ANESTHESIA & ANALGESIA

Journal of the International Anesthesia Research Society, the Society of Cardiovascular Anesthesiologists, the Society for Pediatric Anesthesia, the Society for Ambulatory Anesthesia, the International Society for Anaesthetic Pharmacology, and the Society for Technology in Anesthesia

Abstracts of Posters Presented at the International Anesthesia Research Society 78th Clinical and Scientific Congress Tampa, FL March 27-31, 2004

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Abstracts of Posters Presented at the International Anesthesia Research Society 78th Clinical and Scientific Congress Tampa, FL March 27-31, 2004

IARS 78th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Ambulatory Anesthesia

(S-1) Hamza, M.A., Monday 8:00
(S-2) Kranke, P., Monday 8:00
(S-3) Bekker, A., Monday 8:00
(S-4) Serban, S.I., Monday 8:00
(S-5) Nicolcescu, P.P., Monday 8:00
(S-6) Larijani, G.E., Monday 8:00
(S-7) Larijani, G.E., Monday 8:00
(S-8) Kamel, H.H., Monday 8:00
(S-9) Tang, J., Monday 8:00
(S-10) Iohom, G., Monday 8:00
(S-11) Kaminoh, Y., Monday 8:00
(S-12) Hamza, M.A., Monday 8:00
(S-13) Macario, A., Monday 8:00
(S-14) Kredel, M., Monday 8:00

Circulation - Basic Science

(S-15) Naik, B., Monday 8:00
(S-16) Willert, J., Monday 8:00
(S-17) Kaye, A.D., Monday 8:00
(S-18) Gupta, D.K., Monday 8:00
(S-19) Loepke, A.W., Monday 8:00
(S-20) Rashid, M., Monday 8:00
(S-21) Kold, A.E., Monday 8:00
(S-22) Kehl, F., Monday 8:00
(S-23) Mueller, R.A., Monday 8:00
(S-24) Tse, J., Monday 8:00
(S-25) Howie, M.B., Monday 8:00
(S-26) Damron, D.S., Monday 8:00
(S-27) Damron, D.S., Monday 8:00
(S-28) Damron, D.S., Monday 8:00
(S-29) Deem, S., Sunday 3:00
(Research Awards Panel)

Circulation - Clinical

(S-30) Nonogaki, M., Sunday 8:00
(S-31) Wirtz, S.P., Sunday 8:00
(S-32) Isetta, C.J., Sunday 8:00
(S-33) Shore-Lesserson, L., Sunday 8:00
(S-34) Murphy, G.S., Sunday 8:00
(S-35) Donahue, B.S., Sunday 8:00
(S-36) Fu, E.S., Sunday 8:00
(S-37) Wirtz, S.P., Sunday 8:00
(S-38) Skubas, N., Sunday 8:00
(S-39) Danilov, S.M., Sunday 8:00
(S-40) Wang, S., Sunday 8:00
(S-41) Ito, S., Sunday 8:00
(S-42) Subramaniam, B., Sunday 8:00

Critical Care and Trauma

(S-43) Wahlander, S., Monday 8:00
(S-44) Urban, M.K., Monday 8:00
(S-45) Huang, Z., Monday 8:00
(S-46) Westphal, M., Monday 8:00
(S-47) Agarwal, A., Monday 8:00
(S-48) Johnson, K., Monday 8:00
(S-49) Driessen, B., Monday 8:00
(S-50) MacKenzie, C., Monday 8:00
(S-51) Shang, Y., Monday 8:00
(S-52) Rollins, M.D., Monday 8:00
(S-53) Sabharwal, V., Monday 8:00
(S-54) Spies, C., Monday 8:00
(S-55) Cronin, A.J., Sunday 3:00
(Research Awards Panel)

Economics, Education and Patient Safety

(S-56) Lewis, A., Sunday 8:00
(S-57) Vohra, P.D., Sunday 8:00
(S-58) Weinger, M.B., Sunday 8:00
(S-59) Yarmush, J.M., Sunday 8:00
(S-60) Barach, P., Sunday 8:00
(S-61) Irita, K., Sunday 8:00
(S-62) Overdyk, F.J., Sunday 8:00
(S-63) Hanna, M.N., Sunday 8:00
(S-64) Sidi, A., Sunday 8:00
(S-65) Overdyk, F.J., Sunday 8:00
(S-66) Carter, T.E., Sunday 8:00
(S-67) O'Hara, J.F., Sunday 8:00
(S-68) Kratz, R.D., Sunday 8:00
(S-69) Kratz, R.D., Sunday 8:00
(S-70) Girard, T., Tuesday 8:00
(S-71) Gaba, V.K., Tuesday 8:00
(S-72) Monk, T.G., Tuesday 8:00
(S-73) Szenohradszky, J., Tuesday 8:00
(S-74) Nicolcescu, P.P., Tuesday 8:00
(S-75) Benarjee, A., Tuesday 8:00
(S-76) Jahan, A., Tuesday 8:00
(S-77) Strum, D.P., Tuesday 8:00
(S-78) Strum, D.P., Tuesday 8:00
(S-79) Joshi, G.P., Tuesday 8:00
(S-80) Frasco, P.E., Tuesday 8:00
(S-81) Kranke, P., Tuesday 8:00
(S-82) Kranke, P., Tuesday 8:00
(S-83) Apfel, C.C., Tuesday 8:00

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Equipment & Monitoring

(S-84) Gagnon, C.S., Sunday 8:00
(S-85) Diemunsch, P.A., Sunday 8:00
(S-86) Yamakage, M., Sunday 8:00
(S-87) Lichtenthal, P.R., Sunday 8:00
(S-88) Glick, D.B., Sunday 8:00
(S-89) Otero, P.E., Sunday 8:00
(S-90) Otero, P.E., Sunday 8:00
(S-91) Janelle, G.M., Monday 8:00
(S-92) Redford, D.T., Monday 8:00
(S-93) Redford, D.T., Monday 8:00
(S-94) Redford, D.T., Monday 8:00
(S-95) Fleisher, L.A., Monday 8:00
(S-96) Dworschak, M., Monday 8:00
(S-97) Oshiro, M., Monday 8:00
(S-98) Tong, J.L., Monday 8:00
(S-99) Lallo, A., Monday 8:00
(S-100) Patel, A., Monday 8:00
(S-101) Song, D., Monday 8:00
(S-102) Lieberman, N., Monday 8:00
(S-103) Kling, J.C., Monday 8:00
(S-104) Hino, H., Monday 8:00
(S-105) O'Connor, C.J., Monday 8:00
(S-106) Yajima, S., Monday 8:00
(S-107) Lu, Z., Monday 8:00
(S-108) Soto, R.G., Monday 8:00
(S-109) Schweiger, J.W., Monday 8:00
(S-110) Hamza, M.A., Monday 8:00
(S-111) Rosenbaum, A., Monday 8:00
(S-112) Rosenbaum, A., Monday 8:00
(S-113) Rosenbaum, A., Monday 8:00
(S-114) Xuebing, X., Tuesday 8:00
(S-115) Kakinohana, M., Tuesday 8:00
(S-116) Belda, J., Tuesday 8:00
(S-117) Fan, Q., Tuesday 8:00
(S-118) Zhang, Y., Tuesday 8:00
(S-119) Liu, E.H., Tuesday 8:00
(S-120) Singh, H., Tuesday 8:00
(S-121) Terasako, K., Tuesday 8:00
(S-122) Soto, R.G., Tuesday 8:00
(S-123) Schraag, S., Tuesday 8:00
(S-124) Tang, J., Tuesday 8:00
(S-125) Tang, J., Tuesday 8:00
(S-126) Chan, M.T., Tuesday 8:00

Liver

(S-127) Aggarwal, S., Tuesday 8:00
(S-128) Strum, E.M., Tuesday 8:00
(S-129) Auler, L., Tuesday 8:00
(S-130) Aggarwal, S., Tuesday 8:00
(S-131) Neelakanta, G., Tuesday 8:00
(S-132) Wang, Y.L., Tuesday 8:00
(S-133) Yorozu, T., Tuesday 8:00
(S-134) Miecznikowski, R., Tuesday 8:00

Neuroanesthesia

(S-135) Patel, P., Sunday 8:00
(S-136) Alkire, M.T., Sunday 8:00
(S-137) Hare, G.M., Sunday 8:00
(S-138) Wendling, W.W., Sunday 8:00
(S-139) Sturaitis, M.K., Sunday 8:00
(S-140) Smith, M., Tuesday 8:00
(S-141) Hoffman, W.E., Tuesday 8:00
(S-142) Liu, E.H., Tuesday 8:00
(S-143) Kamel, I.R., Tuesday 8:00
(S-144) Toleikis, J.R., Tuesday 8:00

Obstetric Anesthesia

(S-145) Euliano, T.Y., Monday 8:00
(S-146) Stack, K.E., Monday 8:00
(S-147) Ramanathan, S., Monday 8:00
(S-148) Goodman, E.J., Monday 8:00
(S-149) Ginsberg, S., Monday 8:00
(S-150) Lim, Y., Monday 8:00
(S-151) Sah, N., Monday 8:00
(S-152) Flood, P., Monday 8:00
(S-153) Cohen, S., Monday 8:00
(S-154) Ranasinghe, J., Monday 8:00

Pain - Basic Science

(S-155) Flood, P., Sunday 8:00
(S-156) Kroin, J.S., Sunday 8:00
(S-157) Kroin, J.S., Sunday 8:00
(S-158) Kroin, J.S., Sunday 8:00
(S-159) Kroin, J.S., Sunday 8:00
(S-160) Buvanendran, A., Sunday 8:00
(S-161) Finkel, J.C., Sunday 8:00
(S-162) Lu, Y., Sunday 8:00
(S-163) Nishiyama, T., Sunday 8:00
(S-164) Nishiyama, T., Sunday 8:00
(S-165) Kraft, B., Sunday 8:00
(S-166) Schumacher, M.A., Sunday 3:00
(Research Awards Panel)
(S-167) Schaefer, M., Sunday 3:00
(Research Awards Panel)

Pain - Clinical, Acute

(S-168) Ellis, J.E., Monday 8:00
(S-169) Sickmann, K., Monday 8:00
(S-170) Hall, R.H., Monday 8:00
(S-171) Subramaniam, K., Monday 8:00

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(S-172) Larijani, G.E., Monday 8:00
(S-173) Kumagai, K., Monday 8:00
(S-174) Maroof, M., Monday 8:00
(S-175) Latasch, L., Monday 8:00
(S-176) Latasch, L., Monday 8:00
(S-177) Shah, S.M., Monday 8:00
(S-178) Buvanendran, A., Monday 8:00
(S-179) Raps, F., Monday 8:00
(S-180) Liu, W., Tuesday 8:00
(S-181) Buvanendran, A., Tuesday 8:00
(S-182) Visser, T., Tuesday 8:00
(S-183) Maslovsky, O.P., Tuesday 8:00
(S-184) Aoki, T., Tuesday 8:00
(S-185) Chandralekha, C., Tuesday 8:00
(S-186) Fan, Q., Tuesday 8:00
(S-187) Sutherland, M., Tuesday 8:00
(S-188) Sutherland, M.A., Tuesday 8:00
(S-189) Ono, K., Tuesday 8:00
(S-190) Schraag, S., Tuesday 8:00
(S-191) Dabir, S., Tuesday 8:00
(S-192) Yamaguchi, K., Tuesday 8:00

Pain - Clinical, Chronic

(S-193) Cope, D.K., Monday 8:00
(S-194) Huang, J.J., Monday 8:00
(S-195) Lirk, P., Monday 8:00
(S-196) Sloan, P.A., Monday 8:00
(S-197) Sloan, P.A., Monday 8:00
(S-198) Moric, M., Tuesday 8:00
(S-199) Buvanendran, A., Tuesday 8:00
(S-200) Goldberg, M.E., Tuesday 8:00
(S-201) Yuan, C., Tuesday 8:00
(S-202) Spacek, A., Tuesday 8:00

Pediatric Anesthesia

(S-203) Sun, L.S., Sunday 8:00
(S-204) Sei, Y., Sunday 8:00
(S-205) Whyte, S.D., Sunday 8:00
(S-206) Choi, W., Sunday 8:00
(S-207) Faberowski, L.W., Sunday 8:00
(S-208) Nicolcescu, P.P., Sunday 8:00
(S-209) Weldon, B.C., Tuesday 8:00
(S-210) Frandrup, C.J., Tuesday 8:00
(S-211) Sreevastava, D.K., Tuesday 8:00
(S-212) Sparks, J.W., Tuesday 8:00
(S-213) Radpay, B., Tuesday 8:00
(S-214) Glick, D.B., Tuesday 8:00
(S-215) Walz, J.M., Tuesday 8:00
(S-216) Verghese, S.T., Tuesday 8:00
(S-217) Shinohara, Y., Tuesday 8:00
(S-218) Bryan, Y.F., Tuesday 8:00
(S-219) Bryan, Y.F., Tuesday 8:00
(S-220) Bryan, Y.F., Tuesday 8:00
(S-221) Messieha, Z.S., Tuesday 8:00
(S-222) Sun, L.S., Tuesday 8:00
(S-223) Leyvi, G., Tuesday 8:00

Pharmacology-Basic Science

(S-224) Novalija, E., Sunday 8:00
(S-225) Kitamura, A., Sunday 8:00
(S-226) Archer, D.P., Sunday 8:00
(S-227) Herroeder, S., Sunday 8:00
(S-228) Umeda, E., Sunday 8:00
(S-229) Archer, D.P., Sunday 8:00
(S-230) Whittington, R.A., Sunday 8:00
(S-231) Gingrich, K.J., Monday 8:00
(S-232) Takei, T., Monday 8:00
(S-233) Murphy, P.M., Monday 8:00
(S-234) Kaminoh, Y., Monday 8:00
(S-235) Buvanendran, A., Monday 8:00
(S-236) Kroin, J.S., Monday 8:00
(S-237) Kroin, J.S., Monday 8:00
(S-238) Li, D., Tuesday 8:00
(S-239) Eleveld, D.J., Tuesday 8:00
(S-240) Lee, Y., Tuesday 8:00
(S-241) Lee, C., Tuesday 8:00
(S-242) Bhatt, S.B., Tuesday 8:00
(S-243) Sunaga, H., Tuesday 8:00

Pharmacology-Clinical

(S-244) Michaud, G., Sunday 8:00
(S-245) Trager, G., Sunday 8:00
(S-246) Michaud, G., Sunday 8:00
(S-247) Spacek, A., Sunday 8:00
(S-248) Takagi, S., Sunday 8:00
(S-249) Ruigt, G.S., Sunday 8:00
(S-250) Apfelbaum, J.L., Sunday 8:00
(S-251) Steinberg, D., Monday 8:00
(S-252) Steinberg, D., Monday 8:00
(S-253) Steinberg, D., Monday 8:00
(S-254) Steinberg, D., Monday 8:00
(S-255) Steinberg, D., Monday 8:00
(S-256) Lim, Y., Monday 8:00
(S-257) Horowitz, P.E., Tuesday 8:00
(S-258) Song, D., Tuesday 8:00
(S-259) Song, D., Tuesday 8:00
(S-260) Mathews, D.M., Tuesday 8:00
(S-261) Engelhardt, T., Tuesday 8:00
(S-262) Nicolcescu, P.P., Tuesday 8:00
(S-263) Moller, D.H., Tuesday 8:00
(S-264) Moller, D.H., Tuesday 8:00
(S-265) Yamakage, M., Tuesday 8:00
(S-266) Takasaki, Y., Tuesday 8:00
(S-267) Zhang, Y., Tuesday 8:00

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(S-268) Takada, M., Tuesday 8:00
(S-269) Song, D., Tuesday 8:00
(S-270) Kern, S.E., Sunday 3:00
(Research Awards Panel)

Regional

(S-271) McAllister, J.J., Sunday 8:00
(S-272) Greengrass, R.A., Sunday 8:00
(S-273) Takahashi, S., Sunday 8:00
(S-274) Williams, B.A., Sunday 8:00
(S-275) De Ruyter, M.L., Sunday 8:00
(S-276) Ishikawa, A., Tuesday 8:00
(S-277) Ma, M., Tuesday 8:00
(S-278) Groudine, S.B., Tuesday 8:00
(S-279) Kan, R.K., Tuesday 8:00
(S-280) Yoos, J.R., Tuesday 8:00
(S-281) Nicolcescu, P.P., Tuesday 8:00
(S-282) Schricker, T.P., Sunday 3:00
(Research Awards Panel)

Ambulatory Anesthesia

S-1

COMPARATIVE EVALUATION OF CELECOXIB, ROFECOXIB AND VALDECOXIB IN PREVENTING PAIN AFTER AMBULATORY SURGERY

AUTHORS: **M. A. Hamza**, K. Klein, P. F. White, L. Cox, O. Jaffer, A. Recart;
AFFILIATION: UT Southwestern Medical Center at Dallas, Dallas, TX.

INTRODUCTION: Non-opioid analgesics are commonly administered as part of a multimodal regimen for preventing pain after ambulatory surgery. The COX-2 specific inhibitors allegedly produce comparable analgesia with less risk of platelet dysfunction, gastric mucosa and renal tubular damage than the classical non-selective NSAIDs (1). This randomized, double-blinded, placebo-controlled study compared the three available COX-2 inhibitors, celecoxib, rofecoxib, and valdecoxib, to placebo with respect to their analgesic efficacy when administered prior to surgery.
METHODS: One hundred thirty three consenting outpatients undergoing otolaryngologic surgery were randomly assigned to receive oral Vitamin C 500 mg (placebo), celecoxib 400 mg, rofecoxib 50 mg or valdecoxib 40mg 15-45 min before the induction of anesthesia. The intraoperative medications were standardized in all four groups. A second dose of the same medications were given with the dosage of Vitamin C 250 mg, celecoxib 200 mg, rofecoxib 25 mg or valdecoxib 20 mg, on the morning of first postoperative day. Verbal rating pain scores (0=no pain to 10=worst pain), time from end of surgery to patient achieving Aldrete score of 10 and discharge home criteria (home readiness), and incidences of nausea were assessed at regular time intervals until patient discharge home. In addition, postoperative pain medication and patient satisfaction with pain management (on a verbal rating scale with 1 = highly dissatisfied to 100 = completely satisfied) were assessed at the time of discharge home. A follow-up telephone call was performed 24 h after surgery to assess postdischarge pain and nausea, as well as the patient satisfaction with pain management. Data were analyzed using ANOVA or Chi-square test, with $p<0.05$ considered statistically significant (mean±SD or median and IQR).

RESULTS: Demographic data, intraoperative anesthetic dosages and duration of anesthesia and surgery did not differ among the four study groups. The postoperative pain scores, amount of pain rescue medication, incidence of nausea, time to discharge home, and patient satisfaction with their pain management are summarized in the following table (* $P<0.05$):

	Placebo (n=33)	Cele-coxib (n=34)	Rofe-coxib (n=33)	Valde-coxib (n=33)
Max. pain score until discharge (0-10)	7 (5-8)	4 (2-6) *	4 (2-5) *	4.5 (3-5) *
Postoperative fentanyl (g)	138±99	89±91 *	80±73 *	78±84 *
Nausea until discharge (n,%)	13, 40	8, 25	9, 28	9, 28
Aldrete score of 10 (min)	60±22	48±14*	47±17*	48±16*
Home readiness (min)	166±57	138±39	142±54	143±53
Patient satisfaction at discharge (0-100)	83±17	94±8 *	97±5 *	93±9 *
Max. pain score at home (0-10)	5 (3-6)	3 (1-4) *	3 (0-4) *	3 (1-4) *
Nausea at home (n, %)	9, 27	4, 12	3, 9	5, 15
Patient satisfaction at 24 h (0-100)	84±16	93±11 *	97±6 *	94±10 *

DISCUSSION: Perioperative administration of oral celecoxib, rofecoxib, and valdecoxib were equally effective in reducing the postoperative pain and contributed to a significantly improved quality of recovery in outpatients undergoing otolaryngologic surgery.
REFERENCES: (1) Anesth Analg. 2003;96:987-94

S-2

PATIENT SATISFACTION WITH ANALGESIA AND SAFETY OF INJECTED PARECOXIB FOR POSTOPERATIVE PAIN: A QUANTITATIVE SYSTEMATIC REVIEW

AUTHORS: **P. Kranke**[1], A. M. Morin[2], N. Roewer[1], L. H. Eberhart[2];
AFFILIATION: [1]University of Wuerzburg, Wuerzburg, Germany, [2]University of Marburg, Marburg, Germany.

INTRODUCTION: In addition to opioid analgesics, nonsteroidal anti-inflammatory drugs have been established as useful adjuncts in the management of postoperative pain. Parecoxib is the only parenterally administered cyclo-oxygenase 2 selective inhibitor available so far. The aim of this systematic review was to evaluate efficacy and harm of parecoxib by means of patient satisfaction with the applied analgesic regimen and the observed incidence of adverse effects.
METHODS: We performed a systematic search (MEDLINE, EMBASE, CENTRAL, Science Citation Index, up to June 2003) for full reports of randomized comparisons of parecoxib compared to any other analgesic intervention for the therapy of postoperative pain. Dichotomous data on patient satisfaction with their analgesic regimen were extracted by means of the fraction of patients who rated their medication as “good” or “excellent” compared to "fair" or "poor". Data on any reported adverse effects were extracted. Relative risk (RR) and number-needed-to-treat (NNT) were calculated with 95% confidence intervals (CI) using a random-effects model.
RESULTS: Data from 9 trials were analyzed. In those trials including 1738 subjects, 1013 patients were randomized to receive parecoxib, 218 patients were allocated to an active control (morphine 4 mg, n=84; ketorolac 30-60 mg, n=134) and 507 patients received a placebo. When administered prophylactically the pooled NNT to obtain the desired outcome (“good“ / ”excellent” rating) with parecoxib 20mg and 40mg compared to placebo was 4.5 (RR: 1.42; 95%CI: 0.91-2.24) and 4.0 (RR: 1.40; 95%-CI: 1.10 – 1.79). In the treatment trials the NNT [harm] to obtain the outcome of interest with parecoxib 20mg and 40mg was 2.1 (RR: 3.44; 95%CI: 1.49 – 7.96) and 1.7 (RR: 4.65; 95%-CI: 2.04 – 10.61), 5.3 (RR: 1.43; 95%CI: 1.01-2.02) and 3.7 (RR: 1.62; 95%-CI: 1.21 – 2.16) or [8.3] (RR: 0.85; 955-CI: 0.75 – 0.97) and 50 (RR: 1.03; 95%-CI: 0.89 – 1.18) for the comparisons versus placebo, morphine or ketorolac, respectively. Overall adverse effects for parecoxib 20mg and 40mg were not different from placebo, morphine or ketorolac. Compared to placebo patients receiving parecoxib had significantly less headache (RR: 0.68; 95%-CI: 0.48 – 0.97) and fever (RR: 0.31; 95%-CI: 0.21 – 0.46). The incidence of fever was similarly reduced compared to morphine (RR: 0.27; 95%-CI: 0.12 – 0.62) and ketorolac (RR: 0.15; 95%-CI: 0.07 – 0.33).
DISCUSSION: Injected parecoxib significantly increased patient satisfaction with the analgesic regimen compared to placebo. There is a tendency of parecoxib 40mg being more effective than 20mg without an increased incidence of side effects. Ketorolac and parecoxib are equally effective. Considering the fact that the intraoperative use of parecoxib might be safer compared to ketorolac, parecoxib has the potential to become the non-opioid analgesic of choice for the perioperative period if oral medication is contraindicated.

S-3

A DOUBLE MASKED PROSPECTIVE COMPARISON OF ROFECOXIB VERSUS KETOTOLAC FOR ACUTE POSTOPERATIVE PAIN

AUTHORS: J. Kim, **A. Bekker**, O. Sherman, G. Cuff, A. Lebovits, M. Wajda;
AFFILIATION: New York University Medical Center, New York, NY.

INTRODUCTION. Ketorolac is a commonly used agent to reduce postoperative pain and inflammation in patients who undergo ambulatory orthopedic surgery. However, there is often reluctance to use this drug as a perioperative analgesic because of the potential for gastrointestinal injury and platelet deactivation. Rofecoxib is a selective COX-2 inhibitor with fewer side effects than non-selective NSAIDs (i.e. ketorolac). The aim of this study is to examine whether rofecoxib provides pain relief comparable to ketorolac in patients undergoing arthroscopic knee surgery.
METHODS. With IRB approval, 30 consented ASA I-III patients scheduled for knee arthroscopy were randomly assigned to receive either ketorolac IV 30 mg at the end of the case or rofecoxib 50 mg PO prior to surgery. In addition, patients in the ketorolac group received placebo pill PO preoperatively while patients in the rofecoxib group received a saline injection at the end of the procedure. Fentanyl (1.4 mcg/kg), midazolam (0.07 mg/kg), and propofol (70 mcg/kg/min) were used for intraoperative sedation. Additionally, the surgeon infiltrated the knee with bupivacaine at the end of the procedure. The outcome measures were pain scores (verbal analog scale (VbAS)) and Percocet^{R} use (oxycodone/acetaminophen 5/325 mg) assessed in the postoperative care unit, 6 hours and 24 hours after discharge. Additional endpoints included patient satisfaction and occurrence of side effects. Data were analyzed using independent samples t-tests for continuous variables or chi-squares test for categorical variables. $P < .05$ was considered significant.
RESULTS. The two groups were comparable with regard to age, intraoperative medication use, and duration of surgery. There was no difference either in pain scores or Percocet^{R} use in the PACU or 24 hours after discharge. More patients in the ketorolac group required Percocet within 6 hours after discharge, but the difference was not statistically significant. There were also no differences in the number of patients experiencing any side effects or in patient satisfaction.
DISCUSSION. Preoperative rofecoxib is as effective as ketorolac for the treatment of pain after knee arthroscopy. Although our sample size was too small to show differences in adverse effects, we believe that rofecoxib may be preferred perioperative NSAID because it has minimal effects on platelet function or gastrointestinal bleeding.

Outcome Measurements		
	Ketorolac	Rofecoxib
Age	45.3	44.5
VbAS prior to discharge	.7	.7
VbAS (6 hrs after surgery)	1.7	1.0
VbAS (24 hrs after surgery)	2.8	1.8
Percocet ^{R} in the PACU (n, %)	3/15, 20%	2/15, 13%
Percocet ^{R}, 6 hrs after discharge (n, %)	5/14, 36%	1/13, 8%
Percocet ^{R} 24 hrs after discharge (n, %)	7/14, 50%	5/13, 39%
Side effects (i.e. nausea, vomiting, dizziness)	3/14, 21%	3/13, 23%
Patient satisfaction: Excellent/Very Good (n, %)	9/14, 64%	11/13, 85%

S-4

EVALUATION OF THE EFFICACY OF ROFECOXIB IN THE PERIOPERATIVE MANAGEMENT OF PAIN FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY

AUTHORS: **S. I. Serban**, S. Reuben, W. Joshi, W. Prescott, H. Maciolek;
AFFILIATION: Baystate Medical Center, Springfield, MA.

INTRODUCTION: Recently the COX-2 inhibitor rofecoxib has become available for the management of postoperative pain. The perioperative administration of rofecoxib has demonstrated a significant opioid sparing effect following orthopedic (1,2), abdominal (3), and ENT (4) surgeries. Rofecoxib has also resulted in improved postoperative pulmonary function when administered prior to abdominal surgery(3). The preoperative administration of rofecoxib may be safer than standard NSAIDs since it has no effect on platelet aggregation.
METHODS: After IRB approval, 31 patients undergoing elective laparoscopic cholecystectomy were included in this randomized, double-blinded study. Patients received either placebo (n=15) or rofecoxib 50 mg (n=16) one hour prior to surgery. Baseline pulmonary function tests (FEV-1 and FVC) were obtained. Postoperatively, patients received PCA morphine. Pain scores and morphine use were recorded. In addition, side effects including nausea, vomiting, itching and shoulder pain were recorded.
RESULTS: There were no differences in patients demographics, length of surgery, intraoperative fentanyl use and preoperative FEV-1 and FVC between the two groups. There were no statistical differences between the groups regarding VAS pain scores in the PACU and 3 hours postoperatively. There was a significant difference ($p<0.05$) between the rofecoxib group VAS score (1.8 +/- 1.5) and Control group (3.1 +/- 1.8) at 8 hours post-surgery. There were no significant differences in the pulmonary function tests between the two groups. Total morphine required for the first 8 hours post-surgery was not different in the rofecoxib group (5.4 +/- 6.6) than in the Control group (6.6 +/- 2.4).
CONCLUSIONS: Preoperative administration of rofecoxib 50 mg reduced pain scores at 8 hours; there was no improvement in pulmonary function at 3 or 8 hours postoperatively.
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Summary: Study patients received placebo or rofecoxib prior to laparoscopic cholecystectomy. Preoperatively, PFT's were recorded and postoperatively, total morphine use. The study showed a difference in Morphine use at 8 hours but no difference in PFT's between groups.

S-5

THE SEDATION WITH PROPOFOL THIOPENTAL MIXTURE VERSUS MIDAZOLAM DURING LOCAL ANESTHESIA

AUTHORS: **P. P. Nicolcescu**, I. P. Georgescu, A. I. Georgescu, I. M. Sosea, V. N. Calina, F. O. Purcaru;
AFFILIATION: University Hospital no1 Craiova, Craiova, Romania.

INTRODUCTION: We compared the clinical efficacy and recovery characteristic during plastic surgery under for sedation with Propofol Thiopental mixture versus midazolam during plastic surgery under local anesthesia.
METHODS: After approval by the ethics committee and obtained written informed consent we studied 80 patients (47 male) ASA physical status I-II aged 18- 50 years who were undergoing plastic surgery procedures with local anesthesia. The patients were randomized assigned in two equal groups A and B. No patients were premedicated. The patient's level of sedation was assessed by a blinded observer using the Observer's Assessment of Alertness/Sedation Scale. Five minutes before the surgeons begin infiltrating the operative field with Ropivacaine. The patients including in group A received 2.5 ml bolus iv followed by 15 ml/h Propofol Thiopental mixture (1g Thiopental diluted with 20 ml Propofol 10%) and the patients including in group B received 0.05mg/kg midazolam followed by continuos infusion with 1.5microg/kg/min. Vital signs and sedation scores were subsequently recorded at 5 min intervals until the end of procedure. Cognitive and psychomotor function was evaluated with an original questioner based on TEA test and Bender test. For statistical analysis we used Wilcoxon test and student t test $p<0.05$was considered significant.
RESULTS: The two groups were comparable with respect to age, gender, duration of sedation and local Ropivacaine dosage (61+-14mg group a vs 62+-8mg group B). For all patients the OAA/S score were maintained at a level of 3 throughout the surgical procedures. No major events (respiratory depression, hypotension) and no unpleasant dreaming was noted in both groups. The recovery time of cognitive and psychomotor function was significantly shorter ($p<0.05$) in group A (22+-15minutes) comparatively with group B (56+-27minutes). The sedation level and the incidence of nausea and vomiting were significantly higher ($p<0.05$) in the first 6 hours after surgical intervention in group B.
CONCLUSIONS: The sedation with Propofol Thiopental mixture during local anesthesia is associated with earlier cognitive and psychomotor function recovery comparatively with the midazolam sedation. Both sedation techniques were safe and offered a good comfort for patients. Propofol-Thiopental mixture was more effective in the prophylaxis of PONV after surgical interventions.
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S-6

SYMPTOM EVALUATION IN OUTPATIENTS 24 HOURS AFTER GENERAL ANESTHESIA

AUTHORS: **G. E. Larijani**, M. E. Goldberg, J. B. Dunn, A. Marr, B. Khaleghi;
AFFILIATION: Cooper Hospital, Camden, NJ.

INTRODUCTION: Early discharge after anesthesia is routine. While it is important to emphasize home readiness, recovery from anesthesia and surgery is not complete until the patient has returned to his/her preoperative status. A significant portion of research on recovery has concentrated on minimizing the immediate postoperative symptoms to facilitate patient discharge. Few studies have evaluated recovery after discharge from the hospital. The purpose of this study was to evaluate symptoms in outpatients 24 hours following discharge.
METHODS: Informed consents were obtained in this IRB approved study from 51 patients scheduled to have surgery under general anesthesia on an outpatient basis to evaluate post discharge symptoms. Patients completed a questionnaire prior to surgery, and 24 hours after discharge (via phone). They were asked to rate each question on a 0 to 10 scale. The questionnaire was pilot-tested (N=5) to assure clarity of content. No attempt was made to standardize the anesthetic technique. Data was analyzed using paired student t-test, and Confidence Interval (CI). A $P<0.01$, and/ or 99% CI range was used to demonstrate statistical significance. Data is presented as mean (SD).
RESULTS: Patients had a mean age of 41 years, mean weight of 177 lb and were mostly of female gender (37 f, 14 m). Pre-operatively patients were significantly more tense (4.4±3.5 vs. 1.8 ± 2.8; 37% vs. 12% having a degree of tenseness >5), and significantly more clear-headed (9.4 ±1.3 vs. 7.8 ±2.3; 86% vs. 63% having a value > 8). Twenty-four hours after discharge patients reported feeling significantly more worn-out (5.9±3.5 vs. 3.1±2.9; 51% vs. 16% having a value > 5), more fatigued (5.4±3.1 vs. 3.2 ±3.0; 57% vs. 19.6 % having a value of >5), with less energy (6.9 ±2.5 vs. 4.3 ±2.8; 49% vs. 12% having a value <5) than prior to surgery. Despite the presence of significant feeling impairments, overall satisfaction with the recovery from general anesthesia was rated high by the patients (9.4±0.96). Patients did not report any significant differences in ease of decision-making, or concentration ability 24 hours after discharge.
DISCUSSION: Despite a very high satisfaction rating with recovery from general anesthesia, most patients complained of symptoms representing inadequate recovery. Patients complained of fatigue, exhaustion, not being clear-headed, and having a lack of energy during the first postoperative day. Symptoms such as lack of clear-headed-ness can impair good judgment during recovery and may make the patient dysfunctional even for a short period of time. Lack of energy and feeling of fatigue could interfere with physical activity. This study is a further demonstration that evaluation of recovery from anesthesia should be expanded to include symptoms for at least the first postoperative day.

S-7

MODAFINIL IMPROVES RECOVERY AFTER GENERAL ANESTHESIA

AUTHORS: **G. E. Larijani**, M. E. Goldberg, B. Khaleghi, J. B. Dunn, A. Marr;
AFFILIATION: Cooper Hospital, Camden, NJ.

INTRODUCTION: Recovery from general anesthesia often involves residual sedation, drowsiness, fatigue, and lack of energy that may last hours to days. Modafinil is a wakefulness-promoting agent approved for patients with excessive daytime sleepiness associated with narcolepsy. Some of modafinil's effects appear to be desirable in patients recovering from general anesthesia. The primary objective of this investigation was to evaluate the effect of modafinil on the degree of fatigue and drowsiness in patients after general anesthesia. Secondary objectives included evaluation and effect of modafinil on recovery of cognition as well as subject-reported indicators of behavioral and somatic functions.
METHODS: Thirty-four subjects (24 Female, 10 Male) participated in this prospective, randomized, double blind study approved by our institutional review board. Subjects were ASA I-III, with a BMI <40 without any known significant renal, hepatic, cardiovascular, neurological, gastrointestinal, endocrine, hematologic, or pulmonary diseases and were scheduled to undergo outpatient surgical procedures under general anesthesia. Preoperatively patients were asked to rate various symptoms they had experienced over the pervious 24-hours using a verbal analog scale of 0 to 10, as well as discrete scale when indicated. Postoperatively patients were monitored and cared for according to our institutional standards. Once the patient was able to tolerate oral intake, and met our institutional discharge criteria, the study drug (Modafinil 200 mg or placebo) was administered with a sip of water. Patients were contacted 24 hours after dosing and the same questions were asked to evaluate postdischarge symptoms. The symptom evaluation included headache, dizziness, level of energy, appetite, nausea, pain, vomiting, degree of being tense, clear-headedness, restlessness, fatigue, exhaustion, quality of sleep during the previous night, need for the help of a caregiver, ability to read, comprehend, and communicate. Data was analyzed using unpaired student t-test, chi square statistics, content analysis, and 95% confidence interval.
RESULTS: There were no significant differences in preoperative symptoms, or demographic data, between modafinil and placebo groups. Postoperatively, significantly more patients complained of moderate-to-severe fatigue, feeling worn out, or being exhausted in the placebo group. In subjects recovering from general anesthesia modafinil significantly reduced the degree of fatigue, as well as the incidence of moderate to severe fatigue. Postoperative distress, defined as lack of energy, presence of feeling worn out, fatigue, exhaustion, mental clouding and problem reading was significantly lower in the modafinil group. Two major themes of "alertness" and "energy" were expressed by 71% of the patients receiving modafinil vs. 18% of those receiving placebo.
CONCLUSION: Modafinil significantly improves recovery after general anesthesia. Modafinil may share the same pathway(s), or receptors, as sedatives, hypnotics, or general anesthetics to produce its effect(s). Patients recovering from general anesthesia can significantly benefit from modafinil.

S-8

DOES METOCLOPRAMIDE POTENTIATE MIVACURIUM-INDUCED NEUROMUSCULAR BLOCKADE AND ALTER HEPATOCELLULAR INTEGRITY? THE ROLE OF PLASMA CHOLINESTERASE (PCHE) AND ALPHA-GLUTATHIONE-S-TRANSFERASE

AUTHORS: **H. H. Kamel**;
AFFILIATION: Theodor Bilharz Research Institute, Cairo, Egypt.

INTRODUCTION: This study investigates the effect of metoclopramide on mivacurium-induced neuromuscular blockade and whether plasma cholinesterase (PCHE) activity is actually involved. Alteration in hepatocellular integrity was also investigated by a-glutathione-S-transferase (a-GST) - an early and sensitive marker.
MATERIALS: Forty patients undergoing minor elective procedures (ASA classes I and II) with normal liver functions, were divided after propofol induction into 2 groups (20 patients each): Group (A) received metoclopramide (0.15 mg.kg-1) and Group (B) received saline prior to the administration of mivacurium (0.15 mg.kg-1). Anesthesia was maintained with propofol infusion, nitrous oxide (60% in oxygen) and fentanyl increments.
RESULTS: Using a train-of-four (TOF-Guard) accelerometer, there was no difference in onset time in both groups. Clinical duration (injection time to recovery of T1 25%) was significantly longer by 23% in Group (A). Times to recovery of T1 to 25%, 75% and 90% increased by 22.5%, 28.6% and 29.9% respectively in Group (A) compared to Group (B). Recovery index (recovery of T1 25% - T1 75%) was significantly longer by 44% in Group (A). PCHE activity at baseline showed no significant difference between both groups. Five minutes after metoclopramide, a highly significant decrease (14.4%) in PCHE activity occurred in Group (A). The decrease after mivacurium (at time of maximum block) was insignificant within the 2 groups. As to a-GST, it showed a significant increase in Group (A) 5 minutes after metoclopramide, though within the normal range and resumed initial values at the time of maximum block.
DISCUSSION: Metoclopramide prolongs the duration of mivacurium when given 5 minutes earlier.(1) Since it has no intrinsic neuromuscular blocking activity, this is probably due to its inhibition of PCHE, which is synchronous with alteration in a-GST and is part of its impact on hepatocellular integrity, since PCHE is a hepatocellular marker.(2)
The statistically significant increase of GST, GPT and bilirubin after metoclopramide, indicates subclinical transient liver damage.(3)
CONCLUSION: Metoclopramide prolongs the action of mivacurium probably by inhibiting PCHE activity. Metoclopramide also produces mild, immediate but transient elevation of a-GST - an early sensitive marker of hepatocellular integrity.
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S-9

COMPARATIVE EVALUATION OF ELECTROENCEPHALOGRAPHIC PATIENT STATE INDEX (PSI) AND BISPECTRAL INDEX (BSI) VALUES DURING AMBULATORY ANESTHESIA

AUTHORS: **J. Tang**, P. F. White, R. H. Wender;
AFFILIATION: UT Southwestern Medical Center at Dallas, Dallas, TX.

INTRODUCTION The patient state index (PSI) has been demonstrated to be a useful EEG-based monitor for assessing consciousness during general anesthesia (1). However, concerns regarding the time required to apply the PSI electrodes necessitated the development of a new electrode system (PSArray^2). We designed this study to compare the clinical utility, as well as the sensitivity and specificity of the PSI with the PSArray^2 electrode system to the EEG bispectral index (BIS) using the XP platform. In addition, their ability to predict the level of consciousness during induction and emergence from general anesthesia were evaluated.
METHODS: 19 consenting outpatients scheduled for laparoscopic surgery were enrolled in this prospective study. After application of both the PSI and BIS electrode systems, anesthesia was induced with propofol, 2 mg/kg IV, and fentanyl 1 µg/kg IV. Desflurane 2-6% end-tidal in combination with N_2O 60% was administered for maintenance of anesthesia. The times to display the values from both monitors, and the comparative PSI and BIS values at specific time intervals during the induction and emergence periods were recorded (means±SD, with a= $p<0.05$ vs BIS value; and b= $p<0.05$ vs baseline value).
RESULTS: Both the BIS and PSI values were found to predict the level of consciousness ($p<0.01$). The area under the receiver operating characteristic (ROC) curve for detection of consciousness indicated a similar performance with the PSI (0.98±0.05) and the BIS (0.97±0.05). The PSI exhibited a good correlation with the BIS during both the induction ($r = 0.84$) and emergence ($r = 0.74$) periods. Although application of the PSI electrode required slightly more time than BIS (17±6 vs 13±6 sec, $p>0.05$), the time to display the PSI value was slightly shorter than with the BIS ($p>0.05$). The PSI index also experienced less interference from the electrocautery during surgery (32% vs 72%).
DISCUSSION: The PSI monitor with the newer electrode system appears to possess similar sensitivity and specificity to the BIS monitor in assessing consciousness during induction and emergence from anesthesia. Given the similar time required to apply the electrodes and displayed the value with both EEG monitors, it would appear that the PSI monitor is a viable alternative to the BIS monitor in the ambulatory setting.
REFERENCE: (1) Anesth Analg. 2002;95:1669-74

	Time to apply the electrode (sec)	Time to display the values after application of electrode (sec)	Total time to display values (sec)	EEG values during the perioperative period	Baseline (awake)	Pre-induction	Loss of consciousness	Intubation	Pre-incision	5 min after incision	End of anesthesia	Eye opening	Orientation
BIS	13±6	59±43	74±41		96±3	95±4	77±16	39±9	52±12	45±10	51±11[b]	88±11[b]	93±8
PSI	17±6	47±32	65±33		97±3	92±5	76±16	43±17	39±18	38±15	45±16[b]	81±13	86±9[a,b]

S-10

ABNORMALITIES OF CONTRAST SENSITIVITY AND ELECTRORETINOGRAM FOLLOWING SEVOFLURANE ANESTHESIA

AUTHORS: **G. Iohom**, C. Gardiner, A. Whyte, G. O'Connor, G. Shorten;
AFFILIATION: Cork University Hospital, Cork, Ireland.

BACKGROUND AND OBJECTIVES: *T*o date, the clinical significance of previously described postoperative abnormalities of the visual pathway (1) is unknown. Retinal abnormalities identifiable by electroretinogram (ERG) may signify diminished visual function such as contrast sensitivity (2). This has important safety implications, as some patients resume routine daily activity shortly after discharge.
We tested the hypothesis that disturbances of the visual pathway following sevoflurane general anesthesia i) exist and persist even after clinical discharge criteria have been met and ii) are associated with decreased contrast sensitivity.
METHODS*: W*e performed pattern and full field flash ERG (3) in 10 unpremedicated ASA I patients who underwent N_2O/sevoflurane anesthesia. Electroretinograms and contrast sensitivity (4) were recorded preoperatively, immediately after discharge from the recovery room and two hours after discontinuation of sevoflurane. The time at which post anesthesia discharge score first exceeded 9 was also noted. Data were analysed using paired, one tailed Student's t tests and Pearson's correlation coefficient.
RESULTS: On the full field photopic ERG, b-wave latency was greater at each postoperative time point (31.6 ± 1.1 and 30.8 ± 1.1 ms) compared to preoperatively (30.1 ± 1.1 ms, $p < 0.001$ and $p = 0.03$ respectively). Oscillatory potential (OP2) latencies were greater on discharge from the recovery room compared with preanaesthetic values (23.1 ± 3.1 vs 22.4 ± 3.3 ms, $p = 0.01$) and returned to baseline by two hours after emergence from anesthesia. Also at two hours after emergence from anesthesia i) p50 latency on the pattern erg was greater than at baseline (81.5 ± 17.9 vs 51.15 ± 22.6 ms, $p = 0.004$); ii) n95 amplitude was less compared to preanesthetic values (2.6 ± 0.5 vs 3.3 ± 0.4 uV, $p = 0.003$), and iii) contrast sensitivity was less compared to baseline values (349 ± 153 vs 404 ± 140, $p = 0.048$). A positive correlation was demonstrated between contrast sensitivity and both N95 amplitude and b-wave latency ($r = 0.99$ and $r = -0.55$ at significance levels of $p < 0.005$ and $p < 0.05$ respectively).
CONCLUSIONS: Postoperative electroretinographic abnormalities and associated decreases in contrast sensitivity are consistently present in patients who have undergone N_2O/sevoflurane anesthesia. These abnormalities persist beyond the time at which standard clinical discharge criteria have been met.
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S-11

CARDIAC INDEX DURING INHALATION BOLUS OF SEVOFLURANE (SEBO)

AUTHORS: **Y. Kaminoh**[1], M. Iwaya[2], F. Yanamoto[1], S. Tsujimoto[1], C. Tashiro[1];
AFFILIATION: [1]Hyogo College of Medicine, Nishinomiya City, Japan, [2]Takarazuka City Hospital, Takarazuka City, Japan.

INTRODUCTION: VIMA (volatile induction and maintenance of anesthesia) is one anesthesia technique, which mainly uses inhalation anesthetics, and minimizes the use of intravenous agents, such as muscle relaxants and opioid analgesics. VIMA is suitable for ambulatory anesthesia, because a minimal use of intravenous agents allows patients to wake up quickly from anesthesia, and prevents postoperative nausea and vomiting (PONV) and delirium. Due to noxious stimuli during surgery, the requirement of anesthetics and analgesics changes quickly. Inhalation bolus was defined as a dynamic use of the vaporizer to control the responses to stress caused by surgical procedure (1). The effect of short-duration but high-concentration of sevoflurane on cardiac function has not been evaluated. We intermittently measured the cardiac output before and after inhalation bolus of sevoflurane (sevoflurane bolus: SeBo) by using a non-invasive cardiac output monitor (NICO, Novametrix).
METHODS: Before administering the anesthesia, control values of BP and HR were recorded. Patients received 100% oxygen and 1 micro g/kg of fentanyl 2 minutes before induction of anesthesia. Anesthesia was induced by 8% or 5% sevoflurane and 67% nitrous oxide in oxygen. LMA was positioned without muscle relaxants, and anesthesia was maintained by 1.5% sevoflurane and 67% nitrous oxide. $P_{ET}CO_2$ was controlled to be 35-40 mmHg by mechanical IPPV. BIS monitor was used. Cardiac output was measured every three minutes by NICO. Positive reaction to the noxious stimuli was defined when we saw either a 20% increase of BP or HR compared to the control values, breathing spontaneously, involuntary movement, or a sudden increase of BIS value more than 70. Once a positive reaction was observed, SeBo was started by increasing the inspired sevoflurane concentration to 5% or 8% for 1 minute. If the positive reaction persisted, Ssevoflurane was continued for additional 1 minute in high concentration. If the positive reaction existed after 4 minutes SeBo, a rescue dose of 0.5 micro gram / kg fentanyl was administered.
RESULTS: 29 times of positive reactions were seen in 12 out of 16 patients; 17 by BP, 7 by HR, and 5 by spontaneous breathing. 23 out of 29 positive reactions were treated by SeBo. The table shows the cardiac index before (PRE), during (DUR), and after SeBo (POST). DUR and POST were measured at 3 and 6 minute intervals after PRE, respectively. Cardiac index of POST increased significantly compared to PRE and DUR ($p<0.05$).
DISCUSSION: SeBo treated the positive reaction at a high success rate (79.3%). Cardiac index did not change during SeBo. After SeBo, the cardiac index significantly increased in spite of a high-concentration of sevoflurane. We concluded that the SeBo prohibited the reaction to surgical stimulation, without compromising cardiac function.
REFERENCE: 1) Anesth Analg 94: 1217-22, 2002.

Caridiac index before, during, and after SeBo

	PRE (before SeBo)	DUR (during SeBo)	POST (after SeBo)
Cardiac Index	3.7 ± 0.8	3.7 ± 0.8	4.0 ± 0.8

S-12

ORAL GRANISETRON VS. IV ONDANSETRON FOR ANTIEMETIC PROPHYLAXIS IN OUTPATIENTS UNDERGOING LAPAROSCOPIC SURGERY: A RANDOMIZED, DOUBLE-BLIND COMPARISON

AUTHORS: **M. A. Hamza**, P. F. White, B. Ogunnaike, I. Gasanova, M. Lo, G. Joshi;
AFFILIATION: UT Southwestern Medical Center at Dallas, Dallas, TX.

INTRODUCTION: Granisetron, a 5-HT3 antagonist, has been reported to be effective in the treatment and/or prevention of postoperative nausea and vomiting (PONV) (1). However, the high cost of granisetron has raised questions regarding its cost-efficacy as a routine prophylactic antiemetic in the ambulatory setting. The purpose of this study is to compare the antiemetic efficacy of granisetron (1 mg po) and ondansetron (4 mg IV) when administered for routine prophylaxis against PONV in outpatients undergoing laparoscopic surgery procedures.
METHODS: One hundred and fifteen consenting outpatients undergoing elective laparoscopic surgery with a standardized general anesthetic technique were randomly assigned to one of two antiemetic prophylaxis groups. Group 1 received an placebo pill po 1 h prior to surgery and Ondansetron, 4 mg IV, at the end of surgery. Group 2 received Granisetron 1 mg po 1 h before surgery and saline (1 ml) at the end of surgery. Nausea scores were assessed using an 11-point verbal rating scale, with 0=none to 10=maximal, at 30 min intervals for the initial 4 hours in the postoperative period. In addition, the time to the first postoperative episode of emesis, the number of emetic episodes, and the need for rescue antiemetics were recorded. The incidences of nausea and vomiting were followed up at 24 and 48 hours after surgery. Data were analyzied using t-test, Kruskal Wallis or Chi-square test, with $p<0.05$ considered as statistically significant. Values are expressed as (mean±SD, median and IQR, or number and percentage.
RESULTS: The demographic characteristics were similar in both treatment groups. The results of PONV evaluation in both study groups are summarized in the table (* $P<0.05$):

	Group 1 (Ondansetron)	Group 2 (Granisetron)
Number (n)	57	58
Time to first emetic episode (min)	82±56	65±43
Nausea < 4 h (n, %)	25, 44	28, 48
Vomiting < 4 h (n, %)	14, 25	13, 22
Max. Nausea score < 4 h (1-10)	0 (0-5)	0 (0-5)
Antiemetic rescue < 4 h (n, %)	18, 32	23, 39
Acquisition cost for antiemetics ($)	26.71	47.04
Nausea 4-24 h (n, %)	24, 42	14, 25 *
Vomiting 4-24 h (n, %)	12, 21	8, 14
Nausea 24-48 h (n, %)	9, 16	6, 10
Vomiting 24-48 h (n, %)	2, 4	3, 5

DISCUSSION: Preoperative administration of granisetron,1 mg po, was as effective as ondansetron, 4 mg IV at the end of surgery, in preventing PONV after laparoscopic surgery. Granisetron produced a more sustained antiemetic effect during the first 24 hour postoperative period. However, the acquisition cost of granisetron (1 mg po) was significantly higher than ondansetron (4 mg IV).
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S-13

THE IMPACT OF DESFLURANE AND SEVOFLURANE ON THE RISK OF POSTOPERATIVE NAUSEA AND VOMITING: A SYSTEMATIC REVIEW OF THE PUBLISHED LITERATURE

AUTHORS: **A. Macario**[1], D. Lubarsky[2];
AFFILIATION: [1]Stanford University, Dept. of Anesthesiology, Stanford, CA, [2]University of Miami, Miami, FL.

INTRODUCTION: Avoiding postoperative nausea and vomiting (PONV) is a high priority for surgical patients.The goal of this study was to perform a systematic review of published, randomized controlled trials (RCT) of sevoflurane versus desflurane to compare their effect on PONV.
METHODS: We systematically searched for RCTs of sevoflurane and desflurane in MEDLINE for 1991 - 2003 by using MeSH headings: "sevoflurane" and "desflurane." Trials were included if the study allowed construction of 2 x 2 PONV contingency table (even if PONV was not the primary endpoint), participants had been randomized, and observers blinded. The primary outcomes were the incidence of early (within 4 hours) and late (within 24 hrs) nausea, early and late vomiting, and early and late rescue treatment.
RESULTS: Of 39 identified prospective clinical studies, 20 RCTs were included in our meta-analysis. Studies were excluded, for example, if performed on volunteers (not patients). Pooling the results of the 20 included studies, sevoflurane was associated with a lower risk of PONV compared to desflurane with a relative risk of 0.83 (95% CI, 0.705 - 0.985) and numbers-needed-to-treat = 18 (95% CI, 9 to 210). A total of 631 patients received sevoflurane (overall PONV = 28%) and 631 patients received desflurane (overall PONV = 33%).
DISCUSSION: There is some evidence for a decreased likelihood of PONV with use of sevoflurane. If 18 patients are administered sevoflurane for maintenance of anesthesia, then one less patient will develop PONV than the number that would have if all 18 patients had received desflurane. The impact of baseline patient and study characteristics on the results needs to be further examined.

S-14

DO WEATHER AND MOON CYCLE INFLUENCE POSTOPERATIVE NAUSEA AND VOMITING?

AUTHORS: **M. Kredel**[1], C. C. Apfel[2], D. Bassi[3], N. Roewer[1];
AFFILIATION: [1]Dept. of Anesthesiology, Univ of Wuerzburg, Germany, [2]Outcomes Research Institute and Department of Anesthesiology, Univ of Louisville, KY, [3]Department of Anesthesiology, Univ of Basel, Switzerland.

INTRODUCTION: Numerous risk factors are alleged to influence postoperative nausea and vomiting (PONV)[1, 2]. PONV is also believed to occur more frequently on certain days and one study alleged certain weather conditions to be associated with an increased incidence of PONV[3]. Unfortunately, no detailed information was provided on the meteorological parameters sought to influence PONV. Therefore we tested the hypotheses that static or dynamic meteorological parameters or the phase of the cycle of the moon have an impact on PONV.
PATIENTS AND METHODS: With approval of ethics committee and informed consent data from a survey of 1801 adult inpatients who underwent general anesthesia for elective surgical, urologic, ear, nose and throat, and eye procedures were analyzed. Prophylactic antiemetics were not used. PONV was defined as any nausea and/or vomiting occurring within the first 24 postoperative hours. The air temperature, pressure, water vapor pressure and the general weather situation were obtained from the National Weather Institute in Germany. Patients were divided into categories based on quartiles of air temperature, pressure and water vapor pressure measured on their day of surgery. Dynamic changes towards the proceeding day were categorized into five quintiles. Pearson's chi-square, linear-with-linear-relation test were used.
RESULTS: PONV occurred in 550 out of 1801 patients (30.8%). The observed incidence of PONV and the patient's risk for PONV did not differ within the groups. No correlation could be demonstrated between the weather factors nor the phases of the moon and the observed incidence for PONV. Even when corrected for the patients' risk and other potentially confounding factors in logistic regression analysis no statistically significant impact of the hypothesized factors could be detected.
INTERPRETATION: The data suggest that neither the weather nor the phases of the moon have any clinically relevant effect on PONV after general anesthesia. Thus, it appears more reasonable to estimate the patients risk with validated risk scores based on well proven risk factors[4, 5] instead of overemphasizing numerous suspected but doubtful risk factors.

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Circulation - Basic Science

S-15

RAPID DIRECT INJECTION OF ETHYL ALCOHOL IS ASSOCIATED WITH ACUTE PULMONARY HYPERTENSION AND RIGHT VENTRICULAR DYSFUNCTION IN PIGS

AUTHORS: **B. Naik**[1], J. Willert[1], D. S. Kirby[2], F. Urdaneta[3], E. Lobato[3];
AFFILIATION: [1]Department of Anesthesiology, University of Florida College of Medicine, Gainesville, FL, [2]Anesthesiology Service, Malcom Randall Veterans Affairs Medical Center, Gainesville, FL, [3]Department of Anesthesiology, University of Florida College of Medicine; Anesthesiology Service, Malcom Randall Veterans Affairs Medical Center, Gainesville, FL.

INTRODUCTION: Chemical ablation of hepatic tumors with rapid intravenous injection of 30-60 mL of 100% ethyl alcohol (ETOH) has become commonplace.[1-3] This type of ETOH administration carries the risk of intravenous absorption due to the high vascularity associated with certain tumors. Laboratory data suggest that intravenous ETOH potentiates hypoxic pulmonary vasoconstriction, while its effects on pulmonary hemodynamics and right ventricular function are not well characterized. This study examined the impact of rapid intravenous ETOH infusion on the pulmonary circulation in the absence of hypoxia.
METHODS: 8 adult swine with a mean weight of 42 kg were anesthetized with 1 MAC isoflurane and mechanically ventilated with an FIO_2 of 100%. End tidal CO_2 was maintained between 32 mm Hg and 36 mm Hg. Micromanometer-tipped catheters were placed in the ascending aorta and right ventricle. A balloon-tipped, continuous cardiac output pulmonary artery catheter was introduced through the right internal jugular vein. After a period of stabilization, absolute ETOH was infused through a central venous catheter at a rate of 2 mL/min (approximately 50 mg/kg/min) until a twofold elevation of pulmonary artery pressure (PAP) was reached. The infusion was then discontinued. Data were recorded continuously for 20 minutes. Statistical analysis was performed with ANOVA. A $p<0.05$ was considered significant.
RESULTS: A twofold elevation of mean PAP was achieved in all animals with a mean dose of 123±14 mg/kg of ETOH. Calculated pulmonary vascular resistance increased by 50% ($p<0.05$), with a concomitant increase in heart rate. Right ventricular dP/dT decreased by 40% ($p<0.05$), although cardiac output was maintained. Baseline hemodynamics were restored within 10 minutes of terminating the ETOH infusion.
DISCUSSION: Rapid intravenous injection of absolute ETOH, at lower doses than those used clinically during tumor ablation, produces transient but severe pulmonary vasoconstriction and right ventricular dysfunction. Although short-lived, these events can precipitate acute right ventricular failure and cardiovascular collapse. The clinical implications of this phenomenon merit further study.
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S-16

EFFECTS OF A SILDENAFIL ANALOG, UK 343-664, VERSUS MILRINONE ON A PORCINE MODEL OF ACUTE PULMONARY HYPERTENSION

AUTHORS: **J. Willert**[1], B. Naik[1], D. S. Kirby[2], E. B. Lobato[3], F. Urdaneta[3];
AFFILIATION: [1]Department of Anesthesiology, University of Florida College of Medicine, Gainesville, FL, [2]Anesthesiology Service, Malcom B. Randall Veterans Affairs Medical Center, Gainesville, FL, [3]Department of Anesthesiology, University of Florida College of Medicine; Anesthesiology Service, Malcom B. Randall Veterans Affairs Medical Center, Gainesville, FL.

INTRODUCTION: Inhibition of phosphodiesterase type III (PDEIII) or type V (PDEV) induces pulmonary vasorelaxation, increasing either cyclic AMP or GMP.[1,2] The PDEV inhibitor, sildenafil, has been associated with pulmonary vasorelaxation but is not available for intravenous use.[3] A more potent intravenous sildenafil analog, UK 343-664, has been developed. This study evaluated the effects of UK 343-664 versus milrinone during acute pulmonary hypertension.
METHODS: 24 adult swine were anesthetized with 1 MAC isoflurane and mechanically ventilated with an FIO_2 of 100%. End tidal CO_2 was maintained between 32 mm Hg and 36 mm Hg. Micromanometer-tipped catheters were placed in the ascending aorta, pulmonary artery, and right ventricle. Pulmonary flow was measured with a perivascular probe using transit time ultrasound. Pulmonary hypertension was induced with a continuous infusion of the thromboxane analog, U46619, delivered via a central venous catheter, titrated to produce a twofold elevation of mean pulmonary artery pressure (MPAP). After 30 minutes, the animals were randomized to three groups. Group 1 (n=9) received received 500 µg/kg of UK 343-664 intravenously over 2 minutes; group 2 (n=8) received 50 µg/kg of intravenous milrinone over 10 minutes; and group 3 (n=7) received placebo (10 mL normal saline solution). Data were recorded continuously for 60 minutes. Statistical analysis was performed with ANOVA and t tests. A $p<0.05$ was considered significant.
RESULTS: Pulmonary hypertension was achieved in all animals. The control group had no significant changes in hemodynamics or right ventricular dP/dT following placebo. The administration of UK 343-664 was associated with a significant decrease in pulmonary artery pressure (30.3%; $p<0.05$) and pulmonary vascular resistance (PVR) (42%; $p<0.05$), without systemic vasodilatation; these effects were partially maintained at 30 minutes (17.3% and 39% decrease, respectively; $p<0.05$). Milrinone lowered MPAP by 22% and PVR by 43% ($p<0.05$) at the expense of a 40% decrease in systemic vascular resistance ($p<0.05$). Right ventricular dP/dT was significantly increased with milrinone (by 35%) but not with UK 343-664.
DISCUSSION: During thromboxane-mediated pulmonary hypertension, both UK 343-664 and milrinone produced significant pulmonary vasodilatation. However, UK 343-664 lacked inotropic effects and exhibited relative pulmonary selectivity. In contrast, milrinone was predictably associated with increased right ventricular contractility and systemic vasodilatation. Further studies will define the role of combining intravenous PDEV and PDEIII inhibitors during acute pulmonary hypertension.
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S-17

THE EFFECTS OF ST. JOHN'S WORT IN THE FELINE PULMONARY VASCULAR BED

AUTHORS: **A. D. Kaye**[1], A. M. Fields[2], I. N. Ibrahim[1], T. A. Richards[3], J. Hoover[1];
AFFILIATION: [1]Texas Tech University Health Science Center, Lubbock, TX, [2]Flushing Hospital Medical Center, Flushing, NY, [3]Stanford University Hospital, Palo Alto, CA.

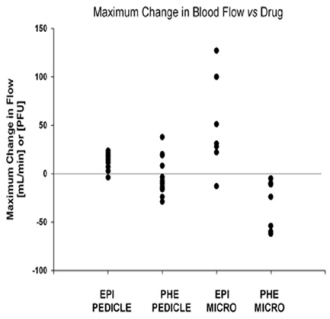
In separate experiments, the effects of L-NIO, an inhibitor of nitric oxide synthase, glybenclamide, a potassium channel blocker, the cyclooxygenase blocker, meclofenamate, nicardipine, a calcium channel blocker, and bicuculline, a GABA receptor blocker were investigated on pulmonary arterial responses of St. John's wort, pinacidil, bradykinin, and other agonist agents during elevated tone conditions induced by the thromboxane A_2 mimic, U46619, in the pulmonary vascular bed of the cat. Lobar arterial perfusion pressure and systemic pressure were continuously monitored, electronically averaged, and permanently recorded. under elevated tone conditions in the isolated left lower lobe vascular bed of the cat. St. John's Wort induced a dose-dependent vasodepressor response that was not significantly altered after administration of L-NIO, glybenclamide, or meclofenamate. Responses to St. John's Wort were significantly reduced after administration of either nicardipine or bicuculline. When the calcium channel blocker nicardipine was administered along with the GABA blocker bicuculline, there was almost complete elimination of the St. John's Wort-induced vasodepressor response. The results of the present study suggest that St. John's Wort has potent vasodepressor activity in the feline pulmonary vascular bed and that this response is mediated or modulated by both a calcium channel and GABA receptor sensitive pathway.

S-18

THE EFFECTS OF EPINEPHRINE AND PHENYLEPHRINE ON PEDICLE ARTERY AND MICROVASCULAR BLOOD FLOWS IN A PORCINE MODEL OF ROTATIONAL MYOCUTANEOUS FLAP

AUTHORS: **D. K. Gupta**, M. F. Massey, M. Cluff, S. W. McJames;
AFFILIATION: University of Utah, Salt Lake City, UT.

INTRODUCTION: Rotational myocutaneous flaps are utilized for complex oncologic reconstruction in a wide variety of clinical settings. Often it is necessary to administer systemic vasoactive agents to maintain systemic arterial pressure close to baseline levels in order to provide adequate perfusion pressure to the brain and other critical organs. However, flap viability may be compromised by the effects of the vasoactive agents on the flap pedicle artery or microvasculature. The aim of this study was to characterize the effects of systemically administered epinephrine and phenylephrine on pedicle artery and microvascular blood flows in a porcine model of rotational myocutaneous flaps.
METHODS: After Institutional Animal Care and Use Committee approval, nine pigs were administered intramuscular ketamine and telazol to induce anesthesia and allow endotracheal intubation and placement of intra-arterial and pulmonary artery catheters for hemodynamic monitoring and intravenous cannulae for fluid and drug administration. Anesthesia was maintained with isoflurane (end tidal 1-1.5% atm) and pancuronium to allow surgical dissection of bilateral vertical rectus abdominus myocutaneous (VRAM) flaps. Intravenous fluid was administered at 10 mL/kg/hr to maintain euvolemia, and blood loss and urine output were replaced at the end of every hour with intravenous fluid. Prior to administration of vasoactive agents via the pulmonary artery catheter, ultrasonic transit flow probes (Transonic Corporation) were placed to measure the blood flow of each VRAM pedicle artery and laser Doppler flow probes (Perimed, Inc.) were affixed to the skin in the center of the myocutaneous flap to measure microvascular perfusion. After baseline hemodynamic measurements, phenylephrine was administered at 20, 40, and 80 mcg/min and the hemodynamic parameters were recorded after appropriate steady-state periods had been achieved. After a washout period, new baseline hemodynamic parameters were recorded before epinephrine was administered at 0.5, 1, and 2 mcg/kg/min. The maximum change in pedicle artery blood flow and microvascular perfusion were compared between drugs utilizing the Wilcoxin signed rank test with $p<0.05$ considered significant.
RESULTS: Fifteen VRAM flaps were created in nine animals. Pedicle artery blood flow decreased in 74% of the animals during phenylephrine infusion while it was augmented by epinephrine ($p = 0.034$). Microvascular perfusion decreased with phenylephrine administration and increased with exposure to epinephrine ($p = 0.028$).
DISCUSSION: Epinephrine augmented both pedicle artery and microvascular blood flow in VRAM flaps while phenylephrine clearly decreased microvascular blood flow despite occasionally augmenting pedicle artery blood flow. Therefore, systemically administered epinephrine may be an appropriate therapeutic option for supporting systemic perfusion pressure during reconstruction with rotational myocutaneous flaps.

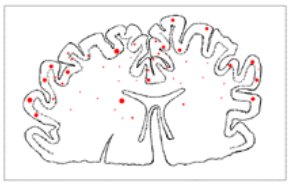


S-19

FUNCTIONAL AND HISTOLOGIC DAMAGE OF THE NEONATAL BRAIN IN A PIGLET LOW-FLOW CARDIOPULMONARY BYPASS MODEL

AUTHORS: **A. W. Loepke**[1], J. Golden[2], J. C. McCann[1], L. Staple[2], C. D. Kurth[1];
AFFILIATION: [1]Institute for Pediatric Anesthesia, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Children's Hospital of Philadelphia, Philadelphia, PA.

INTRODUCTION: Hypothermic low-flow cardiopulmonary bypass (LF-CPB) and deep hypothermic circulatory arrest (DHCA) facilitate surgical repair of complex congenital heart defects. Because outcome studies have documented advantages of LF-CPB compared with DHCA, LF-CPB is becoming more popular, but is still associated with lower intelligence and other neurobehavioral deficits.(1) Whereas neuropathology has been described for DHCA, it remains uncertain after LF-CPB.(2) Our study characterized the neuropathology in a piglet LF-CPB model.
METHODS: Piglets (n=14, age 3-5 days) were anesthetized with fentanyl/ droperidol, intubated, ventilated, and cannulated in the carotid artery and external jugular vein for CPB. Invasive blood pressure, pH, blood gases, cortical blood flow (laser Doppler flowmetry), hematocrit, and glucoses were monitored. Brain, esophageal, and rectal temperatures were recorded. Animals underwent hypothermic CPB with ph-stat management until 22 °C (brain), followed by LF-CPB for 150 min, followed by rewarming, separation from CPB, extubation and recovery for 2 days. Brains were perfuse-fixed and cerebral injury was assessed histologically after H&E staining.
RESULTS: During LF-CPB, MAP was 9±2 mmHg and pump flow of 9±4 ml/kg/min. Cooling and rewarming times were 21±6 min and 36±5 min, respectively. Cerebral cortical blood flow during LF-CPB was 12±6% (n=7) of pre-CPB. After CPB, 5 animals died prematurely: 4 from cardiovascular and 1 from neurologic cause. One day after CPB functional impairment in survivors (n=9) was assessed as mild in 11%, moderate in 33% and severe in 11%; 44% showed no disability. Two days after CPB functional disability improved to mild in 22%, and moderate in 22% animals; 56% animals showed no disability, no animal was rated as severely impaired. Regardless of functional assessment, all animals showed histologic brain damage by 48 hours. Brain damage was moderate to severe in neocortex and hippocampus and mild in basal ganglia, thalamus, white matter, and cerebellum and not observed in the brain stem (Figure 1). Cell death appeared mainly as selective neuronal necrosis in layers 4-6 in neocortex and CA1-4 sections in hippocampus, less so apoptosis; no cerebral infarction was observed. Severity of hippocampal damage inversely correlated with pCO_2 during LF-CPB (r^2=-0.85, p=0.003) and rewarming (r^2=-0.83, p=0.006). Neocortical damage inversely correlated with pCO_2 on rewarming (r^2=-0.84, p=0.005).
DISCUSSION: Brain damage following LF-CPB is similar yet different from that caused by DHCA. The vulnerable areas include neocortex and hippocampus in both, appearing as selective neuronal death and rarely infarction. Neuronal death after LF-CPB appeared as necrosis most often in deep gray matter (layer 4-6), a watershed area. Conversely, neuronal death after DHCA appeared apoptotic, typically in superficial gray matter (layers 2 and 3). Even with pH-stat management, higher pCO_2 during LF-CPB and rewarming reduces brain damage.



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S-20

ANTI-ENDOTOXIN-CORE ANTIBODY LEVELS IN VOLUNTEER BLOOD DONORS

AUTHORS: **M. Rashid**[1], M. Siva[1], R. Stephens[1], M. Grocott[1], M. Contreras[2], M. Mythen[1];
AFFILIATION: [1]Institute of Child Health and Great Ormond Street Hospital, London, United Kingdom, [2]H&I, National Blood Service, Colindale, London, United Kingdom.

INTRODUCTION: Endotoxin plays a central role in sepsis and organ dysfunction after surgery. Levels of one of our natural defences against endotoxin, anti-endotoxin core antibody (EndoCAb), are an independent predictor of post-operative outcome[1]; high pre-operative titres having been associated with a better outcome[2]. However, there is heterogeneity in EndoCAb levels between individuals, within, and across populations, that remains to be explained. The aim of this study was to determine EndoCAb levels in a blood donor population.
METHODS: Blood samples were collected from consented blood donors and the sera separated. EndoCAb levels were determined using an ELISA protocol[3]. Briefly, 100 100µl of diluted test or standard sample were transferred onto an ELISA plate that had been pre-coated with endotoxins from 4 bacterial species and blocked with bovine serum albumin for 1 hour at 37°C. The bound antibodies were then incubated for 1 hour at 37°C with alkaline-phosphatase-conjugated goat-anti-human IgG or IgM antibody. Between each step, the plate was washed with PBS/Tween 20, containing sodium azide. The chromogenic reaction was performed with para-Nitrophenyl phosphate dissolved in a diethanolamine buffer. The reaction was terminated with NaOH and the absorbance read at 405nm. A dual wavelength system with subtraction of a reference wavelength (650nm) was used. The EndoCAb levels of test samples were obtained from a standard calibration curve.
RESULTS: The median IgG EndoCAb level for this population was 141.2 MU/ml (IQR: 84.9 - 238.4 MU/ml). The 95th centile was 576.2 MU/ml. The median IgM EndoCAb level was 226.9 MU/ml (IQR: 138.2 - 365 MU/ml). The 95th centile was 642.6 MU/ml. The cut-off point for hyperimmune plasma in a previous study was 400 MU/ml4. Based on 4 times the median value, the cut-off point for IgG hyperimmunity for this population was 564.8 MU/ml. We identified 27 (5.4%) IgG hyperimmune individuals.
DISCUSSION: The 501 donors screened for EndoCAb levels show a median IgG and IgM level of 141.2 and 226.9 MU/ml, respectively. This is higher than a reported Scottish population where the median for both IgG and IgM was 100MU/ml. In this study individuals differ in their IgG levels by up to 85-fold and in their IgM levels by up to 122-fold. These observed differences between individuals remain unexplained. Possible reasons for these differences may include prior exposure to endotoxins, differences in HLA-genotypes, particularly, class II genes, which may affect differences in antigen presentation, and other factors known to bind endotoxin such as high density lipoprotein cholesterol and bactericidal permeability increasing protein. No correlation between IgG and IgM EndoCAb levels within individuals was observed. Within our population, 5.4% of individuals were IgG hyperimmune.
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S-21

EFFECT OF GI-COUPLED RECEPTOR AGONISTS ON EXTRACELLULAR SIGNAL-REGULATED KINASE (ERK) ACTIVITY IN RATS

AUTHORS: **A. E. Kold**, Z. XU, R. A. Mueller, P. G. Boysen;
AFFILIATION: University of North Carolina at Chapel Hill, Chapel Hill, NC.

INTRODUCTION: Gi-coupled receptor agonists such as adenosine, acetylcholine, bradykinin and morphine have been reported to trigger ischemic preconditioning [1]. ERK activation is an important intracellular signal pathway leading to cardioprotection [2,3]. The purpose of the present study was to investigate the effects of these agonists on ERK activation in rat cardiomyocytes.
METHOD: Cardiomyocytes were isolated from adult male Wistar rats. The cells were treated with the agonists for 10 min and phosphorylated ERK activities were measured with Western blotting.
RESULTS: Adenosine (100 μm) significantly ($P<0.05$) increased both ERK1 (125.1 ± 8.2 % of control) and ERK 2 (129.8 ± 11.3 % of control) activities compared to control. In contrast, acetylcholine, bradykinin and morphine had no effect on ERK activities.
DISCUSSION: It has been reported that acetylcholine, bradykinin and morphine, but not adenosine, trigger ischemic preconditioning by generating reactive oxygen species (ROS) and opening of mitochondrial K_{ATP} channels [1]. In the present study, adenosine but not other agonists phosphorylated ERKs, suggesting the signal pathway for cardioprotective effect of adenosine is unique and different from those other agonists. This finding may help us to understand the diverse signaling events of cardioprotection. Further experiments will better define the signaling mechanism by which adenosine activates ERKs and the role of ERK in the cardioprotective effect of adenosine.
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S-22

DESFLURANE-INDUCED PRECONDITIONING AGAINST MYOCARDIAL INFARCTION IN RABBITS IS MEDIATED BY NITRIC OXIDE

AUTHORS: T. Smul[1], D. C. Warltier[2], J. Kersten[2], P. S. Pagel[2], N. Roewer[1], **F. Kehl**[1];
AFFILIATION: [1]Julius-Maximilians-University, Wuerzburg, Germany, [2]Medical College of Wisconsin, Milwaukee, WI.

INTRODUCTION: Volatile anesthetics induce myocardial preconditioning through a signal transduction pathway that is remarkably similar to that observed during ischemic preconditioning.[1] Nitric oxide (NO)-dependent signalling plays an important role in ischemic preconditioning[2] and it has recently been demonstrated in isolated guinea-pig hearts that sevoflurane-induced preconditioning is mediated through a NO-dependent mechanism.[3] Data on other volatile anesthetics and in situ preparations are lacking. Therefore, we tested the hypothesis that desflurane-induced preconditioning is mediated by nitric oxide.
METHODS: All experimental procedures conformed to the guidelines of the APS and the NIH and were approved by the institutional Animal Care and Use Committee. Barbiturate-anesthetized rabbits (n=34) were instrumented for measurement of hemodynamics, including aortic pressure and cardiac output. All rabbits were subjected to 30-min coronary artery occlusion followed by 3 h of reperfusion. Myocardial infarct size (IS) was assessed with triphenyltetrazolium chloride and area at risk (AAR) was assessed with patent blue. Rabbits were randomized to 4 separate experimental groups and received 0.0 or 1.0 mac desflurane for 30 min that was discontinued 30 min before ischemia and reperfusion in the absence or presence of the unselective nitric oxide synthase (NOS) inhibitor n-omega-nitro-l-arginine (L-NA, 13mg/kg *iv*) 10 min prior to desflurane. Statistical analysis of data was performed with repeated measures ANOVA followed by posthoc Duncan test. Data are mean±SEM.
RESULTS: Systemic hemodynamics during baseline, coronary artery occlusion and reperfusion were not significantly different among groups. There was no significant difference in AAR between groups. IS was 55±7% (IS/AAR) in control experiments. Desflurane significantly (*$p<0.05$) reduced IS to 34±4* and the cardioprotection afforded by desflurane was totally blocked by L-NA (58±4%). L-NA alone had no effect on infarct size (56±7%).
DISCUSSION: The results demonstrate that desflurane-induced preconditioning markedly reduces myocardial infarct size. This beneficial effect is blocked by the NOS-Inhibitor L-NA and suggests that desflurane-induced preconditioning is mediated by NO.
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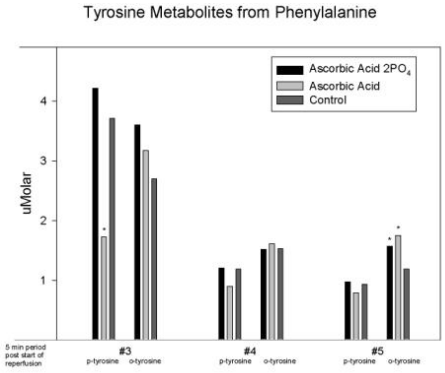
S-23

ASCORBIC ACID 2-PHOSPHATE DOES NOT PREVENT ISCHEMIC DAMAGE IN RAT HEARTS BY SCAVENGING HYDROXYL RADICALS

AUTHORS: **R. A. Mueller**, H. Criswell, S. Perretta;
AFFILIATION: Univ of NC at Chapel Hill, Chapel Hill, NC.

INTRODUCTION: Since the appreciation that cardiac reperfusion-injury was accompanied by the generation of reactive oxygen radicals, many compounds with antioxidant activity have been examined in attempts to prevent radical generation and a loss of cardiac contractile integrity. Esters of ascorbic acid (AA), such as ascorbate –2-phosphate (A2P) are more lipid soluble then AA and more readily pass cell membranes.[1] We previously demonstrated that the relative cardiac protective action of A2P is greater than that of AA on Langendorff perfused rat hearts, after 30 min of ischemia at 37^0C. The present study sought to measure the production of isomers of tyrosine from D-phenylalanine as an index of hydroxyl radical formation during reperfusion of hearts pretreated with A2P, AA or control solution.
METHODS: Sprague-Dawley rat hearts were perfused with Krebs Hensilite solution containing D-phenylalanine (5mM) for recording of dp/dt, diastolic pressure, and maximum systolic pressure achieved. After a 10 minute stabilization period, hearts received (by delivery immediately above the aortic cannula) increasing doses of AA, A2P, or control perfusion solution, at concentrations from 2.3→11.9 mM in 6-5 min periods before ischemia. Contractile responses were recorded at 5 min intervals both before and after a 30 min period of no perfusion (370C). Values were assessed with an analysis of variance. The perfusates collected at 3, 4, and 5 min after the start of reperfusion were assessed for p, o, and m, tyrosine via HPLC with UV detection.
RESULTS: The preischemic dp/dt values of AA and A2P hearts were significantly reduced by all examined concentrations. After a 30 min ischemia period, the recovery of dp/dt was significantly better in A2P exposed hearts relative to AA or control hearts. The postischemic diastolic pressures of A2P hearts were also significantly less than those of control or AA hearts. Tyrosine production was significantly reduced in AA treated hearts relative to control or A2P hearts, (which were similar). (Fig 1)



DISCUSSION: The degradation of ascorbate is protected by substituents at the 2C position, thus higher local concentrations may be achieved with A2P than with molar equivalent doses of AA. The slower heart rate seen with A2P would be expected to delay ischemic contracture, and thus facilitate post-ischemic impairment of function. These data suggest that post ischemic cardiac contracture protection by A2P may be due to its potency to reduce cardiac energy consumption before induction of ischemia, rather than its ability to scavenge oxygen free radicals upon reperfusion.
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S-24

EFFECTS OF CYCLIC GMP ON CONTRACTILE FUNCTION OF MYOCYTES ISOLATED FROM STUNNED MYOCARDIUM INDUCED BY CARDIOPULMNOARY ARREST IN RABBITS

AUTHORS: **J. Tse**, J. Su, P. M. Scholz, H. R. Weiss;
AFFILIATION: UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

INTRODUCTION: Myocardial stunning induced by a brief period of ischemia has depressed function (1). It has been suggested that cyclic GMP (cGMP) may play a protective role against myocardial stunning (2). We hypothesized that the cGMP and cGMP-dependent protein kinase signaling pathway would be altered in the resuscitated stunned myocardium after cardiopulmonary arrest.
METHODS: Fourteen New Zealand White rabbits were included in the experiments with approval from IACUC. Experiments were performed in anesthetized open-chest animals. Cardiopulmonary arrest was achieved for 10 min through ventricular fibrillation and respirator shutdown in seven animals. Ventilation was then resumed and cardiac massage was performed. The heart was defibrillated and allowed to recover for 15 min. Seven sham-operated controls were anesthetized and received same instrumentation without inducing cardpulmonary arrest. Left ventricular myocytes were isolated using collagenase. Myocyte contractile function was measured via a video edge detector. Myocytes were treated with 8-Bromo-cGMP (10^{-5}-10^{-6}M) followed by KT5823 (10^{-6}M, cyclic GMP protein kinase inhibitor). Protein phsophorylation was performed using myocyte extract and [^{32}P] ATP in the prsence and absence of $2.5x10^{-4}$M 8-Bromo-cGMP and $7.5x10^{-4}$M KT5823. Protein eletrophoresis was performed using SDS-polyacrylamide gel. ANOVA was used for statistical analysis. A p value of <0.05 was accepted as significant. All values are expressed as mean ± S.E.M.
RESULTS: The basal percent shortening was significantly depressed in the stunned myocytes when compared with control (3.3±0.1% vs. 5.5±0.3%). 8-Br-cGMP treatment similarly and dose-dependently reduced cell contraction in both stunned (-24%) and control (-25%) myocytes. The negative effect of 8-Br-cGMP was partially reversed by KT5823 in control myocytes, but not in the stunned myocytes. Multiple proteins were specifically phosphorylated when cGMP was present, but the degree of phosphorylation was significantly less in the stunned myocytes.
CONCLUSIONS: The data showed that myocardial stunning reduced the basal contractile function but preserved the negative inotropic response to exogenous cGMP. The results also indicated that the negative inotropic effects of cGMP on the stunned myocardium appeared to be mainly through non-protein kinase pathways.
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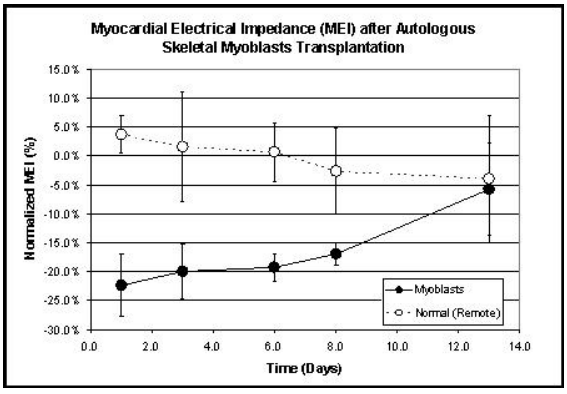
S-25

AUTOLOGOUS SKELETAL MYOBLASTS RESTORE THE ELECTRICAL IMPEDANCE OF INFARCTED SHEEP MYOCARDIUM

AUTHORS: **M. B. Howie**[1], P. I. McConnell[1], C. L. del Rio[1], R. Dzwonczyk[1], D. B. Jacoby[2], R. E. Michler[1];
AFFILIATION: [1]The Ohio State University, Columbus, OH, [2]Diacrin, Inc., Boston, MA.

INTRODUCTION: Autologous skeletal myoblasts can survive within areas of myocardial infarct. However, little is known about the temporal behavior of myoblast integration. Myocardial electrical impedance (MEI) is sensitive to myocardial tissue ischemia, metabolism and fiber alignment. *Hypothesis*: MEI can detect changes in tissue conduction following autologous skeletal myoblast transplantation.
METHODS: Posterior myocardial infarction was induced in 8 sheep by means of coronary microembolization. Myocardial impedance electrodes were placed in remote and infarcted myocardium in both control (n=4) and myoblast (n=4) animals. Myoblasts were injected (3 x 10^8 cells) into areas of infarction and in proximity to the impedance electrodes. Myocardial impedance was measured in awake unsedated animals at 1, 3, 7, and 14 days after transplantation.
RESULTS: Immediately following myoblast transplantation (Day 1), the MEI of infarcted myocardium (381±21Ω) differed from that of remote healthy myocardium (488±33Ω). In control animals, the difference between infarcted and healthy tissue remained unchanged from Day 1 (-19±7%) to Day 14 (-21±4%). In contrast, after myoblast transplantation, the difference decreased significantly over time, from -22±5% (Day 1) to -5±7% (Day 14). By Day 14, MEI in the infarcted region reached control (remote) values (see figure).



DISCUSSION: Autologous skeletal myoblasts transplanted into areas of myocardial infarction restored the MEI to control values. Normalization of the conductive properties of the infarcted myocardium after myoblast transplantation may suggest the timing of myoblast integration and differentiation.
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S-26

SCN5A GAIN-OF-FUNCTION GENE MUTATION LEADS TO ARRHYTHMOGENESIS, ALTERED ACTION POTENTIAL DURATION AND ABNORMAL INTRACELLULAR CA2+ HANDLING IN MOUSE VENTRICULAR MYOCYTES

AUTHORS: K. Chung, **D. S. Damron**;
AFFILIATION: The Cleveland Clinic Foundation, Cleveland, OH.

INTRODUCTION: Long QT (LQT) syndrome is caused by mutations in genes that encode for cardiac ion channels which can drastically affect cardiac action potential duration. If sufficiently increased, these abnormally prolonged action potentials can result in and form the basis of arrhythmogenesis, abnormal handling of intracellular Ca2+ and lethal cardiac arrhythmias. Our objective was to characterize alterations in intracellular Ca2+ handling in mouse cardiomyocytes expressing the human SCN5A gene with the gain-of-function sodium channel mutation (N1325S).
METHODS: All the procedures were approved by the Institutional Animal Care and Use Committee. Freshly isolated ventricular myocytes were obtained from wildtype and transgenic mouse hearts expressing the SCN5A gene. Intracellular free Ca2+ concentration ([Ca2+]i) and myocyte shortening were simultaneously measured using fura-2 (340/380 ratio) and video-edge detection, respectively, in individual field-stimulated myocytes (28ºC, 0.3 Hz). Action potential (AP) recordings were performed using the whole cell patch clamp technique. Statistical analysis was performed using analysis of variance and Bonferroni t-test. Data are reported as means ± SEM.
RESULTS: The resulting phenotype was consistent with clinical LQT syndrome including prolonged QT-interval, increased ventricular action potential duration and high incidence of lethal cardiac arrhythmias. Interestingly, whole cell AP recordings from transgenic myocytes revealed an alternating increase and decrease of AP durations. Resting cell length in wildtype and transgenic cardiomyocytes was 112 ± 5 um and 117 ± 6 um, respectively. Baseline [Ca2+]i in wildtype and transgenic cardiomyocytes was 107 ± 15 nM and 112 ± 11 nM, respectively. Peak [Ca2+]i and shortening in response to field-stimulation were similar in both groups. Time to peak (Tp) [Ca2+]i and Tp shortening were similar in both groups. However, upon return of [Ca2+]i to baseline, transgenic myocytes exhibited a prolonged elevation in [Ca2+]i above baseline, the duration of which was 290 ± 23 msec. Similarly, cardiomyocyte relengthening was also prolonged and the myocyte remained partially contracted during the prolonged elevation in [Ca2+]i. During the prolonged elevation in [Ca2+]i, field-stimulation of the transgenic myocyte resulted in little or no additional transient increase in [Ca2+]i or shortening, but rather triggered the decline of [Ca2+]i to baseline and complete relengthening of the cardiomyocyte.
DISCUSSION: These data demonstrate that the gain-of-function sodium channel mutation in mouse cardiomyocytes results in alterations in AP duration and abnormal intracellular Ca2+ handling causing alterations in cardiomyocyte excitation contraction coupling which may result in lethal cardiac arrhythmias.

S-27

PROPOFOL ATTENUATES THE INOTROPIC RESPONSE TO BETA-ADRENORECEPTOR STIMULATION IN DIABETIC RAT CARDIOMYOCYTES

AUTHORS: **D. S. Damron**;
AFFILIATION: The Cleveland Clinic Foundation, Cleveland, OH.

INTRODUCTION: Activation of myocardial beta-adrenoreceptors represents the primary mechanism for increasing the inotropic state of the heart. We previously demonstrated a propofol-induced inhibition of beta-adrenoreceptor mediated increases in cardiomyocyte shortening via activation of a protein kinase C-dependent pathway (1). Our current objectives are to identify the extent to which propofol alters beta-adrenoreceptor mediated increases in cardiomyocyte inotropy in diabetic cardiomyocytes.
METHODS: All procedures were approved by the Institutional Animal Care and Use Committee. Freshly isolated ventricular myocytes were obtained from normal and diabetic (streptozotocin, 65mg/kg, IP) adult rat hearts. Intracellular free Ca2+ concentration ([Ca2+]i) and myocyte shortening were simultaneously measured using fura-2 (340/380 ratio) and video-edge detection, respectively, in individual field-stimulated myocytes (28ºC). Statistical analysis was performed using analysis of variance and Bonferroni t-test. Data are reported as means ± SEM.
RESULTS: Resting cell length in normal and diabetic cardiomyocytes was 121 ± 6 um and 111 ± 8 um, respectively. Baseline [Ca2+]i in normal and diabetic cardiomyocytes was 129 ± 17 nM and 113 ± 15 nM. Peak [Ca2+]i and shortening in response to field-stimulation were reduced in diabetic cardiomyocytes by 18 ± 6% and 33 ± 7% respectively, compared to normal cardiomyocytes. Time to peak (Tp) [Ca2+]i was unchanged between the two groups, however Tp shortening was prolonged in the diabetic cardiomyocytes. Time to 50% return (T50r) to baseline [Ca2+]i and shortening were also prolonged in the diabetic group. Addition of isoproterenol (ISO, 10-7 M) increased peak [Ca2+]i and shortening by 47 ± 9% and 123 ± 25% in normal cardiomyocytes. In contrast, addition of ISO to diabetic cardiomyocytes increased peak [Ca2+]i by 24 ± 5% whereas peak shortening increased by only 42 ± 16%. Propofol (10-6 M) attenuated ISO-induced increases in peak [Ca2+]i and shortening in normal cardiomyocytes by 9 ± 3% and 11 ± 6%, respectively. In contrast, propofol attenuated ISO-induced increases in shortening by 68 ± 12% whereas peak [Ca2+]i was reduced by 13 ± 7% in diabetic cardiomyocytes.
DISCUSSION: These data demonstrate that beta-adrenoreceptor mediated signaling is diminished in diabetic cardiomyocytes. In addition, the propofol-induced inhibition of beta-adrenoreceptor-mediated increases in [Ca2+]i and shortening are more pronounced in diabetic cardiomyocytes compared with normal cardiomyocytes. These data also suggest that alterations in both Ca2+ cycling and myofilament Ca2+ sensitivity likely explain the effect of diabetes on cardiomyocyte inotropy and that propofol primarily reduces myofilament Ca2+ sensitivity.
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S-28

EFFECT OF INTRAVENOUS ANESTHETICS ON U46619-MEDIATED CONTRACTION IN CANINE CORONARY ARTERIAL SMOOTH MUSCLE

AUTHORS: X. Ding, P. A. Murray, **D. S. Damron**;
AFFILIATION: The Cleveland Clinic Foundation, Cleveland, OH.

INTRODUCTION: Thromboxanes are vasoconstrictor metabolites of the cyclooxygenase pathway and are known to be endogenous regulators of coronary vascular resistance. We previously demonstrated that propofol potentiated vasoconstrictor responses to the thromboxane A2 analog, U46619, in isolated canine coronary artery (1). In the present study, we investigated the extent and mechanism of action by which the intravenous anesthetics, ketamine, thiopental and etomidate, alter the coronary arterial smooth muscle response to U46619.
METHODS: All the procedures were approved by the Institutional Animal Care and Use Committee. Isolated canine coronary arterial rings without endothelium (E-) were suspended in modified Krebs-Ringer buffer for measurement of isometric tension. Cumulative U46619 concentration-response (10-10~10-6 M) relationships were measured in E- rings. The effects of ketamine (10-6~10-4 M), thiopental (10-6~10-4M) and etomidate (10-6~10-4 M) on U46619 response were studied in E- rings. In some experiments, intracellular Ca2+ concentration ([Ca2+]i) was simultaneously measured with tension using Fura-2 (340/380 ratio). The effect of ketamine (10-4M) on [Ca2+]i-tension relationship was assessed. Statistical analysis was performed using analysis of variance and LSD.
RESULTS: U46619 caused dose-dependent contraction E- rings. The maximum response (Rmax) achieved with U46619 was 151 ± 11% (EC50 = –7.32 ± 0.18) of that obtained with 60 mM KCl. Ketamine (10-6 M and 10-5 M) had no effect on the U46619 concentration-response relationship, whereas ketamine (10-4 M) attenuated U46619-induced contraction and decreased Rmax from 151 ± 11% to 109 ± 9%. Similarly, thiopental (10-6 M and 10-5 M) also had no effect on the U46619 concentration-response relationship, whereas thiopental 10-4 M potentiated U46619-induced contraction and increased Rmax from 107 ± 9% to 148 ± 11%. Etomidate (10-6~10-4 M) had no effect on the U46619 concentration-response relationship in coronary arterial rings. Ketamine induced a rightward shift in the [Ca2+]i-tension relationship (i.e. ketamine attenuated myofilament Ca2+ sensitivity).
DISCUSSION: The thromboxane A2 analog, U46619, caused contraction in coronary arterial rings. Etomidate had no effect on U46619-induced contraction in coronary arterial smooth muscle. Clinical concentrations of thiopental had no effect on U46619-induced contraction, whereas supraclinical concentrations of thiopental potentiated U46619-induced contraction in coronary arterial smooth muscle. Clinical concentrations of ketamine attenuated U46619-induced contraction by decreasing myofilament Ca2+ sensitivity.
REFERENCES: (1)Tanaka et al., Anesthesiology 96 (Suppl): A650, 2002.

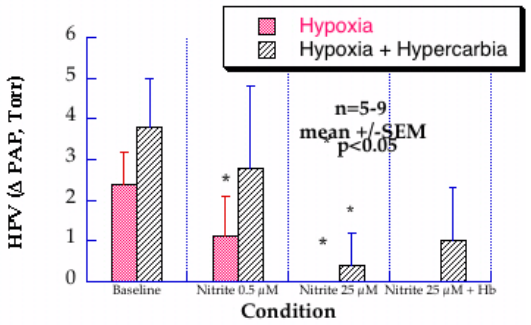
S-29

NITRITE IS A NITRIC OXIDE DONOR AND INHIBITS HYPOXIC PULMONARY VASOCONSTRICTION IN ISOLATED RAT LUNGS

AUTHORS: **S. Deem**[1], J. Moulding[1], M. Hye[1], R. Eveland[1], E. R. Swenson[2];
AFFILIATION: [1]University of Washington, Seattle, WA, [2]Veterans Affairs Puget Sound Medical Center, Seattle, WA.

INTRODUCTION: Nitrite (NO2-) is an oxidative product of nitric oxide (NO). However, this reaction can be reversed under hypoxic and acidotic conditions and is potentiated by free hemoglobin (Hb).2 Nitrite may thus serve as a reservoir and donor of NO, and act as an effective vasodilator. We studied the effect of nitrite on NO generation and hypoxic pulmonary vasoconstriction (HPV) in isolated, perfused rat lungs.
METHODS: Adult Sprague-Dawley rats were anesthetized and euthanized by exsanguination. The lungs were isolated and perfused continuously via a recirculating system, and ventilated with normoxic, normocarbic gas. HPV was assessed as the change in pulmonary artery pressure during ventilation with anoxic, normocarbic gas (FICO2 0.05), or anoxic, hypercarbic gas (FICO2 0.10) for 5 minutes. Endogenous nitric oxide production was inhibited by addition of the L-arginine analog L-NAME to the perfusate. HPV was studied before and after addition of sodium nitrite (NaNO2) to achieve estimated perfusate NO2- concentrations of 0.5 and 25 µM. Exhaled NO was measured continuously using chemiluminescence, and perfusate NO2- was measured electrochemically.
RESULTS: NO2- resulted in a dose-dependent reduction in HPV, an effect that was not reversed by free Hb (Figure 1). NO2- also resulted in a dose-dependent increase in eNO, an effect that was potentiated by hypoxia and hypercarbia/acidosis and that remained in the presence of free Hb. Hypoxic ventilation also resulted in a fall in perfusate nitrite concentration, consistent with generation of NO from nitrite.
DISCUSSION: NO2- is converted to NO when exposed to hypoxic and acidotic conditions in rat lungs. This results in inhibition of HPV. The lowest concentration of NO2- studied approachs that measured in human plasma under normal physiologic conditions, and uder pathophysiologic conditions such as sepsis NO2- concentrations may be much higher. These data suggest that NO2- may act to biopreserve NO activity and thereby modulate pulmonary and/or systemic blood flow under certain conditions, and furthermore that Hb may act to potentiate this effect. This is in contrast to previous observations that suggest that the primary effect of Hb is to inactivate NO and augment vasoconstriction.1

1. Am J Respir Crit Care Med 157: 1181-1186., 1998.
2. J Inorg Biochem 14: 351-358., 1981. Supported in part by a grant from the International Anesthesia Research Society.



Circulation - Clinical

S-30

EFFECTS OF SEVOFLURANE AND PROPOFOL WITH LOW AND MEDIUM DOSES OF FENTANYL DURING OPCAB SURGERY

AUTHORS: **M. Nonogaki**[1], U. Kondo[1], K. Nishiwaki[2], Y. Shimada[2];
AFFILIATION: [1]Yokkaichi Municipal Hospital, Yokkaichi, Japan, [2]Nagoya University Graduate School of Medicine, Nagoya, Japan.

INTRODUCTION: Compared with on-pump CABG, the advantages of off-pump CABG (OPCAB) are known in terms of suppression of release of cytokines and endogenous catecholamines. In this study we investigated the effects on such parameters of sevoflurane and propofol with low and medium doses of fentanyl during OPCAB surgery.
METHODS: Forty patients who were to receive elective OPCAB surgery were enrolled in the study. Written informed consent was obtained from each patient, and approval for the study was obtained from the local research and ethics committee. The patients were divided into four groups: sevoflurane with a low dose of fentanyl (15 mg/kg, LS group); sevoflurane with a medium dose of fentanyl (30 mg/kg, MS group); propofol with low dose fentanyl (LP group); and propofol with medium dose fentanyl (MP group). Anesthesia was induced with 0.08mg/kg midazolam, 2mg/kg fentanyl and 0.1mg/kg vecuronium, and maintained with air-O_2-sevoflurane or propofol and intermittent injection of fentanyl. Before surgery and 1, 2 and 3 hours after graft anastomosis, hemodynamic parameters and plasma adrenalin (AD), noradrenalin (NA), IL-8, IL-6 and IL-10 levels were measured. The time to awakening, the time to extubation after ICU admission and the requirement for postoperative analgesics were also measured. The Kruskal-Wallis test, Mann-Whitney U test, and ANOVA were used for statistical analysis.
RESULTS: There was no significant difference among the four groups in height, weight, age, graft number, ASA-PS, and operation and anesthesia time. The LS group had a significantly shorter time to awakening than the MP group (15.9 ± 15.0 vs. 48.5 ± 24.9 minutes; mean ± SD, p=0.002). There were no significant differences between the four groups in the time to extubation and the plasma AD, NA, IL- 6 and IL-8 levels. However, the IL-10 level was significantly higher in the LS group, compared to the MP group (P = 0.0057). No significant differences in hemodynamic data were observed. Acute pain in the first 24 hours postoperatively was greater in the low dose group than in the medium dose group when anesthesia was maintained with sevoflurane.
DISCUSSION: An increase in the levels of pro-inflammatory cytokines is balanced by a parallel increase of anti-inflammatory cytokines. The cause of the increase in the IL-10 level in the LS group, compared to that in the MP group, is unknown. Sevoflurane was shown to be a good anesthetic for early awakening postoperatively. However, if fentanyl is used with sevoflurane as an anesthetic during OPCAB surgery, a dose of 15 mg/kg fentanyl may be inadequate, because patients treated with this dose required more analgesics, compared to those patients treated with 30 mg/kg fentanyl. Both 15 and 30 mg/kg doses of fentanyl are probably adequate for use of fentanyl with propofol during OPCAB surgery.

S-31

PERCUTANEOUSLY IMPLANTED RIGHT HEART ASSIST DEVICE IN OFF-PUMP CORONARY BYPASS SURGERY

AUTHORS: **S. P. Wirtz**[1], C. Schmidt[1], H. Van Aken[1], E. Berendes[1], H. Scheld[2], D. Hammel[3];
AFFILIATION: [1]Universitätsklinikum Münster, Departement of Anesthesiology and Intensive Care Medicine, Münster, Germany, [2]Universitätsklinikum Münster, Departement of Thoracic and Cardiovascular Surgery, Münster, Germany, [3]Zentralkrankenhaus Links der Weser, Departement of Thoracic and Cardiovascular Surgery, Bremen, Germany.

INTRODUCTION: Off-pump coronary artery bypass (OPCAB) surgery has become increasingly popular avoiding potential risks associated with cardiopulmonary bypass and manipulation of the aorta (1). However, positioning maneuvers to access the coronary arteries on the posterior and lateral cardiac surfaces lead to right ventricular and pulmonary outflow tract distortion causing hemodynamic instability (2). Right heart support (RHS) by temporary assist (RVAD) devices has been proposed to improve hemodynamic stability and safety of OPCAB procedures (3). We report our experience of a consecutive sample of ten patients with multi-vessel coronary artery disease scheduled for beating heart myocardial revascularization with RHS using a percutaneously implanted RVAD.
METHODS: After sternotomy and administration of 400 IU/kg of heparin, a previously inserted central venous catheter was exchanged against an A-Med Jugular Coaxial Cannula® (A-Med Systems Inc., West Sacramento, CA) using a Seldinger-wire and different dilatators to facilitate introduction of the catheter. This cannula consists of two tubes: the outer part was placed into the right ventricle draining blood to the pump; the inner tube was advanced through the ventricular cannula for returning the blood into the pulmonary artery. Transesophageal echocardiography was used to monitor the procedure and guide positioning of the cannula. The cannula was connected to a microcentrifugal pump (A-Med Paraflow Miniature Centrifugal Pump System®) for temporary hemodynamic support during each anastomosis. After completion of the distal coronary anastomosis, the pump flow was adjusted to achieve maximum blood pressure. Then the pump was stopped and arterial blood pressure was recorded. Data were analyzed using unpaired and paired t-tests to compare measurements of anterior (group 1) and posterior and lateral (group 2) wall anastomosis sites.
RESULTS: A total of 27 anastomosis sites were exposed for grafting, with an average of 2.7 per patient (group 1: 10 left anterior descending artery, 3 diagonal branch, 3 1st oblique marginal branch; group 2: 3 right coronary artery, 2 distal left circumflex artery, 6 2nd and 3rd oblique marginal branch). Pump flow to achieve maximal perfusion pressure was significantly higher in group 2. Mean arterial pressure in group 2 but not in group 1 decreased significantly after stopping the pump. Percutaneous insertion of the coaxial cannula in the right jugular vein was feasible without complications.

Table: Pump flow to achieve optimal blood pressure and mean arterial pressure (MAP) with/without pump (mean ± SD)

Group	Pump Flow [l/min]	MAP on pump [mmHG]	MAP off pump [mmHG]	P Value
Group 1	2.4 ± 1.1	63.2 ± 13.6	59.3 ± 14.2	0.146
Group 2	3.1 ± 0.7	67.5 ± 10.5	57.3 ± 15.3	**0.039**
P Value	**0.037**			

DISCUSSION: Percutaneously implanted RHS in OPCAB procedures enables stable hemodynamics for posterior and lateral anastomosis and seems to be a safe and feasible method.
REFERENCES:
1) Ann Thorac Surg, 74: 2088, 2002
2) Eur J Cardiothorac Surg, 19: 34, 2001
3) Ann Thorac Surg, 70: 1083, 2000

S-32

TWO BOLUS OF TRANEXAMIC ACID ARE AS EFFECTIVE AS A CONSTANT INFUSION FOR BLOOD TRANSFUSION SAVING AFTER CARDIAC SURGERY WITH CPB

AUTHORS: **C. J. Isetta**[1], F. Bernage[1], A. Apper-Flory[2], F. Fischer[2];
AFFILIATION: [1]CHU, Fort de France, Martinique, [2]CHU, Nice, France.

INTRODUCTION: Tranexamic acid (AT), an indirect antifibrinolytic agent, reduces blood loss and blood requirements after cardiac surgery with CPB. The therapy should begin before CPB, but the dosages employed are different, from 10 to 150 mg kg-1 (1) body weight followed by a constant infusion of 10 mg kg-1 during 10 hours (2) or by a second intravenous injection after CPB. The aim of this study was to compare the two modes of administration.
METHODS: After IRB approval, informed consent was obtained in 20 patients undergoing bypass surgery with CPB. They were randomly assigned to IV AT group (n = 10) with two AT intravenous injections of 15 mg kg-1 each, before the surgical incision and after the injection of protamine, or to the CI AT group (n = 10) with one AT intravenous injection of 10 mg kg-1 followed by a constant infusion of 1 mg kg-1 during 10 hours. Values expressed as mean ± SD and compared using one-way analysis of variance. A level of $p<0.05$ (*) was considered significant.
RESULTS: The demographic and surgical data were similar in the two groups. There were no differences between coagulation tests. The heparine antagonisation was achieved with protamine (prot), the posology employed was 80 % of the total heparine dose. The given amount of AT was higher in the IV AT group (30 mg kg-1) than in the CI AT group (20 mg kg-1). Plasminogen levels decreased slowly in the 2 groups with plasmin inhibition by a2 antiplasmin (a2AP). In spite of the antifibrinolytic agent presence, a D-Dimers production was observed. Blood loss and blood requirements were the same in the 2 groups (table)
DISCUSSION: Two intravenous injections of AT are as effective as a constant infusion for blood transfusion saving after cardiac surgery with CPB.

REFERENCES:
1 Br J Anesth 1997 ; 78 suppl 2:35
2 Anesthesiology 1995 ; 82 : 383-392

data

	IV TA (10)	CI TA (10)		IV TA (10)	CI TA (10)
TA (mg)	2189 (71)	1538 (140)	Age(year)	66 (8)	63 (9)
BSA (kg/m²)	1.81 (0.1)	1.86 (0.1)	Heparine (IU)	28100 (1400)	29500 (4900)
CPB time (sec)	126 (21)	117 (33)	Protamine (mg)	207 (42)	212 (28)
ACT induction (sec)	119 (5)	127 (126)	a2AP induction (%)	87 (4)	85 (11)
ACT max (sec)	574 (10)	525 (63)	a2AP before prot (%)	63 (20)	68 (13)
ACT 6th PO h (sec)	121 (1)	126 (7)	a2AP 6th PO h (%)	79 (18)	80 (13)
Blood loss 48h (ml)	1020 (138)	946 (880)	D-Dimers induction (µg/L)	425 (47)	473 (375)
Tubes removal (h)	53 (22)	56 (18)	D-Dimers before prot (µg/L)	335 (207)	591 (434)
Tranfused patient (n)	5	4	D-Dimers 6th PO h(µg/L)	1031 (527)	1359 (668)

S-33

USE OF THE HIGH DOSE THROMBIN TIME TO MEASURE HEPARIN ANTICOAGULATION IN HEPARINIZED PATIENTS HAVING CARDIAC SURGERY

AUTHORS: **L. Shore-Lesserson**, J. B. Sanders, M. Stone, D. Harrington;
AFFILIATION: Mt. Sinai Medical Center, New York, NY.

INTRODUCTION: Heparin pre-treatment in cardiac surgical patients often leads to "resistance" to the large dose of heparin required for cardiopulmonary bypass (CPB). This is partially mediated through consumption of anti-thrombin 3 (AT3).[1] Thus, excessively large doses of heparin are given to attain an acceptable activated clotting time (ACT) for CPB. We hypothesize that these large heparin doses are unnecessary. This heparin resistance is related to the ACT technique and may not be seen with an alternative measure of anticoagulation for CPB, the high dose thrombin time (HITT®).[2]
METHODS: After IRB approval and written informed consent, forty-one patients receiving preoperative heparin infusions were randomly assigned to CPB heparin management by either standard ACT or by HITT monitoring. Initial heparin dose was based upon individual patient sensitivity to achieve ACT=480s. An ACT threshold value of 480 sec was accepted which corresponds to a HITT value of 168 sec [HITT package insert]. Perfusionists were blinded to the results of the test to which the patient was not randomized. ACT and HITT were recorded in all patients and the number of sub-therapeutic values was compared between the two tests (chi squared test). Total heparin dose, protamine dose, chest tube drainage, AT3 levels, and fibrin monomer production were compared in the two groups using Student's t-test for parametric data and the Mann Whitney-U test for non-parametric data. All tests were two-tailed and $p<0.05$ was considered significant.
RESULTS: The ACT and HITT groups did not differ with respect to baseline ACT values or heparin sensitivity. Total heparin and protamine doses, and AT3 levels did not differ between groups. Fibrin monomer production increased during and after CPB relative to baseline, but did not differ between groups. In the HITT group, using all time points, the ACT fell below the threshold value 45/122 times (37%) while the HITT fell below the threshold value 23/118 times (19%); $p<0.000001$. In the ACT group, using all time points, the ACT fell below the threshold value 39/99 times (39%) while the HITT fell below the threshold value 19/77 times (25%), $p=0.000004$.
DISCUSSION: HITT measures anti-thrombin effects of heparin at the final common pathway of coagulation and may be less likely to be sub-therapeutic than ACT, which measures a longer portion of coagulation cascade, including the intrinsic portion. Use of HITT led to similar total heparin and protamine doses, chest tube drainage, and markers of fibrin formation to ACT-treated patients. HITT was less frequently sub-therapeutic and may allow for fewer additional heparin doses in patients who seem heparin "resistant" by ACT.[3] HITT may therefore be a safe measure of heparin anticoagulation in patients pre-treated with heparin.
REFERENCES: 1. Anesth Analg 2001;92:66-71 2. Anesth Analg 2000;90: 813-818 3. Br J Anaesth 2001; 87: 844-7

HITT & ACT Values

	Dosing Method	Post-Heparin	CPB 1	CPB 2	CPB 3	CPB 4	CPB 5
HITT Group	HITT	253±63	202±65	227±54	223±67	223±78	206±59
	ACT	582±179	520±83	545±106	535±114	484±66	524±94
ACT Group	HITT	218±99	211±91	226±78	255±111	218±57	329±158
	ACT	592±139	514±109	578±147	546±130	494±163	530±220

S-34

THE EFFECT OF RETROGRADE AUTOLOGOUS PRIMING OF THE CARDIOPULMONARY BYPASS CIRCUIT ON TRANSFUSION OUTCOMES AFTER CARDIAC SURGICAL PROCEDURES

AUTHORS: **G. S. Murphy**[1], J. W. Szokol[1], M. Nitsun[1], D. A. Alspach[1], M. J. Avram[2], J. S. Vender[1];
AFFILIATION: [1]Evanston Northwestern Healthcare, Evanston, IL, [2]Northwestern University Feinberg School of Medicine, Chicago, IL.

INTRODUCTION: A primary determinant of transfusion requirements during cardiac surgery is the inevitable dilution of the red blood cell mass that occurs when the patient is placed on cardiopulmonary bypass (CPB). Retrograde autologous priming (RAP) of the CPB circuit is a recently described technique that involves the replacement of the crystalloid prime with the patients' own blood. After arterial and venous cannulas are placed, blood is allowed to drain by pressure gradients into the CPB circuit, displacing the prime into a collection bag. Data from previous small, prospective, carefully controlled studies suggests that RAP is effective in reducing the number of cardiac patients receiving packed red blood cells (PRBCs) (1-2). The aim of this investigation is to determine the impact of a RAP technique on perioperative transfusion requirements in a large, unselected population of adult patients presenting for cardiac surgery with CPB.
METHODS: The medical records of all patients who underwent cardiac surgical procedures by a single surgeon during the study period were reviewed retrospectively. Data was collected for a 24-month period (2000-2002) when RAP was routinely used on patients undergoing CPB at our institution (RAP group, n=257) and during a 24-month period immediately preceding the introduction of RAP into the clinical practice (no RAP group, n=288).
RESULTS: The two groups were comparable with respect to all demographic data. The groups were closely matched for established risk factors for PRBC transfusions (age, gender, weight, body surface area, emergency and reoperative procedures, CPB time, and initial hematocrit). Although baseline hematocrits were similar, hematocrits on CPB were significantly higher in the RAP group (26% vs. 22%, $P < 0.001$). Patients in the RAP group also received significantly more crystalloid pre- and post-CPB than patients in the no RAP group (3,000 cc vs. 2,700 cc, $P = 0.012$). Although a smaller percentage of patients were transfused PRBCs in the RAP group (44 % in RAP group vs. 51 % in no RAP group), this difference was not statistically significant ($P = 0.083$). The relative risk of requiring PRBCs was only minimally increased in the no RAP group (RR 1.18, 95% CI 0.98 – 1.42). The median total number of PRBC units administered was low in both groups and did not differ significantly (0 in RAP group vs. 0.5 in no RAP group, $P = 0.152$). Red blood cell use was similar in both groups during the intraoperative and postoperative periods. The transfusion of FFP and platelets was not significantly different between the two groups.
DISCUSSION: Retrograde autologous priming resulted in only minimal reductions in blood utilization in a large, unselected group of patients undergoing cardiac surgical procedures.
REFERENCES: 1. J Thorac Cardiovasc Surg 1998; 115: 426-39 2. Ann Thorac Surg 1998; 65: 724-30

S-35

FACTOR V LEIDEN IS ASSOCIATED WITH INCREASED NUMBER OF CORONARY GRAFTS IN A POPULATION OF CORONARY ARTERY BYPASS SURGERY PATIENTS

AUTHORS: **B. S. Donahue**, D. W. Byrne;
AFFILIATION: Vanderbilt University, Nashville, TN.

INTRODUCTION: Although factor V Leiden (FVL) is a risk factor for venous thrombosis [1], data regarding this variant as a risk factor for myocardial infarction and stroke are limited [2]. FVL has not been studied extensively in the coronary surgery population, however, where all patients by definition have coronary disease. Furthermore, thrombophilic mutations in this population may have important clinical consequences [3, 4]. We were interested in whether FVL was associated with more extensive coronary artery disease in this population, using number of bypassed vessels as an indicator for disease severity.
METHODS: Following IRB approval and informed consent, we retrospectively studied 435 adult coronary artery bypass (CAB) patients from the Vanderbilt Cardiac Surgery Registry. FVL status was measured using the technique of Ridker et al[5]. Univariate analysis comparing number of coronary grafts between the FVL subjects and noncarriers consisted of Mann-Whitney test and Student's t-statistic. To rule out confounding variables, stepwise linear regression was used, with the following independent variables: age, gender, ethnicity, diabetes, hypertension, hyperlipidemia, smoking history, current tobacco use, unstable angina, concurrent valve operation, concurrent other cardiac operations, repeat sternotomy, offpump CAB, and FVL.
RESULTS: FVL heterozygosity was identified in 18 patients. Mean number of bypass grafts was significantly different between noncarriers and FVL heterozygotes (3.1 vs 3.8, respectively; p=0.018 by *t*-test; p=0.023 by U-test). Histograms representing these populations are shown in the Figure. Linear regression revealed significant variables as listed in the Table. FVL was associated with an average of 0.7 more CAB grafts.

Table:Linear Regression Model for Number of CAB Grafts

Parameter	Coefficient	Std Error	P
Concurrent valve procedure	-0.880	.144	<0.001
Concurrent other cardiac procedure	-1.084	.253	<0.001
Offpump CAB	-0.982	.151	<0.001
Female gender	-0.394	.104	<0.001
Diabetes	.238	.103	0.021
Factor V Leiden	**.698**	**.238**	**0.004**
Y-intercept	.452	.074	<0.001

DISCUSSION: Number of vessels bypassed during a CAB operation is an important surgical parameter. Increased morbidity [6-8], diabetes [6, 9, 10], and loss of benefits of offpump surgery [8] are associated with increased CAB grafts. All our patients have coronary disease, so results may not be applicable to the general population, or to other groups of patients with vascular disease. Genetic association studies like these also do not imply causality. Validation by other institutions with larger populations will be essential for clarifying these issues [11]. In conclusion, we report an association between FVL and increased number of CAB grafts in a population of cardiac surgery patients, accounting for variables known to affect this parameter. This may have direct clinical relevance, since graft number is associated with morbidity, and genetic factors that determine extent of disease are not fully characterized.
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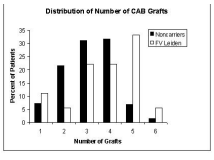

S-36

USE OF THE SECOND DERIVATIVE PHOTOPLETHYSMOGRAM TO ASSESS ATHEROCLEROSIS IN PATIENTS UNDERGOING CARDIOVASCULAR PROCEDURES

AUTHORS: **E. S. Fu**, A. B. Kumar, J. E. Scharf;
AFFILIATION: University of South Florida, Tampa, FL.

INTRODUCTION: Non-invasive pulse wave analysis is useful to evaluate the vascular effects of aging and risk factor associated with atherosclerosis(1). The photoplethysmogram (PPG) detects the changes in the light absorbed by hemoglobin, which in turn reflects the change in blood volume. As shown in the figure below, the second derivative photplethysmogram (SDPPG) consists of a, b, c and d waves in systole and an e wave in diastole. There is an early systolic component (PT1) and late systolic component (PT2) on the raw PPG corresponding to the b and d waves on the SDPPG, respectively. A deepened d wave reflects increased left ventricular afterload as seen with decreased arterial compliance and calculation of the d/a ratio has been used as an indicator of vascular abnormalities (1).
METHODS: Ten patients undergoing cardiovascular procedures were entered into the USF-IRB approved protocol for the mathematical analysis of the PPG. Transmission of the digital PPG was recorded from fingers two, three or four for a period of sixty seconds. The raw ppg was recorded using the Dolphin Medical Pulse Oximeter Software (Hawthorne, CA). Data was sampled at 275 hz and band-pass filtered to remove 60 and 120 hz interference. The d to a ratio was calculated for each subject. Data from patients in the cardiovascular group were then compared to data obtained from ten healthy volunteers.
RESULTS: Patients in the cardiovascular group underwent cardiovascular procedures which included cardiac catheterization, coronary bypass surgery, and aortic aneurysm surgery. Patients in the healthy volunteer group had no presence of cardiac risk factors including smoking, diabetes, and hypertension. The mean d/a ratio was more negative in the cardiovascular patients (-0.367 plus/minus 0.134) than in the healthy volunteers (-0.167 plus/minus 0.100, p=0.001).
DISCUSSION: We found a difference in the d to a ratio between the cardiovascular patients and the healthy volunteers. The second derivative PPG appears to be a useful non-invasive tool to determine the presence of atherosclerotic vessel disease in the perioperative period. Future studies are planned to utilize the second derivative PPG to preoperatively identify patients with clinically significant atherosclerosis independent of chronological age.
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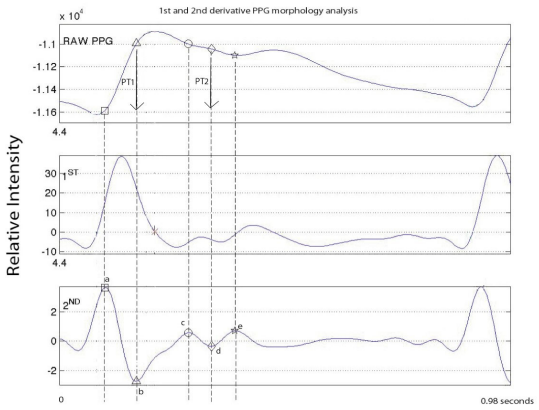

S-37

INFLUENCE OF ANESTHETIC INDUCTION WITH SEVOFLURANE VS. PROPOFOL ON LEFT VENTRICULAR (LV) DIASTOLIC FUNCTION IN PATIENTS WITH CORONARY ARTERY DISEASE (CAD)

AUTHORS: **S. P. Wirtz**, C. Schmidt, H. Van Aken, G. Düsediekerbäumer, C. Flottmann, E. Berendes;
AFFILIATION: Universitätsklinikum Münster, Departement of Anesthesiology and Intensive Care Medicine, Münster, Germany.

INTRODUCTION: Induction of general anesthesia in patients with CAD is often associated with decreases in blood pressure threatening myocardial oxygen balance. LV relaxation throughout early diastolic filling is the most susceptible part of the cardiac cycle to ischemic stimuli (1, 2). Color M-mode Doppler flow propagation velocity (Vp) has been proven to be a quantitative index of LV relaxation (3). Sevoflurane has preconditioning and hence cardioprotective properties (4). Therefore, Vp was measured to assess the impact of anaesthetic induction with sevoflurane vs. propofol on LV diastolic function in patients with CAD.
METHODS: 78 patients with significant CAD were enrolled in this prospective randomized controlled trial. General anesthesia for coronary artery surgery was induced by either sevoflurane or propofol. In addition, sufentanil and cis-atracurium were administered. Before and after induction, colour M-mode Doppler echocardiography was registered in the apical 4-chamber view with the cursor aligned parallel to LV-inflow. Registrations were videotaped for off-line analysis by a blinded investigator. Arterial pressure was measured using a radial artery catheter. Cardiac output (CO) was calculated using echocardiography. Data were analyzed using unpaired and paired t-tests.
RESULTS: Data of 35 patients (15 sevoflurane, 20 propofol) could be included for analysis. Mean age was 65.3 years (range: 45 – 49 years). Mean ejection fraction was 66.9% (range: 30 – 93%). Anesthetic induction resulted in a significant decrease in systolic (SAP), diastolic (DAP), mean (MAP) arterial pressure, and heart rate (HR). Stroke volume (SV) remained unchanged, but CO decreased after induction of anesthesia. Hemodynamic changes were not associated with impairment of LV diastolic function. There were no significant differences between variables in the sevoflurane and propofol group.

Table: Measurements before and after induction of anaesthesia (mean ± SD)

	Time Point	MAP [mmHG]	HR [/s]	SV [mL]	CO [l/min]	Vp [cm/s]
Sevoflurane	**Before**	102 ± 16	64 ± 12	80 ± 16	5.0 ± 1.0	50.3 ± 17.9
After		69 ± 12	52 ± 16	75 ± 12	3.9 ± 1.1	53.0 ± 20.5
p	before/after (paired t-test)	**0.000**	**0.015**	0.064	**0.008**	0.332
Propofol	**Before**	94 ± 20	60 ± 12	83 ± 25	5.0 ± 1.6	48.4 ± 13.1
After		66 ± 12	48 ± 8	80 ± 23	3.7 ± 1.0	48.2 ± 15.4
p	before/after (paired t-test)	**0.000**	**0.000**	0.302	**0.000**	0.910
p	Sevo/Prop after (unpaired t-test)	0.442	0.297	0.568	0.652	0.433

DISCUSSION: Anesthetic induction in patients with CAD — both with sevoflurane and propofol — is safe with respect to LV diastolic function despite a marked fall in cardiac output, blood pressure, and hence coronary perfusion pressure.
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S-38

EFFECT OF PERICARDIOTOMY ON LEFT VENTRICULAR DIASTOLIC FUNCTION IN CARDIAC SURGICAL PATIENTS: A TISSUE DOPPLER STUDY

AUTHORS: **N. Skubas**[1], N. Ryjikov[1], R. Slepian[1], L. Girardi[1], K. Krieger[1], I. Kronzon[2];
AFFILIATION: [1]Weill Medical College/Cornell University, New York, NY, [2]New York University School of Medicine, New York, NY.

INTRODUCTION: The echocardiographic assessment of left ventricular (LV) diastolic function in cardiac surgical patients is usually performed by pulsed-wave Doppler.(1) However, PWD data are preload dependent. Tissue Doppler imaging (TDI) of the mitral valve (MV) annulus allows measurement of LV diastolic properties directly from the myocardium. If the relaxation is impaired, TDI data are independent of preload.(2) TDI data may be influenced by translation and rotation of the heart inside the pericardial sac.(3) We examined the effect of pericardiotomy on the diastolic TDI-derived measurements.
METHODS: After approval of the Institution's Review Board, the LV diastolic properties were prospectively examined with PWD and TDI, before (pre) and after (post) incision and suspension of the pericardium, in 16 cardiac surgical patients in sinus rhythm, with intraoperative transesophageal echocardiography (TEE). Patients with MV or pericardial pathology were excluded. Early (E) and late (A) velocities and E deceleration time (EDT) at the MV tips, and systolic (S), diastolic (D) and reversed atrial (rA) velocities, 1-2 cm inside the left upper pulmonary vein were recorded with PWD. Myocardial early (Em) and atrial (Am) velocities of the septal, lateral, inferior and anterior LV walls were recorded at the MV annulus with TDI at the mid-esophageal 4-, and 2-chamber views. Invasive hemodynamic data were measured as well. Statistical analysis was performed using Student's paired t-test, with P<0.05 significant.
RESULTS: The hemodynamics (data not shown) did not change after pericardiotomy. TEE data (mean±SD) is shown in the table (velocities in cm/sec, EDT in msec).

	TDI				PWD		
	septal	*lateral*	*inferior*	*anterior*			
	Em				E	A	EDT
pre	6.4±1.8	8.9±2¶	8.8±2.9	7±2	49±15	47±13	187±36
post	6±2.2	8.6±2¶	7.9±2.6	5.6±1.4*#	53±15	51±15	195±49
	Am				S	D	rA
pre	8.6±3.4	11±3.8†	11±5.8	11.3±5	48±18	34±15	16±6
post	8.9±3.3	12±4.3†	10.3±3.6	9.6±4.7	39±13	27±9	13±4
	Em/Am				E/A		S/D
pre	0.8±0.3	0.9±0.4	0.9±0.4	0.7±0.4	1.1±0.4		1.6±0.4
post	0.7±0.2	0.8±0.3	0.8±0.4	0.6±0.2	1.1±0.5		1.4±0.4

*: P=0.0015 *vs* pre, ¶: P<0.003 *vs* septal, †: P<0.01 *vs* septal, #: P=0.018 *vs* inferior.
DISCUSSION: Pericardiotomy did not alter the LV diastolic function, classified as abnormal relaxation by TDI (Em/Am<1), and pseudonormal by PWD (E/A>1 and S/D>1). While the Am velocities remained uniform among the LV segments, probably the result of passive lengthening after atrial contraction,(4) we noticed a heterogeneity of Em, with higher velocities prominent in the lateral wall, that may reflect the geometrical arrangement of myocardial fibers. Since Em is associated with the elastic energy stored in systole and released during diastole(2), the significant decrease in anterior Em after pericardiotomy may implicate an active contribution of the intact pericardium on LV relaxation.
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S-39

ANESTHESIA-ASSOCIATED HYPOTENSION IN PATIENTS TREATED WITH ANGIOTENSIN-CONVERTING ENZYME INHIBITORS

AUTHORS: W. Hoffman, L. Brodsky, I. V. Balyasnikova, D. Mayer, **S. M. Danilov**;
AFFILIATION: University of Illinois at Chicago, Chicago, IL.

INTRODUCTION. Preoperative use of ACE inhibitors has been associated with severe hypotension that increases the incidence of vasoconstrictor therapy required to maintain systolic blood pressure. We hypothesize that inter-individual variability in anesthesia-induced hypotension in patients, chronically treated by ACE inhibitors might be predicted by the variability of the level of ACE expression and the degree of ACE inhibition in each individual.
METHODS. Clinical part: 10 patients (4 of which were treated with ACE inhibitors) who were admitted for cardiac surgeries with invasive hemodynamic monitoring were enrolled in the study. The blood pressure (BP) at the time of intubation and the lowest BP measured after induction or during the first 15 minutes of mechanical ventilation without surgical stress were considered for the data analysis. The following hemodynamic parameters were recorded: arterial blood pressure (systolic, diastolic and mean), cardiac output (with cardiac index calculation), mixed venous oxygen saturation (SvO2), pulmonary artery (PA) pressure (systolic, diastolic and mean), pulmonary capillary wedge pressure (PCWP) and systemic and pulmonary vascular resistance. Anesthesia: Premedication: Midazolam 25mcg/kg iv 15 min before induction; Radial art-line, PAC under local + a total of Fentanyl 1mcg/kg iv; Induction: Fentanyl 5mcg/kg; Etomidate 0.1mg/kg; Midazolam 50mcg/kg; Isoflurane 0.3 MAC, O2 in air 50%. Ephedrine was injected for any blood pressure decrease 20 % below a patient's preoperative base line. Biochemical part: ACE level was determined by ACE ELISA. The degree of ACE inhibition was assessed by measuring the ratio of the rates of hydrolysis of two different substrates (HHL and ZPHL) for somatic ACE (Danilov et al. 1996). The measurement of ACE activity with two substrates and calculation of their ratio (ZPHL/HHL) permits quantification of ACE inhibitors and the degree of ACE inhibition.
RESULTS. Hemodynamic response to anesthesia differed in the control group and in patients treated by ACE inhibitors. The changes in the heart rate, arterial systolic and PA diastolic pressure negatively correlated with ACE activity in the control group (r=-0.45, -0.71 and -0.33, respectively), but positively correlated with ACE activity in ACE inhibitor treated patients (r=+1.0, +0.1 and +0.40, respectively). The extent of the correlation of the changes of other hemodynamic parameters with ACE activity/level also shows substantial differences between control and ACEI-treated group.
DISCUSSION. Our results demonstrate that ACE phenotype (ACE level and the efficacy of ACE inhibition) is responsible for differences in hemodynamic responses to induction of anesthesia in patients chronically treated with ACE inhibitors.
Results from this study shows that the measurement of ACE activity and ACE level in patients (especially those under ACE inhibitor treatment) before surgery (and anesthesia) might be used to predict severe hypotension in response to general anesthesia and to provide patients with better treatment during surgery.

S-40

THE EFFECTS OF ANGIOTENSIN II TYPE I RECEPTOR A1166C POLYMORPHISM ON PATIENT HEMODYNAMICSDURING CARDIOPULMONARY BYPASS

AUTHORS: **S. Wang**, S. Zhang, S. Yao;
AFFILIATION: Deparment of Anesthesiology, Union Hospital, Tongji Medical Collage, Wuhan, China.

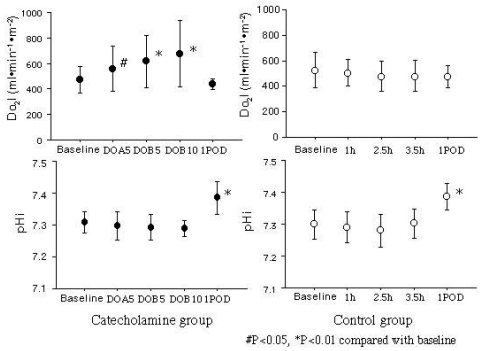
INTRODUCTION: The renin-angiotensin system (RAS) plays a decisive effect on blood pressure regulation in humans. Previous studies reported an association of the 1166 A/C polymorphism of the angiotensin II (Ang II) type 1 receptor gene with high blood pressure. We evaluated the effects of angiotensin II type I receptor (AT_1R) A1166C polymorphism on patient's hemodynamics during cardiopulmonary bypass (CPB).
METHODS: 82 patients scheduled for congenital heart disease correction or valve replacement under mid-hypothermic cardiopulmonary bypass were enrolled. 2 ml of blood sample was extracted from each patient. Gene type was identified by polymerase chain reaction and restriction fragments length polymorphism (PCR-RLFP) method. Patients were divided into mutation group and normal group according to whether there is an A→C replacement in 1166 position of the AT_1R gene code. Mean arterial pressure for each of the patient was recorded continuously at an interval of one minute in the stable period during CPB,which was defined as 20 minutes after the initiation of CPB. And the plasma level of angiotensin II were measured just pre-CPB and 40 minutes after CPB beginning. The relationship between the AT_1R polymorphism and the MAP variation was analyzed.
RESULTS: There are 7 heterozygote patients with AC gene type, 75 homozygote patients with AA gene type. The MAP was increased significantly in mutation group (n=7) than that of in normal group (n=75). They are 64.13±4.99 mmHg and 57.70±7.87 mmHg respectively. And phentolamine requirement were significantly increased in mutation group. Though plasma level of angiotensin II was increased significantly in all of the patients after CPB beginning when comparison with that of pre-cardiopulmonary bypass, but there were no statistical difference between the two groups both on pre-cardiopulmonary bypass or intra-cardiopulmonary bypass. So we conclude that AT_1R A1166C polymorphism results in a dramatically increase in MAP during CPB.
DISCUSSION: During the stable period of CPB, the difference of the MAP between the two groups can be attributed to the gene polymorphism. Increased MAP in mutation group implied the more drastic vascular contraction, which may result in abnormal in tissue perfusion, SIRS or MODS. Consequently it maybe related with some of the CPB complications.

S-41

DOPAMINE AND DOBUTAMINE DID NOT IMPROVE A LOW GASTRIC INTRAMUCOSAL PH FOLLOWING CARDIOPULMONARY BYPASS

AUTHORS: **S. Ito**[1], H. Ito[1], M. Yumoto[1], H. Sasano[1], S. Ito[2], H. Katsuya[1];
AFFILIATION: [1]Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan, [2]Okazaki City Hospital, Okazaki, Japan.

INTRODUCTION: The ischemic injury of gastrointestinal mucosa is believed to cause increased intestinal mucosal permeability, which may result in bacterial translocation and gut-derived endotoxemia and ultimately in multiple organ failure. The gastrointestinal mucosal ischemia can be detected as a decreased gastric intramucosal pH (pHi). The decrease in pHi often occurs after cardiac surgery with CPB. The early correction of low pHi may be useful to prevent bacterial translocation. The effects of additional administration of dopamine and dobutamine on hemodynamics, oxygen metabolism and pHi were examined in the patients following cardiopulmonary bypass.
METHODS: Eighteen patients admitted to our ICU after cardiac surgery with CPB who had low pHi (<7.35) without low cardiac output during infusion of approximately 5 mcg/kg/min of dopamine were enrolled into the study. Five mcg/kg/min of dopamine (DOA5 point) and 5 mcg/kg/min (DOB5 point) and 10 mcg/kg/min (DOB10 point) of dobutamine were additionally administered sequentially to ten patients (catecholamine group). The other 8 patients served as the control (control group). The hemodynamic parameters and pHi and lactate were measured and the parameters in oxygen metabolism were calculated at baseline, at DOA5, DOB5, DOB10 point and on the first postoperative day (1POD) in the catecholamine group. The measurements in the control group were performed at the same time points as in the catecholamine group, at 1 hour, 2.5 hours, and 3.5 hours after the measurement at baseline, and on 1 POD.
RESULTS: There were no significant differences in the parameters measured and calculated at baseline between the catecholamine group and control group. In the catecholamine group, the addition of 5 mcg/kg/min of dopamine or 5 or 10 mcg/kg/min of dobutamine did not increase the VO2I or improved either pHi or lactate although the cardiac index (CI) and global oxygen delivery index (DO2I) increased significantly. The pHi and lactate improved significantly on 1 POD. In the control group, the CI and DO2 and VO2 did not change significantly. Neither the pHi nor lactate changed in the short-term. The pHi and lactate improved significantly in 1 POD such as in the catecholamine group. None of the patients suffered major complications or adverse effects of cateholamines.
DISCUSSION: A decrease in pHi after cardiac surgery using CPB often occurs despite stable systemic hemodynamics. Hypoperfusion and hypothermia during CPB may alter vasoregulation, resulting in the disturbance of the microcirculation in these patients. Increased oxygen delivery by the additional administration of dopamine or dobutamine did not improve the elevated lactate and lowered pHi seen immediately after CPB. The recovery of oxygen utilization at the microcirculation and/or tissue level, which is impaired during CPB, may require at least several to 24 hours.



S-42

PERIOPERATIVE AND LONG-TERM MORTALITY OF DIABETIC AND NONDIABETIC PATIENTS UNDERGOING MAJOR LOWER EXTREMITY AMPUTATIONS

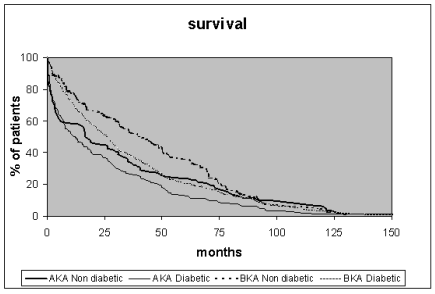
AUTHORS: **B. Subramaniam**, K. W. Park;
AFFILIATION: Beth Israel Deaconess Medical Center, Boston, MA.

INTRODUCTION: Although diabetes mellitus (DM) is listed as an intermediate clinical predictor of cardiac risk by the American Heart Association guidelines (1), it remains controversial whether DM actually increases perioperative cardiac complications in vascular patients (2-4). In this study, we examined whether DM is associated with increased perioperative and long-term mortality in patients undergoing above-knee and below-knee amputations (AKA, BKA).
METHODS: Our quality assurance database was reviewed to identify patients who underwent BKA or AKA from 1990 to 2000. Demographic variables, preoperative comorbidities, and perioperative 30-day mortality were noted from the database. Data on long-term survival of the patients was obtained from the Social Security database available at www.ancestry.com. Proportions were compared by Fisher's exact test and continous variables by t test. Long-term survival was analyzed by Kaplan-Meier analysis. $P < 0.05$ was considered significant.
RESULTS: There were 984 major amputations, 784 BKA and 236 AKA, in 762 patients. Demographics and comorbidities of diabetic and nondiabetic patients are shown in table 1. Diabetics were younger, but had a higher incidence of history of renal insufficienty and CHF, but were otherwise comparable to nondiabetics. There was no difference in 30-day mortality between diabetics and nondiabetics, but AKA carried significantly higher mortality than BKA (21.7 % v. 7.0 %, $P < 0.05$). However, diabetics had a significantly poorer long-term survival either after BKA or AKA (figure 1).

Table 1. (*: $P < 0.05$ vs. diabetics).

	Diabetics	Nondiabetics
Age	65.6 ± 13.6	71.0 ± 14.2 *
Male: Female	278:341	48:195
Hx renal insufficienty	41.6 %	17.5 % *
Hx CHF	31.8 %	24.8 % *
Hx MI	37.9 %	30.8 %
Smoking	57.8 %	66.4 %
Hypertension	66.5 %	56.6 %
BKA (%) / AKA (%)	74.5 % / 25.5 %	78.3 % / 21.7 %

Figure 1. Long-term survival after BKA or AKA



DISCUSSION: Both BKA and AKA are high-risk surgeries with > 5 % perioeprative mortality and triages as such when following the AHA guidelines. Whereas the presence of DM is not associated with an increase in perioperative mortality after BKA or AKA, DM is associated with a poorer long-term survical of amputees. Strategies to improve survival in these patients may include better control of diabetes and beta-adrenergic blockade, but remain to be studied.
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Critical Care and Trauma

S-43

INTRAVENOUS DEXMEDETOMIDINE CAN REPLACE EPIDURAL FENTANYL AS A SUPPLEMENT TO LOW-DOSE EPIDURAL BUPIVACAINE FOR POSTTHORACOTOMY PAIN CONTROL

AUTHORS: **S. Wahlander**, G. Wagener, H. Playford, B. Saldana-Ferretti, R. Sladen;
AFFILIATION: College of Physicians & Surgeons of Columbia University, New York, NY.

INTRODUCTION: Thoracic epidural (ED) analgesia with combined infusions of fentanyl and bupivacaine provides excellent analgesia after thoracic surgery but has inherent limitations including sympathetic block and hypotension, respiratory depression and inadequate analgesia. Dexmedetomidine (Dex) is a selective alpha-2 agonist that provides anxiolysis and anlagesia without respiratory depression. We tested the hypothesis that supplemental intravenous (IV) Dex could provide consistent analgesia when added to low-dose thoracic ED bupivacaine alone.
METHODS: After IRB approval and written informed consent, 28 patients undergoing thoracotomy had thoracic ED catheters placed and tested prior to induction of anesthesia. All patients had their trachea extubated at the end of the case. Adequate postoperative analgesia was defined as a visual analog score (VAS) of <= 3. Patients had their ED loaded with bupivacaine 0.125% postoperatively to establish a VAS <= 3, and were started on a continuous infusion at 4 mL/hr. Patients were randomized to receive supplemental IV Dex infusion at 0.4-0.7 mcg/kg/hr (ED-Dex, n = 14) or saline at the same infusion rate (ED-Placebo, n = 14). For both groups, a "rescue" algorithm to achieve VAS <= 3 was provided by patient controlled epidural analgesia (PCEA) with boluses of 3 mL bupivacaine 0.125%, followed by physician administered ED fentanyl (50 mcg boluses or addition of 2 mcg/mL to the ED infusion) if PCEA was inadequate. Blood pressure (BP), peripheral oxygen saturation (SpO2) and nasal cannula end tidal CO2 were monitored continuously in all patients for 24 hrs after admission from the OR.
RESULTS: Values are expressed as means ±SD. Satisfactory analgesia was achieved in both groups (VAS ED-Dex: 2.31, ED-Placebo: 3.22), which had an equivalent requirement for PCEA bupivacaine (37.8 ± 36.2 vs. 37.4 ± 19.2 mL). However the ED-Dex group required significantly less supplemental ED fentanyl (5.3 ± 17.1 vs 66.1 ± 95.6 mcg, p = 0.039). There were no statistically significant differences in BP, SpO2 or EtCO2 between the two groups. There were no complications related to the study.
DISCUSSION: This study demonstrates that IV Dex is an effective adjunct to low-dose ED bupivacaine in providing adequate analgesia after thoracotomy. It markedly decreases the need for ED opioids without adversely affecting BP. The large SD in the fentanyl requirements is explained by the fact that only one patient in the ED-Dex group needed a significant dose and that eight patients in the ED-Placebo group did not require any fentanyl. This confirms our clinical experience that IV Dex is a valuable "rescue" agent in patients with inadequate ED analgesia. Its use can potentially avoid the sympathetic block and respiratory depression that may occur when ED doses are pushed to higher levels, especially in thoracotomy patients that are "run dry" and often have significant COPD.

S-44

WHEN IS A POSTOPERATIVE TROPONIN POSITIVE FOR AN MI?

AUTHORS: **M. K. Urban**, K. Jules-Elysee, C. Loughlin, W. Kelsey;
AFFILIATION: Hospital for Special Surgery, New York, NY.

INTRODUCTION Perioperative myocardial infarctions (PMI) are difficult to diagnose because perioperative ischemic episodes are often clinically "silent" and objective signs (MB-CPK) do not always provide definitive evidence. The diagnose of a PMI is important, however, since these events are associated with significant complications. Recently, Troponin I elevations have been shown to be a more specific marker for myocardial damage, with levels >0.4ng/ml considered predictive of an acute MI. However, significant levels have not been established for surgical patients.
METHODS At HSS, an orthopedic hospital, during a 12 month period, 725 of 7400 surgical patients were evaluated for a PMI due to acute cardiac symptoms, unstable hemodynamics and/or a history of ischemic heart disease. The PMI protocol consisted of at least two serum Troponin levels drawn every 12 hours or until <0.4 ng/ml, daily 12 lead ECGs, and an echocardiogram (ECHO) on postoperative day 3 to 5 in all patients with Troponin levels>0.4ng/ml. Cardiac symptoms were defined as those indicative of CHF or anginal equivalents.
RESULTS 43 of the 725 patients entered into the PMI protocol had Troponin levels >0.4ng/ml. Seven of these patients (7/45; 16%) had new regional wall motion abnormalities (RWMA) by ECHO and a mean peak Troponin level of 25.7 compared to a mean peak level of 3.4 for the remaining 38 patients. All of the patients with RWMA except one had peak Troponin levels >10ng/ml, this patient had a peak Troponin level of 4.9 after sucessful resuscitation from an intraoperative cardiac arrest with ECG changes which resolved within 24 hours. Of the 38 patients without RWMA, only one had a peak Troponin>10ng/ml, this patient had new ECG lateral T-inversions which resolved within 24 hours.18 patients (18/43) entered into the PMI protocol without RWMA or ECG changes had a mean peak Troponin level of 2.8.
DISCUSSION Using the cardiologist biochemical definition of an acute cardiac event, only ~6% of the patients entered into the PMI protocol had Treponin levels >0.4ng/ml. Only 7 of these patients had RWMA and ECG changes indicative of a PMI, and all but one of them had Troponin levels>10ng/ml. Patients with Troponin levels>0.4 but without RWMA and ECG changes had peak Troponin levels of 2.8. Troponin levels of 0.4ng/ml are probably too low to be indicative of a PMI. In a different surgical population, Adams et.al. reported that postoperative MIs by new RWMA occurred in patients with Troponin levels >3ng/ml. For our orthopedic patients only Troponin levels>3 ng/ml should require further evaluation for myocardial damage.
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S-45

FRUCTOSE-1,6-DIPHOSPHATE ATTENUATES THE DETERIORATION OF PULMONARY FUNCTION IN CANINE OLEIC ACID LUNG INJURY

AUTHORS: Z. Huang[1], Z. Xia[2];
AFFILIATION: [1]Sun Yat-sen Cardiovascular Hospital, Shenzhen, China, [2]Dept . of Anesthesiology, Renmin Hospital, Wuhan University, Wuhan, China.

INTRODUCTION: Mechanical ventilation in patients with acute respiratory distress syndrome remains a challenge because of the conflict between securing adequate gas exchange and furthering lung injury via overdistention. Fructose-1,6-diphosphate (FDP) has been found to prevent tissue injury in a variety of organs including the lung (1). We determined whether FDP could attenuate acute lung injury. Also, we determined whether the mechanism of FDP protection involves the reduction of oxygen free radicals-mediated lipid peroxidation, using malondialdehyde (MDA) as a measure.
METHODS: Sixteen mongrel dogs were anesthetized in the supine position, paralyzed, and mechanically ventilated with 50% oxygen at 15 beats/min with V_T adjusted to achieve a baseline (T_0) end-tidal CO_2 between 35 to 40 mmHg. Acute lung injury was produced by infusion of 0.06 ml/kg oleic acid (OA) solution into the right atrium over a period of 30 min as described (2). Thirty min after the completion of OA injection (T_{30}), animals were randomly assigned into OA group (n=8) or OA plus FDP group (OA-FDP group, n=8). Animals in OA-FDP group received intravenous FDP infusion at 75 mg/kg over a period of 1 min starting at T_{30}, followed by continuous FDP at 5mg/kg/min for 60 min. Animals in the OA group received no drug treatment other than continued ventilation at baseline settings. Arterial blood was sampled at T_0, T_{30}, T_{120} and T_{240} (240 min after OA injection) for the measurement of plasma MDA content as well as the O_2 (PaO_2) and CO_2 ($PaCO_2$) partial pressures.
RESULTS: Baseline parameters did not differ between groups. Both groups received comparable degrees of lung injury. At T30, the PaO2 was significantly (P<0.05) lower and the pulmonary vascular resistance index (PVRI) and intrapulmonary shunt (Qs/Qt) were significantly higher than the corresponding baseline values (135± 30 mmHg, 279± 32 dyn.s-1.cm-5.m2, and 21± 3%, respectively, at T30 versus 218± 22 mmHg, 211± 23 dyn.s-1.cm-5.m2, and 5.5± 0.8% at T0 in OA group; 135± 23 mmHg, 274± 27 dyn.s-1.cm-5.m2, and 21± 3%, respectively, at T30 versus 210± 23 mmHg, 217± 22 dyn.s-1.cm-5.m2, and 5.0± 0.9% at T0 in OA-FDP group). A progressive decrease in PaO2 and increase in PVRI and Qs/Qt were observed in OA group, accompanied by a significant increase in plasma MDA. FDP prevented the significant increase in plasma MDA and attenuated pulmonary dysfunction. At T240, PaO2 in OA-FDP group (165± 23 mmHg) was significantly higher (P<0.01) than that in OA group (105± 15 mmHg), while PVRI, Qs/Qt as well as plasma MDA were lower than those in OA group.
CONCLUSION: Fructose-1,6-diphosphate attenuates pulmonary dysfunction after acute lung injury, which might be attributable to its ability in reducing lipid peroxidation.
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S-46

CARBOXYHEMOGLOBIN FORMATION FOLLOWING SMOKE INHALATION INJURY IN SHEEP INCREASES PULMONARY SHUNT FRACTION

AUTHORS: M. Westphal, P. Enkhbaatar, N. Morita, K. Murakami, L. D. Traber, D. L. Traber;
AFFILIATION: University of Texas Medical Branch, Galveston, TX.

INTRODUCTION: Carboxyhemoglobin (COHb) formation is triggered by the inducible isoform of heme oxygenase (HO-1) catalyzing carbon monoxide (CO) production through breakdown of heme molecules, exposure to CO or even both. In the setting of CO poisoning, COHb is regarded as a reliable marker characterizing both severity of injury and efficacy of treatment strategies (1). The potential problem, however, is that the degree of tissue oxygenation itself may impact on COHb formation (2). The present study was designed as a prospective, laboratory experiment to determine whether the previously described arteriovenous COHb difference in endotoxemia (2) is also existent in the setting of smoke inhalation injury, and to elucidate potential interdependencies between COHb generation, oxyhemoglobin saturation and pulmonary shunt fraction (Qs/Qt).
METHODS: Chronically instrumented ewes (n = 15) were repeatedly subjected to cotton smoke (4 x 12 breaths, < 40 degree C) according to an established technique (3). Before and after each set of smoke inhalation, samples of arterial and matched mixed venous blood were withdrawn and immediately analyzed at the measured body temperature for oxygen and carbon dioxide tensions, oxyhemoglobin saturation and COHb concentrations. At the same time points Qs/Qt, an index of pulmonary ventilation/perfusion mismatch, was determined using standard equation (3). Statistical analysis was performed using either one-way analysis of variance for repeated measurements with appropriate Student-Newman Keuls post hoc comparisons, or linear regression. Data are presented as mean ± SEM and Pearson correlation coefficient, respectively. Significance was set at $P < 0.05$.
RESULTS: Cotton smoke exposure resulted in a progressive increase in arterial and mixed venous COHb concentrations (up to a maximum of 80.5 ± 3.3 and 74 ± 3.7, respectively) that were interrelated with the degree of Qs/Qt ($P < 0.001$), and inversely correlated with both arterial and mixed venous oxyhemoglobin saturation ($r = -0.96$ and -0.93). Although the arteriovenous COHb gradient successively decreased with each set of cotton smoke inhalation, COHb determined in venous blood was lower than in arterial. Similarly, the arteriovenous oxyhemoglobin saturation difference successively decreased over time (34.5% at baseline vs. 9% after the fourth cotton smoke challenge; $P < 0.001$)
DISCUSSION: These findings suggest that tissue dysoxia resulting from CO inhalation is due to an increase in Qs/Qt. In addition, COHb determined in venous blood underestimates arterial COHb content. In the setting of CO inhalation/poisoning, misjudging venous COHb levels could be problematic.
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S-47

COMPARISON OF PREDICTIVE VALUE OF FOUR SCORING SYSTEMS (APACHE II, SOFA, MODS, LODS) FOR OUTCOME IN ICU PATIENTS

AUTHORS: **A. Agarwal**;
AFFILIATION: SGPGIMS, Lucknow, India.

INTRODUCTION: Critical care services consume nearly 20% of health care expenditure. Patients requiring ICU care is increasing and resources are limited. Prediction scoring systems by predicting outcome of patients in early course of disease; helps in directing our limited resources to more patients who would be benefited the most.
AIMS AND OBJECTIVES: To compare four scoring systems in terms of best predictor of outcome; cost effectiveness and predictability of various physiological parameters used individually.o:p>
MATERIALS AND METHODS: 103 consecutive patients admitted to ICU for > 48 hours were included in study. Patients ≤ 16 years and postoperative patients were excluded. Scores were calculated for each scoring system at the time of admission in ICU (Day 1) and 24 hrs later (Day 2). Correct predictive value and cost of each scoring system was calculated. Binary logistic regression analysis was performed to compare the four scoring systems. Survival analysis was done with Kaplan Meier test. Two proportion analysis was done to compare the correct predictive values of scoring systems. P value of ≤ 0.05 was considered as significant.
RESULTS: Correct predictive value of APPACHE II, SOFA, LODS and MODS were 94.2%, 88.3%, 84.5% & 83.3% and cost of scoring (for both days) were INR 520, 630, 790 and 940 respectively.
CONCLUSIONS: APACHE II is the least expensive and has highest correct predictive value. Scoring done on day 2 has a better prediction as compared to day 1. Combined scoring for day 1 and 2 has the best prediction in all the scores. GCS and serum creatinine have significant impact on outcome prediction.
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Table: Correct predictive value of the scoring systems. Two proportion analysis was performed to compare the correct predictive values of all the four scoring systems. * denotes p value <0.05.

Scoring system o:p>	Correct predictive value (%) o:p>		
	Survival o:p>		Expiry o:p>
	For each day	Both days together	Both days together
	o:p>	*o:p>*	*o:p>*
APACHE II(day1)	76.5o:p>	**94.1o:p>**	80.8o:p>
PACHE II (day2)	92.2o:p>		89.3o:p>
ODS (day1)	74.5o:p>	86.3o:p>	67.3o:p>
ODS (day2)	86.3o:p>		80.6o:p>
ODS (day1)	74.5o:p>	88.2o:p>	63.5o:p>
ODS (day2)	80.4o:p>		77.7o:p>
OFA (day1)	74.5o:p>	90.2o:p>	71.2o:p>
OFA (day2)	84.3o:p>		81.6o:p>

S-48

PREDICTING OUTCOMES IN CRITICALLY ILL OCTOGENARIANS

AUTHORS: **K. Johnson**[1], P. G. Boysen[1], A. E. Laubach[2];
AFFILIATION: [1]The University of North Carolina at Chapel Hill, Department of Anesthesiology, Chapel Hill, NC, [2]The University of North Carolina at Chapel Hill, School of Medicine, Chapel Hill, NC.

INTRODUCTION: The number of citizens over the age of 85 is expected to triple by 2030[1], consuming healthcare resources out-of-proportion to the general population [2].These individuals are also more likely to have executed advance directives, and to have thoughtfully considered whether to forego certain types of care, depending on their outcome and the likelihood of returning to a functional status. This study was designed to assess the possibility and reliability of predicting outcomes in the superelderly ICU population[3].
METHODS: After IRB consent, octogenarians admitted to the ICU were enrolled prospectively. Demographic and medical information were obtained via interview, laboratory analysis, and/or chart review. Variables considered include age, gender, baseline support level, domicile (home, SNF) prior to admission, HR at ICU admission, type of ICU, medical history, ICU interventions, and organ system failure. The data were used in a formula of logistic regression to make predictions regarding potential outcomes.
RESULTS: Preliminary evaluation of 66 octogenarians consecutively admitted to the ICU setting over a 2-month period was made. Thirty were female (45.5%), average age was 83.8 ± 3.7, and average HR at admission was 80.4±17.5. Exactly 50% of these patients performed independent ADLs prior to admission. Forty-six patients (70%) were admitted to medical ICUs, while 20 patients (30%) were admitted to surgical ICUs. Fifty-one (77.3%) required no invasive interventions, such as PAC, mechanical ventilation, or vasopressor use, and only 18 (27%) had organ system failure. Thirty-five patients (53.0%) were discharged home, 22 (33.3%) were discharged to a skilled nursing facility, and 9 (13.6%) died. The logistic regression formula accurately predicted the actual outcome in 43 out of 66 patients (65%). Further analysis of these 43 patients showed variability in the predictive quality of the model based on the outcome variable. For example, 35 of the 66 patients were discharged home and the model accurately predicted this outcome in 34 of the 35 patients (97.1%). However, 22 of the 66 patients were discharged to a SNF and the model only accurately predicted this outcome in 4 of the 22 patients (18%). Of the 9 patients who died, the model accurately predicted this outcome in 5 patients (55.6%).
DISCUSSION: Analysis of our data indicate that a mathematical model will predict the likelihood of discharge to home following ICU admission. The power of the study is limited as regards patients who die or are discharged to a SNF. Increasing our database may further refine our ability to advise these patients as to potential outcome, assist patients and families in decision-making, provide realistic goals for medical interventions, and improve resource utilization.
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S-49

QUANTIFICATION AND CONFIRMATION OF TWO HEMOGLOBIN-BASED OXYGEN CARRIERS (HEMOPURE® AND HEMOLINK™) IN HUMAN AND EQUINE PLASMA BY LC-MS/MS

AUTHORS: F. Guan[1], C. Uboh[2], L. Soma[1], Y. Luo[1], J. S. Jahr[3], **B. Driessen**[1];
AFFILIATION: [1]University of Pennsylvania, School of Veterinary Medicine, Kennett Square, PA, [2]PA Equine Toxicology & Research Laboratory, Department of Chemistry, West Chester University, West Chester, PA, [3]University of California, School of Medicine, Department of Anesthesiology, Los Angeles, CA.

INTRODUCTION: Hemoglobin glutamer-250 (Hemopure®), an ultrapure solution of glutaraldehyde-polymerized bovine hemoglobin, and Hemoglobin raffimer (Hemolink™), a solution of human hemoglobin cross-linked and polymerized with o-raffinose, have been developed as temporary blood substitutes currently under clinical investigation (Phase III), and Hemopure® has recently been approved for use in humans in South Africa. However, the potential of these hemoglobin-based oxygen carriers (HBOC's) to increase O_2-carrying capacity of circulating blood and thus to improve tissue O_2 delivery makes them excellent candidates for abuse in human and equine athletes. Currently, there are no specifically developed detection methods for HBOC's available. Techniques used to quantify HBOC's include bedside hemometers (HemoCue®) or co-oximeters to measure Hb content. The purpose of our study was to develop a reliable technique for quantitative and qualitative determination of Hemopure® and Hemolink™ in human and equine plasma using liquid chromatography-mass spectrometry (LC-MS).
METHODS: Hemopure® and Hemolink™ solution was each added to control human or equine plasma and extracted by solid-phase extraction. The extract was dried at 80°C under a stream of air or nitrogen. The dried extract was dissolved in 0.5 mL of NH_4HCO_3 (50 mM, pH 7.8), and 0.025 mL of trypsin (0.4 mg/mL in H_2O) was added. The mixture was briefly mixed and incubated at 37°C for 3 h. An aliquot of 0.02 mL was injected into LC-MS for detection of tryptic peptides from digestion of HBOC's. The tryptic digestion was necessary to distinguish between equine, bovine and human Hb.
RESULTS: Digestion of Hemopure® by trypsin resulted in a peptide with the sequence of 'AVEHLDDLPGALSELSDLHAHK' that is related to the amino acid residues #69-90 in bovine Hb's alpha chain. This sequence is very specific for bovine Hb's alpha chain and could not be found in other proteins such as Hb of other species including the horse, as concluded from the Fasta search results against the current 'Swissprot' database. For Hemolink™, a tryptic peptide was found to be specific for human Hb's alpha chain and its sequence is 'VADALTNAVAHVDDMPNALSALSDLHAHK' that is related to the amino acid residues #63-91. The two peptides mentioned above were targeted for quantification and confirmation of Hemopure® and Hemolink™, respectively, by LC-MS/MS. The LC-MS method allowed detection of Hemopure® and Hemolink™ at concentration ranges of 0.25-5.00 mg/mL and 0.05-5.00 mg/mL, respectively, in human and equine plasma with external calibration. The limits of detection were 0.25 mg/mL (Hemopure®) and 0.05 mg/mL (Hemolink™), respectively.
DISCUSSION: The LC-MS method developed for quantitative and qualitative determination of Hemopure® and Hemolink™ was selective and specific. It can be used in studies determining pharmacokinetic profiles of the two HBOCs as well as in detection and confirmation of performance enhancers in samples from human and equine athletes.

S-50

TRANSFUSION PREDICTORS, PRACTICES, AND STUDY FOR TRAUMATIC ACETABULAR (AFX) AND SPINE FRACTURES (SFX)

AUTHORS: S. Sawant, **C. MacKenzie**, S. Decau, J. Kufera, A. Jones, J. Hess;
AFFILIATION: University of Maryland, Baltimore, MD.

INTRODUCTION: Orthopedic surgery for AFx and SFx causes major blood loss[1].We examined retrospective data on AFx and SFx surgery from the Shock Trauma Center (STC), Baltimore,to: identify predictors of red cell (PRBC) transfusion, evaluate appropriateness of PRBC use and determine a sample size for prospective randomized study of liberal versus restrictive transfusion strategy.
METHODS: After IRB approval, charts of all patients undergoing AFx repair or multilevel SFx stabilization in 2000 were reviewed. PRBC, cell saver and estimated blood loss (EBL) were checked with blood bank and intraoperative fluid records. Laboratory data were obtained from an electronic database. Appropriate transfusion was defined as occurring when hemoglobin (Hb)10-6 g/dl. The sample size calculation for prospective study of Hb 9-10 g/dl versus 6-7 g/dl assumed no PRBC transfusion occurred to determine Hb < 10g/dl for liberal and < 7g/dl for restrictive strategies. Statistics used chi-squared and t-tests, ANOVA, bivariate correlation and linear regression.
RESULTS: 125 patients underwent 131 surgical procedures (6 had multiples). Thoracic SFx (15/30) and complex AFx (32/58) had greatest ($P < 0.02$) transfusion incidences. EBL was greater ($P < .001$) in complex than simple AFx. Among 125 patients 60 received intraoperative PRBC, 34 cell saver, and 90 received PRBC during hospitalization. No patients were under transfused but 10/60 were over transfused. Pre-operative Hb < 10 g/dl correlated (r=0.62) with EBL.
DISCUSSION: The 74% incidence of transfusion among these two orthopedic procedures suggests they would be a good model for prospective multicenter study. Complexity of AFx and type of surgery and pre-operative Hb predicted need for PRBC. Eight trauma centers with same recruitment capabilities as STC could enter the 850 patients necessary within 2 years, to detect a 5% difference in transfusion strategy with 96% power.
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S-51

INFLUENCE OF HETASTARCH ON INSULIN SENSITIVITY DURING HEMORRHAGIC SHOCK IN RABBITS

AUTHORS: **Y. Shang**, S. L. Yao, S. Y. Yuan;
AFFILIATION: Department of Anesthesiology, Xiehe Hospital, Wuhan, China.

INTRODUCTION: Stress (shock, infection, trauma, etc.) may induce decline of insulin sensitivity [1]. Insulin sensitivity index (ISI) is used to evaluate the insulin sensitivity recently. Hetastarch (HES) has proved to be many advantages including attenuation of the excess stress [2]. However, whether the HES has any effect on the insulin sensitivity remains unclear. We hypothesized that HES ameliorates the insulin sensitivity through attenuation of the stress hormones secreted during hemorrhagic shock.
METHODS: Hemorrhagic shock was induced by withdrawal of blood until mean arterial pressure was maintained at 45mmHg. 45 mins later, rabbits were randomized into two groups: group H (n=7) resuscitated with 6% HES and group L (n=7) resuscitated with LR (Lactate Ringer's solution). HES or LR (6ml•kg^{-1}) was infused respectively in 5 mins. LR (6ml •Kg^{-1}• h^{-1}) was given subsequently to maintain the basic fluid requirement. Blood samples were achieved to measure plasma epinephrine, norepinephrine, cortisol, glucagons, insulin, and blood glucose at baseline, 30 min shock, and 30 min, 60 min, 120 min after resuscitation. Epinephrine and norepinephrine were measured by fluorescence spectrophotometry. Cortisol, glucagons and insulin were measured by radioimmunoassay. ISI (1 / [Insulin (μIU / ml) x Glucose (mmol / L)]) was calculated.
RESULTS: The concentrations of epinephrine, norepinephrine and glucagons in group H decreased significantly after resuscitation, which were lower in group H than those in group L 120 min after resuscitation (P<0.01). The level of cortisol in circulation did not change significantly after resuscitation in group H, but it was higher than that in group L 120 min after resuscitation (P<0.05). The concentration of insulin in group H rised after resuscitation. Blood glucose concentration was suppressed after it reached climax 30 min after resuscitation in group H, which was lower 60 min after resuscitation in group H than that in group L (P<0.05). Epinephrine correlated with ISI (r=-0.437, P<0.01) and norepinephrine correlated with ISI (r=-0.575, P<0.01). ISI declined to minimum 30 min after resuscitation in group H. It improved gradually and was higher than that in group L after 120 min resuscitation from then on (P<0.05).
DISCUSSION: Stress hormones result in insulin resistance during hemorrhagic shock. The decline tendency of insulin sensitivity is inhibited by HES resuscitation. Amelioration of insulin sensitivity benefits from the decrease of hormone concentration in circulation lessened by HES.
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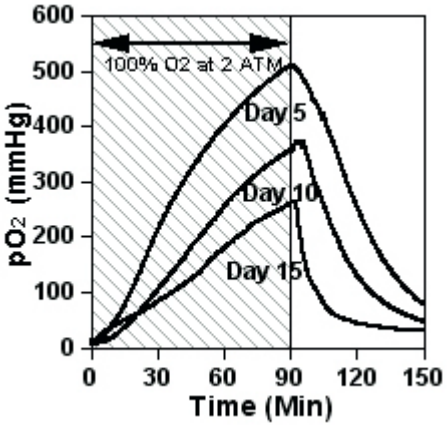
S-52

WOUND OXYGEN LEVELS DURING HYPERBARIC OXYGEN TREATMENT IN A RAT MODEL

AUTHORS: **M. D. Rollins**, T. K. Hunt, H. W. Hopf;
AFFILIATION: University of California, San Francisco, San Francisco, CA.

INTRODUCTION: Hyperbaric oxygen (HBO) is thought to improve wound healing by increasing oxygen delivery. There are however, few data quantifying the effect of HBO on wound oxygen levels. These are required to better understand the effects and mechanisms of HBO therapy. We therefore characterized the changes in wound pO_2 during and after HBO treatment.
METHODS: A mesh cylinder wound model was implanted subcutaneously in 18 Sprague-Dawley rats (Day 0). The HBO treatment group (n=10) received 100% O_2 at 2.0 atmospheres, 90 minutes BID for 15 days. Control rats (n=8) only received exposure to HBO during measurement. On days 5, 10, and 15, the wound pO_2 was measured with a polarographic electrode before, during, and for more than an hour after an HBO treatment. An ANOVA with Scheffe's post hoc test was used for within group comparison and a t-test used to compare between groups.
RESULTS: The average wound pO_2 values of the treatment group are shown in the figure. Both the peak pO_2 and the pO_2 1 hour after HBO treatment were significantly greater than baseline on all days in both the treatment ($p < .01$) and control group ($p < .05$). The peak pO_2 attained during HBO exposure and one hour after decreased significantly in the treatment group on day 15 compared to day 5 ($p < .01$, $p < .05$ respectively). No significant differences were found in pO_2 values within the control group across the three days measured. Analysis between groups demonstrated the treatment group attained a significantly higher peak pO_2 on day 5 as compared to control ($p < .05$).
DISCUSSION: Oxygen tension in a rat dead space wound model increased markedly above baseline during HBO treatment on all days measured, and remained significantly elevated for more than an hour after treatment ended. The dead space wound model represents an extreme case of the increased intercapillary distance seen in wounds. The prolonged elevation of oxygen supports the effectiveness of HBO in oxygen delivery to hypoxic wounds. In the HBO treatment group the overall rise in pO_2 decreased over the 15 days. This illustrates changes in not only oxygen delivery, but also consumption, and may represent combined effects from angiogenesis and changes in capsular thickness, size of wound dead space, and total cellularity. These results demonstrate that the pO_2 within a wound during and after an HBO treatment changes as a wound heals, and suggest dynamic biological interactions affecting the degree of wound pO_2 increase during and after HBO treatment. Future studies are needed to ascertain the specific changes occurring in the wound during a course of HBO treatment.
REFERENCES: Supported by NIH GM 27345 and The Whitaker Foundation



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COLLOID INFUSION AND BLOOD TRANSFUSION FOLLOWING SUBARACHNOID HEMORRHAGE

AUTHORS: **V. Sabharwal**, A. Deogaonkar, A. Camel, P. Rasmussen, M. Mayberg, M. DeGeorgia;
AFFILIATION: Cleveland Clinic Foundation, Cleveland, OH.

INTRODUCTION: To optimize cerebral blood flow and prevent ischemia, patients with vasospasm after subarachnoid hemorrhage (SAH) are often treated with colloids and blood transfusions. In critical care, controversy exists regarding colloid use(1) and thresholds for blood transfusion(2). We sought to determine the effect of colloid use and transfusion on blood pressure, intravascular volume, and outcome in patients with vasospasm after SAH.
METHODS: A retrospective analysis of 76 SAH patients admitted to the Neurological Intensive Care Unit between January 2000 and July 2002 was conducted recording demographic data, hemoglobin/hematocrit levels, number of packed red cell transfusions, treatment with colloids or crystalloids, average systolic, diastolic, and mean arterial pressures and fluid balances during vasospasm. Wilcoxon rank sum test, Fisher's Exact test and univariable logistic regression analysis were used for statistical analysis.
RESULTS: Of 76 patients, 42 (55.3%) developed vasospasm. Thirty-two (78%) received colloids. There was a trend towards a lower cumulative fluid balance (+ 1,622 ml) in the colloid group vs. crystalloid group (+ 2,114 ml)(P=0.75). There was a trend towards higher median systolic pressures in the colloid group (188.3 vs.162 mm Hg) but also greater pressor use in the (53.1% for a mean of 6.5 days vs. 44.4% for a mean of 5.2 days) (P=0.09). On admission the mean Hgb/Hct was 12.6±1.7/36.8±4.6.Twenty-three (54.8%) were transfused an average of 3.4±1.8 units of packed red cells. The average threshold triggering transfusion was a mean Hgb/Hct of 10.0±0.8/29.8±2.1. Patients who were transfused were 2.6 times more likely to have a poor outcome (P=0.15). Mean length of stay in transfused patients was 22.2 ±11.9 days versus 17.3 ±12.6 days in non-transfused patients.
DISCUSSION: There was a trend of worse outcome in transfused patients. Outcomes were the same in patients who received colloids versus crystalloids. Further studies are needed to determine the relative contributions and optimal targets of each component of triple H therapy.
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S-54

HLA-DR MONOCYTE EXPRESSION IN CANCER PATIENTS UNDERGOING SURGERY AFTER VACCINATION

AUTHORS: **C. Spies**;
AFFILIATION: Charite Medical Center, Humboldt-University, Berlin, Germany.

OBJECTIVE: The immune functions of cancer patients are thought to be impaired and their balance can be expected to shift from Th1 to Th2. In particular, an altered function of monocytes in patients with head and neck carcinoma was found, which might be associated with an increased postoperative infection rate indicating immediate postoperative immune suppression before the onset of infections. The aim of the study was to determine the HLA-DR monocyte expression after vaccination in patients with a tumor of the upper gastrointestinal tract undergoing surgery.
METHODS: In this ethically approved study, 21 patients with aerodigestive tract cancer were included. Patients were randomized to one of the following groups: The vaccine-group (n=11) and the placebo-group (n=10). Patients of the vaccine-group were vaccinated with Hemophilus influenza a/b (MUTAGRIP, MSD) two times (day 1 and day 3). Blood samples to assess the immune response to vaccination were taken at baseline (day 1) until day 5. Expression of HLA-DR on monocytes was analyzed by flow cytometry. Statistical analysis: ANOVA
RESULTS: Basic patient characteristics did not differ between groups. In the vaccine-group a significant increase of HLA-DR monocytze expression ($p< 0.02$) occurred after second vaccination with Hemophilus influenza compared to the placebo group. With respect to the safety of the vaccination neither an anaphylactic reaction nor infection, SIRS or SEPSIS after surgery occurrred.
CONCLUSIONS: Even if cancer patients have an altered immune function, patients undergoing surgery for the upper gastrointestinal tract might benefit from an adjuvant preoperative vaccination with Hemophilus influenza with respect to an increase in HLA-DR monocytes expression. This might be explained as a recovery of the patient`s immunological function.

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MELATONIN DOES NOT PREVENT POSTOPERATIVE CIRCADIAN RHYTHM DISRUPTION

AUTHORS: **A. J. Cronin**, M. Davies, N. DiVittore;
AFFILIATION: Hershey Medical Center, Hershey, PA.

INTRODUCTION: The purpose of this study is to determine if perioperative melatonin administration preserves postoperative circadian rhythm. Previous studies have demonstrated that sleep[1] and secretion of the nocturnal circadian hormone, melatonin,[2] are both inhibited in postoperative patients. Because administration of melatonin restores sleep by entraining the circadian rhythm in humans with some sleep disorders,[3] this study describes the effect of surgery on the circadian rhythm and the ability of melatonin therapy to prevent this derangement.
METHODS: After IRB approval and written informed consent, patients scheduled for vaginal hysterectomy were randomized to receive placebo or 3.0 mg melatonin at 9 P.M. beginning on the 5th preoperative night and ending on the 5th postoperative night. To monitor the circadian rhythm of activity, subjects wore a movement recorder from the 10th preoperative day until the 10th postoperative day. The circadian activity index (CAI) (total activity 6 A.M.-10 P.M./total activity 10 P.M.-6 A.M.) was calculated for each 24-hour period. To confirm delivery of melatonin and to monitor the circadian hormonal rhythm, urinary excretion of 6-sulfatoxymelatonin (6-SM), the chief metabolite of melatonin, was measured from 10 P.M. until 10 A.M. prior to the 5th preoperative night, on the 1st postoperative night, and on the 10th postoperative night. Comparison between the melatonin and placebo groups of the CAI on the first 3 postoperative days was made using t-tests, and repeated measures ANOVA with post hoc Dunnetts' test was used to compare the preoperative CAI to the CAI on the first 10 days following surgery.
RESULTS: Urinary excretion of 6-SM decreased ($p \leq 0.05$) from preoperative levels on the first postoperative night in the placebo group. Melatonin administration increased nocturnal 6-SM excretion above preoperative levels, but had no significant effect on postoperative circadian rhythm of activity. The CAI postoperatively was significantly different from the preoperative CAI ($p < 0.0001$), and this loss of circadian amplitude persisted throughout the 10 day study period. There were differences in both the night and the day activity, but the loss of DAYTIME activity was more prominent.
DISCUSSION: While the finding of a decrease in the circadian rhythm of activity after surgery was expected, its severity and persistence was surprising. A decrease in 6-SM excretion on the first postoperative night suggests that the decrease in the amplitude of the circadian rhythm of activity corresponds to a decrease in the amplitude of the output of the internal pacemaker. However, administration of melatonin to restore nocturnal 6-SM excretion to presurgical levels did not cause a corresponding restoration of the circadian rhythm of activity to presurgical levels.
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Economics, Education and Patient Safety

S-56

COMPLEMENTARY AND ALTERNATIVE MEDICINE IN THE OPERATING SUITE

AUTHORS: **A. Lewis**, I. Osborn, R. Roth;
AFFILIATION: Mt. Sinai School of Medicine, New York, NY.

INTRODUCTION: Interest in complementary and alternative medicine (CAM) is becoming prevalent for surgical patients. (1) Innovative music has been developed to complement intraoperative analgesia. The Monroe Institute (Virginia, USA) produces binaural beat music called hemispheric synchronization (Hemi-Sync) to be listened to intraoperatively. (2) A previous study established that listening to Hemi-Sync intraoperatively decreases the amount of analgesia required for bariatric patients, but failed to show a difference in analgesia requirement for lumbar surgical patients. (3) The current double-blind randomized study employed desflurane and a 25-ug induction bolus of fentanyl, rather than isoflurane and a 100-ug induction bolus, and observed the effects of listening to Hemi-Sync intraoperatively on the amount of analgesia required and on postoperative measures.
METHODS: Consented lumbar discesctomy patients were randomized to listen to either Hemi-Sync or a blank tape. Following endotracheal intubation and prone positioning, headphones were applied. Baseline blood pressure and heart rate were determined after ten minutes of tape play. The concentration of desflurane was adjusted in 0.5% increments every five minutes to maintain the bispectral index between 40 and 60. Fentanyl was administered in boluses of 25-ug every five minutes if heart rate was 15% above the baseline or if systolic blood pressure was 20% above the baseline. Ephedrine or labetalol were administered if blood pressure was 40% below or above baseline, respectively. The headphones were removed at the initiation of skin closure. Amount of fentanyl per kilogram per minute was compared using a student's t-test. An anesthesiologist-rated questionnaire was completed postoperatively and a patient-rated questionnaire was completed the day after surgery.
RESULTS: 6 patients listened to Hemi-Sync and 7 listened to the blank tape. There was no significant difference in the amount of fentanyl administered (0.0108 ug/kg/min (0.01) v. 0.013 ug/kg/min (0.02)) (p=0.75), the concentration of desflurane (2.7% (.2) v. 2.2% (0.7)) (p=0.16), or the cumulative postoperative scores (13 (5) v. 17 (4)) (p=0.16) for patients listening to the blank tape versus those listening to Hemi-Sync. There was no significant difference in baseline heart rate (66 bpm (11) v. 63 bpm (6)) (p=0.5); there was a significant difference in baseline systolic blood pressure (115 mg Hg (10) v. 103 mg Hg (7)) (p=0.03).
DISCUSSION: These results suggest that using Hemi-Sync to complement intraoperative analgesia does not affect the amount of analgesia required, extubation in the operating suite, or postoperative nausea and pain. Because patients listening to Hemi-Sync had a lower baseline blood pressure, it may be concluded that listening to Hemi-Sync reduced baseline blood pressure.
REFERENCES: (1) Journal of Alternative and Complementary Medicine 2002; 8 (3): 351-6.
(2) Anaesthesia 1999; 54: 769-73.
(3) Anesthesia and Analgesia 2003; 96; S-1-S-293.

S-57

ATTITUDES OF MEDICAL STUDENTS AND HOUSESTAFF TOWARDS MEDICAL ERRORS AND ADVERSE EVENTS

AUTHORS: **P. D. Vohra**[1], J. Mohr[1], C. Daugherty[1], M. Wen[2], P. Barach[3];
AFFILIATION: [1]University of Chicago, Chicago, IL, [2]University of Utah, Salt Lake City, UT, [3]University of Miami, Miami, FL.

BACKGROUND: Patient safety research creates an opportunity to explore how academic health centers respond to the challenge of providing exceptional educational opportunities to medical students and housestaff without compromising safe, high quality patient care. [i] [ii] [iii] [iv].
PURPOSE: This study examines the process by which physicians-in-training (PITs-medical students and housestaff) respond to adverse events in patient care and incorporate safety lessons into their daily practice at an urban teaching hospital.
METHODS: 563 PITs were invited to complete an anonymous electronic questionnaire on a secure website. Questions assessed their knowledge of methods to improve patient safety, beliefs in their ability to reduce medical errors, and their experiences with sentinel events. Questions were categorized into five domains: *knowledge*, *self-efficacy, awareness of safety culture, beliefs about barriers/facilitators*, and *awareness of human factors*. Each category was scored on a 100-point scale; summing the five scales formed the *Patient Safety Score* (PSS) with a 500-point maximum.
RESULTS: 158 PITs completed the questionnaire, of which 29% had been exposed to an adverse event (n=41). Mean PSS score was 306 (SD=54). Mean scores for the specific domains were: knowledge – 68 (SD=14), self-efficacy – 61 (SD=21), safety culture – 53 (SD=14), barriers/facilitators – 77 (SD=13), human factors – 47 (SD18). PITs exposed to adverse events reported a lower overall awareness of human factors in errors (p=0.0017) and a lower awareness of the hospital's safety culture (p=0.033). Older respondents scored higher on measures of self-efficacy than younger PITs (p=0.042).
CONCLUSIONS: The exposure of PITs to medical errors and adverse events appears to negatively affect their attitudes toward patient safety. Early exposure to these events may decrease error reporting by negatively affecting their willingness to adopt future safety practices into their training. More years of training may increase reported self-efficacy in dealing with adverse events. The low means on the domains of human factors and safety barriers provides support for the development of a formal safety curriculum. The learning experience about patient safety of housestaff exposed to adverse events is not positive, and lessons about adverse events have not been incorporated into their training. A patient safety curriculum that teaches PITs about patient safety and the need to learn from adverse events in a constructive manner is needed.
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PRELIMINARY ANALYSIS OF VIDEOTAPED ANESTHESIA EVENTS

AUTHORS: **M. B. Weinger**[1], J. Slagle[1], N. Ordonez[1], S. Jain[2];
AFFILIATION: [1]San Diego VA Hospital, San Diego, CA, [2]Univ. of California San Diego, La Jolla, CA.

INTRODUCTION: To improve patient safety, it is critical to understand how clinical systems actually work and why adverse events occur. We evaluated whether the prospective study of "non-routine events" (NRE) identified dysfunctional clinical system attributes or potentially dangerous conditions. NRE are defined as any event that is perceived by care providers or skilled observers to deviate from ideal care for that patient in that clinical situation.
METHODS: After IRB approval and informed written consent, we studied 349 elective surgical cases representing a cross-section of general anesthetic techniques, surgical procedures, and patient complexity. Before each case, baseline data were obtained. A trained observer, a data-logging computer, and audio and video recording equipment were positioned in the operating room (OR) to obtain a clear view of the anesthesia workspace without interfering with patient care. In addition to videotaping, the observer continuously recorded all of the participant's activities (Anesthesiology 87:144-155, 1997) and the occurrence of key intraoperative events including possible NRE. Workload and vigilance were also measured. Data collection began when the patient entered the OR and ceased when the patient and provider left the OR. Post-case surveys and a brief NRE questionnaire (JAMIA 9: S58-63, 2002) were completed by the primary anesthesia provider as soon as possible after the case. Relevant information was abstracted from the medical records. Data were deidentified prior to entry into an electronic database. Clinical experts reviewed each NRE-containing case and, using standardized rating systems, scored NRE type, patient impact events (PIE; e.g., tachycardia, cardiac ischemia, etc.), NRE severity, and putative contributory factors. A second clinician reviewed these codings and consensus was obtained.
RESULTS: 114 of 349 (32.7%) completed anesthetic cases contained a non-routine event. There was more than one NRE in 28 (24.6%) of NRE-containing cases (overall total of 152 NRE). The patient was impacted in 110 of NRE (72.3%) and 23 (15.1%) led to injury. The 152 NRE yielded 232 different PIE 39% of NRE led to ≥2 PIE. Of all PIE, 22.2% were airway related (e.g., failed intubation, laryngospasm), 16.6% were cardiovascular (e.g., bradycardia, hypotension), 11.7% were pulmonary (e.g., hypoventilation, desaturation, bronchospasm), and 11.3% were surgical (e.g., vascular laceration). A preliminary analysis of putative contributory factors is shown in the Table.
DISCUSSION: These initial results demonstrate the feasibility of real-time data collection, including videotaping, in the operating room and suggest the potential value of studying anesthesia NRE. Substantial human subjects and privacy issues had to be overcome. The use of this conceptual framework permits the capture of rich data on a large number of cases. Future detailed statistical analyses are expected to generate important new testable hypotheses and promising interventions to enhance anesthesia patient safety. Supported by grants from AHRQ and the VA HSR&D

Categorization of Putative Contributory Factors in Prospective Anesthesia NRE		
Patient Disease / Unexpected Patient Response	87	57.2%
Provider supervision, knowledge, experience, or judgment	68	44.7%
Equipment failure or usability	40	26.3%
Surgeon / surgical factors	33	21.7%
Logistical / system factors	28	18.4%
Communication	27	17.8%
Preoperative preparation	23	15.1%
Other / Miscellaneous	21	13.8%
Patient Positioning	19	12.5%
Adverse drug event	19	12.5%

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WHO IS CURRENT WITH THE BCLS/ACLS PROTOCOLS?

AUTHORS: **J. M. Yarmush**, J. D. Weinberg, M. Apergis, B. R. Wilkow, J. SchianodiCola;
AFFILIATION: New York Methodist Hospital, Brooklyn, NY.

INTRODUCTION: New BCLS/ACLS protocols were introduced in 2000. Are recently trained caregivers attuned to these changes?
METHODS: Three randomly selected groups of local area anesthesia residents (AR) (n=50), medical students (MS) (n=50), and ambulance personnel (AP) (n=50) were given a multiple-choice survey of 13 BCLS/ACLS questions. Questions 1-2 dealt with chest compressions. Questions 3-6 dealt with choking victims, family presence during CPR, automated external defibrillators (AEDs), and airway devices, respectively. Questions 7-9 dealt with rescue breathing, bicarbonate and calcium channel blockers, respectively. Questions 10-13 dealt with stable and unstable tachycardias, refractory ventricular fibrillation, outdated drugs, and mixed general information, respectively. Some of the questions contained the right answers for both the old protocol (1992) and the new protocol (2000).
RESULTS: AR and AP knew significantly more than MS about chest compressions, AEDs and the use of medications in refractory ventricular fibrillation. MS seemed to be distracted by the old protocol answers. AP knew significantly more than AR and MS about rescue breathing. Again, differences disappeared if old protocol answers were included. AP were only moderately knowledgeable of bicarbonate, calcium channel blockers and mixed general information but were significantly more so than AR and MS. AP and MS were not well informed about outdated drugs but were significantly more so than AR. AR were significantly more familiar than MS and AP about family presence during CPR and airway devices. The majority of AR, MS, and AP were ignorant about choking victims and only mildly knowledgeable about stable and unstable tachycardias.
DISCUSSION: The majority of AR and especially AP knew the BCLS protocol and the new drugs used in refractory ventricular fibrillation while many of the MS were still stuck on the older versions. Both the AR and MS were unsure of how to deal with calcium channel blockers. AP were more knowledgeable about calcium channel blockers but were unfamiliar with airway device usage. All groups were unsure of how to deal with choking victims, bicarbonate and outdated drugs, and the new data on stable and unstable ventricular tachycardia. Much information about BCLS/ACLS protocols is not making its way to AR and especially MS. AP are more up to date. Medical educators should place greater emphasis on the new BCLS/ACLS protocols and introduce this subject early in medical education. AP have the basics of breathing and circulation in hand but seem to be wanting in updated knowledge of the airway. They would benefit from greater education of the upper airway.

Correct answers for BCLS / ACLS survey			
	Anesthesia Residents	Medical Students	Ambulance Personnel
Q1	34 / 50*	20 / 50*^	36 / 50^
Q2	30 / 50*	3 / 50*^	26 / 50^
Q3	8 / 50	5 / 50	1 / 48
Q4	48 / 50*#	10 / 50*	11 / 50#
Q5	48 / 50*	30 / 50*^	42 / 50^
Q6	37 / 50#	16 / 50^	1 / 50#^
Q7	31 / 50#	21 / 48^	49 / 50#^
Q8	2 / 50#	9 / 47	17 / 50#
Q9	9 / 50#	11 / 45^	27 / 48#^
Q10	16 / 47	16 / 44	7 / 46
Q11	34 / 50*	8 / 44*^	35 / 49^
Q12	2 / 50*#	16 / 46*	15 / 49#
Q13	0 / 50#	8 / 45^	25 / 50#^

* = AR significantly different than MS
# = AR significantly different than AP
^ = MS significantly different than AP

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CARDIAC ARREST AND DEATH DURING ANESTHESIA SECONDARY TO IATROGENIC HYPERKALEMIA

AUTHORS: E. Richmond, D. Lubarsky, **P. Barach**;
AFFILIATION: Univeristy of Miami, Miami, FL.

INTRODUCTION: Potassium is critical to the maintenance of cellular polarization and transmission of electrical impulses. Alterations in the normal balance between intracellular and extracellular potassium concentrations can lead to life-threatening arrhythmias. Severe hyperkalemia reduces the resting membrane potential to the point at which conduction of electrical impulses ceases. Medication misadminstration is the most common intraoperative adverse event.
METHODS: We present 2 cases of hyperkalemic arrest and death, in addition to reviewing the morbidity and mortality directly attributable to iatrogenic hyperkalemia cardiac arrest/death in the National Practitioner Database Bank (NPDB).
RESULTS: A 44 kilo, 78 year old female with intraoperative serum potassium level of 2.9 meq/L was administered 20 meq KCL 90 minutes after aortic abdominal aneurysm vacular clamp. Cardiac arrested ensued and was unrescucitatible. In second case, 6 kilo neonate was given 8 mEQ instead of 0.8 meq KCL, developed ventricular fibrilation and was rescucitated with no apparent sequalea. The NPDB reports 17 cases of morbidity and/or mortality due to potassium injection by physicians over the past 20 years. The outcomes range from severe burn due to infiltration of IV fluid to death. Cases went to court and resulted in monetary settlements or physician license suspensions. Twelve of those cases resulted in death, with settlements ranging from $80,000 to $1,300,000. In two fatalities the administration of potassium was deliberate. Three pediatric cases were reported, one an infant who went into cardiac arrest and brain damage. A 77 year old patient recieved 30 meq of KCL IV push, coded, was resuscitated, but suffered permanent neurologic impairment, and lead to payment of $528,600. Fatalities were due to excessive doses and rapid infusion. A 47 year old female, with serum potassium of 2.2 meq/L intraoperatively was administered 30 meq KCL, twelve minutes later patient sustained cardiac arrest and died. Anesthesiologist was charged with manslaughter, and case was settled for $1,300,000. Mistakes in potassium administration varied from giving the wrong concentration, inappropriate doses, rapid infusion, injecting oral form intravenously, giving potassium iodide instead of potassium chloride, to mistakenly injecting potassium.
CONCLUSION: Potassium replacement for intraoperative hypokalemia is rarely beneficial and has a high harm potential. Most cases do not get reported so reported incidence is low and near misses are not reported. Despite clearly written and communicated rules about rate and dose of replacement harmful perioperative KCL overdosing continues to occur. We recommend removing all concentrated potassium from the perioperative settings to align with national standards, and according to JCAHO recommendations. Potassium should only be repleted in diluted form using infusion pump controlled administration.
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3. www.jcaho.org

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ANESTHESIA-RELATED CARDIAC ARREST AND ITS OUTCOME IN JAPANESE SOCIETY OF ANESTHESIOLOGISTS-CERTIFIED TRAINING HOSPITALS: AN ANALYSIS OF 3,855,384 ANESTHETICS OVER 4 YEARS

AUTHORS: **K. Irita**[1], Y. Kawashima[2], Y. Iwao[3], K. Tsuzaki[4], N. Seo[5], K. Morita[6];
AFFILIATION: [1]Kyushu University, Fukuoka, Japan, [2]Teikyo University, Tokyo, Japan, [3]Kyorin University, Mitaka, Japan, [4]Keio University, Tokyo, Japan, [5]Jichi Medical School, Tochigi, Japan, [6]Okayama University, Okayama, Japan.

INTRODUCTION: The Japanese Society of Anesthesiologists (JSA) conducts an annual survey of intraoperative life-threatening events in JSA Certified Training Hospitals by sending and collecting confidential questionnaires (1). We determined the incidence, causes, and outcome of anesthetic-related cardiac arrest by analyzing data obtained from the surveys conducted between 1999 and 2002.
METHODS: Between January 1999 and December 2001, 2,443 cases of cardiac arrest were registered, of which 183 cases were reported to be anesthesia-related cardiac arrest (AR-CA). The total number of anesthesia patients available for this analysis was 3,855,384. Statistical analysis was performed by the chi-square test. A p value less than 0.05 was considered significant. ASA-PS 1 and 2 were defined as good PS, while ASA-PS 3 and 4 were defined as poor PS.
RESULTS: The incidence of AR-CA in the operating theatre was 0.47 per 10,000 anesthetics. Among AR-CA patients, 16% died (5.5% in the operating theatre, 4.4% by the 7th postoperative day, 6.0% after the 8th postoperative day), 3.8% developed vegetative state, and 77.6% survived without any sequelae. The incidence of AR-CA was analyzed in relation to age, ASA-PS, and surgical sites. The incidence of AR-CA was high both in newborns/infants and in the elderly. ASA-PS correlated well with the incidence of AR-CA and subsequent mortality rate (p<.0001). In patients with good PS, the incidence of AR-CA and subsequent mortality rate were 0.33 per 10,000 anesthetics and 9.9%, respectively. The incidence of AR-CA and subsequent mortality rate were higher in emergency patients than in elective patients. The incidence of AR-CA was highest in patients undergoing cardiac surgery. The incidence was higher in patients under general anesthesia combined with regional anesthesia than in those under general anesthesia alone. The mortality following AR-CA was higher in patients receiving general anesthesia than in those receiving general anesthesia combined with regional anesthesia. Causes of AR-CA included problems in medication (44%), ventilatory problems (20%), problems in airway management (12%), problems in infusion or transfusion (9%), and inadequate vigilance (9%). The leading cause of medication error was drug overdose/selection error, followed by inadvertent high spinal anesthesia. Mortality rates of AR-CA due to ventilatory problems and problems in airway management were 31% and 38%, respectively, which were significantly higher than that due to problems in medication, 11%.
DISCUSSION: Emergency, poor PS, neonate/infant, elderly, and cardiac surgery patients were at higher risk of AR-CA. The mortality rate was high in the same population. The mortality rate was also high in AR-CA caused by airway/ventilatory problems. Considerable effort is required to improve airway/ventilatory management and medication. It is also suggested that more experienced anesthesiologists should participate in the perioperative management of patients at risk.
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MINIMIZING RISK OF NEEDLE STICK DURING REGIONAL ANESTHESIA TECHNIQUES

AUTHORS: **F. J. Overdyk**, D. Rowe, N. Weber;
AFFILIATION: Medical University of South Carolina, Charleston, SC.

INTRODUCTION: Risks of blood borne infection after a needle sticks from hollow bore needle are a serious occupational hazard to anesthesia practitioners[1]. A variety of IV catheters have become available with mechanisms that reduce the possibility of needle sticks[2]. However, regional anesthesia kits remain a likely source of needle stick injury, as their manufacturers have not yet adopted this technology. In this study, we analyzed the mechanics of placing a subarachnoid block (SAB) in terms of the number of occasions a practitioner is exposed to a potentially infectious hollow bore needle and subsequently choreographed a sequence of hand movements that would minimize this exposure.
METHODS: After institutional approval, we closely examined ten right-handed anesthesia residents performing a subarachnoid block using a Baxter™ (BD) Spinal Anesthesia Tray. We analyzed their hand/arm movements and documented the number of potentially infectious exposures (PIE) to a hollow bore needle previously used on the patient (PIN- potentially infectious needle). A PIE constituted any one of the following three occurrences:
(1) Resident capped a PIN.
(2) Resident transferred a PIN between the patient and the tray.
(3) Resident left an exposed PIN on the tray or on the sterile field.
We then choreographed a specific sequence of hand/arm movements designed to minimize PIE's. The essential elements of this technique are:
(1) Disconnect the local anesthesia syringe from its needle, leaving the needle in the patient's back as a placeholder whilst swapping or filling syringes.
(2) Never handle two needles simultaneously.
(3) Never recap a PIN.
After instruction in this technique for 15 minutes, we observed the same residents performing a SAB and counted the number of PIE's.
RESULTS: The total number of PIE's during the ten SAB's prior to instruction in the choreographed technique was 72, and the average per resident was 6.5. After instruction, these numbers dropped to 26 and 2.9 respectively, with the remaining PIE's involving transfer of a single PIN between patient and kit. There were no needle sticks in either arm of the study.
CONCLUSION: The probability of being stuck with a potentially infectious needle whilst placing a SAB block or epidural catheter can be greatly reduced by using a simple sequence of hand/arm movements that is easily learned. Although, our sample numbers were insufficient to determine a ratio of PIE's to needle ticks, we suspect this relationship is directly proportional and this technique may cut needle sticks during regional anesthesia in half.
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PERIOPERATIVE PAIN MANAGEMENT EDUCATION: A SHORT REGIONAL ANESTHESIA COURSE COMPARED WITH TRADITIONAL TEACHING AMONG MEDICAL STUDENTS

AUTHORS: **M. N. Hanna**, D. B. Keck, T. Mancuso, M. Donnelly, C. Montgomery, P. Sloan;
AFFILIATION: University of Kentucky, Lexington, KY.

INTRODUCTION:Previous research has demonstrated that a brief course on pain management will improve knowledge and attitudes about analgesic use among medical students.[1] Senior medical students, as part of a required course, [2] were exposed to regional anesthesia techniques for perioperative pain control. The purpose of this study was to compare a short clinical course on regional anesthesia techniques for perioperative pain management with traditional teaching given to final-year medical students.
METHODS: During a one-month clerkship in Anesthesiology, 40 final-year medical students received instruction on regional techniques for perioperative pain management. Group 1 (20 students, study group) received a two-hour course on regional techniques for pain management which included a brief lecture, audiovisual, live model, video and hands-on cadaver presentations, in addition to written materials. Group 2 (20 students, control) received detailed written material covering the subject taught to group 1. Both groups were told they would be examined on the course content and completed an objective structured clinical examination (OSCE) [3] at two-weeks post-instruction. This one-station, 15 minute OSCE used a standardized patient, a blinded and trained observer, and tested student performance of regional anesthesia techniques including indications, side effects, anatomy, landmarks, and use of local anesthetics. In addition, Group 1 completed a 9-item evaluation using a 5-point Likert scale (1=strongly disagree; 5=strongly agree) of the short regional course.
RESULTS: The OSCE included 11 items assessing regional anesthesia performance by the students. The study group performed better on each individual item, as well as on total performance scores, compared with the control group ($p < 0.05$). Total mean (S.D.) performance scores were 36.2 (7.3) and 14.8 (8.4) for the study group and control group respectively. Specific mean item scores for patient position, anatomy landmarks, technique demonstration, and side effect knowledge were 2.2 (1.1) and 0.5 (0.8), 4.6 (1.8) and 0.6 (1.1), 2.4 (1.3) and 0 (0), and 2.4 (0.8) and 0.8 (1), for the study group and control group respectively. All students rated (mean, SD) the short clinical course highly (4.7, 0.5); especially with regard to faculty enthusiastic (4.9, 0.3), clinical skills presented clearly (4.8, 0.4), and presentation of new information (4.7. 0.5).
DISCUSSION: 1) Medical students receiving a short structured clinical course on regional techniques of pain management out-performed students with control instructional format at 2 weeks post-instruction. 2) Significant learning among medical students receiving the structured clinical course seems to have taken place in all aspects of regional pain management techniques. 3) Senior medical students were very enthusiastic for the short clinical regional course.
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S-64

INITIAL EXPERIENCE IN INCORPORATING ADVANCED SIMULATION TO THE ISRAELI NATIONAL BOARD EXAMINATION IN ANESTHESIA - THE EXAMINEES' PERSPECTIVE

AUTHORS: H. Berkenstadt, A. Ziv, R. Dach, **A. Sidi**;
AFFILIATION: Sheba Medical Center, Tel Hashomer, Israel.

INTRODUCTION: The Israeli board examination in anesthesiology has been traditionally based primarily on oral discussion of clinical cases. The call for increased objectivity and standardization along with the need to evaluate examinees' clinical competence, as well as the increased experience and recognition in the validity of anesthesia simulators, have led the Israeli Anesthesia Board to incorporate new evaluation tools and various simulation modalities in order to evaluate examinees' clinical skills in an authentic and realistic setting. The guiding concept in developing the examination was that it would encompass a minimum-requirements task-driven, performance assessment.A possible obstacle to such modification in the examination format could be the examinees' resistance to radical change. The objective of this survey was to evaluate examinees' perspectives of the new examination design.
METHODS: 34 candidates for Anesthesia Board specialization were examined according to the new examination format, which included 5 hands-on simulation-based task-driven stations including: 1. Trauma management; 2. Resuscitation; 3. Operating room crisis management; 4. Regional anesthesia; 5. Mechanical ventilation. SimMan (stations 1 and 2), HPS simulator (station 3), a standardized patient-actor (station 4) and a standard ventilation machine (station 5) were employed, and emergency room or operating room environment were simulated as needed. All examinees had no previous experience in simulation-based training but underwent an orientation session two weeks prior to the examination. Participants completed a feedback questionnaire immediately after the examination and prior to publication of results.
RESULTS: Most participants - 79% (trauma management), 70% (resuscitation), 76% (OR crisis management), and 75% (regional anesthesia or mechanical ventilation) - reported that they were able to demonstrate their clinical skills better then in a traditional oral examination. Only a small minority (6%, 6%, 3% and 11%, respectively) claimed the new modality was inferior to the traditional oral examination.
DISCUSSION: This pilot survey demonstrates that anesthesia specialization examinees with minimal experience in medical simulation training prefer realistic simulated environments and modalities as a set-up to demonstrate clinical competence in comparison to the conventional oral examination. This study supports further evaluation of simulation as an evaluation and accreditation tool.

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EVALUATION OF A WIRELESS, HANDHELD COMPUTER NETWORK IN THE OPERATING ROOM OF AN ACADEMIC MEDICAL CENTER

AUTHORS: **F. J. Overdyk**, M. McEvoy, T. B. Chafin, J. Burnette, S. Caporossi, V. Bansal;
AFFILIATION: Medical University of South Carolina, Charleston, SC.

INTRODUCTION: Although wireless access to medical databases has been used in anesthesia for preoperative evaluations[1], we developed an intraoperative wi-fi (wireless) network and evaluated the impact on patient care, resident education and daily workflow of handheld computers (HC) wirelessly connected to our anesthesia server and the Internet.
METHODS: Five anesthesia residents in different stages of training evaluated three different brands (Toshiba e740, Dell Axim X5, and Compaq Ipaq3900) of HC with wi-fi capability (built-in or external wireless network interface cards (NIC)) and the PocketPC™ operating system. Cisco Systems 352 access points provided wireless coverage of our operating rooms (OR), recovery room (RR), holding area, and anesthesia offices. Our departmental Website was modified to include a 'mobile' page, allowing faster downloads and easier viewing on the HC's. An Odyssey Client (Funk Software.com) provides HIPAA compliant, secure access to preoperative evaluations, laboratory data, radiology studies, and office notes. A Web enabled form allows residents to log adverse events to our quality assurance database directly from the OR or RR. Similar Web enabled forms allow equipment and medications to be ordered from our anesthesia workroom and pharmacy during cases. Residents can update their ACGME case log (https://www.acgme.org/residentdatacollection/), log their work hours as mandated by the new AAMC 80 hour week, evaluate faculty (https://www.e-value.net/), and manage their email from their HC. The residents evaluated the performance of the wireless HC's through a simple survey.
RESULTS: All residents agreed the HC's provided immediate and point of care access to Internet based reference material useful for their daily casework. Similarly, all residents agreed the wireless HC's improved their daily workflow by improving communication with faculty, anesthesia techs, and fellow residents. Furthermore, all residents believed the wireless HC facilitates their compliance with mandatory database requirements (ACGME, QA) and increases their efficiency by allowing immediate, remote access to schedules, assignments, and e-mail. Eighty percent believed intraoperative Internet access was not distracting from patient care.
Only the Compaq HC (Orinoco™ (Proxim) external NIC), and the Toshiba e740 (internal NIC) provided reliable access to all the features described in methods, although the battery life of the Toshiba was rated unacceptable. All users were pleased with the data transmission rates and found the small display screen acceptable. No instances of interference between HC's and OR electronic equipment were noted, nor was our cellular phone communication in the OR disrupted.
CONCLUSION: Our initial evaluation of a wireless HC network for the OR suggests this technology has potential to improve the efficiency of residents' daily activity and accelerate their learning, although a more rigorous evaluation that includes the impact on OR vigilance and patient outcome is forthcoming.
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S-66

PROGRAM ENRICHMENT - TEACHING PROFESSIONALISM: SHOULD WE?

AUTHORS: **T. E. Carter**[1], P. Arciaga[1], J. S. Jahr[1], J. Tetzlaff[2], S. Steen[1];
AFFILIATION: [1]King Drew Medical Center, Los Angeles, CA, [2]Cleveland Clinic Foundation, Cleveland, OH.

INTRODUCTION: The Accreditation Council for Graduate Medical Education and the American Board of Anesthesiology (ABA) requires compliance with six core competencies -- professionalism is one of them (1,2). The ABA 2003 manual states: "Residents must demonstrate a commitment to carrying out professional responsibilities, adherence to ethical principles and sensitivity to a diverse patient population (3)." We evaluated a teaching module that included a pre- and post-test and a didactic lecture assessing improvement.
METHODS: As part of the resident education curriculum, a 30 minute presentation was scheduled to present a didactic lecture on Professionalism. No specific cases or tutorials were presented. Ten relevant questions, which were not directly addressed in the lecture, were administered as a pre- and post-test to members of the Anesthesiology Department of King/Drew Medical Center, including faculty, residents, and rotating students from UCLA. Feedback from the presentation and descriptive statistics were used to evaluate the results.
RESULTS: The faculty and Dean of the Medical School, residents, and students, on validated feedback, commented favorably on the lecture, including presentation, slides, and style. However, focus and additional time allotment was suggested, including specific question-matched case examples, and interactive tutorials. Specifically, of the 6 faculty members who were pre-tested, 2 of 3 which were post-tested, demonstrated a 10% improvement. Of 11 residents who were pre-tested, 9 of them completed the post-test and only one showed 10% improvement. One who scored 100% on the pre-test, did not take the post-test. Of the 3 medical students who took the pre-test, one significantly improved his performance by 30%. No individuals' scores decreased.
DISCUSSION: It is important to note that the lecture did not specifically cover the questions asked. Based on these initial findings, it is clear that the lecture should include specifics to cover relevant/topical aspects of professionalism included in the tests. For this to occur, educational modalities must be designed, which may include simulation of conditions relevant to anesthesiology and medicine in general.
In conclusion, as a result of these findings, we are developing:
a. Relevant, test questions to administer in a non-biased method, for which we provide a pre- and post-test following a didactic presentation of compelling topics in professionalism.
b. Teaching modules with examples in interactive sessions.
c. A published residency manual that documents clearly expected behaviors and actions (punctuality, honesty, politeness, team cooperation) as the patient's advocate.
d. The above permits performance evaluations, which may document improvement based on personal observations by faculty, colleagues, and support teams members.

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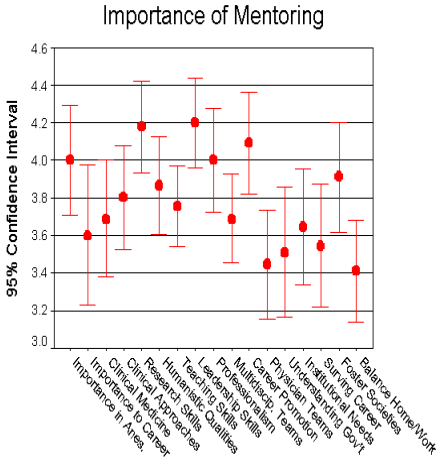
S-67

PARTICIPANT OPINION OF MENTORSHIP TO PROMOTE PROFESSIONAL GROWTH WITHIN AN ANESTHESIOLOGY ACADEMIC DEPARTMENT

AUTHORS: **J. F. O'Hara**, M. Hewson, B. Bierer, S. Stevens, A. Schubert;
AFFILIATION: Cleveland Clinic Foundation, Cleveland, Ohio, OH.

INTRODUCTION: A mentor is a person who has acquired experience and seniority; who is more than a teacher or colleague; who serves as a sponsor, advisor and role-model; who has the time to counsel and support more junior people; a person whose high standards of excellence a protégé can emulate[1,2]. This study surveyed physicians in an academic anesthesiology department with the purpose of identifying the importance of mentoring to promote professional growth within the work environment.
METHODS: Fifty-two anesthesiologists in an academic, tertiary care facility with a large residency program (>100 residents) were asked to complete a survey that was compiled by the study authors (table). The items generated were perceived to include relevant and appropriate issues for these physicians. The anesthesiologists were asked to rate items using a Likert scale (1 = not important to 5 = very important). Data are presented as mean scores and standard deviations. Confidence intervals were used to check significant differences among ratings.
RESULTS: The response rate of surveys completed was 86% (45/52 anesthesiologists). 71% of the respondents rated mentoring as important/very important. However, only 46% indicated that mentoring has been important/very important in their career so far. As presented in the figure below, the top five items reflecting respondents' perceptions of the importance of mentoring for professional growth were: research skills = 4.16 ± .85, leadership strategies = 4.14 ± .79, career promotion = 4.12 ± .78, professionalism = 4.04 ± .91, and advancing in state and national anesthesiology societies = 3.97 ± .97. Maintaining a balance between career and family/personal life was rated the lowest (3.44 ± .9, p<.05).



CONCLUSIONS: General anesthesiologists in this study view mentoring favorably. Mentoring is seen as most important in research, leadership, career promotion, professionalism, and advancing in state and national anesthesiology societies. These observations suggest these anesthesiologists may benefit from an organized mentoring program to promote professional growth in specific areas. Faculty development programs are being developed based on the most important items identified by the survey. Ongoing research will investigate the success of this tailored approach for organizing a structured mentoring program.
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S-68

ASSESSING FACULTY SATISFACTION WITH A FACULTY INCENTIVE PLAN

AUTHORS: **R. D. Kratz**, F. K. Orkin, B. Mets;
AFFILIATION: The Penn State Milton S. Hershey Medical Center, Hershey, PA.

INTRODUCTION: This study assessed the satisfaction of anesthesiology faculty in one academic health center with the current incentive payment plan to establish a baseline for evaluating the effectiveness of a new, productivity-based incentive plan for clinical and non-clinical activities.We developed a survey to be used before and annually after the implementation of the new plan to assess its incremental effectiveness. We report the results of the survey administered before implementation of the new incentive plan.
METHODS: A survey was developed using 19 statements with a five-point Likert scale: strongly disagree, disagree, neutral, agree, or strongly agree. Additional questions inquired about length of time in the department and specialty areas. Two open-ended questions allowed faculty to share experience with other plans and express concerns that were not addressed in the survey. With IRB approval, the anonymous survey was distributed to current clinical faculty members and to those faculty who had resigned during the past year. Summary statistics and contingency tables were prepared (SPSS 11.5), with exact probabilities computed (StatXact 5); P less than 0.05 was considered to indicate statistical significance.
RESULTS: Of the 26 current clinical faculty and four faculty who had left the department during the last year, 20 current and all four former faculty completed the survey. Among current faculty 80% did not understand how their most recent incentive amount was determined, 70% did not feel they had received adequate time, and 35% did not feel they had the other resources needed to make progress towards their yearly goals. Concerning the current plan, 40% felt it did not influence their productivity, and over half disagreed with statements that it motivated them to provide patient care, educational activities, research, or administrative activity. Only 35% could agree that they are highly satisfied with the current incentive plan. Faculty were more likely to be satisfied if they felt collegiality and support (P=0.0011), were in the department longer than 5 years (P=0.0347), and felt they had adequate time (P=0.0221) and other resources (P=0.0081). Those who resigned were more likely to have their level of productivity influenced by the incentive (P=0.0349) but otherwise responded similarly.
DISCUSSION: These data suggest that the current incentive plan is ineffective in motivating faculty. As we implement our new incentive plan, we must effectively communicate the details of this plan and ensure the goals set are aligned with the resources provided. These data will also provide a base from which to evaluate the success of our efforts.

S-69

DEVELOPMENT OF A GOAL-BASED INCENTIVE PLAN FOR MOTIVATING ACADEMIC ANESTHESIOLOGY DEPARTMENTS

AUTHORS: **R. D. Kratz**;
AFFILIATION: The Penn State Milton S. Hershey Medical Center, Hershey, PA.

INTRODUCTION: In the past many chairs of departments of anesthesiology have had full discretion and no formal guidelines for dispensing incentives.Our current chairman envisions the department moving to a program with more structure: one that not only rewards past effort but also looks to the future and motivates personal development. Our departmental faculty feel strongly that a goal-based program is more desirable than a value based or standards based program. No prior literature has been found relating goal-based incentive programs to anesthesiology departments.
METHODS: The literature in medical, psychological, and business journals relating to goal theory was reviewed. Goal setting theory was developed in the psychological literature. It was then expanded into business practice, but only recently have applications related to medicine been documented.
RESULTS: Five general rules of goals have emerged from the laboratory experiments and field studies (1,2,3,4).
1. Focused goals inspire. Three to five goals are preferable to six or more goals.
2. Specific goals generate higher performance than general goals. Specific goals are observable and measurable.
3. Difficult, achievable goals generate higher performance than easy goals or impossible goals.
4. Worker participation elicits increased commitment and motivation.
5. Specific feedback, both negative and positive, inspires increased levels of performance.
DISCUSSION: The Goal Setting Model can be applied to an anesthesiology department.
Goals are established individually by the chairman and faculty. Then the chair and faculty meet to determine mutually agreeable goals. At the same time they determine measurement criteria for goal achievement. It is important to ensure that the resources necessary for goal achievement are available. Then follow up for feedback and evaluation allows for continuous improvement.
Goal-based incentive plans can be developed which not only reward past effort but also encourage future growth in faculty by aligning their effort with the interests of the department (5). Good communication between the chairman and the faculty is required for success. We will be implementing a goal-based incentive plan and evaluating its effect on productivity and faculty satisfaction.
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S-70

MOLECULAR GENETIC TESTING FOR MALIGNANT HYPERTHERMIA IS SAFE AND COST EFFECTIVE

AUTHORS: **T. Girard**, S. Treves, E. Voronkov, H. Ginz, A. Urwyler;
AFFILIATION: University of Basel, Departments of Anesthesia and Research, Basel, Switzerland.

INTRODUCTION: For more than 30 years the in-vitro contracture test (IVCT, also called caffeine/halothane contracture test, CHCT) was the only appropriate diagnostic tool for malignant hyperthermia (MH) susceptibility. MH has been linked to the locus of the skeletal muscle type ryanodine receptor (RYR1) and more than 30 mutations of this gene were identified in MH susceptible (MHS) individuals. More recently the European MH Group has published guidelines for the molecular genetic detection of MH susceptibility(1). The aim of this study was to establish the applicability of these guidelines, potential advantages for the patients and economic impact of genetic testing.
METHODS: All patients referred to our MH investigation unit since 2001 were included. Every patient with a known RYR1 mutation in his family was investigated by molecular genetic methods and scheduled for IVCT in case of negative genetic results. Patients from families without mutations underwent IVCT without genetic investigations. IVCT was performed following the protocol of the European MH Group(2). Genetic analyses were done by PCR amplification of genomic DNA and restriction enzyme digestion as described earlier(3).
RESULTS: Two hundred and eight individuals underwent diagnostic procedures for MH between January 2001 and April 2004. Sixty-seven from families with known MH mutations 32 (48%) were mutation carriers and thus diagnosed MHS. IVCT followed negative genetic testing in 20 patients and 19 were diagnosed MHN (95%), while one was MH equivocal (contractures to halothane but not to caffeine). The negative predictive value was 0.99.
If estimated costs are US$ 6000 per IVCT(4) and US$ 200 per mutation tested, then calculated cost savings were US$ 178,600.
DISCUSSION: In families with known MH mutations, genetic testing is beneficiary because IVCT is not needed in mutation carriers. According to autosomal dominant inheritance of MH susceptibility, careful patient selection leads to approximately 50% of positive genetic tests. Costs savings are thus around US$ 300,000 per 100 patients from families with known RYR1 mutations. Although the negative predictive value of genetic testing was 0.99, maximal patient safety still requires IVCT to exclude MH susceptibility due to the heterogeneity of this disease.
Genetic testing in MH reliably confirms MH susceptibility in individuals bearing familial MH mutations and improves anesthesia risk management.

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S-71

CORRELATION OF THE INTRAOPERATIVE BISPECTRAL INDEX SCORE (BIS) WITH INCIDENCE OF POSTOPERATIVE COGNITIVE DISORDERS (POCD) IN THE GERIATRIC POPULATION

AUTHORS: **V. K. Gaba**, D. M. Mathews, B. Zhaku, G. G. Neuman;
AFFILIATION: Saint Vincent's Catholic Medical Center, Saint Vincent's Hospital, New York, NY.

INTRODUCTION: Past studies (1-2) have shown that elderly patients undergoing non-cardiac surgery have a 10% incidence of postoperative cognitive disorder (POCD) at three months post surgery. However, there has been no study correlating the patient's hypnotic state, with POCD. We conducted a study to determine if the depth of the patient's hypnotic state, as determined by the Bispectral Index Score (BIS), correlated with POCD.
METHODS: Our study is a double-blind, prospective, randomized study of patients aged more than 65 years, undergoing major abdominal, non-cardiac thoracic, orthopedic, or vascular surgery. Patients were randomized to 1 of 2 BIS levels: 30-40 or 50-60. Cognition was assessed preoperatively, and repeated postoperatively on day 3 and day 90, using a battery of neuropsychological tests. We also determined the Confusion Assessment Method (CAM) score on day 3 postoperatively, to assess the prevalence of postoperative delirium, which could potentially confound the assessment of cognitive function. The POCD was compared between the 2 groups and to a third group age and gender matched control subjects not undergoing surgery.
RESULTS: 62 geriatric patients were randomized between the 2 study groups. 34 patients were maintained at an intraoperative BIS of 30-40, and 28 patients were maintained at an intraoperative BIS of 50-60. 20 age and gender matched subjects were studied as controls. The baseline characteristics of the 3 groups are as shown in the table. The prevalence of delirium was 33% and 26% in the groups with BIS of 30-40 and 50-60 respectively. This is similar to the incidence of delirium reported in other studies. There was no correlation between the BIS level and prevalence of delirium postoperative (P=0.71).

DISCUSSION: From the above results, it appears that the hypnotic state, as determined by the intraoperative BIS, has no correlation with postoperative delirium. The last patient accrued to the study will be assessed for the day 90 POCD in November 2003. The final analysis will therefore be presented at the meeting.

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2. Anesthesiology 96: 1351-7, 2002.

Baseline characteristics of the cases and controls

	Patients with BIS maintained at 30-40	Patients with BIS maintained at 50-60	Control subjects
Number of subjects	34	28	20
Age: Range, Mean +/- 2SD	64-87, 74.41±11.96	65-77, 69.7± 6.88	62-82, 71.18± 10.06
Sex: Ratio of males to females	0.62	0.75	0.82
College Education: (Percentage)	17.6	39.28	35
ASA score of 2, 3 and 4 respectively (Percentage)	17.6, 64.71, 17.6	32.14, 42.86, 25	Not Applicable
Duration of Anesthesia: Range, Mean (minutes)	60-480, 190.78	60-420, 161.04	Not Applicable
Delirium: Prevalence as per CAM score(Percentage)	33.33	26.32	Not Applicable

S-72

TOURNIQUET USE DURING TOTAL KNEE ARTHROPLASTY IS ASSOCIATED WITH POSTOPERATIVE COGNITIVE DYSFUNCTION IN ELDERLY PATIENTS

AUTHORS: **T. G. Monk**[1], D. T. Webster[2], C. W. Garvan[1], P. F. Gearen[1];
AFFILIATION: [1]University of Florida College of Medicine, Gainesville, FL, [2]Keystone Orthopedics, Hazel Crest, IL.

INTRODUCTION: Postoperative cognitive dysfunction (POCD) is common in elderly patients following major, non-cardiac surgery.[1] However, little is know about the risk factors for this complication. This prospective longitudinal study was designed to evaluate the relationship between surgical risk factors and POCD in elderly patients undergoing orthopedic surgery.
METHODS: After obtaining informed consent, 153 patients undergoing elective orthopedic surgery were enrolled in the study. Exclusion criteria included age <60 years, central nervous system disorder, drug abuse, severe depression, or a preoperative score < 24 on the Mini-Mental State Examination. All patients completed neurocognitive testing before, at hospital discharge, and 3 months after surgery. Patients were identified as having POCD if the Z score on two individual tests or the combined Z score was 1.96 indicating cognitive decline from baseline test scores. Orthopedic surgical procedures were classified as total hip arthroplasty (THA), total knee arthroplasty (TKA), or other (non-joint bone or soft tissue surgery). Surgical risk factors were defined as tourniquet use, intramedullary reaming, intramedullary instrumentation for bone alignment, and the use of cement during the procedure. All data is expressed as mean ± SD. The relationship between surgical risk factors and POCD at hospital discharge and 3 months after surgery were examined using univariate methods (t test, Chi-square tests) with $p < 0.05$ considered significant.
RESULTS: The mean age of the patients was 69.7 ± 6.4 years. They had an educational level of 13.7 ± 3.0 years and a baseline MMSE of 28.8 ± 1.3. The overall incidence of POCD at hospital discharge was 39.5% and at 3 months after surgery was 14.1%. The incidence of POCD was significantly higher in TKA (49.3%) compared to both THA (34.7%) and other (24.1%)orthopedic procedures ($p < 0.05$) at hospital discharge. However, at 3 months after surgery, POCD was similar among the groups (12.8% - 15.2%, $p = 0.9$). The relationship between surgical risk factors and the occurrence of POCD is shown in the table.
DISCUSSION: POCD is common in elderly patients after orthopedic surgery. The only predictive surgical risk factors were TKA surgery and tourniquet use which occurs during TKA surgery. One possible mechanism for POCD is intraoperative embolic events. Our findings suggest that tourniquet use may predispose patients to the formation of thrombi that enter the circulation when the tourniquet is released.
REFERENCE: 1. Lancet 1998; 351:857-61.

The Relationship Between Surgical Risk Factors and POCD After Orthopedic Surgery

Surgical Risk Factors	Hospital Discharge (% of Patients)	3 Months Postoperative (% of Patients)
Tourniquet Use	No - 29.7% Yes - 49.3%* (p = 0.2)	No - 9.8% Yes - 18.6% (NS)
Intramedullary Reaming	No - 39.0% Yes - 41.1% (NS)	No - 14.1% Yes - 14.3% (NS)
Intramedullary Instrumentation	No - 34.1% Yes - 41.8% (NS)	No- 15.0% Yes - 14.1% (NS)
Use of Cement	No - 36.4% Yes - 41.3% (NS)	No - 14.8% Yes - 13.6% (NS)

No indicates risk factor not present; Yes indicates risk factor present
NS = not significant; * indicates significance with p , 0.05

S-73

PRIMARY OR REVISION TOTAL HIP OR TOTAL KNEE ARTHROPLASTY IN PATIENTS 80 YEARS AND OLDER

AUTHORS: E. M. Strum, **J. Szenohradszky**, T. Ayoub, V. Zelman, E. J. McPherson, P. D. Lumb;
AFFILIATION: USC, Los Angeles, CA.

INTRODUCTION: As the population ages, more and more patients over the age of 80 require total hip and knee arthroplasty surgery. The purpose of this retrospective study was to determine the preoperative medical conditions and any intraoperative and early postoperative medical problems in this population of patients. All of the patients had one or more unilateral primary or revision total hip arthroplasty (THA) or total knee arthroplasty (TKA).
METHODS: After IRB approval, we reviewed data of 59 patients (71 arthroplasties) 80 years or older who underwent unilateral primary or revision THA or TKA performed by one surgeon between 1993 and 1998. Measured values were expressed as mean ± SEM. All comparisons were performed using one-way ANOVA and unpaired t test with Welch correction. Differences were considered significant at $P<0.05$.
RESULTS: The 59 patients (16 males and 43 females) ranged in age from 80 to 95 (83.8 ± 0.4 [mean ± SEM]). 75% were 80 to 85 years old, 20% were 86 to 90 years old, and 5% were 91 to 95 years old. ASA PS grades were II-IV. During the study period, 23 patients (23 arthroplasties) had unilateral primary THA and 4 patients (8 arthroplasties) had revision THA. 24 patients (26 arthroplasties) had primary TKA and 8 patients (14 arthroplasties) had revision TKA. Combined general and epidural anesthesia was used for 31 arthroplasties. In 30 arthroplasties, general anesthesia alone was used; in six arthroplasties, epidural; and in two arthroplasties, spinal anesthesia was used. In 26 arthroplasties, pulmonary artery catheter was inserted; in 29 arthroplasties, a Cordes central venous line was used. A radial artery catheter was used on all but one of the patients. There were more complications after primary or revision THA (in 70% or 100% of arthroplasties, respectively) than after primary or revision TKA (23% or 7% of arthroplasties, respectively). There were statistically significant differences in tourniquet times between the primary and revision TKA patients, and differences in estimated blood loss and hospital stay between primary and revision THA and TKA patient groups. There was no perioperative mortality. 1.7% of the patients died within 3 months after surgery, 6.1% died within 4 years after surgery, and 8.2% died within 5 years after surgery.
DISCUSSION: Data from the retrospective chart review suggest that unilateral primary or revision THA or TKA for patients 80 years of age or older is a safe procedure with improved performance of surgery, optimal anesthetic management and close perioperative monitoring technique associated with appropriate use of available technology. Patients reviewed had a high frequency of preoperative medical conditions that might have predisposed the patients to a variety of perioperative complications.

S-74

PROPOFOL ANESTHESIA VERSUS PROPOFOL THIOPENTAL ANESTHESIA IN LAPAROSCOPIC CHOLECISTECTOMY. CLINICAL OUTCOME AND COST ANALYSIS

AUTHORS: **P. P. Nicolcescu**, P. O. Florea, I. I. Georgescu, A. I. Georgescu, N. C. Calina, I. N. Sosea;
AFFILIATION: University Hospital no1 Craiova, Craiova, Romania.

INTRODUCTION: We examined 2 anesthetic technique with respect clinical outcome and anesthetic cost.
MATERIAL AND METHODS. After ethic committee approval and informed consent, we prospectively studied 30 patients (23 female) ASA physical status I-II scheduled for elective laparoscopic cholecistectomy.The patients were and randomized into 2 equal groups: a Propofol group (A) and a Propofol Thiopental mixture group (B).All patients were premedicated with diazepam 10 mg po 40 min before surgical intervention.General anesthesia was induction with Atropine 0,5 mg,fentanyl 2microg/kg. In the group A patients received Propofol 2.5 mg/kg iv for the induction followed by 100 microg/kg/min for maintenance. In the group B patients received 5 ml Propofol-Thiopental mixture (1g Thiopental diluated with 20 ml Propofol 10% in the same syringe) for induction followed by 30ml/h.Vecuronium 0,1mg/kg were given and patients were intubated. and they were ventilated with O2 50%. At the end of the surgery the neuromuscular blockade was not reversed. For each patients we monitored: age, gender, body weight, duration of anesthesia (min), duration of surgery (min), respiratory and hemodinamic parameters, time to extubation (min). Emesis score, pain score, Ramsey scale, and recovery score were made at 0, 30, 60 min, 4, 8, 12, 24 hours in the PACU. Data are presented as mean +- SD. Fisher exact test was used to compare categorical data (nausea and vomiting) and the Mann Whitney U test was used for the comparison of means $p<0.05$ was significant
RESULTS Our results were summarized in table 1.
CONCLUSIONS: Continuos infusion of Propofol Thiopental mixture offers a similar hypnosis like propofol during surgical intervention. Our results show that for outpatient laparoscopic cholecistectomy surgery both the techniques we describe offer similar anesthesia and emergence. Continuos infusion of Propofol Thiopental mixture determined low cost, absence of injection pain and low risk of microbial contamination.
REFERENCES: Anesth Analg 1998; 86:731-8
Anesthesiology 1999; 90:1746-55

Table 1

	Group A	Group B
Age	37±21	36±25
Gender		
-female	11	12
-male	4	3
Body weight (kg)	63±27	63±18
Duration of anaesthesia (min)	49±25	48±27
Duration of surgery (min)	33±24	35±19
Time to extubation (min)	10±9	10±13
Nausea	5	5
Emesis	2	2
Total nausea and emesis	7	7
Heart rate	75±14	76±12
Mean blood pressure	78±6	75±8
Cost (USD)	75	45

S-75

PERIOPERATIVE AIRWAY MANAGEMENT IN MORBIDLY OBESE PATIENTS UNDERGOING OPEN GASTRIC BYPASS SURGERY - A RETROSPECTIVE ANALYSIS

AUTHORS: **A. Banerjee**[1], J. K. Wright[1], J. Stamler[1], M. Guerrero[1], P. K. Janicki[2];
AFFILIATION: [1]Vanderbilt University Medical Center, Nashville, TN, [2]Hershey Medical Center, Hershey, PA.

INTRODUCTION: The perioperative airway management in the morbidly obese surgical patients remains controversial, with several studies providing conflicting results as to the incidence and extent of difficult intubation and postoperative airway management in this group of patients. The open gastric bypass represents a standardized surgical procedure, performed under general endotracheal anesthesia in morbidly obese group of patients. The aim of the present study was to retrospectively analyze and characterize the large cohort of morbidly obese patients undergoing open gastric bypass surgery in single tertiary academic medical center, in respect to the types of preoperative airway evaluation, details of the perioperative airway management and the early postoperative outcomes.
MATERIAL AND METHODS: After institutional IRB approval, the archived, computerized anesthesia records (including preoperative evaluation) of 470 subsequent patients undergoing open gastric bypass in the single academic medical center were extracted and analyzed for several demographic and perioperative anesthetic variables. Demographic characteristics included gender, body mass index (BMI) and the history of the previous surgeries (with particular emphasis on the previous airway management history). The preoperative airway evaluation (performed by the staff nurse practitioner in the Preoperative Evaluation Clinic) included previous history of difficult airways and Mallampati score. The intraoperative airway information included number of attempts to intubate, evaluation of the direct laryngoscopic view, the incidence of use laryngeal mask airways (LMA), and fiberoptic assisted intubation. The postoperative evaluation included the incidence of extubation in operating room versus postoperative anesthesia care unit (PACU), use of ventilator and/or other ventilation assisting devices in PACU, as well as the incidence of extubation after leaving PACU. These data were compared with the available computerized perioperative records of remaining patients undergoing general anesthesia in the same period of time. The comparison between groups was made using Chi-Sq test (or t test when appropriate) and $P<0.05$ was defined as statistically significant.
RESULTS: The demographic characteristics and the perioperative airway management data for all analyzed patients are summarized in Table 1. The values of BMI were 53.5 +/- 8.9 and 28.3 +/- 3.6 in the open gastric bypass and control group, respectively ($p<0.05$). No statistically significant differences ($p>0.05$) were found for all analyzed perioperative airway management parameters in the open gastric bypass group and the remaining surgical patients (control group).
CONCLUSIONS: Morbidly obese patients undergoing open gastric bypass do not differ significantly from the non-non morbidly patients undergoing different surgical procedures under general endotracheal anesthesia in respect to the frequency of difficult intubations, intraoperative airway management and the methods of postoperative airway management.

Table 1. Demographic and perioperative data

	Gastric Bypass Patients (N=470)	Control (N=15,240)
Gender (female / male)	4.8*	1.1
Airway Mallampati Class:1 / 2 / 3 / 4 (% of total)	27 / 47.5 / 25 / 0.5*	48 / 41 / 10 / 1
Number of patients with history of difficult airways (% of all with previous surgical history)	0.7	0.59
Fiberoptic Intubation: awake fiberoptic / LMA followed by fiberoptic (% of total intubations)	4 / 18 / 1	3 / 14 / 2
Direct intubation: Easy / Difficult / Impossible (% of all intubated)	82 / 17.5 / <0.1	86 / 13.5 / <0.1
Direct Laryngoscopic View1 / 2 / 3 / 4 (% of all intubated)	62.6 / 29.1 / 6.2 / 2.1	69 / 19 / 11 / 1
Number of Intubation Attempts: 1 / 2 / 3 / 4 (% of all intubated)	85.3 / 11.7 / 2.3 / 0.7	77 / 18 / 4 / 0.9
Patients leaving OR withmask / t-piece / ventilator (% of all intubated)	74.1 / 21.8 / 4.1	71 / 19 / 11
Patients extubated in OR / PACU / ICU (% of all intubated)	78 / 22 / 1	70 / 29 / 1

S-76

FAILED POSTOPERATIVE EXTUBATIONS ARE AVOIDABLE

AUTHORS: **A. Jahan**, J. Hoban, V. Sabharwal, M. Popovich;
AFFILIATION: Cleveland Clinic Foundation, Cleveland, OH.

INTRODUCTION Endotracheal intubation is performed as part of many anesthetic techniques. In most cases, anesthesiologists are able to decide, prior to induction, whether or not a patient will be extubated at the end of a case. In addition to the patients that are anticipated to remain intubated, there lies a group of patients who are kept intubated secondary to unanticipated reasons. We refer to this as an *aborted extubation*. An aborted extubation is a clinical situation when a patient that was anticipated to be extubated at the end of a case, cannot be safely extubated. Many studies have focused on unanticipated ventilatory problems in the post anesthesia care unit (PACU) after extubation, but none have evaluated situations resulting in *aborted extubations*. We are in the process of prospectively examining the reasons and frequency of aborted extubations in hopes of decreasing their incidence and associated morbidity.
METHODS This is an ongoing prospective study from a tertiary care center. All patients whom, prior to induction, were clearly anticipated to be extubated but remained intubated where included (i.e. aborted extubations). Additionally, all patients reintubated within 1 hour of being extubated in the operating room were included. Emergency cases, patients arriving in the operating room intubated, and patients with either cardiothoracic, neurosurgical, otolaryngical, obstetrical or pediatric procedures were excluded. The staff anesthesiologist involved with induction was contacted to determine whether or not extubation was anticipated at the end of the case. The total number of elective cases were determined. All cardiothoracic, neurosurgical, otolaryngical, obstetrical and pediatric cases were excluded. Additionally, any case where the patient was obviously expected to remain intubated was excluded. The diagnosis for the aborted extubation was made based on a variety of clinical information and categorized into one of the following: Excessive anesthetic drugs, respiratory problems, hemodynamic instability, unanticipated intraoperative surgical event, hypothermia, unanticipated airway difficulties and other. Disposition from PACU was noted.
RESULTS A total of 28 aborted extubations were identified from 5275 elective cases (0.53%). Fifteen of the 28 patients (54%) were *aborted extubations* secondary to anesthetic drugs. The remaining aborted extubations were due to hemodynamic instability (2), respiratory problems (3), unanticipated intraoperative course (5), unanticipated difficult intubation (1), other (1), while one patient had both hemodynamic instability and respiratory problems. Of the 15 patients with aborted extubations secondary to anesthetic drugs only one required admission to the intensive care unit while 7 of the 13 patients with problems other than anesthetic drugs required admission to the ICU.
CONCLUSION Our results show that the primary cause of aborted extubations was avoidable: 54% were due to excessive anesthetic. Even though the overall incidence of aborted extubations is low, 0.53%, efforts should be made to eliminate all avoidable aborted extubations.

S-77

DURATION-DEPENDENT MODEL OF TIME ESTIMATES FOR DUAL PROCEDURE SURGERIES

AUTHORS: **D. P. Strum**[1], J. H. May[2], L. G. Vargas[2];
AFFILIATION: [1]Queen's University, Kingston, ON, Canada, [2]University of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: Improved models of surgical times are needed to forecast the duration of surgeries with known precision and reduced costs. Dual procedure surgeries (provider-ordered) are difficult to model because permutations (order-dependent combinations of the same CPT codes) occur and conventions do not exist to deal with or eliminate them. We investigated a duration-dependent model of dual procedure surgeries (CPTL-S) because that model was expected to improve time estimates by explaining more of the variability in surgical procedure times while eliminating coding permutations.
METHODS: With institutional approval, we studied retrospectively 10,737 dual procedure surgeries and 46,322 single CPT surgeries performed at a large teaching hospital (1). We used a multivariate linear model to study factors associated with variability in total time (TT) and surgical time (ST). To eliminate coding permutations we designated the longest procedure as CPTL and the shortest as CPTS. To test the ability of a duration-dependent model to detect variability in LnTT and LnST, we fitted a 7-factor main effects model of the general form: where MTEL = median time estimate for CPTL, MTES = median time estimate for CPTS, Anes = type of anesthesia, SPL = surgical specialty of CPTL, SPS = surgical specialty of CPTS, Emerg = emergency status (yes or no), and age. We conducted the analyses using the natural logarithm (ln) of TT and ST because of previous indications of lognormality (2). To furnish MTEs, single CPT surgeries were summarized by their medians and matched to CPTL-S component codes using lookup tables. Surgical specialties (1-20) were assigned using main headers from the CPT classification.
RESULTS: All 7 independent factors were significant ($p < 0.00$) and together explained 70.5% of the variability in lnTT. Independent factors ordered by decreasing importance (by factor F-ratio) were MTEL Anes, MTES, Emerg, Age, SPECL, and SPECS. Results were similar for ST. ANOVA Table for lnTT (r2 = 70.5%, n = 9,876 CPTL-S surgeries)

Indep Factor	Sum Squares	DF	Mean Square	F Ratio	P-value
MTEL	757.556	1	757.556	6249.135	0.0000
Anes	62.071	3	20.690	170.677	0.0000
MTES	10.2264	1	10.2264	84.359	0.0000
Emerg	2.501	1	2.501	20.672	0.0000
Age	1.1534	1	1.154	9.518	0.0020
SPL	11.003	17	0.647	5.339	0.0000
SPS	7.548	18	0.419	3.459	0.0000
Error	1192.012	9833	0.121		

CONCLUSIONS: This research identified factors associated with variability in dual procedure surgeries. A duration-dependent dual procedure model (CPTL-S) proved superior to a provider-ordered model reported previously (3). The sources of variability in dual procedure surgeries must be understood to improve modeling of multiple procedure surgeries and in turn to improve surgical schedules.
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1. Bashein et al: Anesthesia Analgesia 1985; 64:425-431
2. Strum et al: Anesthesiology 2000; 92:1160-67.
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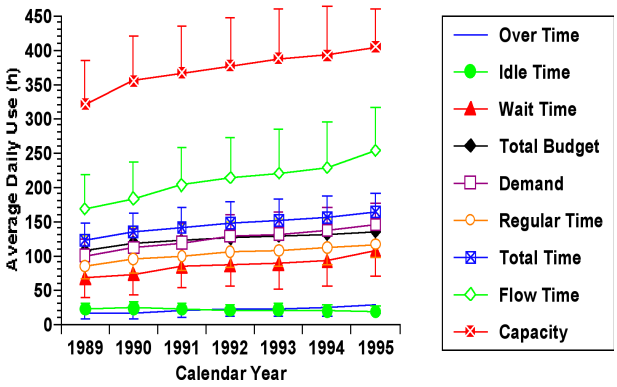
S-78

EVALUATION OF SURGICAL SERVICES USING SURGICAL SCHEDULE OUTCOMES

AUTHORS: **D. P. Strum**[1], L. G. Vargas[2];
AFFILIATION: [1]Queen's University, Kingston, ON, Canada, [2]University of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: To evaluate surgical schedules and inform scheduling policies, we parameterized surgical schedules. We described 9 schedule outcome parameters that quantitate individual surgical schedules. Multiple schedule outcomes were aggregated to evaluate institutional production of services over time (institutional service outcomes).
METHODS: With institutional approval, we studied 58,703 surgeries performed in 18 operating rooms over 1,651 weekdays at a large academic medical center (1). Parameterized surgical schedules were evaluated using historical case records and computerized subroutines written in common LISP. Schedule outcomes evaluated included wait time, total time, regular time, overtime, idle time (unused regular time), flow time (wait time + surgical time), surgical demand, capacity, and budgeted time. Schedule outcomes were aggregated using Excel and trends in schedule service outcomes over time were tested using multivariate ANOVA (Systat). Weekend days and holidays were omitted from analyses to reduce confounding factors.
RESULTS: All parameterized schedule outcomes increased ($p < 0.00$) over 7 years studied (capacity, regular time, flow time, wait time, overtime, etc) except idle time and that decreased ($p < 0.00$, $n = 58,703$ surgeries).

Aggregate Schedule Outcomes (mean ± SD) for Surgical Services



CONCLUSIONS: Methods to evaluate surgical schedules and thus institutional services must be refined and documented in the literature before widespread use of these outcome measures may commence. Aggregate schedule outcomes reflect institutional service outcomes. Additional studies are needed to investigate the impact of surgical scheduling and institutional policies on these parameterized schedule outcomes.
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S-79

USE OF SIMPLE PRACTICE GUIDELINES REDUCES ANESTHESIA DRUG COSTS

AUTHORS: S. Hindocha[1], **G. P. Joshi**[2], L. Duffy[2], C. Whitten[2];
AFFILIATION: [1]University of Manchester, Manchester, United Kingdom, [2]University of Texas Southwestern Medical Center at Dallas, Dallas, TX.

INTRODUCTION: With increasing focus on cost containment, many hospitals have implemented numerous initiatives to reduce pharmaceutical costs. These include education of practitioners and limiting access to drugs. However, utilization of these methods usually generates only short-term results. The implementation of practice guidelines for use of drugs has been shown to reduce costs without adversely affecting clinical outcome (1). We report the use of simple practice guidelines as an approach to reduce anesthesia-related costs with sustained financial benefits.
METHODS: A committee consisting of anesthesiologists and pharmacy personnel reviewed anesthesia-related drug costs. Simple practice guidelines were developed for the most expensive drugs (i.e., propofol, rocuronium and ondanesetron). These guidelines suggested that propofol be used only in patients undergoing ambulatory surgery and in those patients at high risk of postoperative nausea and vomiting (PONV), as well as for sedation during regional or local anesthesia. Thiopental should be used for all others cases. Rocuronium should be used only if there is a need for rapid tracheal intubation and succinylcholine was contraindicated. Vecuronium should be used for all other cases. Ondansetron should be used only in patients at high risk of PONV and only in combination with droperidol, dexamethasone, or metoclopramide. When these drugs were ordered from the operating room satellite pharmacy, it was required that the anesthesia attending justify their use. Drug usage was collected 6 months before (i.e., October 1999 to March 2000) and after the implementation of the program (i.e., April 2000 to December 2000). In addition, the number of surgical procedures performed every month and the need for treatment of PONV (with ondansetron) in the postoperative anesthesia care unit (PACU) was also noted. Data were analyzed using F test with a $P<0.05$ considered statistically significant.
RESULTS: The average monthly usage (and the costs) of the drugs evaluated was significantly lower after the implementation of the cost saving program. The average costs savings from the implementation of guidelines were $ 10,800 per month. The number of cases performed per month were similar before and after the implementation of guidelines. There was no increase in the need for ondansetron in the PACU after the implementation.
DISCUSSION: Our study has shown that the use of practice guidelines and need for justification of the drug use (even within the practice guidelines) significantly reduced the anesthesia drugs costs. We have also demonstrated that these financial benefits are sustainable without increasing adverse events.
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S-80

THE IMPACT OF THE JCAHO PAIN INITIATIVE ON PERIOPERATIVE OPIATE CONSUMPTION AND PACU LENGTH OF STAY

AUTHORS: **P. E. Frasco**, T. Trentman;
AFFILIATION: Mayo Clinic Scottsdale, Scottsdale, AZ.

INTRODUCTION: In October of 2002, Mayo Clinic Scottsdale participated in a survey conducted by the Joint Commission for Accreditation of Healthcare Organizations (JCAHO). Assessment of compliance with the Joint Commission's pain initiative was part of this survey. The pain initiative represents an effort on the JCAHO's part to improve pain management.
Mayo Clinic Scottsdale's (MCS) peri-operative services responded to the JCAHO pain initiative in September 2001 (prior to the survery) by utilizing a standardized pain assessment tool, i.e. implementing the numeric pain scale. In addition, all physician and allied health providers were instructed to assess for pain in all patients admitted for surgery and pain management as guided by the pain scale was emphasized in the post anesthesia care unit (PACU). We hypothesized that increased organizational emphasis on pain management led to increased immediate peri-operative opiate use and prolonged PACU stays.
METHODS: We reviewed 225 anesthesia records before the JCAHO pain initiative was instituted at MCS (2000) and an additional 225 records after the pain initiative (2002). We did not use patients from 2001 since the initiative was adopted by the instituion in September 2001. This population represents 25 patients from each of our top 9 diagnostic related groupings (DRGs) by yearly case volume. The nine DRGs that were included were 148/149 (Major small & large bowel procedures with and without coexisting conditions (cc)), 209 (Major joint/limb reattchment procedures of the lower extremity), 334/335 (Major male pelvic procedures w/ and w/o cc), 358/359 (Uterine/adnexa procedures for non-malignancy w/ and w/o cc) and 499/500 (Back/neck procedures not including spinal fusion w/ and w/o cc). The charts were reviewed for intra-operative and PACU opiate use and PACU length of stay. Dosages of fentanyl, sufentanil, meperidine and hydromorphone were expressed as morphine equivalents using standard potency conversions. PACU length of stay was measured from time of admission to time when discharge criteria were met.
RESULTS: There were no significant differences in patient age and gender between the groups. The data for perioperative morphine equivalents and duration of PACU time are summarized in Table 1. There were statistically significant differences in total perioperative morphine and postoperative morphine equivalents between the patients in year 2000 versus those in 2002. There were no diffences in intraoperative morphine equivalents or in total PACU time.

COMPARATIVE RESULTS

	TOTAL MORPHINE (MG)	INTRAOP MORPHINE (MG)	POSTOP MORPHINE (MG)	PACU TIME (MIN)
2000	40.36	33.64	6.72	104.70
2002	46.19	35.76	11.24	95.98
P VALUE	P < 0.001	P > 0.05	P< 0.0001	P > 0.05

DISCUSSION: We detected an overall increase in the average consumption of morphine equivalents between the two periods of time (2000 versus 2002). This increase was most significant during the immediate postoperative period in the post anesthesia care unit. This increase in morphine utilization in the PACU was not associated with an increased length of stay. We conclude that this increase in morphine equivalents may be explained by compliance with the JCAHO pain initiative.

S-81

PATIENTS´ ASSESSMENT OF THE PERIOPERATIVE PERIOD: GENERATING ITEMS FOR A PILOT QUESTIONNAIRE

AUTHORS: **P. Kranke**[1], L. Eberhart[2], I. Celik[3], W. Buendgen[1], M. Simon[2], N. Roewer[1];
AFFILIATION: [1]Department of Anesthesiology, University of Wuerzburg, Wuerzburg, Germany, [2]Department of Anesthesiology, University of Marburg, Marburg, Germany, [3]Department of Surgery, University of Marburg, Marburg, Germany.

INTRODUCTION: Patient satisfaction with healthcare in the perioperative setting forms a complex psychological construct that cannot be separated neither into technical care vs. nursing vs. physicians care vs. education or trust, nor in anesthesia- vs. surgery- vs. nursery-related items. Therefore, we aimed to develop a psychometric questionnaire covering satisfaction with the perioperative care (1 day before until 1-2 days after the operation) for use during continuous quality improvement and as a means for adding patient values and concerns to clinical outcomes (i.e. in clinical trials). The aim of this initial step was to generate a comprehensive item list for constructing a pilot questionnaire.
METHODS: A list of possible relevant items relating to satisfaction with the perioperative setting was created using systematic literature search, and results of a survey with open questions among patients (P), relatives (R) and healthcare professionals (H). The generated list of 198 items was re-distributed to another subgroup of patients (n=99), relatives (n=64)), and healthcare professionals (n=111) who rated each item on a 5-point likert scale ("extremely important" = 5 to "not important at all" = 0).
RESULTS: Using factorial analysis 12 main categories could be identified: specific solicitudes concerning the preoperative (n=16) and perioperative (n=18) period, injuries/morbidity (n=6), pain perception (n=20), general somatic symptoms (n=64), physical mobility/self determination (n=15), emotional well being (n=20), physical/emotional support (n=21), housing/catering (n=14), achievement of objectives (n=5). Assessment and weighted pooling of the results led to 66 items that could be further condensed to 41 key items by the elimination of identical meanings or linguistic redundancy. The 10 most important issues were (ranking from "1"=most important to "41"=less important of the respective groups are given in parenthesis): physicians anticipate the patients wishes and act accordingly (P: 3., R: 2., H: 1.), sufficient/ tidy sanitary facilities (P: 1., R: 3., H: 12.), gagging on tracheal tube (P: 5., R: 1., H: 9.), injured teeth (P: 6., R: 4., H: 3.), achievement of personal objectives with the operation (P: 2., R: 13., H: 17.), timely information on results/success/complications of the procedure (P: 4., R: 11., H: 6.), sufficient information on therapy/treatment (P: 9., R: 7.,H: 4.), pain free state as soon as possible (P: 10., R: 8., H: 13.), quick and understandable information on results from any examinations (P: 12., R: 12., H: 13.), pain under control (P: 18., R: 6., H: 8.).
CONCLUSION: The applied process assures that patients´ concerns and preferences were given appropriate weight without neglecting expert knowledge in the construction process of a tool to assess patients assessment of the perioperative period. The inclusion of the entire core process of the perioperative pathway takes into account the circumstance that separating this process remains problematic.

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PATIENTS´ ASSESSMENT OF THE PERIOPERATIVE PERIOD: GENERATING A PILOT QUESTIONNAIRE AND PSYCHOMETRIC TESTING

AUTHORS: **P. Kranke**[1], I. Celik[2], N. Roewer[1], M. Simon[3], W. Buendgen[1], L. Eberhart[3];
AFFILIATION: [1]Department of Anesthesiology, University of Wuerzburg, Wuerzburg, Germany, [2]Department of Surgery, University of Marburg, Marburg, Germany, [3]Department of Anesthesiology, University of Marburg, Marburg, Germany.

INTRODUCTION: Various methods have been used to quantify patient satisfaction with perioperative care. Most are narrowly focused due to the neglect of patients attitudes and concerns during the development or due to the fact that the core process of the perioperative pathway was subdivided into various aspects (i.e. physicians vs. caring professions, anesthesia vs. surgery, "hotel service" vs. medical service. In a previous step of comprehensive and weighted (patients vs. relatives vs. healthcare professionals) item generation we identified 41 key issues that should be further evaluated and processed in a pilot questionnaire using psychometric methods. The aim was to generate a validated and consistent questionnaire to evaluate patients assessment of the perioperative period (approximately 1 day prior to surgery until the first or second postoperative day).
METHODS: Relevant outcomes and circumstances were presented to inpatients as statements in an iterative approach at various institutions (university hospitals, private surgery centers) in Marburg and Wuerzburg, Germany. Patients were asked to rate the given statements on a 4-point likert-scale ranging from "1" (= at no time / not at all true) to "4" (=all of the time / wholly true).
RESULTS: In a first step, the 41 most relevant issues of the item generation phase were presented to 157 patients. The obtained ratings were subjected to qualitative and quantitative reliability analysis. Items were eliminated due to lacking responses of more than 10% of the cohort or because a statement was not an issue for more than 90% of patients resulting in impaired discriminating properties. Items with inter-item correlation below 0.2 were eliminated. Based on 114 eligible assessments out of 157 patients the calculation of Crohnbach´s alpha was 0.82 for the revised questionnaire with the remaining 33 items. In a second step these 33 items were regrouped and again presented to subsequent patients in the aforementioned institutions. Reliability testing confirmed good positive inter-item correlation. Crohnbach´s alpha was calculated to be 0.78. Compliance with this final tool was excellent. Randomized distribution of the questionnaire using other layout or other order (chronological order of the statements according to the perioperative path of the patient vs. random order vs. grouping due to main categories) was irrelevant for the results in both steps.
CONCLUSION: Qualitative and quantitative psychometric testing confirms the reliability of the developed questionnaire. Anesthesia-related issues play a relevant role in the final set of items. Factors that determine results of the patients´ assessment of the perioperative period, robustness across different patient populations, correlation with other tools (visual analog scale, willingness to pay) or sub-categories of perioperative course (i.e.: recovery) have yet to be determined in subsequent investigations.

S-83

HOW MUCH ARE PATIENTS WILLING TO PAY FOR ANTIEMETIC TREATMENT?

AUTHORS: **C. C. Apfel**[1], A. Turan[2], H. Kerger[3], M. Kredel[4], T. Gan[5];
AFFILIATION: [1]Outcomes Research Institute and Department of Anesthesiology, Univ of Louisville, KY, [2]Dept. of Anesthesiology, Trakya University, Edirne, Turkey, [3]Dept. of Anesthesiology, Mannheim University Hospital, Mannheim, Germany, [4]Dept. of Anesthesiology, Univ of Wuerzburg, Germany, [5]Department of Anesthesiology, Duke University, Durham, NC.

Due to increasing pharmacoeconomic pressure, costs-effectiveness analyses are also increasing in the field of postoperative nausea and vomiting (PONV).[1]However, cost-benefit analyses may be more appropriate as it converts the clinical outcome or effectiveness in monetary units. Using a questionaire it was demonstrated that US citizens were willing to pay US$56 for an antiemetic that would completely prevent PONV.[2] As direct translation into different countries may be difficult due to differences in income or the cultural background we sought to repeat this investigation in two European centers, Germany and Turkey.
At the evening after surgery 200 adults patients who underwent elective surgery completed an interactive computer questionaire on demographics, the value of avoiding PONV, and their willingness to pay for an antiemetic.
Patients were willing to pay € 56 (€2.50-€100; median, 25%-75%) and € 67.50 (€38.38-€97) in Germany (G) and Turkey (T), respectively. The corresponding values for patients who developed nausea (n=34 and n=31) were € 96 (€50.66-€129) and € 80 (€57-€97) and for patients who developed vomiting (n=23 and n=10) €99 (€51-€144) and € 60.58 (€27.82-€71), for G and T, respectively. In Germany, 85% and 90% of patients considered the prevention of nausea and vomiting as being important (>=50 on a 0-100 mm VAS), respectively. The corresponding figures in Turkey were 94% and 94%, respectively. In a logistic regression model independent predictors to be willing to pay more than €50 were high importance allocated to the prevention of nausea 4.8 (odds ratio; 95% confidence interval 2.3-9.8), non-smoking status 3.1 (1.5-6.3), nausea on that day after anesthesia 2.2 (1.05-4.8), and the center 2.1 (1.1-4.3). Patients associated a value of about €56 to €67.50 for an completely effective antiemetic to prevent PONV. To our surprise this is quite similar to the previously published study in the US but it emphasizes hwo important our patients value the prevention of PONV.

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2. Gan T, Sloan F, Dear G, El Moalem HE, Lubarsky DA. How much are patients willing to pay to avoid postoperative nausea and vomiting? Anesthesia and Analgesia 2001; 92:393-400.

Equipment & Monitoring

S-84

A SMALL LEAK IMPAIRS PRE-OXYGENATION WITH VITAL CAPACITY OR TIDAL VOLUME BREATHING

AUTHORS: **C. S. Gagnon**, L. P. Fortier, F. Donati;
AFFILIATION: Maisonneuve Rosemont Hospital, Montreal, PQ, Canada.

INTRODUCTION: Pre-oxygenation techniques are effective provided that there is a tight seal betweeen the mask and the face. In practice, leaks occurs frequently. The most common pre-oxygenation procedure requires breathing 100% oxygen for 3-5 min (1). To shorten pre-oxygenation time, a method involving four deep breaths in 30 seconds has been proposed (2). In the event of a leak, it was hypothesized that a shorter pre-oxygenation period could be more effective than a longer time. Therefore, this study compares 3 min of tidal volume breathing with 4 vital capacity breaths in 30 seconds as pre-oxygenation methods in the presence or absence of a leak.
METHODS: Twenty (14 F, 6 M) healthy adult volunteers, aged 21-56 yr, were pre-oxygenated by 4 different methods in a randomized, cross-over design, using 6 L/min of fresh oxygen flow supplied to a circle circuit: 1) tidal volume breathing for 3 min, no leak; 2) four vital capacity breaths in 30 seconds, no leak; 3) tidal volume breathing for 3 min, with leak; 4) four vital capacity breaths in 30 seconds, with leak. The leak was created with a piece of nasogastric tube # 18, 5 cm long, taped under the edge of the mask. Inspired and expired O2 and CO2 were sampled by a canula at the nose. Primary outcome measurement was the end-tidal oxygen fraction (FeO2) at the end of the preoxygenation period. A paired sudent's t-test with Bonferroni correction was applied and a P value < 0.05 was used to indicate statistically significant differences.
RESULTS: With no leak, the FeO2 was greater after tidal volume breathing for 3 min than after 4 vital capacity breaths in 30 seconds (P < 0.001). Introduction of a leak decreased the FeO2 significantly to approximately 60% (P < 0.001), regardless of the pre-oxygenation method (Table 1). End-tidal CO2 was significantly lower (P<0.001) after 4 vital capacity breaths than after 3 min of tidal volume breathing with or without a leak.

FeO2 (mean % +/- SD) at the end of pre-oxygenation			
	Leak	**No leak**	**P value**
Tidal volume 3 min	61+/-8	89+/-3	< 0.001
Vital capacity 30 sec	59+/-11	76+/-7	< 0.001
P value	0.574	< 0.001	

DISCUSSION: A leak as small as 4 mm of internal diameter markedly decreases FeO2 at the end of pre-oxygenation. This was observed, using a 6 L/min fresh gas flow of oxygen, both with normal breathing for 3 min and 4 deep breaths in 30 seconds. Thus, none of these techniques is superior with a small leak. However, in the absence of a leak, normal breathing for 3 min provides a higher FeO2 is obtained than 4 deep breaths in 30 seconds.
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S-85

EVALUATION OF GAS HUMIDIFYING DEVICES AS MEANS OF INTRAPERITONEAL ROPIVACAINE ADMINISTRATION FOR LAPAROSOPIC SURGERY

AUTHORS: **P. A. Diemunsch**, L. Oehlkern, J. Y. Pabst, T. Pottecher, B. Geny;
AFFILIATION: CHRU, Strasbourg, France.

INTRODUCTION : Intraperitoneal administration of ropivacaine (R) (Naropine*, Astra Zeneka) during laparoscopic surgery has been shown to improve postoperative analgesia. The administration of R may be more efficient when injected before the beginning of surgery at the moment of insufflation of the pneumoperitoneum rather than at the end of the procedure (1). Moreover, the humidification of pneumoperitoneal gas might improve analgesia and reduce postoperative hypothermia (2) . The aim of this study is to evaluate the possibility of intraperitoneal R administration using CO_2 humidification systems. This administration route was studied in a laboratory setting using 2 different humidifying devices.
METHODS: A pneumoperitoneum insufflator (162*, Stryker MI), preset to a maximum pressure of 12mmHg, delivered CO_2 to a gas humidifier. Two different gas humidifiers, humidifier A (Airlife* , Allegiance II), and humidifier B (CO2 Humidifier20432033* , Karl Storz, Germany) were used in 2 separate experiments. The humidifier (A or B) was filled with a 0.2 or 0.75% R solution. After exiting the humidifier, the CO_2 was directed into a calibrated phial containing 25 cc of a 50% methanol-in-water mix. The concentation of R collected in the methanol-H_2O mix was then measured using high performance liquid chromatography (HPLC). For humidifier A, the measurements were first performed at temperatures of 20° C, every 15 minutes for 90 minutes. After having placed the humidifier in a controlled heating device, the measurements were performed in the same fashion at 50° C. Humidifier B had an inbuilt thermostat and measurements were made every 30 minutes for 60 minutes at a temperature of 50° C. Each sample was analyzed in triplicate, and results are reported as the mean of the observed values for each sampling. The R concentrations are expressed as the amounts of R delivered for each 15-minute period by the system A, or for each 30-minute period by the system B.
RESULTS: The average CO_2 inflow into the experimental systems was of 2.3+/-0.4L/min. Table 1 shows the amount of R delivered by the humidifier A under 3 experimental conditions.
Using humidifier B, no amount of R could be detected, neither at 30 nor at 60 minutes.
DISCUSSION: R, when delivered by evaporation-based humidifiers, is present in minute or non-measurable quantities, under ambient or heated conditions. R is not efficiently delivered with the evaporation process, and this means of administration is inappropriate for clinical application. Other means of delivery, as aerosols or ultrasonic nebulizers, should be studied to assess the feasibility of simultaneous CO_2 humidification and intraperitoneal administration of local anesthetics during laparoscopy.
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Table 1: Quantity of R delivered by system A under 3 experimental conditions

R Concentration; mg/mL	T °C	Quantity of R delivered in 15 min; mean± SD (range)
7.5	50	370.8 ± 55.1 ng (270 - 420)
7.5	20	82.1 ± 11.3 ng (75 -102)
2.0	20	66.5 ± 44.7 ng (34 -174)

S-86

FACTORS AFFECTING THE CONCENTRATION OF CO IN THE BREATHING CIRCUIT AND THE CONCENTRATION OF ARTERIAL COHB DURING LOW-FLOW ISOFLURANE ANESTHESIA IN SMOKING AND NON-SMOKING SUBJECTS

AUTHORS: **M. Yamakage**, S. Yoshida, S. Iwasaki, M. Mizuuchi, A. Namiki;
AFFILIATION: Sapporo Medical University School of Medicine, Sapporo, Japan.

INTRODUCTION: Smokers have a high incidence of postoperative respiratory complications, and smoking can also increase the concentration of carboxyhemoglobin (COHb) up to 5%~10%, leading to cardiac events during anesthesia. Carbon monoxide (CO) can be produced from degradation of isoflurane by soda lime, especially with dry soda lime or by the use of a low-flow anesthetic technique. Some carbon dioxide (CO2) absorbents that contain few or no strong bases have become available for clinical use. We investigated the concentration of CO in the anesthetic circuit and the concentration of arterial COHb during low-flow isoflurane anesthesia in smoking and non-smoking subjects using various kinds of CO2 absorbents with and without strong bases.
METHODS: Sixty ASA physical status I or II adult patients were enrolled in this study. Thirty patients who were smoking up to the operating date and 30 patients who had never smoked were selected as smoker group and non-smoker group, respectively. Anesthesia was maintained with isoflurane and nitrous oxide (1 L/min)/oxygen (1 L/min). Ventilation was controlled to maintain end-tidal partial pressure of CO2 between 34 and 38 mmHg. The end-tidal isoflurane concentrations were adjusted to 1.0%. Each group (smoker or non-smoker group) randomly divided into three groups according to the type of CO2 absorbent used. The CO2 absorbents used were Wakolime A, Dragersorb Free, and Amsorb. Gas samples for measurement of CO (Carbolyzer, mBA-2000) were obtained from the inspiratory limb of the circle system at 0, 1, 2, 3, and 4 hrs after exposure to isoflurane. Concentrations of arterial COHb were measured at the same time as the measurement of CO concentrations in the breathing circuit. Concentrations of CO in the breathing circuit and arterial COHb were compared using linear regression analysis. In all comparisons, $P < 0.05$ was considered significant.
RESULTS: In the smoking groups there were no significant differences in CO concentrations in the circuit between the groups, and the CO concentrations did not change significantly during the study period (3.1 to 48.2 ppm). There were also no significant differences in the arterial COHb values between the groups, and the COHb concentrations remained constant (1.5% to 9.7%). There was a significant linear correlation between the concentrations of CO and COHb ($r = 0.86$, $n = 30$, $P < 0.001$). In the non-smoking groups all of the parameters remained constant at low levels (1-5 ppm and < 2%), and they were independent of the type of CO2 absorbents tested.
DISCUSSION: The major sources for increased intraoperative CO exposure are related to patient attributes, such as smoking status and number of cigarettes smoked before the operation. The results of this study indicate that low-flow isoflurane anesthesia with a conventional CO2 absorbent can be used safely in clinical practice.

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8500 POET® IQ -AN ACCURATE ANESTHESIA GAS MONITOR?

AUTHORS: **P. R. Lichtenthal**, R. G. Loeb, S. E. Morgan;
AFFILIATION: University of Arizona, Tucson, AZ.

INTRODUCTION: While many companies sell respiratory gas monitors, most of these are OEM; only a few companies manufacture gas monitor benches. Criticare Systems, Inc., a longtime manufacturer of gas analyzer benches, recently released a new product, the 8500 Poet® IQ. This sidestream analyzer uses non-dispersive infrared (NDIR) technology to identify and measure CO_2, N_2O and five halogenated anesthetics, and a fast polarographic cell to measure O_2. The object of this study was to determine the accuracy and stability of this new respiratory gas analyzer as compared to an industry-standard analyzer (Datex AS3).
METHODS: For a period of four weeks we conducted daily quality checks on both gas analyzers. Each was calibrated prior to the study by a factory-authorized technician . The analyzers were used clinically during the study period; they were located in the same operating room, and were used simultaneously for every case. Both analyzers were tested every morning for their ability to correctly analyze a series of 9 precision gas mixtures (Scott Medical Products), each of which contained CO_2. The analyzer sample lines were connected to computer-controlled solenoid valves that simulated respiratory rates of 10, 30, 60 breaths per minute by switching the inflow path between test gas and room air every 3, 1, or 0.5 second, respectively. Stable end-tidal values were recorded from each analyzer's display. Data from both analyzers for each of the 9 gases at 3 respiratory rates were collected. The average of the daily readings during the study (mean), day-to-day variation (SD), and the average error (bias) were then calculated.
RESULTS:
• Both analyzers had stable readings over the 4-week course of the study (day to day standard deviation <2%).
• The 8500 Poet® IQ tended to over-read at high CO_2 values (3.5mmHg bias at 74mmHg), while the Datex AS3 tended to under-read at high CO_2 values (-1.5mmHg bias at 74mmHg)
• N_2O slightly decreased CO_2 precision with both monitors (due to N_2O broadening), and decreased CO_2 accuracy of the 8500 Poet® IQ (7.0mmHg bias at 74mmHg)
• Desflurane (8%) dramatically increased the CO_2 rise time of both monitors (as indicated by decreased accuracy at higher respiratory rates), while helium (63%) modestly decreased the CO_2 rise time of both monitors (as indicated by increased accuracy at high respiratory rates)
• Both monitors accurately detected and quantified mixed anesthetic agents (1% sevoflurane and 1% isoflurane)
• The Datex AS3 had a faster O_2 rise time (i.e., increased accuracy at high respiratory rates)
• Water vapor, carbon monoxide (2%), and ethanol vapor (0.13%) did not affected measured gas concentrations with either monitor.

Accuracy ± day-to-day precision, measuring O_2 and CO_2 in 9 test gases (10 breaths per minute)

Test gas CO_2 concentration (mmHg)	8500 Poet measured CO_2 concentration	Datex AS3 measured CO_2 concentration	Test gas O_2 concentration (%)	8500 Poet measured O_2 concentration	Datex AS3 measured O_2 concentration
4.6	5.0 ± 0.0	4.3 ± 1.0	30	29.3 ± 0.6	29.6 ± 0.5
4.6	5.9 ± 0.4	4.1 ± 0.3	30	30.6 ± 0.9	29.9 ± 0.4
4.6	5.0 ± 0.0	4.8 ± 0.8	30	31.9 ± 0.5	30.0 ± 0.9
35	35.1 ± 0.6	35.0 ± 0.7	30	32.1 ± 0.6	30.3 ± 0.5
35	35.2 ± 0.4	34.4 ± 0.5	30	31.6 ± 0.6	27.6 ± 0.5
35	32.3 ± 0.5	31.4 ± 0.5	30	29.5 ± 0.9	29.3 ± 0.6
74	77.5 ± 0.8	72.6 ± 0.5	30	30.3 ± 0.7	29.8 ± 0.4
74	80.9 ± 0.8	73.7 ± 0.7	70	70.5 ± 0.8	64.1 ± 1.5
74	76.9 ± 1.5	72.0 ± 1.1	93	97.9 ± 2.6	91.9 ± 0.4

CONCLUSION: The CSI 8500 Poet® IQ is a stable respiratory gas monitor that accurately measures gas concentrations for at least 4 weeks without recalibration.

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CHARACTERIZATION OF DESFLURANE WITH MASS SPECTROMETRY

AUTHORS: **D. B. Glick**[1], M. Cohn[2], Y. Bryan[3], G. Gautam[3];
AFFILIATION: [1]University of Chicago, Chicago, IL, [2]UOP, Chicago, IL, [3]university of chicago, Chicago, IL.

INTRODUCTION: Because of the size and expense of anesthesia systems that rely on mass spectrometry to gauge agent concentrations, they have been replaced by more compact infrared technology. Infrared technology is well suited for determining the concentration of inhaled and exhaled anesthetic agents in the operating room. When more than one anesthetic agent is in the anesthesia circuit however, infrared analysis is unable to give accurate concentrations of each. Depending on fresh gas flows, an inhaled agent with a long half-life that no longer registers on an infrared system can affect total MAC up to 1 hour after it has been discontinued (1). In such situations, mass spectrometry is clearly superior. Because analysis with mass spectrometry predated the clinical popularity of desflurane, its pattern has not been described in the chemistry or anesthesia literature. We characterized the mass spectrometry fractioning pattern of desflurane.
METHODS: Samples of desflurane were collected in two separate fashions. To evaluate the mass spectrometry pattern for high concentrations, the sample was drawn from a tube containing liquid desflurane. To determine the pattern for clinically relevant concentrations, samples were drawn from the expiratory limb of an anesthesia circuit at end-tidal concentrations of 2%, 4%, and 6%.
RESULTS: The pattern for the high concentration samples resembled the pattern predicted by a standard mass spectrometry modeling program—there was a single spike at 168 (the molecular weight of desflurane). The samples with lower concentrations all had spikes at 51, 69, and 101. There was almost no unfractured desflurane at 168.
CONCLUSIONS: To determine the concentrations of more than one volatile anesthetic agent simultaneously, a system other than an infrared-based monitor must be developed. Mass spectrometry has the potential to provide this information. We have taken the first step in this quantitative undertaking by identifying the mass spectrometry pattern of desflurane at clinically relevant concentrations.
REFERENCE: 1. Anesthesiology 1998; 88:914-21.

S-89

INCREASING DESFLURANE CONCENTRATIONS BY SERIAL CONNECTION OF TWO TEC 6 VAPORIZERS

AUTHORS: **P. E. Otero**[1], M. Rebuelto[1], R. E. Hallu[1], J. Aldrete[2];
AFFILIATION: [1]School of Veterinary Medicine, Buenos Aires, Argentina, [2]Arachnoiditis Foundation Inc., Birmingham, AL.

INTRODUCTION: The inability to reach MAC concentrations of anesthetics with low gas flows has been an impairment for a greater popularity of this approach. A vaporization system capable of rapidly increasing the desflurane concentrations delivered to the circuit, without modifying the FGF, was developed.
METHODS: Two agent-specific, concentration-calibrated, injection, thermo-compensated by heat, vaporizers (Tec 6, Ohmeda, Inc, USA) were calibrated by the manufacturer with oxygen as the carrier gas to deliver 0-18% desflurane(1). Anesthetic concentrations (%) were determined by placing the sampling head from an anesthetic gas analyzer (Oxyanga Eku, Leiningen, Germany) previously calibrated for accuracy, into a corrugated tube (22 mm internal diameter, 60 cm length). When desflurane concentrations were above the maximal limit of accuracy of the gas analyzer (19.9%), the vaporizer output was diluted 1:1 with 100% oxygen. Each vaporizer was tested at 200, 300, 400, 500 and 1000 mL/min at 1, 2.5, 5, 10, 15 and 18 % at the dial settings. Oxygen 100% was used as carrier gas. The first vaporizer received FGF from the oxygen flowmeter and the second vaporizer received as carrier gas the output of the first vaporizer. Wasted gas was eliminated by a gas-scavenging system.
The dial was set to deliver desflurane concentrations of 1, 2.5, 5, 7,5, 10 and 15% for each vaporizer at oxygen flow rates of 200, 300, 400, 500 and 1000 mL/min. Each measurement was repeated 6 times; between measurements the vaporizer was turned off and the oxygen flow rate increased until no anesthetic agent concentration was detected at the exit end of the last vaporizer. Then it was started again. The differences between expected (the simple addition of the maximum values, previously determined for each vaporizer) and the actually measured values were determined. Results are reported as mean ± standard deviation. Results were analyzed using the ANOVA method. Significance was set at a 5% level.
RESULTS: The final outflow of desflurane concentrations increased after connecting serially 2 vaporizers without modifying the FGF; however, the total output was lower than the expected (Figure 1). No difference was noted at every FGF level.
DISCUSSION: The addition of desflurane to the carrier gas of the second vaporizer appeared to modify the expected final concentration that could be due to the Tec 6 vaporizer design as back-pressure is generated prevents the concentration from reaching a precisely double value (2). Desflurane concentrations increased by serially connecting two agent-specific vaporizers without modifying FGF and keeping the vaporizers outside the breathing system. This approach deserves further studies on low flow and closed circuit anesthesia, to reach higher constant and predictable final anesthetic concentrations up to 27%, in the case studied.
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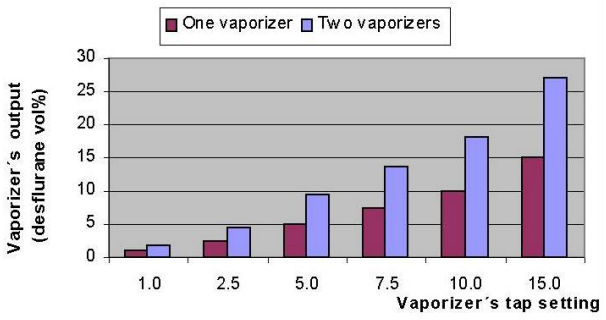

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INCREASING HALOTHANE CONCENTRATIONS BY SERIAL CONNECTION OF FOUR VAPORIZERS

AUTHORS: **P. E. Otero**[1], M. Rebuelto[1], R. E. Hallu[1], J. Aldrete[2];
AFFILIATION: [1]School of Veterinary Medicine, Buenos Aires, Argentina, [2]Arachnoiditis Foundation Inc., Birmingham, AL.

INTRODUCTION: To reach high anesthetic concentrations of halothane (HAL) during induction with low gas flows, a VOC system capable of increasing HAL concentrations delivered to the circuit without modifying the FGF was designed by placing several vaporizers in series.
METHODS: Four agent-specific vaporizers (Muraco Medical Ltd., Japan) were used in this study. Vapour concentrations (%) were determined using an anesthetic gas analyzer (Oxyanga Eku, Germany). Each vaporizer was tested at 0.2, 0.3, 0.5 and 1.0 L/min at its maximal tap setting (4%) for defining the actual gas output. Oxygen 100% was used as carrier gas. Vaporizers were serially connected to each other, increasing in one each time. Thus, the first vaporizer received FGF from the oxygen flowmeter, the second vaporizer received as carrier gas the output of the first vaporizer, and so on.
The dial was set at 4% for each vaporizer at oxygen flow rates of 0.2, 0.3, 0.5 and 1.0 L/min. Each measurement was repeated 6 times.Differences between expected (defined as the simple addition of the maximal actual values previously determined for each vaporizer) and measured values were calculated and possible significant differences were determined by a Students t test. ANOVA was used for comparing vaporizers output for different flows. The significance was set at a 5% level.
RESULTS: The delivered HAL concentration after connecting serially 2, 3 and 4 vaporizers increased with each vaporizer addition, however, the final output was significantly lower than the mathematical expected end result (table 1). Statistically significant differences between 1.0 L/ min flow and other flows were detected.
DISCUSSION: After connecting serially 2, 3 and 4 vaporizers delivered final HAL concentration increased with each vaporizer addition, however, the final output was lower than the expected. This difference may be due to the fact that carrier gas composition for vaporizers 2, 3 and 4 contained partly HAL. It seems that the anesthetic vapour of the carrier gas flow mixes with the anesthetic present in the vaporization chamber, where saturation pressure exists, resulting in the impairment of the carrier gas capability for vaporization (1). The decrease on final concentration was repeated along vaporizers and the influence was higher as the number of connected vaporizers increased. Approximation to final anesthetic concentrations may be calculated by means of the following equation:
Final output$_{1\text{-}4}$ (%) =[(vapour$_d$ Σ 1-4) - (vapour$_e$ Σ $_{2\text{-}4}$) x 100] / [FGF + (vapour$_d$ Σ $_{1\text{-}4}$) - (vapour$_e$ Σ $_{2\text{-}4}$)]
where: vapour$_d$ = vapour delivered by each vaporizer; vapour$_e$ = vapour extracted by each vaporizer.
This technique may be an alternative to rapidly induce inhalation anesthesia with low flow or closed circuit anesthesia, as it provides fairly constant and predictable final anesthetic concentrations.

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Table 1. Mean (SD) halothane output (%)

FGF (Oxigen)	2 vaporizers		3 vaporizers		4 vaporizers	
L / min	expected	mea-sured	expected	measured	expected	measured
0.2	8.72 (0.07)	7.90 (0.06)	11.78 (0.11)	10.97 (0.05)	14.25 (0.10)	13.37 (0.12)
0.3	8.82 (0.07)	7.93 (0.05)	11.97 (0.09)	10.83 (0.09)	14.40 (0.08)	13.32 (0.04)
0.5	8.83 (0.07)	7.88 (0.04)	11.97 (0.09)	10.67 (0.05)	14.35 (0.10)	13.37 (0.05)
1.0	8.62 (0.09)	8.27 (0.05)	11.78 (0.12)	11.37 (0.15)	14.40 (0.12)	13.62 (0.08)

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TEMPORAL PERFORMANCE OF THE T-LINE™ TENSYMETER (CONTINUOUS NON-INVASIVE BLOOD PRESSURE MANAGEMENT DEVICE) VERSUS CONVENTIONAL INVASIVE RADIAL ARTERY TONOMETRY IN SURGICAL PATIENTS

AUTHORS: **G. M. Janelle**[1], S. Gallant[2], A. Butler[3], M. Wilson[3], N. Gravenstein[1];
AFFILIATION: [1]University of Florida, Gainesville, FL, [2]Tensys Medical Inc., San Diego, CA, [3]Tensys Medical, Inc., San Diego, CA.

INTRODUCTION: Tensys Medical, Inc. has introduced the T-line (TL-100) continuous non-invasive blood pressure monitor which produces a beat-to-beat, high fidelity radial arterial pressure (A-line) waveform on any conventional patient monitor with an invasive blood pressure input. The overall accuracy of this monitor in surgical cases as measured against a contra-lateral A-line has been validated. Accuracy data including Bland-Altman and pooled regression data statistics have shown conformance exceeding the AAMI Standards for non-invasive blood pressure monitors. Since the T-Line is a *continuous* monitor which produces a real-time waveform, it is important to know how well the T-line performs over time contrasted to an A-line.
METHODS: After IRB approval and informed consent, 25 adult patients were studied with the following criteria: 1)normal bilateral Allen´s test and 2) left vs. right arm oscillometric mean BP difference < 10 mmHg. The T-line processing algorithms extract, calibrate, and display arterial pressure waveforms from pulsations sensed non-invasively over the radial artery. A T-line sensor was placed over the contralateral radial artery to the A-line. All data were zero referenced to the cranial midline and simultaneously recorded from both the T-line and A-line. Data were sampled at 160hz, imported into a Microsoft Excel database, and separated into 10-beat data sets for comparison with simultaneous A-line values as controls. The sampled recordings were subsequently post-processed for beat-to-beat comparison over the entire surgical period. Specifically, calculations for mean error of mean, systolic and diastolic pressures were made for each 10-minute period of recording. Each 10-minute epoch was then plotted and analyzed using time series analysis. Conventional descriptive statistical measures were also computed for these data.
RESULTS: Cumulative recording time was 35.8 hours, with a range of 10 minutes to 181 minutes per patient. The average duration of recording was 86 minutes; therefore, fewer epochs were analyzed for longer durations. Mean difference of the mean pressure begins at 0.2 mmHg and peaked at 0.5 mm Hg over time (range -0.4 to 0.5 mmHg, Figure 1). Mean differences of systolic and diastolic pressures peaked at 0.8 and 1.3 mmHg over time, respectively. There were no significant differences in errors over time compared to baseline measurements in systolic, mean, or diastolic pressures.
CONCLUSIONS: There is no degradation in accuracy or performance over the course of monitoring with the use of the T-line system compared to A-line measurements. Furthermore, the T-line requires no incremental maintenance such as saline flushing of an indwelling catheter, catheter repositioning, or other interventions to maintain patency or reduce the possibility of infection.

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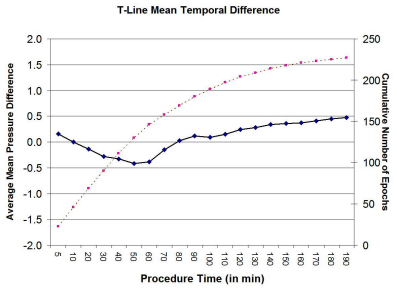

S-92

EVALUATION OF EAR TRANSMISSION AND FOREHEAD REFLECTANCE OXIMETRY IN INTRAOPERATIVE SURGICAL PATIENTS

AUTHORS: **D. T. Redford**, P. Lichtenthal, S. J. Barker;
AFFILIATION: University of Arizona, Tucson, AZ.

INTRODUCTION: Pulse oximetry is the standard of care in the operating room and ICU. Recent studies have demonstrated potential differences in response time for detection of adverse events between finger and forehead sensors. This study evaluates the accuracy and reliability of the new Max-Fast forehead sensor, used with the Nellcor N595 oximeter, compared to a new ear sensor, the Tip Clip (TC-I), used with a Masimo SET Radical oximeter, in stable surgical patients.
METHODS: Following IRB approval, 17 adult surgical patients undergoing general anesthesia were enrolled prospectively. Probes from 4 pulse oximeters were attached; Nellcor N595 with the Max-Fast forehead sensor, Nellcor N200 with the D25 finger sensor, Masimo SET Radical with the Adt LNOP finger sensor and the Masimo SET Radical with the TC-I ear sensor. The digit sensors were optically shielded from one another. SpO2 and pulse rate values from these oximeters were recorded digitally to a laptop computer at a frequency of 1Hz. The mean of the two digit sensors was calculated, as were the bias and precision. Error was defined as the difference between the forehead sensor or the ear sensor and the mean of the 2 digit sensors during stable patient conditions. The bias (mean error), precision (SD of the error) and E7% (% of time that the error was > 7% in stable conditions) were calculated for the forehead sensor and TC-I. Paired t-tests were used to compare values, with significance determined by $p<0.05$.
RESULTS: Data are presented as mean (±SD). The mean age of the patients was 48 (±16) years. The mean length of surgery was 75 (±26) minutes. The mean bias and precision of the digit sensors were -0.1 (±0.9) and 0.5 (±0.4) respectively. The mean bias and precision of the forehead sensor were –4 (±7) and 3 (±5) and for the TC-I were -0.5 (±0.8) and 0.7 (±0.4). The mean E7 differed between the forehead [13 (±26)] and TC-I [1 (±2)], sensors $p=0.035$. In 18% of patients, the forehead E7% was greater than 20% of the duration of the surgical procedure while the ear E7% was never greater than 20%.
DISCUSSION: Studies from 12 years ago reported that reflectance oximetry sensors performed poorly(1). Despite advancements in technology, this study demonstrates similar poor performance of the forehead reflectance pulse oximeter. The Max-Fast sensor attached to the N595 oximeter demonstrated an unacceptable bias and precision and was in error by more than 7% for more than 20% of the total operative time in 18% of patients. In contrast, the TC-I sensor performed well with a small bias and precision.
REFERENCES: 1) J Clin Monit 1991; 7:102-103

S-93

INTRAOPERATIVE PERFUSION CHANGES AT TWO PULSE OXIMETRY MONITORING SITES: THE DIGIT VS. THE NARE

AUTHORS: **D. T. Redford**, P. Lichtenthal, S. J. Barker;
AFFILIATION: University of Arizona, Tucson, AZ.

INTRODUCTION: Routine monitoring of the surgical patient includes pulse oximetry. Most commonly the sensor is attached to a digit. Intraoperative changes in peripheral perfusion may occur, especially in patients in whom the body temperature is not maintained. As peripheral temperature decreases, peripheral perfusion may also decrease. It is possible, although uncommon, that this decrease may cause difficulties in monitoring pulse oximetry. Therefore an alternate monitoring site should be available. Here, we evaluate the nare as a potential alternate site. We evaluated changes in perfusion to the digits and the nares in surgical patients, using the Perfusion Index (PI), as measured by the Masimo SET Radical pulse oximeter (Masimo, Irvine, CA).
METHODS: Following IRB approval, 17 adult surgical patients undergoing general anesthesia were enrolled prospectively. In addition to routine monitoring, sensors from 2-pulse oximeter were attached. The Masimo Adt LNOP sensor was attached to a finger and the Masimo TC-I sensor was attached to a nare. Each probe was attached to a Masimo radical oximeter. The PI values from these two oximeters were recorded digitally to a laptop computer at a frequency of 1Hz. The change in PI from the beginning of the case to end of surgery was calculated for each monitoring site. Paired t-tests were used to compare values, with significance determined by $p<0.05$.
RESULTS: Data are presented as mean (± SD). The mean age of the patients was 48 (±16) years. The mean length of surgery was 74.8 (±26.1) minutes. The PI for the finger was 6 (±2) at the beginning of the case and decreased by 2 (± 3) at the end of the case. The PI for the nare was 2.0 (±0.9) at the beginning of the case and decreased by 0 (± 2) at the end of the case. The decrease in the digit was significantly greater than that of the nare, $p<0.001$.
DISCUSSION: We evaluated the perfusion to the digit and the nare simultaneously in surgical patients. Although the surgery was of short duration, we found statistically significant decreases in perfusion to the digits. This decrease may not be clinically significant. However, in longer cases or in more critically ill patients such changes may become clinically significant. In contrast, we demonstrated no change in perfusion to the nare during surgery. Although further research is needed in critically ill patients, these data suggests the nare may be a useful alternate site for monitoring pulse oximetry, as perfusion is maintained to this site.

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EVALUATION OF THE NARES AS A SITE FOR OXIMETRY MONITORING IN INTRAOPERATIVE SURGICAL PATIENTS

AUTHORS: D. T. Redford, P. Lichtenthal, S. J. Barker;
AFFILIATION: University of Arizona, Tucson, AZ.

INTRODUCTION: Routine monitoring of the surgical patient includes pulse oximetry. Most commonly the sensor is attached to a digit. There are times when peripheral perfusion is low, causing poor monitor performance. Therefore we evaluated the new Masimo Tip Clip sensor (TC-I) for use in a new site, the nare.
METHODS: Following IRB approval, 17 adult surgical patients undergoing general anesthesia were enrolled prospectively. Four pulse oximeters and sensors were attached; Nellcor N200 with a D25 finger sensor, Masimo SET Radical with an Adt LNOP finger sensor, Masimo SET Radical with a TC-I ear sensor and the Masimo SET Radical with a TC-I nare sensor. The digit sensors were optically shielded from one another. SpO2 and pulse rate values from these four oximeters were recorded digitally to a laptop computer at a frequency of 1Hz. The mean of the two digit sensors was calculated, as were the bias and precision of the two sensors. Error was defined as the difference between the ear or the nare sensor and the mean of the 2 digit sensors during stable patient conditions. The bias (mean error) and precision (SD of the error) as well as the E7% (% of time during which the error was greater than 7% in stable conditions) were calculated for the ear and the nare sensors. Paired t-tests were used to compare values, with significance determined by $p < 0.05$.
RESULTS: Data are presented as mean (± 75). The mean age of the patients was 48 (±16) years. The mean length of surgery was (±26) minutes. The mean bias and precision of the digit sensors were -0.2 (±0.9) and 0.5 (±0.4) respectively. The mean bias and precision of the ear sensor were –0.5 (±0.7) and 0.7 (±0.4) respectively. Similarly, the bias and precision for the nare sensor were –0.2 (±0.7) and 1 (±1). The mean E7 was 1 (± 2) minutes for the ear and 0.7 (±1) minutes for the nare, p=0.28. In none of the 17 patients was E7% greater than 20% of the duration of the procedure.
DISCUSSION: In this population of patients the bias and precision of the TC-I was similar whether it was placed in the nare or on the ear. Both the ear and the nare sites demonstrated very small E7%, indicating a high degree of monitoring reliability for both of these sites. The E7% for the nare site tended to be lower than the ear, although this did not reach statistical significance. Our data demonstrate the nare and the ear may both be useful as sites for monitoring patients who are otherwise difficult to monitor using pulse oximetry.

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THE UTILITY OF GOAL-DIRECTED INTRAOPERATIVE FLUID ADMINISTRATION USING THE HEMOSONIC TRANSESOPHAGEAL DOPPLER MONITOR IN WHIPPLE PROCEDURES

AUTHORS: L. A. Fleisher, M. A. Kalish, C. Krug, A. J. Rowlingson;
AFFILIATION: Johns Hopkins University School of Medicine, Baltimore, MD.

INTRODUCTION: Goal-directed intraoperative fluid adminstration using a transesophageal doppler monitor has recently been shown to decrease hospital length of stay in one randomized trial involving a mixed group of general, gynecologic and urologic surgery associated with a blood loss >500cc .(1) These results need confirmation before they are diffused. Therefore, we performed a small pilot study in patients undergoing one type of major abdominal surgery and compared our results to historical controls.
METHODS: A total of 10 patients undergoing a Whipple procedure were studied. Intraoperative volume expansion was guided by the esophageal doppler (Hemosonic device, Arrow International) to maintain maximal stroke volume. This cohort was compared to 45 patients who underwent the procedure during the same time period but were only monitored with a central venous pressure catheter.
RESULTS: The Hemosonic group had an average age of 63 $\pm$ 9 years, which was similar to the controls (63 $\pm$ 12 years). The Hemosonic group had a larger percentage of females (70% versus 38%). Surgery lasted an average of 6.2 $\pm$ 1 hour with an EBL of 1095 $\pm$ 774 cc in the Hemosonic group. Postoperative length of stay (LOS) was reduced in the Hemosonic group (8.5 $\pm$ 2.3 days) compared to historical controls (10.7 $\pm$ 7.2 days).(p=N.S.) The median LOS was 8.4 and 8.0 days, respectively in the Hemosonic and Control groups. Thus, for the 'typical' patient, there was no effect. However, the maximum LOS were 13 and 49.0 days, respectively, for HemoSonic and Control patients. Similarly, the 75th percentile values were 9 and 12, respectively. Thus, 25% of Control LOS were above 12 days while 1 patient (10%) of the Hemosonic study group had LOS that exceeded 12 days.
CONCLUSIONS: Our pilot study suggests that goal-directed intraoperative fluid adminstration with a transesophageal doppler is associated with a reduced incidence of prolonged LOS in Whipple sugery. Therefore, the economic benefit of HemoSonic may be through its ability to reduce the
likelihood of extended stays presumably by reducing the likelihood of adverse events. This is where the potential benefit for reducing health case costs may be realized. A large scale randomized trial is required to confirm these and previous findings.
(1) Anesthesiology 2002;97:820-6

S-96

NEAR INFRARED SPECTROSCOPY DURING DEFIBRILLATOR THRESHOLD TESTING

AUTHORS: K. Skhirtladze, G. Tenze, G. Reining, M. Weigl, M. Czerny, **M. Dworschak**;
AFFILIATION: University Hospital Vienna, Wien, Austria.

BACKGROUND: Intermittent interruptions of the cerebral perfusion during defibrillator (ICD) threshold testing has been implicated with ischemia-typical EEG changes and a drop in jugular venous oxygen saturation (SjO_2)(1,2). Cerebral oxygen saturation (ScO_2) determined by near infrared spectroscopy (NIRS), a non-invasive method to evaluate brain oxygenation, also drops after induction of ventricular fibrillation. Preliminary data indicate that patients with low cardiac output show increased release of neuron specific enolase after ICD testing as compared to patients with a normal output (3). However, the association between cerebral desaturation and ventricular pump function during ICD testing has not yet been evaluated.
METHODS: We studied 34 consecutive patients who had to undergo elective ICD placement because of drug refractory ventricular fibrillation. Cardiac output was determined preoperatively either by echocardiography or by ventriculography. Depending on their calculated ejection fraction (EF), patients were assigned to either the "normal" (EF > 30%, n = 21) or the low cardiac output group (EF < 30%, n = 13). The NIRS optode (INVOS 3100A) was attached to the right forehead and ScO_2 readings were continuously monitored throughout the procedure. They were stored on a computer when stable for off-line analysis. Before induction of ventricular fibrillation, the spontaneously breathing patients received 0.1 mg/kg etomidate IV and respiration was assisted to achieve $petCO_2$ values in the normal range.
RESULTS: With administration of supplemental oxygen (4 l/min) via facemask, there was no statistically significant difference between groups in regard to baseline ScO_2 (70 vs. 68%, P = NS). Changes from baseline, but not absolute values, were weakly correlated with the duration of cardiac arrest for all patients (r^2 = 0.11, P = 0.002). This association, however, was much greater in patients with EF < 30% (r^2 = 0.48). The degree of cerebral desaturation during fibrillation was similar in both groups during the first episode of cardiac arrest (-3.7 vs. -3.2%, P = NS) but appeared to be less marked during subsequent fibrillations in low cardiac output patients.
CONCLUSION: During ICD testing, the degree of cerebral desaturation seems to be closer associated with the duration of arrests in patients with decreased left ventricular pump function. Over-reading of ScO_2 by INVOS 3100 at low (< 60%) and under-reading at high SjO_2 (> 60%) possibly contributed to our results (4). These findings most likely reflect a diminished recovery of cerebral oxygenation in the low output group in conjunction with regional redistribution of cerebral blood flow (5). This would make these patients more susceptible for neurologic injury and could explain the tendency towards a greater release of neuron specific enolase after ICD testing.
REFERENCES: 1) J Clin Monit 1997,13:303; 2) J Thorac Cardiovasc Surg 1995,109:565; 3) Crit Care Med 2003,31:2085; 4) Anaesthesia 1998,53:13; 5) JACC 1999,33:1196

S-97

THE COMPARISON OF PULSE AMPLITUDE VARIABILITY OF FOREHEAD SENSING AND FINGER SENSING PULSE OXIMETER DURING INCREASED CARDIAC SYMPATHETIC ACTIVITY

AUTHORS: **M. Oshiro**, K. Kamizato, S. Abe, M. Kakinohana, K. Sugahara;
AFFILIATION: University of the Ryukyus, Okinawa, Japan.

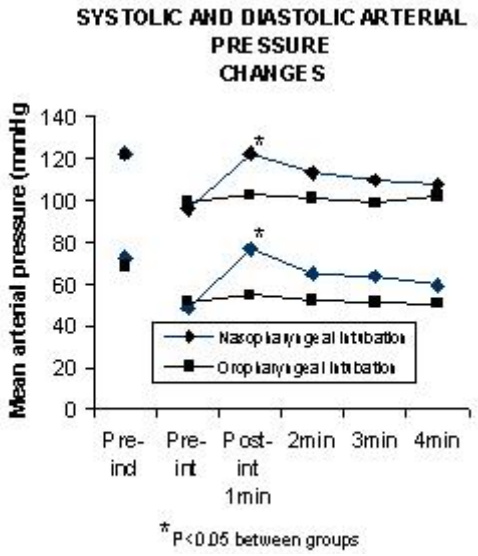
INTRODUCTION: Finger sensing pulse oximeter is very useful monitor for observation of patient's oxygenation status. However, sometimes it cannot detect patient's peripheral pulse waves due to peripheral vasoconstriction associated with increased sympathetic activity. Forehead sensing pulse oximeter became available recently, which was reported its effectiveness even in the patient with peripheral vasoconstriction. We therefore compared pulse amplitude variability of forehead sensing and finger sensing pulse oximeter during increased cardiac sympathetic activity induced by cold stimulation, and then verified its effectiveness.
METHODS: After obtaining written informed consents, 7 adult volunteers were studied. Heart rate variability (HRV) (Mem Calc ™; Suwa Trust, Tokyo, Japan), forehead sensing pulse oximeter (N-595; Nellcor, US) and finger sensing pulse oximeter (M-1020A; HP, US) were monitored. Pulse amplitude was monitored by a personal computer (PowerBook G3; Apple Computer, US) through MacLab (AD Instruments, US) attached to pulse oximeter. Before and after cold stimulation by ice put on abdominal skin for 10 seconds, we measured the ratio of Low-frequency component (LF; cardiac sympathetic activity) to high-frequency component (HF; cardiac parasympathetic activity) in HRV and pulse amplitude of forehead and finger. Data are presented as mean ± SD, paired t-test was used to analyze each variability and p-value < 0.05 was considered statistically significant.
RESULTS: Measurement was done twice on each patient, total 14 times. After cold stimulation, LF to HF ratio was significantly increased from 1.26 ± 1.46 to 2.30 ± 2.67, (p=0.049). pulse amplitude of forehead was also significantly increased from 331.4 ± 34.7 to 356.8 ± 16.5 mV, (p=0.027). On the other hand, amplitude of finger was significantly decreased from 5.15 ± 0.34 to 3.58 ± 0.59 V, (p<0.0001).
CONCLUSION: Our results suggest that forehead sensing pulse oximeter is more effective than finger sensing pulse oximeter to detect peripheral pulse waves during increased cardiac sympathetic activity.

S-98

PRESSOR RESPONSES TO THE INSERTION OF OROPHARYNGEAL AND NASOPHARYNGEAL AIRWAYS

AUTHORS: **J. L. Tong**, J. E. Smith;
AFFILIATION: University Hospital Birmingham, Birmingham, United Kingdom.

INTRODUCTION: Oropharyngeal and nasopharyngeal airways are widely used to help maintain patent airways in anesthetized or comatose patients. The pressor response to the insertion of oropharyngeal airways has been found to be of little clinical significance (1), but the response to the insertion of nasopharyngeal airways has not been investigated. This study aimed to compare the cardiovascular responses to the insertion of oropharyngeal and nasopharyngeal airways.
METHODS: After local Ethics Committee approval and informed consent, 24 patients, ASA status 1 or 2, aged 16 to 65 years, requiring nasotracheal intubation for elective maxillofacial surgery under general anesthesia, received a standardized anesthetic comprising fentanyl, propofol, atracurium and isoflurane in oxygen and nitrous oxide. After 3 minutes bag-mask-valve ventilation, patients were randomly allocated to receive either a Guedel oropharyngeal airway or a nasopharyngeal airway. After the insertion, patients' lungs were ventilated for 4 more minutes. Indirect arterial pressure and heart rate measurements were taken at one minute intervals. The maximum arterial pressures and heart rates were analyzed using t-tests. Within group data were analyzed using repeated measures ANOVA.
RESULTS: The two groups were similar with respect to age, weight and sex distribution. There was a significant decrease in systolic pressure following the induction of anesthesia. Following nasopharyngeal intubation, there was a significant rise in systolic pressure (Post-int) above pre-intubation (Pre-int) levels, though not above pre-induction (Pre-ind) levels. There were no significant changes in the oropharyngeal intubation group. At one minute post-intubation, systolic pressure in the nasopharyngeal intubation group was significantly greater than that in the oropharyngeal intubation group. Diastolic pressure followed a similar pattern. In both groups, heart rates fell after induction and fell further after intubation, and at 4 minutes post-intubation, were significantly lower than pre-induction and pre-intubation levels. There were no significant differences in heart rates between the two groups.
DISCUSSION: Stimulation of the nose and nasopharynx may account for the significant hypertensive response to nasopharyngeal intubation. Anesthesiologists should be aware that this could have an adverse effect in patients with poorly controlled hypertension, critical myocardial ischaemia or raised intracranial pressure (2).
REFERENCES: (1). Anaesthesia 1990; **45:** 629-33. (2). Anesth Analg 1975; **54:** 687-90.



S-99

COMPARISON BETWEEN THE PAXPRESS™ AND THE PROSEAL™ LARYNGEAL MASK AIRWAY DURING GENERAL ANESTHESIA

AUTHORS: **A. Lallo**, M. Lacroix, P. Drolet;
AFFILIATION: University of Montreal, Montreal, PQ, Canada.

INTRODUCTION: The Paxpress (PAx) is a new pharyngeal airway device consisting of a curved tube with a gilled tapered distal tip. Ventilation occurs through an open rectangular hooded window in the front. Airway seal is provided by an oropharyngeal low pressure cuff. It has been shown to be an easily inserted, effective airway device (1). The purpose of this prospective, randomized study is to compare the efficacy of the PAx with that of the Proseal laryngeal mask airway (PLMA) during anesthesia in terms of ease of insertion, efficacy of seal, adequacy of ventilation and incidence of regurgitation.
METHODS: Patients undergoing elective surgical procedures under general anesthesia were randomized to receive either the PAx (n=50) or the PLMA (n=50). Each patient swallowed a methylene blue capsule prior to anesthesia. Induction was standardized using fentanyl, propofol and rocuronium. The study devices were inserted by a single experienced user 2 minutes after muscle paralysis. Insertion time and number of attempts were noted. Oropharyngeal leak pressures were measured at 50% and 100% of the maximum recommended cuff volumes for each device. A fiberscope was used to evaluate and grade the view of the glottis through the device. Volume-controlled ventilation at 10 ml/kg was then instituted. Peak airway pressure and end-tidal CO2 were noted two minutes later. Anesthesia was maintained with sevoflurane 1 to 1.5 MAC. Airway devices were removed when the patients regained conciousness, and were inspected for blood or methylene blue staining. A structured interview was conducted 24 hours after surgery to evaluate the presence of sore throat, dysphagia and dysphonia.
RESULTS: The two study groups were comparable with respect to demographic characteristics and duration of surgery. Insertion time was longer for the PAx than for the PLMA. There was no statistical difference in the number of attempts or the failure rate between the two groups. The oropharyngeal leak pressure was higher for the PLMA at 50% but not at 100% of the maximum recommended volumes. There was no difference with respect to the incidence of blue stains on parts of the devices in direct contact with the airway. Blood was seen more often on the device and dysphagia was more frequent and more severe in the PAx group.
DISCUSSION: The PAx is an acceptable alternative to the PLMA for positive pressure ventilation during routine surgery. However, it takes slightly more time to insert and is associated with higher peak airway pressures and end-tidal CO2. The PAx is also more traumatic and is associated with more postoperative discomfort than the PLMA.
REFERENCES: (1)Can J Anesth, 50, 495-50, 2003

Variable		PAx	PLMA	P value
Insertion time (s)		52±44	34±23	0.0003
Attempts (1/2/3/Failure)		38/8/2/2	42/5/1/2	NS
Oropharyngeal leak pressure				
-50% recommended volume		18±8	22±7	0.016
-100% recommended volume		27±7	30±7	NS
Fiberscopic view of the cords (obstructed 1/2/3/4 unobstructed)		8/16/9/15	4/10/19/15	NS
Peak airway pressure (cmH2O)		19±6	16±4	0.0268
EtCO2 (mmHg)		33±4	31±3	0.04
Blood on device (yes/no)		28/20	9/39	0.0001
Blue stains upon removal (yes/no)		5/43	4/44	NS
24h postoperatively (none /light /moderate/ severe)	Dysphagia	10/13/15/6	24/15/7/2	0.002
	Dysphonia	27/11/6/0	33/12/2/1	

S-100

COMPARISON OF THE POLYVINYL CHLORIDE TRACHEAL TUBE VS. THE SILICONE TRACHEAL TUBE IN AIRWAY MANAGEMENT WITH THE INTUBATING FASTRACH-LMA

AUTHORS: **A. Patel**, R. Dorian, J. Chen, L. Rodriguez;
AFFILIATION: St.Barnabas Medical Center, Livingston, NJ.

INTRODUCTION: The Fastrach intubating laryngeal mask airway has become an invaluable tool in anesthesiology for the management of difficult airways. This randomized, prospective, comparative study was undertaken to test our hypothesis that a standard polyvinyl chloride tube can be used as an effective alternative to the pre-packaged silicone tube.
METHODS: One hundred patients were randomly allocated into two groups undergoing general anesthesia. Intubation was attempted with the Fastrach LMA using either a PVC tube, using a modified method of insertion, or with the standard silicone tube packaged with the Fastrach LMA. The number of attempts, failures, adverse events and level of training was recorded. The number of attempts was up to four per patient, at which time another method for securing the airway was elected. Data was analyzed using the two tail independent t-test. Frequency values were analyzed using the Chi-Square test.
RESULTS: The Fastrach LMA effectively established an airway in all patients. The successful intubation rates (83% in the PVC group and 80% in the silicone tube group) were not statistically different.
DISCUSSION: In 1997, Brain 1 introduced the blind intubating technique through the Fastrach LMA. This technique has had success rates that have varied between 70- 99%. Our study demonstrated that a standard PVC tube (with a success rate of
83 %) could be used as an effective alternative to the pre-packaged silicone tube.
REFERENCES:
1: Brain AI, Verghese C, Addy EV, and Kaplan A, Brimacombe J: The Intubating LMA I: Development of a new device for intubation of the trachea. Br. J Anaesth. 1997; 79: 699-703.

Parameters	n	Age (yrs)	Successful intubations		Failed intubations		P value
			n	%	n	%	
Silicone tube	51	48.7	41	(80.39)	10	(19.61)	P = 0.638 (not significant)
PVC Tube	49	42.4	41	(83.67)	8	(16.33)	

S-101

COMPARATIVE EVALUATION OF A STANDARD MACINTOSH BLADE AND A MODIFIED VIEWMAX BLADE

AUTHORS: **D. Song**, M. A. Hamza, P. F. White;
AFFILIATION: UT Southwestern Medical School, Dallas, TX.

INTRODUCTION: The availability of a laryngoscope blade that could improve visualization of the glottic structures without requiring excessive force for tracheal intubation would be helpful in reducing the perioperative morbidity and mortality related to a difficult laryngoscopy (1). The Viewmax® laryngoscope blade (Rusch Inc., Duluth, GA/ Truphatek International Limited, Israel) is a modified laryngoscope blade that incorporates an unmagnified optic side port to a standard Macintosh (MAC) blade. This modification allows for an alternative direct view of the glottis from a position 1 cm behind the left tip of the blade while still allowing the standard direct view provided with a MAC-3 blade (2).
METHODS: Following IRB approval and informed consent, 12 ASA status 1-2 females undergoing surgical procedures requiring general anesthesia and trachea intubation were enrolled in this ongoing study. The preanesthesia airway evaluation included thyromental distance, sternomental distance and maximal mouth opening distance. Anesthesia was induced with propofol 2 mg/kg IV and fentanyl 50-100 µg IV, followed by rocuronium 0.6 mg/kg IV for muscle relaxation. According to the last digit (odd or even) of patients' hospital ID number, either the standard MAC-3 or Viewmax blade was first chosen for laryngoscopy. After viewing the larynx structure (without intubation), the first blade was withdrawn and the second blade (MAC or Viewmax) was used to repeat the laryngoscopy. A strain gauge handle (Model MG100, Truphateck®) was used with both the blades to measure the peak axial forces applied by the anesthesiologist along the handle (vertically) during the laryngoscopy. After viewing the larynx structure with the second blade, tracheal intubation was performed. The grades of view of larynx structure during the laryngoscopy were classified as: Grade 1 = most of the glottis is visible (including anterior and posterior commissure); Grade 2 = only posterior portion of the glottis is visible; Grade 3 = only the epiglottis is visible; and Grade 4 = only the soft palate is visible. In addition, anesthesiologist's satisfaction with the Viewmax laryngoscope was evaluated with a verbal rating score from 0 (minimum) to 100 (maximum). Data were analyzed using paired t-test, with a p- value less than 0.05 considered statistical significant (mean±SD).
RESULTS: The patients' demographic characteristics include age 51±15 yr, height 158±5 cm, weight 72±18 kg, thyromental distance 9.6±1.2 cm, sternomental distance 16.2±1.7 and maximal mouth opening 5.4±0.8 cm. The results of laryngoscopic views and peak intubation forces are summarized in the table:

	MAC-3 blade	Viewmax blade
View of larynx Grade 1 (n)	6	5
View of larynx Grade 2 (n)	6	7
View of larynx Grade 3 and 4 (n)	0	0
Peak force (KgF)	11.9±5.9	9.1±5.3 *
Satisfaction (0-100)		79±23

* = P<0.05
DISCUSSION: Use of the Viewmax blade was comparable to the MAC-3 blade but associated with less applied forces during the laryngoscopy procedure.
REFERENCES: 1) Biboulet, et al. Can J anaesth 2001; 48: 326-32. 2) Markowitz, et al. J Clin Anesth 2002; 14: 604-7.

S-102

TRUVIEW^{R} BLADE IMPROVES LARYNGEAL VIEW AND REDUCES AIRWAY TRAUMA IN COMPARISON TO MACINTOSH BLADE – A PRELIMINARY REPORT

AUTHORS: **N. Lieberman**, H. Abu Ras, L. Lemberg;
AFFILIATION: Hillel-Yaffe Medical Center, Hadera, Israel.

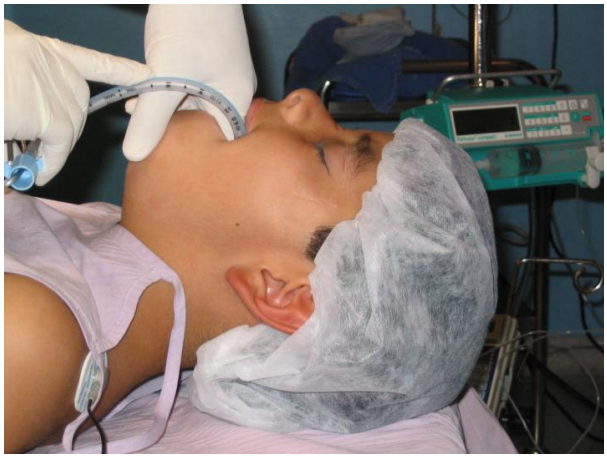
INTRODUCTION: Sore throat is a well known complication of laryngoscopy and intubation and is a sign of airway trauma (1). The optical system of the new Truview^{R} blade, (Truphatek,Israel) offers the possible advantage of improved laryngeal view (LV) and was already shown to facilitate intubation in situations of difficult intubation in a previous study (2). The aim of the study was to compare the force applied and signs of airway trauma for Truview^{R} (TV) and Macintosh (M) blades in healthy patients undergoing general anesthesia.
MATERIAL AND METHODS: After obtaining human experiments committee approval, healthy 18-80 years old, elective surgical patients undergoing general anesthesia and intubation were included in a prospective and randomized comparison. Excluded were patients with expected intubation problems. For each case the best laryngeal view obtained (BLV), force used, time to intubation (TTI), anesthesiologist satisfaction (on a scale of 1-10) and signs of trauma (immediately, in the PACU, and 24 hours later) were recorded for TV and M blades. Two tails student T-test was used to determine the significance of the difference in the mean value for each parameter measured. $P<0.01$ was considered significant.
RESULTS: After signing the informed consent 14 males and 8 females, ASA I and II were randomly assigned to laryngoscopy and intubation with TV or M blades. A single consultant (ARH) performed all laryngoscopies. The average age, weight, and height, were 35 ± 13years, 77.9 ± 18kg and 172 ± 9.8cm accordingly. We found a significantly greater subjective grade of ease of intubation and satisfaction when using the TV compared to M (9.8 ± 0.4 vs. 7.2 ± 2.2 and 9.9 ± 0.3 vs. 7.2 ± 2.2 respectively, $p< 0.01$). The BLV was significantly better with the TV (1 ± 0) compared with the M (2 ± 0.7) ($p<0.0001$). The force used during intubation was greater with the M (6.9 ± 1.9 kg) as were time to BLV (9.4 ± 6.6sec), and TTI (16.1 ± 8.3sec) when compared to TV (6.5 ± 1.0kg, 5.4 ± 3.3sec, and 8.3 ± 4.1sec accordingly), although not reaching statistical significance. In 2 out of 13 patients intubated with the M blade there were trauma signs (immediate and delayed), none in the TV group.
DISCUSSION: The new blade TV caused less trauma and improved visualization and the anesthesiologist satisfaction was greater when compared to the Macintosh blade.
REFERENCES: 1. Br J Anaesth;1987;50:587
2. Lieberman N, accepted for presentation in the next ASA meeting

S-103

DIGITAL INTUBATION TODAY: AN UNDERESTIMATE TECHNIQUE WITHIN REACH OF YOUR HAND

AUTHORS: **J. C. Kling**, F. Ariza, S. Pino;
AFFILIATION: Fundacion Cardioinfantil, Bogota, Colombia.

INTRODUCTION: Digital intubation is one of numerous techniques of blind intubation that had been described many years ago, which has been replaced by modern techniques, although it is an alternative for some advance vital support guidelines without laryngeal reflexes. The objetive of this work is to evaluate the efficacy, applicability and hemodynamic response to digital intubation on surgical patients in comparison to direct laryngoscopy to determine its usefullness at present time.
METHODS: This is a randomized controlled prospective trial involving 80 patients over 12 years old for elective surgery in which general anesthesia with endotracheal intubation was required, excluding those who had indications for rapid sequence or direct vision intubation, those who were under effects of beta-adrenergic antagonists and calcium entry blockers. We evaluated the airway predictors. After standarized induction of anesthesia, were randomizing each patient to one group (Group 1= Digital intubation, Group 2= Direct Laryngoscopy). Blood pressure and heart rate had been recorded an the intubation procedure had done, after that, we registered again the hemodynamic values, as well as the time spent on the procedure. The ubication of tube was confirmed (by touch in group 1 and by auscultation in group 2) and recorded too. Both procedures had done by skilled professionals.
RESULTS: There is not any significative differences between both around demographic and airway caracteristics. The average spent at the intubation procedure was 28 sec for digital intubation and 22 sec for laryngoscopy group. It had not been esophagical intubation in any groups; in digital intubation group were aborted 6 procedures because of technical difficulties to touch the arytenoids cartilages, while in the laryngoscopy group were aborted 3 procedures, because of difficult laryngoscopy. Digital confirmation method was a succesfull in all cases. The average finger longitude of the operator was 8.1 cms. The hemodynamic values have had a ($P<0.001$) for blood pressure and heart rate. There has not been any complications derivated from the procedure.
DISCUSSION: Digital intubation technique is valid, even on adults and pediatrics patients, in easy or difficult airways, expected or not, without important hemodynamic changes, neither complications. It is only limitation in some patients is constituted by the finger longitude of the operator. Digital confirmation method of tube ubication is highly sensitive.
It is important to have in mind digital intubation on difficult situations like a useful tool, because literally on those cases **we could have the solution in our hands.**
REFERENCES: Sutera PT, Gordon GJ. Digitally assisted tracheal intubation in a neonate with Pierre Robin Syndrome. Anesthesiology 1993; 78: 983-4.



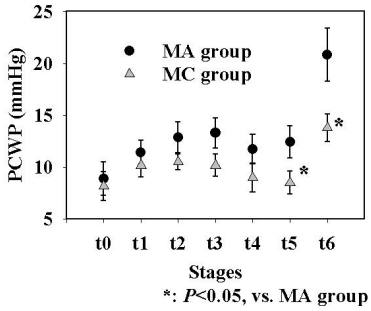
S-104

CARDIOVASCULAR CHANGES INDUCED BY LARYNGOSCOPY IN PATIENTS UNDERGOING CABG SURGERY

AUTHORS: **H. Hino**[1], T. Tateda[1], I. Yamanaka[1], T. Suzuki[2], K. Asano[2];
AFFILIATION: [1]St. Marianna Univ.School of Medicine, Kawasaki, Japan, [2]Saitama Medical Center / School, Kawagoe, Japan.

INTRODUCTION: Laryngoscopy and tracheal intubation often cause marked sympathetic response, resulting in catastrophe in CABG patients. Cardiovascular responses to laryngoscopy are reported in normal patients but not in CABG patients. Our aim was to evaluate whether the McCoy (MC) blade attenuates blood pressure response better than the Macintosh (MA) blade by measuring pulmonary artery pressures and serum catecholamine levels.
METHODS: With IRB approval, 13 patients undergoing CABG were randomly assigned to the MC group (n=6) or MA group (n=7). We attached electrocardiogram (ECG) electrodes and noninvasive blood pressure cuff and then cannulated a radial artery and right internal jugular vein under local anesthesia to continuously monitor systolic arterial pressure (sAP), central venous pressure, mean pulmonary artery pressure (mPA), and pulmonary capillary wedge pressure (PCWP). Heart rate (HR) was calculated from ECG lead II. Data measured pre-induction were considered baseline data. Anesthesia induction was standardized to fentanyl 2 mcg/kg, midazolam 0.04 mg/kg, and vecuronium 0.1 mg/kg under 100% oxygen. Three min after induction, the laryngoscope was inserted and the epiglottis elevated for 20 sec with no mechanical response to right ulnar nerve train-of-four ratio stimulation. Experimental stages were t0=before induction, t1=after induction, t2= laryngoscope insertion, t3=1 min after t2, t4=3 min after t2, t5=5 min after t2, and t6=intubation. All data was recorded by an observer blinded to the blade type used. Serum catecholamine (adrenaline, noradrenaline, and dopamine) levels were measured 1 min after induction and 2 min after insertion. Data were analyzed by ANOVA. P<0.05 was considered significant.

RESULTS: There were no differences in patient demographics or between-group baseline values. MC group showed significantly less increase in sAP during laryngoscopy (106.33±5.26 mmHg) than did MA group (147.86±4.66 mmHg, P<0.05). Reduction in MC group blood pressure was seen at t3 and t5, but increase in blood pressure was not inhibited during t6. There was no significant difference in between-group HRs at all stages. Increase in PCWP at t5 and t6 was significantly less in MC group (Figure). mPA at t5 was significantly less in MC than MA group but not during the intubation phase. There was no significant difference in mean percent change of noradrenaline and dopamine concentration between groups after laryngoscopy, but greater inhibitory effect in the percent change rate of epinephrine concentration was seen in MC versus MA group (MC, 64.53±11.58%; MA, 107 .14±19.28%; P<0.05).
DISCUSSION: MC blade laryngoscopy attenuated increases in sAP, mean PA, PCWP, and epinephrine concentration during the intubation phase in CABG patients, possibly because of the smaller area stimulated by laryngoscopy with this blade type. Our result indicate an advantage of the MC blade over the MA blade in reducing hemodynamic responses to laryngoscopy and tracheal intubation in CABG patients.



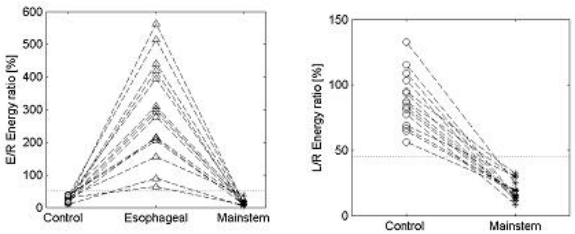
S-105

IDENTIFICATION OF ENDOTRACHEAL TUBE MALPOSITION USING COMPUTERIZED ANALYSIS OF BREATH SOUNDS

AUTHORS: **C. J. O'Connor**, H. A. Mansy, R. A. Balk, R. H. Sandler;
AFFILIATION: Rush Medical College, Chicago, IL.

INTRODUCTION: Endotracheal tube (ETT) malpositioning may produce significant hypoxemia if placed in a bronchus or the esophagus. Current methods of correct ETT position rely primarily on detection of end-tidal CO_2, but this modality may be unavailable in non-hospital/ emergency settings or low cardiac output states, and may not reliably detect endobronchial intubation. Auscultation of breath sounds can frequently be inaccurate. The purpose of this study is to quantify breath sounds using electronic stethoscopes placed over each hemithorax and epigastrum to detect ETT malposition.
METHODS: Following Human Investigation Committee approval and informed consent, ventilation sounds were obtained in 15 healthy, non-obese subjects undergoing general surgery. While in the supine position, 2 electronic were placed at the bilateral axillary lines and a 3rd stethoscope placed over the epigastrium. Anesthesia was induced, intubation of the trachea performed with bronchoscopy, and the ETT positioned 3 cm above the carina, after which 3 tidal volume breaths of ~ 500 mL were given. Breath sounds were recorded with a digital recorder. A 2nd ETT was placed in the esophagus, the stomach emptied, the breathing circuit attached to this ETT, and a similar series of breaths given. The stomach was emptied, the ETT removed, and the tracheal ETT advanced fiberoptically into the right mainstem bronchus (RMB). 3 breaths were administered, after which the ETT was withdrawn into the standard tracheal position. Acoustic signals were digitized and the energy in each acoustic signal was calculated as the mean squared amplitude of each sensor output. The acoustic energy ratios between the 3 positions were then calculated. Breath sound spectra were calculated using the Fast Fourier Transform for each 4096-point data segment after windowing with the Hanning window. Energy ratios for the 3 ETT locations were compared using the Wilcoxon signed-rank sum test.

RESULTS: Total energy ratios accurately identified 13/15 esophageal intubations, although accuracy was poor for the RMB intubation where 10/15 were misclassified using total energy ratios. Accuracy was increased to 100% for all malpositions by using band-pass filtering during analysis of the acoustic signals (p<0.001) (Fig 1 and 2, showing epigastrium/right chest (E/R) and left/right (L/R) energy ratios, respectively). The 100% separation using energy ratios suggest a high sensitivity and specificity for detection of both esophageal and RMB intubation.
DISCUSSION: These preliminary results suggest that this device, when incorporated into a simple 3-component electronic stethoscope-type device, may be an accurate, portable, and inexpensive mechanism to detect ETT malposition in situations where $ETCO_2$ may be unavailable or unreliable. Further studies will determine the applicability of this device to a more diverse and heterogeneous group of patients.
REFERENCES: 1 ieee eng med bio mag 16:105-17; 1997; 2) med bio eng comp 40:526-32; 2002



S-106

THE EFFECT OF CAROTID ARTERY PALPATION ON THE SIZE OF THE RIGHT INTERNAL JUGULAR VEIN UNDER POSITIVE PRESSURE VENTILATION

AUTHORS: **S. Yajima**, Y. Kobayashi, Y. Aoyama, M. Sekiguchi, A. Ishikawa, H. Sakurai;
AFFILIATION: National Hospital Tokyo Medical Center, Tokyo, Japan.

INTRODUCTION: Right internal jugular vein (IJV) cannulation has become one of the most popular central venous access routes. Various techniques including palpation of carotid artery (CA) are used to increase success rate of cannulation. However, it is possible that CA palpation will decrease the size of IJV and thereby make IJV cannulation more difficult. This study was designed to investigate the effect of CA palpation on the IJV size.
METHODS: After obtaining informed consent, 11 patients (6 men and 5 women; age range, 14-75 yr; BMI range, 17.9-24.7) who had a plan of general endotrachial anesthesia were participated to this study. Exclusionary criteria included limited neck mobidity and history of IJV cannulation. The size of the right IJV was measured by Hitachi EUB-450 ultrasound machine with a 7.5-MHz surface probe. After endotrachial intubation, mechanical ventilation (peak pressure=20mmH2O) was started under general anesthesia with a mixture of oxygen, nitrous oxide and sevoflurane. All patients was placed in the supine position with their heads unsupported and necks straight on the bed. The ultrasound probe was placed on the right neck at the level of cricoid cartilage, and was applied perpendicularly on the skin as gently as to keep underlying venous structure. After hemodynamic and ventilatory stability were established, cross-sectional area of right IJV was measured at the end of inspiration. Measurement was repeated three times on the same condition and the results were averaged to describe the baseline value (BV). Subsequently similar measurements were made at the same site palpating over the skin of the right CA with minimal pressure to feel palpation and averaged data of IJV area (maneuver value, MV). The differences between BV and MV, were analyzed statistically by using paired Student's *t* test, where $P<0.05$ was considered significant.
RESULTS: Mean IJV size (BV versus MV) was 1.75 (95% CI 1.27-2.23) cm^2 and 1.05 (95% CI 0.67-1.43) cm^2, respectively. IJV size was significantly decreased by means of CA palpation ($p<0.001$).
DISCUSSION AND CONCLUSION: There are many techniques for right IJV cannulation to increase IJV size and locate the anatomic structure. CA palpation is distinctly beneficial to confirm anatomic landmark without ultrasound guidance before puncture. However, our results clearly showed that CA palpation should decrease IJV size. A success rate of IJV cannulation should correlate to the size of IJV, if performed on the similar condition. Consequently CA palpation should be avoided during IJV puncture, if the anatomic landmark could be established before puncture.

S-107

EFFECT OF DIFFERENT CALIBRATIONS OF ACCELEROMYOGRAPHY ON DETERMINATION OF DOSE-RESPONSE RELATIONSHIP OF VECURONIUM

AUTHORS: **Z. Lu**, B. Yu;
AFFILIATION: Ruijin Hospital, Shanghai Second Medical University, Shanghai, China.

Recent studies showed a short-time stabilization wasn' t enough for getting a stable response to train-of-four(TOF)stimulation, which leads to false results on onset and recovery times of muscle relaxants. However, no study is performed in estimating the effect of short-time stabilization on dose-response relationship of muscle relaxants. We hypothesized the dose-response relationships of vecuronium obtained after a short-time stabilization without 50Hz tetanus stimulation wasn't similar to that after a long-time stabilization with 50Hz tetanus stimulation.
METHOD: Acceleromyography (TOF-GUARD) was used to determine dose-response curve of vecuronium in 10 patients (ASA I-II) . For each patient, either hand was chosen as control hand, the other hand was test hand. In test hand, a three-minute stabilization after AUTO I calibration was performed. In control hand, a 5-s, 50Hz tetanus stimulation was applied before AUTO I calibration, then TOF stimulation was going on for 20 min. After stabilization, the dose-response relationship for vecuronium was determined using the cumulative dose-response technique. A total dose of 40 µg.kg-1 was given in four doses of 10 µg.kg-1. If 90% or more depression was achieved after two incremental dose, the third dose was omitted. ED50, ED90, ED95 and slope (probit/log) were obtained and compared between control hand and test hand.
RESULTS: There were no significantly differences on ED50, ED90, ED95 and slope, test hands vs control hands.($P>0.05$)
DISCUSSION: Our finds showed that the dose-response relationship obtained after a three-minute stabilization isn't significantly different from that obtained after a 5s, 50Hz tetanus stimulation plus a 20-miunutes stabilization. It is common for investigators to allow only 1-3 min to elapse between initial transducer calibration and drug administration, because a long time (20 min or more) is rarely available in a busy medical center. Girling1 found a short stabilization led to longer onset and shorter recovery times. Kopman2 pointed out that a short-time stabilization wasn't enough to achieve a stable baseline, but a 5s, 50Hz tetanus considerably accelerated this procedure. However, results of current study implicated 3-minutes stabilization without tetanus stimulation was acceptable to research dose-response relationship of muscle relaxants.

Dose-response relationships of vecuronium in control hand and test hand

	ED_{50}	ED_{90}	ED_{95}	Slope(logit / log)
Test hand	26.0±8.2	42.6±12	48.8±14	6.0±0.7
Control hand	23.8±6.3	40.6±11.2	47.2±13.5	5.8±1.4

REFERENCES:
1 Girling KJ, Mahajan RP: The effect of stabilization on the onset of neuromuscular block when assessed using acclerometry. Anesth Analg 1996; 82: 1257-60

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S-108

AIRWAY PRESSURE RELEASE VENTILATION IMPROVES PULMONARY FUNCTION DURING LAPAROSCOPIC GASTRIC BYPASS

AUTHORS: **R. G. Soto**, M. M. Murr, R. A. Smith;
AFFILIATION: University of South Florida, Tampa, FL.

INTRODUCTION: Previously we observed increased efficiency of ventilation during Airway Pressure Release Ventilation (APRV) in patients undergoing laparotomy (1) and laparoscopy (2). Whether this is realized in significantly obese patients (Body Mass Index >35 kg/m^2) is unknown. Therefore, we compared pulmonary mechanics and gas exchange during total intravenous anesthesia and conventional mechanical ventilation (CMV) versus APRV in these patients.
METHODS: Anesthesia and neuromuscular blockade were induced and sustained with propofol and rocuronium in patients undergoing laparoscopic gastric bypass. All patients were initially ventilated via CMV (Dräger Evita 4), with a tidal volume (Vt) of 7 to 8 mL/kg and a respiratory rate (RR) sufficient to keep $PaCO_2$ between 38 and 42 mmHg guided by $PetCO_2$. Fraction of inspired oxygen concentration (F_IO_2) was titrated to produce SpO_2 of at least 90%. Appropriate instruments were used to determine Vt, RR, MV, peak airway pressure (Paw), mean Paw, respiratory system compliance (C_{RS}), and expired CO_2 concentration. Expired gas was collected and CO_2 was measured and multiplied by MV to estimate CO_2 elimination and compute alveolar ventilation (V_A) and physiological dead space ($V_D$phys). The gradient between partial pressure of CO_2 in the arterial blood and end-tidal gas [P(a-et)CO_2)] was calculated. After stable pneumoperitoneum was established, patients were randomly assigned to receive alternating 15-min trials of CMV and APRV. Cross-over trials were repeated four-times. APRV was given at the same RR as CMV, but Vt was set by adjusting CPAP to a level that when intermittently released produced a $PaCO_2$ between 38 and 42 mmHg. Release time was titrated to permit exit of volume from lungs (i.e., until zero gas flow), then airway pressure and lung volume were rapidly reestablished with a reapplication of pressure. Data were collected after each study period, summarized as mean±SD and compared with a repeated measures analysis of variance.
RESULTS: Ten-patients 44 ± 10 years old and 133 ± 8 kg underwent laparoscopic procedures with a mean intraperitoneal pressure of 18 ± 5 mmHg. There were no significant intragroup differences in F_IO_2 (0.30 ± 0.10), or cardiovascular/pulmonary function between the four trials of CMV or APRV, thus data were pooled for summary (Table).
DISCUSSION: Less MV and a smaller P(et-a)CO_2 gradient with similar $PaCO_2$ reflect a significant reduction in physiological dead space ventilation and increased efficiency of ventilation during APRV. Since respiratory compliance was similar and mean Paw was greater, increased lung volume may reflect less atelectasis during APRV, which might be particularly advantageous in morbidly obese patients in the immediate postoperative period. We conclude that APRV provides more efficient alveolar ventilation with lower peak airway pressure and greater accuracy of $PetCO_2$ as a reflection of $PaCO_2$ than does CMV.
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1. *Anesthesiology* 1998;89:334-40.
2. *Anesthesiology* 1999;90:1888-89.

CMV vs. APRV in bariatric patients

	CMV	APRV
MV (L / min)	8.47 ± 1.30	6.99 ± 2.14*
V_{phys} (L / min)	2.06 ± 0.68	1.50 ± 0.71*
P(a-t)CO_2 (mmHg)	3.5 ± 2.5	1.5 ± 2.9*
Peak Paw (cmH_2O)	34.5 ± 5.4	25.7 ± 4.0*
Mean Paw (cmH_2O)	8.1 ± 2.5	16.6 ± 3.3*
C_{RS} (mL / cmH_2O)	21.4 ± 2.9	22.5 ± 4.9

S-109

APPLICATION OF VEST™ AIRWAY CLEARANCE SYSTEM DURING BILATERAL LUNG WASHOUT FOR TREATMENT OF ALVEOLAR PROTEINOSIS

AUTHORS: **J. W. Schweiger**, R. A. Smith, A. B. Kumar;
AFFILIATION: University of South Florida, Tampa, FL.

INTRODUCTION: Alveolar proteinosis is an uncommon pulmonary disorder associated with progressive deposition of lipoproteinaceous material within alveoli.This process eventually produces hypoxemia due to an alveolar-capillary oxygen diffusion limitation which if untreated, may progress to respiratory failure. Conventional treatment is bilateral whole lung lavage.
METHODS AND MAIN RESULTS: A 54-yr-old male was referred to our institution by his regular pulmonologist. Six-years earlier the patient had been diagnosed with pulmonary alveolar proteinosis and experienced progressive shortness of breath and severe dyspnea on exertion. Subsequently, he underwent bilateral therapeutic whole lung lavage (BTWLL). The patient reported "almost immediate improvement in his shortness of breath," and returned to work within 4-weeks. However, similar symptoms recurred over recent 4-months. Hence, he was referred for another BTWLL. Patient was placed on an OSI™ spinal table and intermittently positioned prone to facilitate complete drainage of lavage fluid. He was fitted with the Advanced Respiratory Vest™ before induction of general anesthesia (propofol) and muscle relaxation (succinylcholine). He was intubated with a left-sided 41-Fr double lumen tracheal tube (DLT). After confirming DLT position, left lung was isolated. Then, 0.75-1L was instilled with each lavage under passive drainage by gravity. Following cessation of flow, the drainage port was temporarily closed and the Vest™ was oscillated in 10-minute increments. The fluid was allowed to drain while vest still oscillated. This was repeated (10-times) until drainage was clear and for 30-minutes patient was allowed to rest while undergoing mechanical ventilation with PEEP (10cmH_2O). After rest and reconfirmation of DLT position, lavage procedure was repeated (9-times) on right side. After procedure, DLT was replaced with a standard tracheal tube and patient was transferred to SICU, and was extubated 6-hours later. The patient was discharged to home the following morning, and was seen 2-weeks later in pulmonary clinic. He reported "complete resolution of all symptoms."
DISCUSSION: We observed that the Advanced Respiratory Vest™ Airway Clearance System is a useful adjunct to facilitate BTWLL. It is highly effective at breaking up the lipoproteinaceous material adherent within the alveoli, and thus allowing easier extraction during the lung lavage. Theoretically, device provides better distribution of chest percussion than manual or handheld pneumatic chest percussion. Although the Vest™ System requires anesthesiologist's attention during application, it relieves OR personnel from having to perform manual or pneumatic chest percussion. Thus, Vest™ System appears an effective and useful adjunct during BTWLL, but future research should be conducted to confirm efficacy.

S-110

OPTIMAL TIMING OF THE RELIEFBAND ACUSTIMULATION FOR ANTIEMETIC PROPHYLAXIS IN PATIENTS UNDERGOING PLASTIC SURGERY

AUTHORS: **M. A. Hamza**, P. F. White, D. Song, J. E. Coleman, M. Luby, A. D. Macaluso;
AFFILIATION: UT Southwestern Medical Center at Dallas, Dallas, TX.

INTRODUCTION: Postoperative nausea and vomiting (PONV) are among the most common reasons for delayed recovery after surgery (1,2). The purpose of this study was to determine the optimal use of a transcutaneous acupoint electrical stimulation device, the ReliefBand, when used for antiemetic prophylaxis before and/or after plastic surgery.
METHODS: Following institutional approval and informed consent, 96 ASA 1-2 patients receiving general anesthesia for major plastic surgery were randomly assigned to one of the three treatment groups: Group 1 received the ReliefBand treatment for 30 min before surgery; Group 2 received the ReliefBand treatment for 72 h after surgery, and Group 3 received the ReliefBand treatment both 30 min before surgery and 72 h after surgery. The device was applied at the P6 acupoint on the median aspect of the patient's wrist. All patients were premedicated with midazolam 20 ug/kg IV. Anesthesia was induced with propofol 1.5-2 mg/kg IV, and sufentanil 0.1 ug/kg IV, and was maintained with sevoflurane 1-2% end-tidal, and a sufentanil IV infusion, 100 ug/kg/h. Ondansetron, 4 mg IV, was administrated to all patients at the end of surgery. The postoperative pain was controlled using PCA morphine for 24 h after surgery. Postoperative nausea was assessed using an 11-point verbal rating scale (with 0=none to 10=maximum) at 30-min intervals in the first 4 h after surgery, and then at 24 and 72 h after surgery via follow-up phone calls. In addition, patient satisfaction with their antiemetic treatment was assessed using a 100-point verbal rating scale (with 1=none to 100=maximum) at 72 h after surgery. Data were analyzed using ANOVA, Kruskal-Wallis test and chi-square test with Yates correction, with $p<0.05$ considered statistically significant.
RESULTS: The three treatment groups were comparable with respect to demographic data, duration of anesthesia, and intraoperative dosages of propofol and sufentanil, as well as the postoperative PCA morphine requirement. The incidences of PONV and severity of nausea, as well as the patient satisfaction scores are summarized below. Values are numbers (n), percentages (%), mean±SD or median and range (interquartile).

	Group 1 (n=32)	Group 2 (n=32)	Group 3 (n=32)
Nausea < 4h (n, %)	18, 56	12, 38	10, 31*
Vomiting < 4h (n, %)	7, 22	3, 9	4, 12
Maximum nausea score <4 h	3 (0-7)	0 (0-4)*	0 (0-3)*
Rescue antiemetics < 4 h (n, %)	13, 40	7, 22	6, 19
Nausea 4-24 h (n, %)	19, 59	11, 34*	11, 34*
Vomiting 4-24 h (n, %)	6, 18	4, 12	3, 9
Maximum nausea score 4-24 h	5 (0-8)	0 (0-3)*	0 (0-4)*
Nausea 24-72 h (n, %)	7, 22	2, 6	3, 9
Patient satisfaction	86±14	94±10*	95±9*

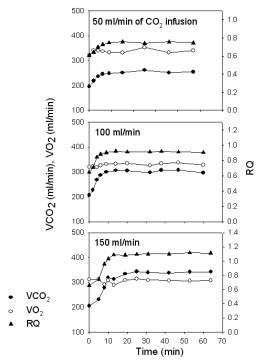
* = P<0.05
DISCUSSION:
The ReliefBand was most effective in the prevention of PONV when administered before and after surgery. The preoperative use of this acustimulation device was less effective in reducing nausea and vomiting after surgery than use of the ReliefBand after surgery. Despite the use of both ondansetron and the ReliefBand, these patients still experienced high incidences of PONV (34-59%) during the first 24 hours after plastic surgery.
REFERENCE: (1) Anesth Analg 2001; 92: 629-35; (2) Anesth Analg 1997; 84: 712-4.

S-111

NEW MEASUREMENT OF AIRWAY VO_2 AND VCO_2, USING THE HALDANE TRANSFORMATION, CAN DETECT PHYSIOLOGICAL PERTURBATIONS DURING NON-STEADY STATE

AUTHORS: **A. Rosenbaum**, H. C. Howard, D. Botros, P. H. Breen;
AFFILIATION: University of California - Irvine Medical Center, Orange, CA.

INTRODUCTION: Airway opening measurement of O_2 uptake (VO_2) and CO_2 elimination (VCO_2) is a challenging task, mainly because of errors in flow measurement. The Haldane transformation[1] solves this problem by utilizing the inert gas, N_2, where the product of inspired N_2 fraction and volume equals the product of the expired values (N_2 conservation principle). This relationship allows inspired volume to be expressed as a function of expired volume (or vice versa), avoiding flow measurement errors between inspiration and expiration. Traditionally, the Haldane transformation requires steady state. However, we hypothesized that the Haldane transformation can be used during nonsteady state.
METHODS: We designed a bench setup that includes a ventilator (60% O_2), mechanical lung, and an ethanol combustion system sealed inside an airtight chamber. An occlusive roller pump circulated gas, at constant flow rate, between the mechanical lung and the metabolic chamber. We developed a mixing device (bymixer[2]) for the measurement of mixed inspired and expired gas fractions. We constructed a fast response temperature and humidity sensor[3] to correct flow to standard temperature and pressure, dry (STPD) conditions. After attaining steady state at a VO_2 of 300 ml/min (VCO_2 of 200 ml/min), we started a CO_2 gas infusion into the chamber. We captured data for 60 minutes, with more frequent measurements immediately after beginning the CO_2 infusion. We tested 3 CO_2 infusion rates of 50, 100 and 150 ml/min, which resulted in final respiratory quotients ($RQ=VCO_2/VO_2$) of 0.83, 1.0 and 1.16 respectively.
RESULTS: The figure shows changes in VO_2, VCO_2 and RQ in one experiment. After the start of the CO_2 infusions, VCO_2 and RQ displayed immediate and progressive increases to plateau at their final values by about 12 min. VO_2 was remarkably constant before and during the CO_2 infusion. The other 3 experiments displayed almost identical results.
DISCUSSION: During the CO_2 infusion, that RQ (and VCO_2) increased steadily and progressively to its plateau value and VO_2 remained constant, supports measurement of accurate VO_2, using the Haldane transformation, during non-steady state conditions. This finding contrasts with the classical requirement for equilibrium before invoking nitrogen conservation. The rise time for VCO_2 and RQ resulted mostly from the time needed for CO_2 equilibration from the metabolic chamber (site of CO_2 infusion) to the mechanical lung. Early detection of critical metabolic events during anesthesia should provide an important diagnostic tool for patient care (e.g., early detection of pulmonary embolus, compromised venous return during laparoscopic insufflation of the peritoneal cavity). Patient studies are needed to test these clinical questions.
REFERENCES: 1. Ann Biomed Eng 2000; 28: 1159-1164. 2. Anesth Analg 2003; 97: In Press. 3. U.S. Patent Number 6,014,890; 2000.
Support by: NIH R01 HL-42637 and NCRR M01 RR00827.

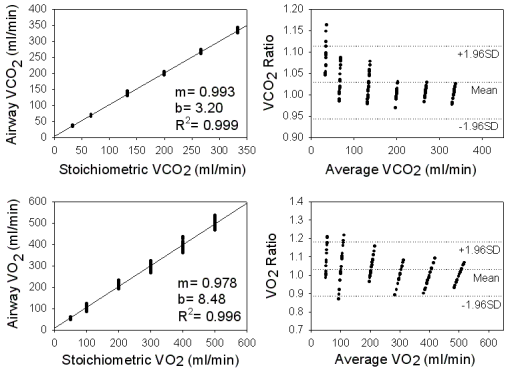


S-112

NEW INDIRECT CALORIMETRY MEASUREMENT, USING THE HALDANE TRANSFORMATION, MEASURES ACCURATE VO_2 AND VCO_2 DURING HIGH O_2 FRACTION VENTILATION

AUTHORS: **A. Rosenbaum**, H. C. Howard, B. J. Kavoossi, P. A. Lee, P. H. Breen;
AFFILIATION: University of California - Irvine Medical Center, Orange, CA.

INTRODUCTION: The Haldane transformation[1] is commonly used to non-invasively measure O_2 uptake (VO_2). Because N_2 is an inert gas, the product of inspired N_2 fraction and volume equals the product of the expired values (N_2 conservation principle). This relationship allows inspired volume to be expressed as a function of expired volume (or vice versa), avoiding flow measurement errors between inspiration and expiration. However, during high inspired O_2 fraction (FiO_2) breathing, N_2 fractions become small and limit the accuracy of the Haldane transformation (traditionally during FiO2 > 0.6). We have developed an indirect calorimetry measurement, based on the N_2 conservation principle system, with several innovative components. We hypothesized that this new methodology would allow accurate measurements of VO_2 and VCO_2 (CO_2 elimination) during high FiO_2.
METHODS: Our measurement system is composed of: 1) new, fast response, accurate, and compact in-line mixing chamber (bymixer)[2] for the measurement of mixed gas fractions; 2) new fast response temperature and humidity sensor[3] for the correction of flow to standard temperature and pressure, dry conditions (STPD); 3) accurate clinical monitor to measure pneumotachometer flow and gas fractions (Datex Ultima); and 4) custom computer algorithm that automatically performs the complex calculations. We designed a unique bench setup, using ethanol combustion, to test the measurement system operating during open circuit ventilation with FiO_2 of 0.8. VO_2 was tested over the range of 49.9-499.3 ml/min (VCO_2 of 33.3-332.8 ml/min). Five consecutive measurements were taken on 4 separate days (total of 120 trials).
RESULTS: Average error for VCO_2 and VO_2 was 2.5±3.9% and 3.0±7.5% respectively. Average respiratory quotient (RQ) was 0.666±0.037. Linear regression showed an excellent correlation; slope, Y intercept and R^2 were 0.99, 3.20 and 0.999 for VCO_2, and 0.98, 8.48 and 0.996 for VO_2, respectively. Bland & Altman ratio analysis demonstrated good agreement (Figure).
DISCUSSION: High FiO_2 is commonly required for respiratory compromised patients. Previously, under these circumstances, VO_2 measurement by the N_2 conservation principle was impossible or prone to large errors. We have developed a measurement system, with the above-described new components, that allows for VO_2 measurement under high FiO_2 conditions, resulting in remarkable accuracy and repeatability. We believe that overcoming this obstacle of high FiO_2 may contribute to the routine use of VO_2 measurement during anesthesia, and provide the anesthesiologist with an invaluable clinical tool.
REFERENCES: 1. Annals Biomed Eng 2000; 28: 1159-1164. 2. Anesth Analg 2003; 97: In Press. 3. U.S. Patent Number 6,014,890; 2000.
Support by: NIH R01 HL-42637 and NCRR M01 RR00827.

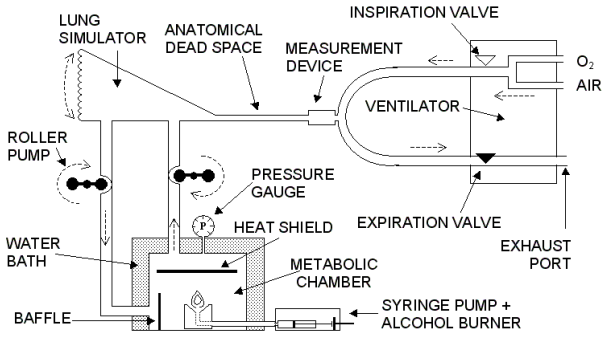


S-113

ENHANCED METABOLIC LUNG SIMULATOR GENERATES ACCURATE AND WIDE RANGE OF VCO_2 AND VO_2 FOR INDIRECT CALORIMETRY METHODOLOGY RESEARCH

AUTHORS: **A. Rosenbaum**, C. Kirby, H. C. Howard, D. Botros, P. H. Breen;
AFFILIATION: University of California - Irvine Medical Center, Orange, CA.

INTRODUCTION: As medicine moves forward towards non-invasive monitoring, indirect calorimetry (airway O_2 uptake, VO_2, and CO_2 elimination, VCO_2) offers an attractive modality for the measurement and investigation of metabolic rate and gas exchange. However, indirect calorimetry methodology research in humans is problematic because of difficulty to control metabolic indices and inability to execute extreme perturbations. Furthermore, high precision reference measurements are not available during human studies. In a previous paper[1], we reported the design of a metabolic lung simulator, which utilized alcohol combustion as a gold standard. We now report two innovative enhancements to that design. First, a new wickless burner allows for measurements to be taken with inspired O_2 fraction (FiO_2) < 0.6. Second, we have eliminated ventilation-induced pressure fluctuations within the metabolic chamber, which stabilize the combustion process.
METHODS (see figure): As described previously[1], the system is composed of a ventilator, a mechanical lung simulator, an airtight chamber (incorporating an alcohol combustion system), and an occlusive roller-pump that circulated gas flow between the lung and the metabolic chamber. A precision syringe pump supplied the burner with an adjustable, metered amount of liquid ethanol. The new system has the following new features: 1) The wick burner was replaced with a customized temperature-stable, wickless burner that allowed a consistent delivery of ethanol. 2) A second roller pump was placed upstream of the mechanical lung to stabilize pressure within the metabolic chamber (no respiratory cycle pressure fluctuations). A pressure gauge, located on the metabolic chamber, permitted synchronization of the two roller pumps, to maintain inner chamber pressure near 0 cmH_2O.
RESULTS: The new system allowed measurements of VCO_2 and VO_2 down to 33.3 and 49.9 ml/min, respectively. Compared to measurements utilizing mixed inspired and expired gas fractions, average error, during FiO2 of 0.6, was 0.07±2.41% and 1.11±2.88% for VCO_2 and VO_2, respectively. The average respiratory quotient (RQ) was 0.66±0.01. During FiO_2 of 0.4, average error was 2.1±3.1% and 3.6±3.1% for VCO_2 and VO_2 respectively. Average RQ was 0.66±0.01.
DISCUSSION: Indirect calorimetry methodology is important to many medical fields, such as intensive care, anesthesiology, sports medicine, cardiology and the basic sciences[2]. Therefore, a highly reliable, accurate, and versatile bench investigation system is needed in order to further investigation in this area. The high accuracy of our new metabolic lung simulator, and its ability to operate under low FiO_2 conditions, will significantly contribute, we believe, to the field of indirect calorimetry methodology research.
REFERENCES: 1. A.S.A. Scientific Meeting, 2003, Abstract A-526. 2. Bursztein S et al. Baltimore, William & Wilkins 1989; pp. 119-172.
Support by: NIH R01 HL-42637 and NCRR M01 RR00827.



S-114

CHANGES OF A-LINE AUTOREGRESSIVE INDEX AND BIS DURING INDUCTION AND TRACHEAL INTUBATION IN THE ELDERLY

AUTHORS: **X. Xuebing**, S. Shouzhang, Y. Yan, X. Lixin;
AFFILIATION: Department of Anesthesiology, The First People's Hospital of Guangzhou, Guangzhou, China.

INTRODUCTION: A-line autoregressive index (AAI) and bispectral index (BIS) has been used to reflex the anesthesia depth during induction and tracheal intubation. Previous data had showed that BIS is useful for anesthesia depth monitoring in the elderly, while we had no idea about AAI use for the elderly. The purpose of this study was to compare AAI and BIS during induction and tracheal intubation in elderly patients.
METHODS: After Hospital Research Committee approval and informed consents, 40 ASA grade I-II patients (age 20~80 years old) without obvious auditory and psychiatric dysfunction undergoing general surgery procedures using a standardized general anaesthetic technique were enrolled into this study. According to the patients age, the patients were distributed into group E (age≥60, n=18) and group Y (age<60, n=22). No premedication was given. Upon arrival to the operating room, all patients received AAI monitor (Danmeter A/S Co, Denmark) and BIS monitor (HDX-1, Harbin, China). MAP, HR were also recorded continuously. Tracheal intubation was performed following induction with midazolam0.06mg/kg, fentanyl 4μg/kg, propofol 0.5mg/kg and vecuronium 0.1mg/kg. The changes of AAI, BIS, MAP, HR were recorded at baseline before induction, after induction, during intubation and post-intubation 1, 3, 5 minutes.
RESULTS: MAP and HR in both groups decreased significantly by anaesthesia induction, increased sharply by tracheal intubation and then nearly returned to the baseline. The values of AAI and BIS are shown in the table as mean ± SD.

Table: AAI and BIS at different time points in Group E and Group Y

	E -AAI	E-BIS	Y-AAI	Y-BIS
T_1	74.9±15.7	76.6±18.3	83.8±15.0	86.1±12.0
T_2	25.3±6.0$^{\#}$	26.3±5.2$^{\#}$	50.7±3.7$^{\#}$	52.0±4.6$^{\#}$
T_3	31.8±9.1**	34.8±12.3**	64.2±11.1**	62.0±11.9**
T_4	35.6±10.6**	35.2±10.3**	68.1±13.1**	68.3±9.0**
T_5	31.9±8.2**	32.0±10.3**	63.1±11.1**	64.5±14.9**
T_6	25. 8±8.1	28.5±11.3	54.7±7.3*	58.8±13.9*

T_1, baseline before induction; T_2, after induction; T_3, just intubation; T_4, 1 minute after tracheal intubation; T_5, 3 minutes after tracheal intubation; T_6, 5 minutes after tracheal intubation. $^{\#}$: $P < 0.01$, T_2 vs. T_1; *: $P < 0.05$, **: $P < 0.01$, T_3, T_4, T_5 and T_6 vs. T_2.
DISCUSSION: Though AAI not BIS returned to T_1 level at T_6, the changing tendency of AAI and BIS in both groups were identical at all time points. This implicated that AAI, a quantitative auditory evoked potential, could be used for anesthesia depth monitoring for the elderly without obvious auditory dysfunction during induction and tracheal intubation.
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1.Minerva Anestesiol 66,398-402,2000
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S-115

INTRAVENOUS KETAMINE CAN INCREASE THE PROCESSED EEG VARIABLES, BUT NOT THE SYMPATHETIC RESPONSE DURING SEVOFLURANE ANESTHESIA IN HUMAN

AUTHORS: **M. Kakinohana**, E. Okuno, H. Nishi, M. Ohshiro, Y. Miyata, K. Sugahara;
AFFILIATION: University of the Ryukyus, Nishihara, Japan.

INTRODUCTION: Although the effect of ketamine on the EEG variables duirng propofol infusion had already been studied, interaction between sevoflurane and ketamine on the EEG variables has not been studied. In this study, we investigated the effect of intravenous ketamine on sympathetic activity, processed EEG variables, e.g, bispectral index (BIS), 95 % spectral edge frequency (95% SEF) during sevoflurane anesthesia.
METHODS: After obtaining written informed consents, 18 patients (20 – 45 y.o, ASA PS I) were randomized to two groups, ketamine administration group (K) or saline administration group (S). All patients were received with intramuscular 0.5 mg of atropine and 0.04 mg / kg of midazolam, as premidication. After the anesthetic circuit was prefilled with 5 % sevoflurane with 100% oxygen, induction of anesthesia was performed. Tracheal intubation was facilitated with 0.1 mg / kg of vecuronium. All patients received 1 MAC of sevoflurane in 6 L/min of oxygen after tracheal intubation. 5 min after intubation, 1 mg/ kg of ketamine (10 mg/mL) in Group K, or 0.1 ml/kg of saline in Group S was injected intravenously. Blood pressure (BP), heart rate (HR), Heart rate variability (HRV) and EEG (Makin 2 ™ ; Suwa Trust, Tokyo, Japan), and BIS were monitored until 10 minutes after ketamine or saline administration. Two-way repeated measures analysis of variance followed by post-hoc test were used to analyze BP, HR, HRV, BIS and 95% SEF. A p-value < 0.05 was considered statistically significant.
RESULTS: There were no significant difference bwtween Group K and Group S in BP, HR, HRV, BIS and 95% SEF before ketamine injection. In both groups, neither BP or HR changed significantly after administration of ketamine or saline. After injection of ketamine in Group K, BIS and 95% SEF were increased significantly (BIS; 48.2 ± 8.4 to 72.9 ± 12.0, 95 % SEF; 11.3 ± 3.2 to 19.8 ± 2.9), but those changes were not observed after injection of saline in Group S. In both Groups, however, the ratio of low-frequency component to high-frequency component (cardiac sympathetic activity) did not change after injection of ketamine or saline.
CONCLUSION: Our results demonstrated that ketmaine can induce the increase of processed EEG variables, but not HR, BP or the sympathetic activity during sevoflurane anesthesia. It was suggested that sevoflurane can suppress the effect of ketamine on autonomic nervous system, and that processed EEG variables may be inadequate index for depth of anesthesia under the additional ketamine administration during sevoflurane anesthesia

S-116

EFFICIENCY OF THE ANACONDA™ (ANESTHETIC CONSERVING DEVICE) USED WITH SEVOFLURANE IN PIGS

AUTHORS: M. Soro[1], M. J. Alcantara[1], M. Santos[2], G. Aguilar[1], F. Tendillo[2], **J. Belda**[1];
AFFILIATION: [1]Hospital Clinico Universitario de Valencia, Valencia, Spain, [2]Research Unit. Clinica Puerta de Hierro, Madrid, Spain.

INTRODUCTION: The Anesthetic Conserving Device (AnaConDa; Hudson RCI, Sweden) is a new device for anesthetic vapours delivery. The AnaConDa consists of an anesthetic gas exchanger, which absorbs some of the expired anesthetic vapor by means of an activated carbon filter, and desorbs some of it in the next inspiration. A syringe pump delivers the volatile anesthetic in liquid status to the AnaConDa where the anesthetic is vaporized (1). A clinical study showed that due to the physical properties of the AnaConDa, the isoflurane sedation of ICU patients requires small volumes of isoflurane, and it is environmentally safe (2). However not all the anesthetic is retained in the device; in part pass through the filter and it is eliminated to the atmosphere. This study aimed to evaluate the concentration of anesthetic loss from the AnaConDa filter (efficiency) at different sevoflurane end-tidal concentrations.
METHODS: Four experimental animals were anesthetized (Large-White pigs, mean weight = 17.7 Kg). After endo-tracheal intubation, the animals were connected to a Evita respirator (Dräger, Germany) and mechanical ventilation was adjusted to achieve an end-tidal CO2 between 35 and 40 mmHg. Due to the 100 mL of dead space produced by the device, we readjusted VT to avoid rebreathing and hypercarbia. Sevoflurane was delivered by means of the AnaConDa, which was placed at the Y- piece of the ventilator circuit and the endotracheal tube. In each animal incremental end-tidal concentrations of sevoflurane from 0.5 to 3% in 0.5% steps were adjusted. After 15 minutes of steady state at each end-tidal concentration, expiratory gases were collected in a Douglas bag for 10 minutes and analyzed thereafter. Anesthetic concentrations were measured using a standar clinical monitor (Julian v 2.02, Drager, Germany). Percentage of gas loss (mean + SD) was plotted against end-tidal anesthetic concentrations.
RESULTS: The figure 1 shows the Efficiency plot i.e. loss of sevoflurane through the filter (Y axis) related to the adjusted end-tidal concentrations (X axis). Minute volume was of 6.1 + 0.2 l/min.
DISCUSSION: For a determined minute volume ventilation the loss of sevoflurane from the AnaConDa filter increases exponentially as end-tidal concentration increases. This can be explained knowing that the active carbon in the filter has a certain absorption capacity and when it is loaded with more Sevoflurane the effiency goes down. However, for end-tidal concentrations of 1% or less, there is a maximal efficiency and the loss of anesthetic is negligible. These results confirm the interest for the potential application of the AnaConDa with sevoflurane around 1% concentration in the ICU settings without significant ambient pollution.
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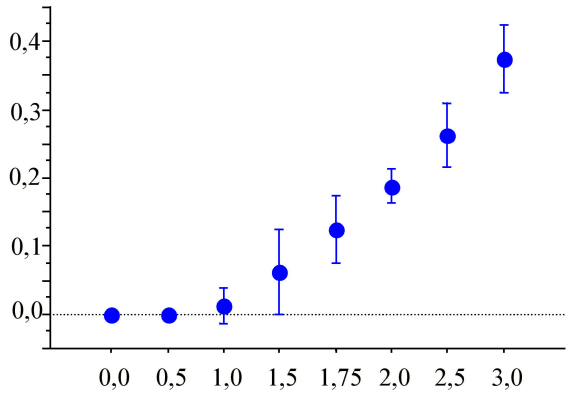

S-117

COMPARISON OF THE ANAESTHETIC METHODS OF MEDIUM-FLOW, LOW-FLOW CLOSED CIRCUITS AND LOW-FLOW CLOSED CIRCUITS COMBINED WITH BISPECTRAL INDEX MONITORING FOR THE USE OF SEVOFLURANE

AUTHORS: **Q. Fan**[1], R. Eltringham[2], B. Yu[1], R. Craven[3];
AFFILIATION: [1]Rui Jin Hospital, Shanghai Second Medical University, Shanghai, China, [2]Department of Anaesthesia, Gloucestershire Royal Hospital, Gloucestershire, United Kingdom, [3]Deparement of Anaesthesia, Gloucestershire Royal Hospital, Gloucestershire, United Kingdom.

INTRODUCTION:The aim of this study was to establish which anaesthetic method provides the best conditions for the use of sevoflurane by comparison between medium-flow closed circuit anaesthesia (MFCCA) and low-flow closed circuit anaesthesia (LFCCA) and low-flow closed circuit anaesthesia combined with bispectral index (BIS) monitoring.
METHODS: Ninety-six ASA I-II patients presenting for elective low abdominal or pelvic surgery under general anaesthesia were randomly divided into three groups, according to the anaesthetic system used. Group A, used medium-flow closed circuits, Group B, low-flow closed circuits and Group C, low-flow closed circuits combined with bispectral index monitoring. There were 32 patients in each group. The fresh gas flow was delivered at a rate of 1500ml per minute in Group A and 500ml per minute in groups B and C. The sevoflurane was delivered through a Komesarroff vaporizer, which was placed on the inspiratory limb of the circle. The delivered concentration of sevoflurane from the Komesarroff vaporizer in Groups A and B, was adjusted as clinically indicated, while in Group C, it was adjusted according to the BIS value (at 46 +/- 10).
RESULTS:The end-tidal sevoflurane concentrations in groups A, B and C, were 1.4 +/- 0.2MAC, 1.1 +/- 0.2MAC and 0.8 +/- 0.2MAC respectively. The consumption of sevoflurane in groups A, B and C was 13.3 +/- 1.6ml per hour, 9.6 +/- 1.5ml per hour and 7.5 +/- 1.8ml per hour respectively. The end-tidal sevoflurane concentration and the consumption of sevoflurane in Group C was less than that of Group A ($P<0.01$) or Group B ($P<0.05$). The times to regain consciousness in Groups A, B and C were 14.3 +/- 3.3minutes, 10.5 +/- 2.8minutes and 7.5 +/- 2.6minutes respectively. The times to full orientation in Groups A, B and C were 24.5 +/- 6.1minutes, 17.4 +/- 5.5minutes and 12.7 +/- 4.8minutes respectively. The times to regain consciousness and full orientation in Group C were less than that of Group A ($P<0.01$) and Group B ($P<0.05$). The incidence of nausea and vomiting in Groups A, B and C was 14.5% +/- 2.6%,10.1% +/- 2.3% and 7.5% +/- 2.1% respectively. The incidence of nausea and vomiting in Group C was lower than that of Group A ($P<0.01$) and Group B ($P<0.05$).
DISCUSSION: Low-flow closed circuit anaesthesia, combined with bispectral index monitoring has the advantages of the lowest consumption of sevoflurane, the shortest time to regain consciousness and the lowest incidence of nausea and vomiting. It was shown to be an excellent method for the administration of sevoflurane with important financial considerations.

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DOES THE LOCATION OF ELECTRICAL STIMULATION FOR ELECTROCONVULSIVE THERAPY AFFECT THE SEIZURE DURATION, HEMODYNAMIC RESPONSE OR BISPECTRAL INDEX VALUES?

AUTHORS: **Y. Zhang**, P. F. White, A. Okupa, L. Perdue, L. Thornton, M. J. Downing;
AFFILIATION: UT Southwestern Medical Cen, Dallas, TX.

INTRODUCTION: In recent years, electroconvulsive therapy (ECT) has become more widely used to treat severe medication-resistant depression. The three commonly used electrode locations are: 1) unilateral temporal, 2) bilateral temporal, and 3) bilateral frontal. A previous study indicated that EEG-BIS value immediately before the ECT stimulus was applied could be useful in predicting the seizure time; however, the BIS values on awakening were highly variable (1). Since the effect of electrode location on physiologic responses to ECT has not been previously studied, we proposed a study to compare the EEG and hemodynamic responses to the three commonly used electrode locations for ECT.
METHODS: After IRB approval, 12 ASA I-III patients (age 33~87) undergoing an acute series of ECT treatments were involved in this study. The electrode locations were placed according to a randomized ECT stimulus assignment. All patients received the same anesthetic technique consisting of premedication with glycopyrrolate 3 μg/kg IV, induction of anesthesia with methohexital, 1 mg/kg IV, and with muscle relaxation succinylcholine, 1 mg/kg IV. The BIS values were recorded at the following specific end-points: (1) pre-anesthesia (baseline) , (2) before ECT, (3) post-ECT maximum (after the end of the motor seizure), (4)post-ECT minimum (after the end of the EEG seizure), and (5) awakening (eye opening in response to a verbal command). In addition, the duration of the motor and EEG seizure activity, mean blood pressure (MAP), and heart rate (HR) values were recorded. Data were expressed as mean±SD; with $p<0.05$ considered statistically significant.
RESULTS: The motor and EEG seizure times were slightly shorter in unilateral group than bi-temporal or bi-frontal groups (36 vs 43 and 47 sec, and 50 vs 57 and 57 sec, respectively, $P>0.05$). However, there were no differences in the hemodynamic response or BIS values among the three electrode placement groups.

	Unilateral (n=16)	Bi-temporal (n=26)	Bi-frontal (n=22)
Motor seizure time(s)	36±10	43±10	47±8
EEG seizure time(s)	50±10	57±12	57±10
BIS Baline	97±2	96±3	97±1
Post-ECT max	63±16	60±12	62±15
Post-ECT min	48±12	52±15	47±9
Awakening	71±18	72±16	69±18
MAP(mmHg) Baseline	100±11	97±11	95±14
Post-ECT max	118±18	115±20	119±24
Awakening	104±15	98±10	95±12

CONCLUSION: The electrode placement may have some effects on the duration of seizure activity; However, the patterns of EEG-BIS and hemodynamic responses to ECT were similar irrespective of the location of the electrical stimulus.
REFERENCES: 1), Anesth Analg 2003; 96:1636-39

S-119

MONITORING OXYGENATOR EXPIRATORY ISOFLURANE CONCENTRATIONS AND THE BISPECTRAL INDEX TO MEASURE ISOFLURANE REQUIREMENTS DURING CARDIOPULMONARY BYPASS WITH MODERATE HYPOTHERMIA

AUTHORS: **E. H. Liu**, S. S. Dhara;
AFFILIATION: National University Hospital, Singapore, Singapore.

INTRODUCTION: Bispectral index (BIS) monitoring is commonly used to guide anesthetic depth during cardiac surgery. [1] While isoflurane requirements are expected to fall during hypothermic cardiopulmonary bypass, this has not been previously quantified in relation to BIS. Oxygenator expiratory gas having equilibrated with the patients' blood can reflect blood concentrations of anesthetics. [2] Analysis of this gas is analogous to measuring the end tidal anesthetic concentrations. We measured isoflurane concentrations in the oxygenator expiratory gas while using BIS to guide management of anesthetic depth.
METHOD: IRB approval and consent from 40 patients undergoing elective coronary artery surgery with hypothermic cardiopulmonary bypass were obtained. Anesthesia was induced with propofol and maintained with isoflurane. A continuous morphine infusion was used for analgesia. During bypass, oxygenator fresh gas flows were set at 2L/min and adjusted to maintain pH stat acid base balance. Isoflurane was delivered using a Drager Vapor 19.3 vaporizer in the fresh gas pathway of a Sarns 2000 bypass machine. Oxygenator expiratory gas was sampled without contamination from room air. During the rewarming phase, isoflurane concentrations required to maintain the BIS between 40 and 50 were measured with a Drager Narkomed agent analyzer. Rewarming was gradual and there was minimal variation in the BIS during gas analysis at specified nasopharyngeal temperatures.
RESULTS: There was a significant difference in isoflurane requirements at 30ºC and at 37ºC (0.41% vs. 0.98%) There was a positive correlation between temperature and isoflurane requirements during rewarming from 30°C to 37°C, Pearson coefficient 0.777. (Table)
DISCUSSION: This method may help in quantifying volatile anesthetic requirements during cardiopulmonary bypass, with BIS monitoring. This study suggests that isoflurane requirements are reduced during moderate hypothermia. However, the relative contributions of the effects of temperature and isoflurane on the BIS cannot be quantified. Further study is required to assess if BIS has the same relationship with anesthetic depth during hypothermia, as it does in normothermia.
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Anesthesiology 1989; 71:519-25

Mean (se) expiratory isoflurane concentrations between 30 and 37 degree Celsius

Temperature (degree Celsius)	Expiratory Isoflurane%
30	0.41 (0.02)
31	0.43 (0.02)
32	0.49 (0.02)
33	0.54 (0.02)
34	0.62 (0.03)
35	0.72 (0.03)
36	0.88 (0.03)
37	0.98 (0.02)

S-120

BIS CORRELATES BETTER THAN 95% SEF WITH BLOOD PROPOFOL CONCENTRATIONS WITH EQUILIBRATION LAG BETWEEN BLOOD CONCENTRATIONS AND CNS PHARMACODYNAMIC EFFECT DURING INITIAL STAGES OF INFUSION

AUTHORS: **H. Singh**[1], K. Hirota[2], M. Kudo[2], A. Matsuki[2];
AFFILIATION: [1]University of Texas Medical Branch, Galveston, TX, [2]University of Hirosaki School of Medicine, Hirosaki, Japan.

INTRODUCTION: Following propofol infusion, there may be considerable equilibration lag between blood and brain concentrations, thereby affecting correlation between blood propofol concentrations and CNS pharmacodynamic effect monitored by bispectral index (BIS) and 95% spectral edge frequency (SEF) values. This study determined the correlations between blood propofol concentrations and BIS and 95% SEF values at three clinical endpoints, i.e.,0.5-h postinduction, 2-h postinduction (or termination of infusion) and eye opening
METHODS: Following Institutional Review Board approval, 23 ASA 1-2 male/female patients undergoing elective surgery were studied. Anesthesia was induced with propofol 2mg.kg^{-1}, fentanyl 1.5ug.kg^{-1} and vecuronium 0.1 mg.kg^{-1} iv and maintained with propofol infusion, 10 mg.kg^{-1}.h^{-1} and fentanyl boluses 1 ug.kg^{-1} every 30-min. BIS and 95% SEF were recorded using an EEG monitor (A-1000, BIS 3.0 algorithm, Aspect Medical System, MA, USA) and blood samples for measuring propofol concentrations by high performance liquid chromatography were drawn at 0.5-h postinduction, 2-h postinduction (or termination of infusion) and eye opening.
RESULTS: Total doses of propofol and fentanyl administered were 1616.6+/-741.5 mg and 341.3+/-172.5 ug, respectively. The BIS and 95% SEF values at baseline, 30-min, 115.8+/-16.5-min (2-h postinduction or termination of infusion) and 151.6+/-41.5-min (eye opening) were 94+/-5, 36.4+/-7.5, 38.2+/-2.7 and 73.2+/-7.7; and 22.4+/-4.2, 14.7+/-3.5, 15.4+/-2.3 and 20.5+/-3.4, respectively. The blood propofol concentrations and correlation coefficients are shown in the table below.
DISCUSSION: BIS correlated better than 95%SEF with blood propofol concentrations[1]. Correlation coefficients for BIS vs. propofol concentrations were higher at 115.8+/-16.5 and 151.6+/-41.5 min as compared to 30-min. This suggests considerable equilibration lag between blood and brain concentrations of propofol during initial stages of infusion. An animal study in sheeps suggested disequilibrium between blood and brain concentrations with marked hysteresis for 30-min following propofol infusion[2]. Further studies in humans may address the issue of hysteresis between blood and brain concentrations of propofol and pharmacodynamic effect monitored by BIS and 95%SEF following propofol infusion.
REFERENCES: 1. BJA 78:180-84,1997. 2. Acta Anaesth 43:209-11,1999.

Propofol concentrations vs. BIS and 95% SEF values (Correlation coefficients)

Endpoints (Number)	Time (min)	P. Conc. (ug)	BIS vs P. conc. (r)	95%SEF vs P. conc. (r)
1 (23)	30	4.71+/-1.23	0.13	0.01
2 (23)	115.8+/-16.5	6.15+/-2.24	0.46	0.21
3 (23)	151.6+/-41.5	2.05+/-0.73	0.34	0.09
1+2+3 (69)		5.67+/-2.05	0.71	0.4

S-121

COMPARISON OF SPECTRAL EDGE FREQUENCY 90 BETWEEN GOS WITH PENTAZOCINE AND GOS WITH EPIDURAL ANESTHESIA DURING SURGERY

AUTHORS: **K. Terasako**;
AFFILIATION: Hamawaki orthopedic hospital, Hiroshima, Japan.

INTRODUCTION: Prevention of intraoperative recall is one of the most important goals of monitoring anesthesia adequacy. The purpose of the present study is to compare electrocortical activities between GOS (1% sevoflurane, 66% nitrous oxide) with epidural lidocaine and GOS with intravenous pentazocine anesthesia during surgery.
METHODS: Sixteen patients aged 17-72 yr scheduled for open reduction of leg fractures were randomly assigned to GOS with intravenous pentazocine group (group P) and to GOS with epidural lidocaine group (group E). General anesthesia was induced in all patients with 4 mg/kg thiopental, 0.1 mg/kg vecuronium, and 3% sevoflurane in a mixture of oxegen and nitrous oxide followed by direct laryngoscopy and tracheal intubation. After tracheal intubation the vaporizer setting was decreased until end-tidal concentration reached 1% for sevoflurane. Inspiratory nitrous oxide concentration was adjusted to 66 %. The EEG was recorded, analyzed, and stored by a p-EEG monitor system (Drager, Lubeck, Germany). Spectral edge frequency 90 (SEF90) values were recorded blindly. To maintain systolic blood pressure from 90 to 120 mmHg, pentazocine was infused intravenously in group P and lidocaine was infused via epidural catheter in group E. After surgery was started, when SEF90 values stabilized more than 30 seconds three points were picked up randomly from the computer record.
RESULT: Systolic blood pressure and heart rate at the time SEF90 value was adopted were not different between the groups. SEF90 of group P (lt 16.7 $\pm$ 3.58 Hz, rt 16.3 $\pm$ 3.69 Hz) was significantly larger than that of group E (lt 10.9 $\pm$ 1.25 Hz, rt 11.6 $\pm$ 1.07 Hz) both in left and right sides. One patient required ephedrine (4 mg) to maintain a mean arterial pressure above 60 mmHg in the epidural group. None of the enrolled patients developed intraoperative memory.
DISCUSSION: To our knowledge, the processed EEG has not been previously applied to compare general anesthesia using pentazocine and combined epidural-general anesthesia at the same end-tidal concentration of sevoflurane during surgery. We have adopted systolic blood pressure between 90-120 mmHg as a standard indicator of adequate depth of anesthesia. And also in this study we used power spectral analysis of an EEG. The frequencies of 10.9 Hz and 11.6 Hz in SEF90 observed in group E in the present study are comparable to the predicting arousal from general anesthesia with isoflurane or propofol (1) and isoflurane-nitrous oxide anesthesia (2). However, the frequencies of 16.7 Hz and 16.3 Hz in group P are not comparable. These results, combined with the fact that none of the enrolled patients developed intraoperative memory, suggest that in group P the patients were kept under "light" anesthesia in terms of cortical electrical activities.
1. Br J Anaesth 1996;77:179-184.
2. Acta Anaesth Scand 1991;35:693-699.

S-122

THE BISPECTRAL INDEX IS PREDICTIVE OF EPISODES OF APNEA DURING MONITORED ANESTHESIA CARE

AUTHORS: **R. G. Soto**, E. S. Fu, R. A. Smith;
AFFILIATION: University of South Florida, Tampa, FL.

INTRODUCTION: Procedures performed under monitored anesthesia care and sedation are popular and prevalent, however a concern exists regarding the safety of these procedures, especially when performed outside of the operating room. We have previously shown that the incidence of apnea during MAC is high, and that it is poorly detected with standard monitoring (1). Bispectral Index (BIS) is a parameter derived from the bipolar scalp encephalogram that has been shown to provide an estimate of the depth of consciousness during anesthesia and sedation. Anesthesiologists primarily use BIS to assure that patients are unaware during general anesthesia. If apnea can be shown to correlate with depth of consciousness, that is with the level of BIS, then a potential improvement in safety during MAC/sedation could be achieved.
METHODS: 58 patients undergoing MAC anesthesia were monitored with BIS for level of consciousness, and capnography for apnea detection. Sedation was administered with propofol +/- fentanyl at the discretion of the provider. All patients received oxygen via nasal cannula as needed to maintain SpO2 >94%. The anesthesia provider was blinded to BIS and capnography data. Apnea for more than 60s as detected by capnography triggered notification of the anesthesiologist, who managed the patient appropriately. At the conclusion of the case the anesthesia provider was asked to determine the deepest level of sedation achieved using standard ASA definitions of sedation/analgesia (minimal, moderate, or deep). Categorical data were analyzed using Pearson's chi squared test. Logistic regression analysis was used to examine association between apnea and demographics, procedures, sedatives, and analgesics.
RESULTS: Incidence of apnea increased as depth of consciousness (as measured by BIS) decreased (minimum BIS in apnea group 45.6+/-17.9, versus 66.4+/-16.9 in the non-apnea patients). The age, sex, and weight of patients experiencing apnea was similar to that of patients without apnea, as were history of smoking, alcohol, COPD, and sleep apnea. The ability of the anesthesia provider to rate the depth of anesthesia did not correlate with the incidence of apnea.
DISCUSSION: As previously shown, the incidence of apnea during MAC is high, and although it can be reliably *detected* by capnography, apnea cannot be reliably *predicted* with current standard monitors. Monitoring depth of consciousness, however, allows for a new level of patient safety during MAC procedures. As depth of consciousness decreases below 70, the incidence of apnea increases significantly, with a positive predictive value of 0.75 at a BIS of 60. Limiting depth of sedation, and thereby depth of consciousness, to a BIS score >70 should prevent most cases of apnea during sedation cases.
REFERENCES
1. *Anesth Analg* 2003;96:S-147.

S-123

INFLUENCE OF BISPECTRAL INDEX SIGNAL UPDATE ON PERFORMANCE TO DISCRIMINATE LOSS AND RECOVERY OF CONSCIOUSNESS

AUTHORS: **S. Schraag**;
AFFILIATION: University of Ulm, Ulm, Germany.

INTRODUCTION. A key feature of any depth of anesthesia parameter is the ability to differentiate between consciousness and unconsciousness [1]. The scientific assessment of this feature is often based on a calculated prediction probability (P_k) of how accurate the transition from consciousness to unconsciousness and vice versa is detected by the respective variable [2]. This probabilistic approach depends on the allocation of the dichotomous variables. We report the dependence of P_k and performance of BIS on the signal update time delay.
METHODS. After obtained institutional ethic`s committee approval and written informed consent, the BIS recordings of 28 patients which were enrolled in a pharmacodynamic study were analysed. Anesthesia was induced with propofol 1.5 mg/kg and maintained with Desflurane with a baseline Remifentanil-TCI of 2 ng/ml.
Mean BIS values as well as the prediction probability (P_k) were calculated just when patients lost (LOC) and recovered (ROC) consciousness. These results were compared with those obtained 15 and 30 seconds thereafter to adjust for the time that is required for the computation of a full signal update from the raw EEG signal, according to manufactures´ information and previous literature [3]. Pairwise comparison for differences in performance indices were accomplished statistically using z-scores for grouped data with an overall significance value of 0.05. Grouped and paired comparisons were performed with an Excel-Macro (PKDMACRO).
RESULTS. Probability values are listed in the table below (*denotes significance against LOC/ROC). For comparison, a baseline BIS value obtained15 seconds before the respective observation is given.

Criteria for LOC	**Baseline -15**	**LOC**	**LOC+15**	**LOC+30**
BIS value (mean, 95% CI)	78.4 (71.0-85.9)	65.1 (55.9-74.4)	53.9 (44.9-63.0)	43.4 (36.2-50.5)
P_k (mean ± SEM)	n.a.	0.66 ± 0.07	0.79 ± 0.06	0.89 ± 0.04
p-value			0.00025	0.000021
Criteria for ROC	**Baseline -15**	**ROC**	**ROC+15**	**ROC+30**
BIS value (mean, 96% CI)	70.6 (66.9-74.4)	72.8 (69.1-76.4)	75.8 (71.8-79.8)	79.1 (74.8-83.4)
P_k (mean ± SEM)	n.a.	0.57 ± 0.07	0.66 ± 0.07	0.72 ± 0.06
p-value			0.0039	0.00012

DISCUSSION. The results show a relevant influence of the timing to collect and allocate clinical data for calculating prediction probability (P_k) and thus to describe the performance of depth of anesthesia parameters to correctly identify loss and recovery of consciousness. This fact may in part explain the large variation of P_k values reported in the literature[4]. As an example, we report from bispectral index data. However, this fact may in principal be valid for any EEG derived parameter.
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S-124

COMPARISON OF PATIENT STATE INDEX (PSI) AND BISPECTRAL INDEX (BSI) RESPONSE TO PROPOFOL AND DESFLURANE DURING AMBULATORY SURGERY

AUTHORS: **J. Tang**, P. F. White, R. H. Wender;
AFFILIATION: UT Southwestern Medical Center at Dallas, Dallas, TX.

INTRODUCTION: Both the physical state analyzer (PSA) and the bispectral index (BIS) monitors have been utilized to improve the titration of intravenous (IV) and volatile anesthetics, thereby facilitating the early recovery from general anesthesia (1,2). This study was designed to compare the use of the two cerebral monitors during a standardized general anesthetic technique.
METHODS: Nineteen patients undergoing general anesthesia were monitored simultaneously using the PSA (with the PSArray[2]) and BIS (with the XP platform) monitors. All patients were premedicated with midazolam (2 mg IV) and anesthesia was induced with propofol 2 mg/kg IV. Anesthesia was initially maintained with desflurane 3% and nitrous oxide 60% in oxygen. During surgery, the patients were administered bolus doses of propofol (20 mg IV), or the inspired concentration of desflurane was increased or decreased by 2%, and the changes in PSA and BIS values were subsequently recorded at 1, 3 and 5 min intervals. Data were analyzed using Student's *t*-test for continuous variables, paired *t*-test for intragroup differences, and Chi-square test for categorical data. (a, $p < 0.05$ vs before administration of propofol bolus or desflurane)
RESULTS: Both groups were similar with respect to their demographic characteristics. The PSA monitor appeared to be comparable to the BIS with respect to changes after bolus doses of propofol or alterations in the desflurane concentration (Table).
DISCUSSION: The PSA monitor appears to be a viable alternative to the BIS monitor for titrating both intravenous (propofol) and volatile (desflurane) anesthetics during surgery.
REFERENCES: (1) Anesthesiology. 2002;97:82-9; Anesth Analg. 2002;95:1669-74

	Before propofol bolus	1 min after bolus	3 min after bolus	5 min after bolus	Before des-flurane increased	1 min after change	3 min after change	5 min after change	Before des-flurane decreased	1 min after decreased	3 min after decreased	5 min after decreased
BIS	65±14	59±9[a]	51±11[a]	49±10[a]	57±11	54±10	54±10	48±10[a]	40±7	44±7	46±10[a]	49±10[a]
PSA	56±14	51±10	42±9[a]	41±9[a]	55±12	51±11	47±10[a]	43±7[a]	29±5	32±7	35±8[a]	40±11[a]

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ASSESSMENT OF PATIENT STATE INDEX (PSI) AND BISPECTRAL INDEX (BIS) VALUES DURING THE RECOVERY PERIOD AFTER OUTPATIENT SURGERY

AUTHORS: **J. Tang**, P. F. White, R. H. Wender;
AFFILIATION: UT Southwestern Medical Center at Dallas, Dallas, TX.

INTRODUCTION: The EEG-based patient state index (PSI) monitor has been demonstrated to assess consciousness during general anesthesia (1,2). Due to the failure of the PSI to return to the pre-induction baseline value with recovery of consciousness, it has been suggested that a difference may exist between the PSI and bispectral index (BIS) with respect to their sensitivity to residual (subhypnotic) levels of volatile anesthetic drugs (1). This study was designed to evaluate the relationship between the PSI and BIS values and the residual end-tidal desflurane concentrations during the early recovery period from general anesthesia.
METHODS:19 consenting outpatients scheduled for laparoscopic surgery were enrolled in this prospective study. Both the PSI (with PSArray[2]) and the BIS (with XP platform) were applied prior to induction of anesthesia. Anesthesia was induced with propofol, 2 mg/kg IV, and fentanyl 1 µg/kg IV. Desflurane 2-6% end-tidal in combination with N_2O 60% was administered for maintenance of anesthesia. Comparative PSI and BIS values along with the end-tidal concentration of desflurane at specific time intervals during the emergence period were recorded (means±SD; a, $P<0.05$ vs PSI value; b, $p<0.05$ vs Baseline value).
RESULTS: Even though the PSI exhibited a good correlation with the BIS during emergence period ($r = 0.74$), the PSI values were consistently lower than the BIS values. Interestingly, the PSI values displayed a better correlation with the end-tidal concentration of desflurane than the BIS at the times of eyes opening ($r = 0.56$, $r = 0.1$, respectively) and extubation ($r = 0.71$, $r = 0.31$, respectively).
DISCUSSION: The PSI appears to be more sensitive to the residual levels of desflurane than the BIS monitor during the early postoperative period.

REFERENCE: (1) Anesth Analg. 2002;95:1669-74; (2) Anesthesiology. 2002;97:82-9

	PSI	BIS
Baseline	97±3	96±3
End of anesthesia	45±16[b]	51±11[b]
Eye opening	81±13[b]	88±11[b]
Extubation	81±14[b]	89±13
Following commands	83±13[b]	91±9
Orientation	86±9[b]	93±8[a]

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COGNITIVE FUNCTION AFTER BIS-GUIDED ANESTHESIA

AUTHORS: **M. T. Chan**[1], T. Gin[1], B. C. Law[2], D. L. Chan[3], L. Chow[1];
AFFILIATION: [1]Chinese University of Hong Kong, Hong Kong, Hong Kong Special Administrative Region of China, [2]Kwong Wah Hospital, Hong Kong, Hong Kong Special Administrative Region of China, [3]North District Hospital, Hong Kong, Hong Kong Special Administrative Region of China.

INTRODUCTION: Deep level of anesthesia has been associated with cognitive impairment after surgery.[1] BIS monitoring may allow better titration of anesthetic depth. The purpose of this study was to determine whether BIS-guided anesthesia will prevent postoperative cognitive dysfunction (POCD).
METHODS: This study was approved by the Clinical Research Ethics Committee. All patients gave written informed consents. Ninety-eight elderly (> 60) patients undergoing non-cardiac surgery were randomly allocated to receive either BIS-guided or routine care anesthesia. Anesthetic regimen was determined by the attending anesthetists but generally consisted of propofol, isoflurane or sevoflurane, fentanyl, morphine and nitrous oxide. Anesthetic depth in the BIS group titrated to achieve a BIS value between 40 and 60. Routine care group received anesthesia according to clinical response. BIS values were recorded in all patients but were blinded to the anesthetists in the routine care group. Cognitive function was recorded before and three months after surgery using a self-reported 25-items cognitive failure questionnaire (CFQ).[2] CFQ scores range from 0 to 100. A score of 0 indicates normal cognitive function. POCD was defined as an increase in CFQ score > 1.96 standard deviation from the preoperative value of the group. Incidences of POCD and other variables were compared between groups using Fisher's exact test and unpaired t test, respectively. Logistic regression was used to identify risk factors for POCD. *P* value < 0.05 was statistically significant.
RESULTS: Four patients (4.1%) were loss to follow up. Patient characteristics did not differ between groups. BIS monitoring was associated with earlier tracheal extubation and lower volatile agent consumption. Although not achieving statistical significance, patients receiving BIS monitoring had a lower incidence of POCD compared with routine care group, $P = 0.09$. Our data also identified pre-existing cognitive dysfunction (CFQ > 17), odds (95%CI) = 2.1 (1.1-5.1), and prolonged duration of anesthesia (> 2 h), odds (95%CI) = 8.3 (2.0-19.7), as significant risk factors for POCD.
DISCUSSIONS: Our data showed a trend towards better cognitive outcome after BIS-guided anesthesia. These result indicate that a larger trial involving elderly patients undergoing long (> 2) hours of major surgery is warranted to demonstrate a statistically significant benefit with BIS monitoring.

REFERENCE

1. Anesthesiology 2001;95:A-52
2. Arch Clin Neuropsychol 1999;14:735-6
3. Br J Anaesth 1996;96:179

Patient characterics and perioperative variables

	BIS-guided group (*n* = 45)	Routine care group (*n* = 47)	*P* Values
Age (year)	70 ± 8	73 ± 8	0.10
Gender (M:F), *n*	20 : 25	19 : 28	0.82
Duration of surgery, h	4.2 ± 2.2	4.0 ± 2.1	0.14
Time to obey command, min	8.3 ± 1.8	10.7 ± 2.1	0.03
End-tidal volatile concentration (MAC-equivalent)	0.39 ± 0.08	0.51 ± 0.85	<0.01
Time averaged BIS values	51.5 ± 4.4	38.4 ± 5.8	<0.01
CFQ at baseline	13.1 ± 5.9	12.4 ± 6.2	0.78
CFQ 3 months after surgery	19.7 ± 10.6	22.8 ±11.1	0.17
Incidence of POCD, *n* (%)	6 (13%)	11 (25%)	0.09

Liver

S-127

EFFECT OF BLOOD CHEMISTRY ON INTRACRANIAL PRESSURE IN CANINE MODEL OF ACUTE HEPATIC FAILURE PERFUSED WITH BIOARTIFICIAL LIVER SUPPORT SYSTEM

AUTHORS: **S. Aggarwal**, R. C. Lopez, J. F. Patzer II;
AFFILIATION: University of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: A common and life-threatening complication of acute hepatic failure is rising intracranial pressure (ICP), with concomitant decrease in cerebral perfusion pressure (CPP), that is refractory to treatment. While the pathophysiology of elevating ICP is not well understood, perfusion with a bioartificial liver may serve to delay or prevent rising ICP. This study presents a retrospective analysis of ICP measurements in a canine D-galactosamine (D-Gal) acute liver failure model supported with a novel Bioartificial Liver Support System (BLSS) for possible correlation with survival, BLSS perfusion, physiologic and blood chemistry parameters.
METHODS: A preclinical evaluation of a novel BLSS, based on fresh porcine hepatocytes suspended in a hollow fiber bioreactor, was performed with 15 purpose-bred male hounds, one-three years old, 25-30 kg, administered a lethal dose of 1.5 g/kg D-Gal. The animals were divided into two primary groups: (1) no BLSS support (control, n=6) and (2) BLSS support starting at 16-26 hrs post D-Gal administration (n=9). The animals, maintained under isoflurane anesthesia, were invasively monitored for arterial pressure, central venous pressure (CVP), extradural ICP, pulmonary arterial pressure (PAP), urinary output, and end-tidal CO_2, and blood chemistries. Experimental endpoint was death, death equivalent (inability to sustain systolic blood pressure > 80 mmHg for 20 minutes despite maximal fluids and 20 g/kg/min dopamine infusion), or euthanasia at 60 hours.
RESULTS: After 12-24 hours all animals developed evidence of liver failure, showing increased levels of hepatocellular enzymes, ammonia, and lactate, hemodynamic instability, elevated ICP, elevated prothrombin time, and metabolic acidosis. Survival time is marginally prolonged for BLSS-supported animals compared with non-supported animals (p=0.05, by pair-wise log-rank censored survival time analysis). Group 1 (control) average ICP tended to rise throughout an experiment. ICP increased until the intiation of BLSS support in Group 2, at which point it stabilized. ICP and nominal blood chemistry liver failure indicators such as aspartate transaminase (AST), alanine transaminase (ALT), ammonia, and lactate tended to rise as liver failure progressed in all animals (Table 1). However, ICP was uncorrelated with any measured blood chemistry marker ($r^2 < 0.09$ for all ICP/blood chemistry correlations).

Table 1: Average ICP and blood chemistries at indicated times post D-Gal administration

	Control Group					BLSS-supported Group				
Time	ICP	AST	ALT	NH_3	Lactate	ICP	AST	ALT	NH_3	Lactate
0		26	32	20	2.8		26	38	11	2.5
16	23	197	146	12	3.7	25	273	242	7	2.5
24	31	1141	1199	15	4.1	25	549	705	9	3.9
32	33	2762	3633	29	3.3	35	1377	2056	16	2.8
40	36	4112	6171	69	3.9	32	2748	4397	23	4.4
48	51	5977	9740	85	4.6	31	4507	7915	42	5.7
56		3199	5733	57	6.3	25	5073	9098	80	9.4

ime post d-gal, hr; icp, mmhg; ast, iu/l; ast, iu/l; nh_3, mmol/l, lactate, mg/dl

DISCUSSION: Lack of correlation of ICP with liver enzymes, ammonia, and lactate indicates that these are not contributing factors in ICP elevation. Stabilization of ICP in BLSS-supported animals indicates that elevated ICP may be caused by substances (not identified) that are dialyzed through BLSS support. Blood chemistry markers that are correlated with and predictive of ICP elevation, such as cytokines, remain to be identified.

S-128

TRANSFUSION-FREE LIVING-DONOR LIVER TRANSPLANTATION

AUTHORS: **E. M. Strum**, J. Szenohradszky, V. Zhang, R. V. Patel, N. Jabbour, P. D. Lumb;
AFFILIATION: USC, Los Angeles, CA.

INTRODUCTION: Liver transplantation (LT) has become mainstream surgical therapy for patients with end-stage liver disease. A disproportionate increase of patients requiring LT has led to a prolonged waiting period and sicker recipients. Consequently, Jehovah's Witness (JW) patients, who refuse blood-product transfusion, are usually excluded from LT. Living-donor liver transplantation (LDLT) allows LT to become an elective surgery. A transfusion free (TF) procedure for JW patients can be achieved by combining blood augmentation and conservation; acute normovolemic hemodilutioon (ANH); intraoperative cell salvage (ICS); and individual-component therapies such as albumin, cryoprecipitate, factor VIIα, aprotinin, and aminocaproic acid.
METHODS: 38 cases of LDLT from 9/1998 to 6/2001 were reviewed retrospectively. All of them were separated into TF (n=8), and transfusion-eligible (TE, n=30) groups, with age, gender, and etiologies identified. With the combined technique of LDLT and transfusion-free strategies, we accomplished 8 cases of LT for JW patients. Patients in the TE group did not receive preoperative erythropoietin augmentation, since its use was not approved for non-JW patients. The induction of general anesthesia was with etomidate or ketamine and succinylcholine, and was maintained with isoflurane in oxygen and cisatracurium. Invasive monitors (arterial line, pulmonary artery catheter, and central venous line) were used. Preoperative clinical characteristics, intraoperative variations, and postoperative outcomes were compared. Data and outcomes were analyzed by using the Mann-Whitney U-test and Fisher's exact test. A P value < 0.05 was considered statistically significant in all tests.
RESULTS: The severity of liver disease was similar in both groups. The preoperative hematocrit levels of patients in the TF group were significantly higher then in the TE group, because of erythropoietin augmentation. Estimated blood loss, surgery time, and postoperative hematocrit values were similar in both groups. No blood products were used in TF patients, while 80% of TE patients received a median of 4.5 ± 3.5 units of packed red cells. The intensive care unit and hospital stay were similar in both groups. The mean postoperative follow-up is 817 ± 325 and 672 ± 224 days in the TF and TE patients, respectively. The re-operation and overall patient's survival rates were 25% and 100%, respectively, in the TF patients; and 30% and 90%, respectively, in the TE patients.
DISCUSSION: Living-donor-liver transplantation can be done successfully without blood-product transfusion in selected patients; e.g., Jehovah's Witnesses. Preoperative preparation, intraoperative cell salvage, and acute normovolemic hemodilution are essential. These techniques may be applied widely to all patients for several other surgical procedures. Chronic blood product shortages, as well as the known and unknown risk of blood products, should serve as the driving force for development of transfusion-free technology.

S-129

FAST-TRACKING OF LIVER TRANSPLANT RECIPIENTS. DO THE ANESTHESIA DRUGS AFFECT IT ?

AUTHORS: **L. Auler**, R. Diaz, R. Miecznikowski, G. Gouvea, J. Martinho, A. Cerqueira;
AFFILIATION: Bonsucesso General Hospital, Rio de Janeiro, Brazil.

INTRODUCTION. Previous studies have demonstrated the advantages and the safety of fast-tracking protocols for orthotopic liver transplant (OLT) recipients1,2, but because of the complications and that the surgery is almost always in an emergency scenario, physicians still have doubts about do it or not. The aim of this study was to examine if the total intravenous anesthesia could be a safe technique for fast-tracking OLT recipients.
METHODS. The anesthesia protocol for OLT recipients was: infusion of propofol 75 – 200mcg/kg/min, remifentanyl 0.1 –1.0mcg/kg/min, atracurium 10-15mcg/kg/min and aprotinin 200.000 UI/h (until the anastomoses of the hepatic arteries). The patients were monitored with 5-lead ECG, SpO2, end-tidal CO2 , MAP, CVP, PAP, SvO2, CO, CI, blood temperature, urine output, peripheral nerve stimulation, and BIS. Extubation criteria were: awake state, positive reflexes, neuromuscular reversal, body temperature, not hypoxemic, ETCO2 < 50 mm Hg, VT of at least 7 ml/kg, hemodynamically stable. We evaluated the first 30 patients of our group between October 19 and June 12. Diagnosis of liver disease were viral (53%), cholestatic (17%), alcohol (13%) and other (17%). The youngest patient was 11yr, the oldest was 63yr, and 63% were male. There were 5 cases of living right lobe recipients. We excluded from the protocol the pediatric patients, and the fulminant hapatic failure patients who were already intubated when arrived in the operating room (OR).
RESULTS. Of 30 consecutive transplant cases studied, 22 (73,3%) were successfully fast-tracked in the OR, right before going to the ICU. The MELD score of the recipients was determinant in the extubation time in the OR and in the ICU.
DISCUSSION. We could see with this new protocol, based on a total intravenous anesthesia, that this drugs, remifentanyl and propofol, which are metabolized quickly, made a huge improvement in the outcomes when the aim is recovery fast. These patients could be extubated fully awake as soon as the surgery was over, and consequently they went to the ICU without sedatives, endotracheal tubes or mechanical ventilation, what decreased pulmonary complications and post-operative infections.
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S-130

TK VERSUS UW PRESERVATIVE SOLUTION: HEMODYNAMIC AND METABOLIC CHANGES DURING ORTHOTOPIC LIVER TRANSPLANTATION (PART II)

AUTHORS: **S. Aggarwal**, R. Nicolau-Raducu, R. Planinsic, C. Boucek, I. Hilmi;
AFFILIATION: University of Pittsburgh Medical Center, Pittsburgh, PA.

INTRODUCTION: In our previous study we demonstrated that when donor livers were preserved with Histidine-Tryptophan-Ketoglutarate (HTK) and were *not* flushed with lactate Ringer's solution prior to reperfusion the incidence of post reperfusion syndrome (PRS, defined as decrease in MAP > 30 % from baseline value) was 40 % in comparison to 25 % when the donor livers were preserved with University of Wisconsin (UW) solution and were flushed with lactate Ringer's solution.
The purpose of this study was to determine if the donor liver's preserved with HTK and flushed with lactate Ringer's solution prior to reperfusion reduces the incidence of PRS during orthotopic liver transplantation (OLT).
METHODS: After IRB approval, 60 adult patients undergoing first OLT were studied. Depending on preservation solutions used patients were divided into 3 groups. Each group included 20 patients. Prior to reperfusion, in group 1, the liver preserved with HTK was not flushed via the portal vein with cold lactate Ringer's solution, group 2 the liver preserved with HTK was flushed with cold lactate Ringer's solution, and group 3 the liver preserved with UW was flushed with cold lactate Ringer's solution . Variables measured included systemic hemodynamic and metabolic profile at I + 60 (baseline), III + 30 s (30 seconds after reperfusion), III + 5 (5 minutes after reperfusion), III + 30 (30 minutes after reperfusion) and III + end (final sample). Data are presented as mean value ± standard deviation (SD). Statistical analysis was done using Mann- Whitney U test ($p < 0.05$).
RESULTS: as shown in table.
DISCUSSION: 1) There was no diference in incidence of PRS (25%) in patients where donor liver was preseved either with HTK (group 2) or with UW solution (group 3) and flushed with cold lactate Ringer's solution, however incidence of PRS was 40% in patients where livers were preserved with HTK solution and *not* flushed 2) The duration and the dose of epinephrine infusion required to support MAP was lesser in patients who received liver preserved with HTK and flushed with lactate Ringer's solution. 3) Lesser increase in serum lactate and base deficit in patients with liver's preserved with HTK indicates better graft function
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2. Journal of Critical Care, 8 (3), 154-160, 1993.

Variables	Group	I+ 60	III + 30 s	III + 5	III + 30	III + end
HR beats / min	1	81±15	66±12*	80±8*	84±13*	84±14*
	2	78±15	79±19	86±15	86±14	85±24
	3	90±16	82±21	95±14	95±13	97±14
MAP mmHg	1	74±11	56±13	68±11	74±10	71±8
	2	78±10	59±14	69±17	74±9	77±19*
	3	77±9	60±13	67±11	71±11	69±9
K^+ mmol/l	1	4±0.5	4.8±1.2	3.7±0.6	3.7±0.5	3.8±0.6
	2	3.7±0.6	4.1±0.8*	3.5±0.8*	3.2±0.6*	3.6±0.6
	3	3.9±0.7	5.2±1.1	3.9±0.9	3.8±0.7	3.8±0.6
BE mmol/l	1	-2.2±2.5	-3.2±3.4	-2.6±2.9	-2.7±3.3	-4±3.4
	2	-3.4±2.4	-2.2±3.8	-3.4±3.3	-3.0±2.3	-2.3±5.3
	3	-4.1±3.3	-5.7±2.9*	-5.1±3.3*	-4±2.9	-3.4±3.6
Lactate mmol/l	1	2.4±2.3	6.1±1.9	5.7±1.7	5.6±2.3	5.8±2.9
	2	2.1±0.9	5.8±2.1	5.8±2.1	5.6±2.4	5.6±3.1
	3	3.8±2.6*	9±3.7*	8.7±3.5*	8.3±3.8*	8.1±3.6*

* $p < 0.05$ statistically significant between groups

S-131

REPERFUSION CHARACTERISTICS DURING ORTHOTOPIC LIVER TRANSPLANTATION: EFFECT OF MARGINAL DONORS

AUTHORS: **G. Neelakanta**, A. Chikyarappa, M. Braunfeld, H. Nourmand, R. Steadman, K. Manoochehri;
AFFILIATION: David Geffen School of Medicine at UCLA, Los Angeles, CA.

INTRODUCTION: Shortage of organ donors and longer waiting list for orthotopic liver transplantation (OLT) patients has resulted in acceptance of "marginal livers " from organ donors previously considered unacceptable. However, marginal donor livers are at a higher risk of I/R injury. We hypothesized that in patients undergoing OLT, liver graft from marginal donor is associated with higher serum potassium and greater hemodynamic perturbations during reperfusion of grafted liver.
METHODS: After IRB approval, adult patients under going primary OLT were studied prospectively. Exclusion criteria were patients unable to consent, fulminant liver failure, and/or renal failure. Marginal liver was defined as presence of ≥ 3 following factors in the organ donor. Age ≥ 60 years, number of hospital days ≥ 5 days, systolic hypotension ≤ 70 mm Hg > 1 hour, use of two or more vasopressors, cardiac arrest duration ≥ 30 min, peak serum sodium > 165 mEq/L, liver enzymes ≥ 3 times normal, microvesicular fat content ≥ 25%. Non heart beating donors were considered marginal. Arterial blood serum K^+ was determined 10-min prior and 1, 2, 3, 4, and 5 min after starting portal reperfusion. Hemodynamic difficulty during reperfusion was graded according to the duration of hypotension (systolic BP = 80 mm Hg) and total amount of vasopressor use. They were graded as none (no hypotension, no vasopressor use), minimal (no hypotension, neosynephrine < 500 mcg, epinephrine <50 mcg), moderate (hypotension in spite of use of neosynephrine > 500 mcg, epinephrine > 50 mcg and/or nor epinephrine infusion) and severe (major dysrhythmias and/or cardiac arrest). Serum K^+ levels were analyzed as area under the curve (AUC) of values during the 5 min. The two groups were analyzed by fisher's exact test.

RESULTS: Total 32 patients had OLT (control i.e. donors with two or less of above-mentioned adverse factors, n=26, and marginal n=6). Patient preoperative data is shown in table 1. Reperfusion hemodynamic data was as follows; control vs. marginal (none 11 vs. 1, minimal 10 vs. 3, moderate 5 vs. 2, severe 0 vs. 0). Patients with marginal livers had higher K^+ AUC than controls (mean ± SEM 25.8± 1.24 vs. 20.8± 0.9, p value 0.003). There was no difference in the hemodynamic difficulty between the groups (p=0.48, 80% power not achieved).
DISCUSSION: Results from this ongoing study show that marginal livers are associated with higher release of K^+ during portal venous reperfusion. Measures such as portal venous flushing of liver via IVC, controlled release of portal vein, and immediate treatment of hyperkalemia may be important in patients receiving marginal liver. Further study is indicated before conclusion regarding hemodynamic difficulty during reperfusion due to marginal livers may be drawn.

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	Control Group	Marginal Group
n	26	6
Age , yrs (Mean± SD)	56 (10)	59 (7)
Gender	17 M, 9F	4M, 2F
Weight, Kg (Mean± SD)	81 (18)	76 (12)
Child-Turcotte-Pugh score (Mean± SD)	8 (2)	9 (2)
MELD score (Mean± SD)	14 (8)	17 (11)
K^+ (AUC) (Mean± SD)	20.8 (0.9)	25.8 (1.2)
Reperfusion difficulty		
none	11	1
minimal	10	3
moderate	5	2
severe	0	0

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PROTECTIVE EFFECTS OF PROPOFOL ON THE HEPATIC ISCHEMIC-REPERFUSION INJURY DURING NORMOTHERMIC PARTIAL HEPATECTOMY

AUTHORS: **Y. L. Wang**[1], S. L. Yao[2], Y. Shang[2];
AFFILIATION: [1]Department of Anesthesiology, Qian-Fu-Shan Hospital, Ji'nan, Shandong Province, China, [2]Department of Anesthesiology, Xiehe Hospital, Wuhan, Hubei Province, China.

INTRODUCTION: Effect of propofol on free radical mediated oxidative to cardiac muscle has been conformed. It can protect cardiac ischemic-reperfusion injury. But the protective effects of propofol on the hepatic ischemic-reperfusion injury during normothermic partial hepatectomy unknown.
METHODS: Twenty four patients undergoing elective partial hepatectomy in normothermic status were divided into two groups randomly. Observe group, the propofol solution were perfused intravenous continuously from the beginning of induction to the peritoneal suturing with the rate of 4 $mg \bullet kg^{-1} \bullet h^{-1}$. Control group, the propofol infusion were substituted with normal saline by equivalencing method. Venous blood samples were taken in five time points separatively as to measure the concentrations of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), glutamyl transpeptidase, blood glucose, bilirubin, superoxide dismutase (SOD) and malondialdehyde (MDA).
RESULTS: The concentrations of AST, ALT and blood glucose increased significantly during operation compared with those of preoperative values ($p<0.05$) in both groups. SOD increased and MDA decreased significantly in observe group compared with that of control group ($p<0.05$) at the same time.
CONCLUSION: It seems that propofol is an available protective agent during normothermic partial hepatectomy as to relieve the hepatic ischemic-reperfusion injury.
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S-133

BLOOD VOLUME SHIFT AND REDUCTION OF HEPATIC BLOOD FLOW DURING THORACIC EPIDURAL BLOCK

AUTHORS: **T. Yorozu**[1], T. Iijima[1], H. Miyao[2], M. Matsumoto[3], Y. Kubota[1], Y. Iwao[1];
AFFILIATION: [1]Dept. of Anesthesiology, Kyorin University School of Medicine, Tokyo, Japan, [2]Saitama Medical Center, Saitama Medical School, Saitama, Japan, [3]Federation of National Public Service Personnel Mutual Aid Associations, Tachikawa Hospital, Tokyo, Japan.

INTRODUCTION: Epidural block induces hypotension, which may become a postoperative risk factor. This hypotension is mainly due to sympathetic nerves blockade. Consequently, epidural block is considered to alter distribution of blood, which may be a mechanism behind hypotension. Since pulse dye densitometry (PDD) enables to monitor circulating blood volume (BV) 1) simultaneously with central blood volume (CBV) and hepatic blood flow (HBF) 2), the distribution of blood can be evaluated on bed-side. The authors applied PDD to evaluate the distribution of blood after epidural block during operations.
METHODS: Twenty patients (ASA 1 or 2) scheduled for elective abdominal surgeries were informed the nature of this study and the consent was obtained. An epidural catheter was inserted into 7 to 12 thoracic level. After the induction of anesthesia, the patients were intubated for mechanical ventilation. Anesthesia was maintained with sevoflurane 1-2% and nitrous oxide 67% in oxygen. When the hemodynamics was stabilized after incision, the first measurement of PDD (Nihon Kohden Corp., DDG analyzer DDG-2001™, Tokyo) was performed (pre-EDB). When the data of PDD was obtained 15 min after the injection of indocyanine green (ICG), 0.1mg/kg of 1% mepivacaine was injected into the epidural space. After 20 min from the epidural injection, the second measurement of PDD was performed (post-EDB). The arterial hemoglobin concentration (Hb, g/dL), mean arterial pressure (MAP, mmHg) and heart rate (HR, /min) were measured both at pre- and post-EDB. Cardiac output (CO, L/min), plasma dye clearance rate of ICG (K, /min), BV (L) and CBV (L) were computed by PDD. Stroke volume (SV, mL) and HBF were calculated by CO/HR and K*BV/0.8(extraction rate: 0.8), respectively
The data are expressed as mean ± SD. The statistical differences between the values of pre-and post-EDB were analyzed by Student's paired t test. Multiple regression analyses were performed to clarify the prominent factors of changes of the values.
RESULTS: MAP, HR and CO significantly decreased after epidural block, while BV did not change. CBV, SV, K and HBF significantly decreased. Multiple regression analyses showed that higher age significantly related to the more reduction of K.
DISCUSSION: Our study delineates the mechanism of hypotension during thoracic epidural block. Thoracic epidural block induced significant blood volume shift from central compartment to peripheral compartment. Accordingly reduced venous return and negative chrnotropic effect significantly reduced CO. Consequently, reduced CO caused significant reduction of HBF. The reduction of K, which reflected HBF, was more prominent in older patient. A treatment to counteract the reduction of CO has to be considered in aged group to preserve hepatic circulation during thoracic epidural anesthesia.
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Table Hemodynamic parameters at pre- and post-EDB

	Pre-EDB	Post-EDB	%reduction
Hb (g/dL)	12.0±1.2	11.5±1.4*	4%
MAP (mmHg)	96±13	84±17*	13%
HR (/min)	78±15	67±13*	14%
CO (L/min)	6.4±2.4	4.8±1.9*	25%
SV(ml)	81±22	70±21*	12%
K (/min)	0.213±0.04	0.188±0.04*	2%
BV (L)	4.9±1.0	5.0±1.1	
CBV (L)	2.00±0.41	1.83±0.48*	8%
HBF (L/min)	1.32±0.41	1.17±0.37*	11%

*: $p<0.01$; Post-EDB values significantly decreased from pre-EDB values

S-134

LIVING RELATED LIVER DONORS AND PATIENT CONTROLLED EPIDURAL ANALGESIA. GOOD NEWS FOR THE DONORS

AUTHORS: L. Auler, **R. Miecznikowski**, R. Diaz, G. Gouvea, L. Pacheco, M. Enne;
AFFILIATION: Bonsucesso General Hospital, Rio da Janeiro, Brazil.

INTRODUCTION. A severe worldwide shortage of organs for transplantation and the long waiting time have led to an increase acceptance of living donor liver transplantation for treatment of end-stage liver disease. Since Raia1 first performed living related liver transplantation in 1989, thousands of cases were described2,3. Because completely healthy patients undergo major surgery for altruistic motives, concerns have been raised about its safety for the donor4. Even the smallest pain felt by the donor is considered a collateral effect poorly accepted in this situation. The aim of this study was to know if the use of thoracic epidural catheter with patient controlled epidural analgesia (PCEA) in the donors could be considered effective in postoperative pain control, and if it was safe.
METHODS. Since December 2001, when we started our Live Donor Liver Transplant Program, we performed nine transplants with live donors (5 right livers, 1 left liver, and 3 left lobe, according French nomenclature). All donors were submitted to a large sub-costal incision that always results in significant postoperative pain. In eight of these donors, a thoracic epidural catheter with PCEA was chosen as the method for pain control. Our protocol was to keep the epidural catheter/ PCEA with the combination of ropivacaine 0,1%, fentanyl 4mcg/ml, and epinephrine 2mcg/ml for at least 72 hours.
Results. In the postoperative period, all donors presented coagulation disorders caused by liver resection. The pain stayed bellow 30 in the international analog scale (IAS) in all donors with PCEA, range from 0 to 100mm. The catheters were pull out only when the PT was about 70%, and no complications of epidural catheter were observed with these rules, >72 hours and PT >70%.
DISCUSSION. In conclusion, the thoracic epidural catheter with PCEA was considered an effective and safe method for control live liver donor pain. Our results show that this protocol decreases post-operative pulmonary complications, days in the ICU and hospital dischart. And also show that if we wait for the coagulation tests become normal, it is a safe technique of post-operative analgesia.
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Neuroanesthesia

S-135

ISOFLURANE AND CASPASE INHIBITION REDUCE CEREBRAL INJURY IN RATS SUBJECTED TO FOCAL CEREBRAL ISCHEMIA

AUTHORS: **P. Patel**[1], S. Inoue[1], D. Davis[1], J. Drummond[1], D. Cole[2];
AFFILIATION: [1]University of California, San Diego, San Diego, CA, [2]Mayo Clinic, Scottsdale, AZ.

INTRODUCTION: Although isoflurane can reduce ischemic neuronal injury after short post-ischemic recovery intervals, recent data have shown that this neuroprotective efficacy is not sustained. Delayed apoptotic neuronal death, mediated in part by activation of caspases, contributes to the gradual increase in the size of the infarction such that the neuroprotective efficacy is not manifest after a recovery period of at least 2 weeks. These data suggest that isoflurane, although capable of reducing early excitotoxic cell death, may not inhibit ischemia-induced apoptosis. If so, then it is conceivable that the prevention of apoptosis by a caspase inhibitor might provide neuroprotection in addition to that provided by isoflurane. The present study was conducted to test the hypothesis that isoflurane mediated neuroprotection can be made more long lasting with the administration of z-VAD-fmk, a broad spectrum caspase inhibitor.
METHODS: Fasted Wister rats were anesthetized with isoflurane and were randomly allocated to awake-zVAD, awake-vehicle, isoflurane-zVAD or isoflurane-vehicle groups (n=16 per group). Animals were subjected to focal ischemia by filament occlusion of the middle cerebral artery. Pericranial temperature was servo-controlled at 37 °C throughout the experiment. In the awake groups, isoflurane was discontinued and the animals were allowed to awaken. In the isoflurane group, isoflurane anesthesia was maintained at 1.5 MAC during the ischemic interval. After 60 min of focal ischemia, the filament was removed. Before and after ischemia, daily injections of zVAD or vehicle were administered icv via an implanted cannula for 14 days. Animals were killed 14 days after ischemia. The volume of cerebral infarction and the number of intact neurons in the peri-infarct cortex were determined by image analysis of H&E; stained brain sections.
RESULTS: Infarction volume was less in the isoflurane-zVAD group (23±11 mm3, mean±SD) than in isoflurane-vehicle, awake-vehicle, and awake-zVAD groups (82±31 mm3, 86±31 mm3 59±25 mm3, $p < 0.01$, $p < 0.01$, $p < 0.05$, respectively). In comparison to both vehicle treated groups, the administration of zVAD significantly decreased infarction volume ($p < 0.01$, respectively). The number of intact neurons within the peri-infarct cortex was significantly less in the awake-vehicle group than in the other three experimental groups ($P<0.01$).
DISCUSSION: The results of the present study indicate that a combination of isoflurane and a broad spectrum caspase inhibitor can produce neuroprotection that is evident even after a recovery period of 14 days. This combination demonstrated greater efficacy that the administration of z-VAD-fmk alone. These findings are consistent with the premise that ongoing apoptosis contributes to the enlargement of cerebral infarction during the recovery period and its inhibition can provide sustained neuroprotection.

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LIDOCAINE INACTIVATION OF THE RAT AMYGDALA BLOCKS THE HYPERALGESIC RESPONSE OF LOW-DOSE HALOTHANE

AUTHORS: **M. T. Alkire**, L. A. Gorski, S. V. Nathan;
AFFILIATION: University of California, Irvine, CA.

INTRODUCTION: The hypothesis that a unitary mechanism of anesthesia exists that explains all facets of anesthetic action through a single mechanism is now considered less plausible than a multiple mechanisms/multiple sites hypothesis. To further the latter idea, the mechanisms and sites involved in anesthetic action need identification. Inhalational anesthetic agents cause a hyperalgesic response at doses around 0.1 MAC **[1]**. Given the known role of the amygdala in modulating spinal pain processing through descending pathways **[2]**, and the fact that low-dose halothane primarily first affects brain activity in the amygdala **[3]**, we hypothesized the amygdala could be a brain site involved with mediating halothane induced hyperalgesia, as at least one mechanism of anesthesia. We tested this hypothesis by noting the pain sensitivity of rats to electrical shock at a hyperalgesic dose of halothane in the presence and absence of amygdala inactivation using lidocaine microinjections and compared these findings to control measurements made in air.
METHODS: Following IACUC approval 60 male Sprague-Dawley rats underwent stereotaxic bilateral cannula implantation surgery with cannula aimed at the amygdala (AP 2.65, ML 5.0, DV 8.3). One week later animals were divided into 4 groups and 20 min prior to footshock sensitivity testing in an airtight inhibitory avoidance apparatus during exposure to either air or 0.1MAC halothane they received intra-amygdala 0.2 microliters of either buffer or 4% lidocaine. Sensitivity was determined by applying a slowly increasing ramp current and noting the mA value at which the rat flinched. At least 3 measurements were made per animal. Histology verified cannula placement for a number of animals (suggesting appropriate coordinate selection, but complete histology remains pending at submission). Data are means +/- SD.
RESULTS: Consistent with prior work, 0.1MAC halothane caused a significant ($p<0.005$) hyperalgesia, decreasing the flinch threshold by 25% to electrical footshock pain versus air exposed-control animals given buffer into their amygdala (see figure). Air-control animals given intra-amygdala lidocaine did not have a change in sensitivity compared with buffer injected animals, suggesting that the amygdala does not have a tonic influence on pain processing. However, consistent with our site specific hypothesis, intra-amygdala lidocaine prevented the 0.1MAC halothane hyperalgesic response ($p<0.005$).
DISCUSSION: Halothane-induced hyperalgesia critically depends on the functioning of the amygdala. These findings serve to establish that the amygdala may be one brain site involved with mediating at least one mechanism of anesthesia, namely hyperalgesia. Coupled with prior work, these data suggest hyperalgesia occurs because low dose halothane specifically activates the amygdala and causes a change in gating of spinal pain signals through a descending modulatory pathway.
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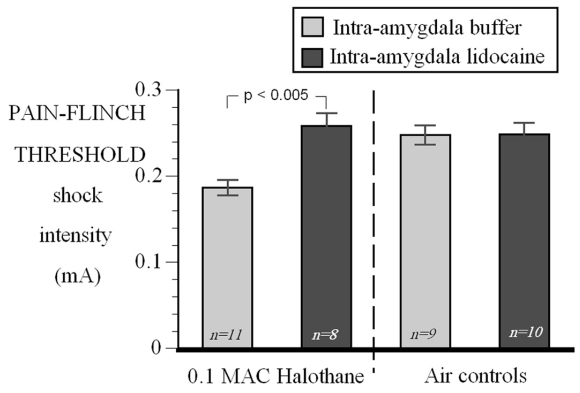

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ANEMIA INCREASES RAT CEREBRAL CORTICAL NNOS PROTEIN LEVELS AT CLINICALLY RELEVANT HEMOGLOBIN CONCENTRATIONS

AUTHORS: **G. M. Hare**[1], C. Mazer[1], X. Li[2], M. S. Cheung[2], R. Qu[1], A. J. Baker[1];
AFFILIATION: [1]University of Toronto, Toronto, ON, Canada, [2]Biotechnology Centre for Applied Research and Training, Seneca College, Toronto, ON, Canada.

INTRODUCTION: Increased cerebral cortical neuronal nitric oxide synthase (nNOS) expression has been identified following exposure to hypoxic environmental conditions (1) and may mediate the associated compensatory increase in cerebral blood flow (CBF) observed during hypoxic hypoxia (2). As such, nNOS may contribute to neuroprotective mechanisms directed at optimizing CBF during hypoxia.We recently reported an increase in cerebral cortical nNOS mRNA levels during acute anemia (3), raising the possibility that nNOS may also protect the brain from “anemic hypoxia”. The current study tests the hypothesis that acute hemodilutional anemia causes cerebral hypoxia triggering an increase in cerebral nNOS protein levels at clinically relevant hemoglobin concentrations.
METHODS: Anesthetized ventilated rats underwent tail artery and vein cannulation for monitoring of arterial pressure and performing hemodilution. Hemodilutional anemia was achieved by exchanging 30 $ml{\cdot}kg^{-1}$ of blood with pentastarch over 10 minutes. Hemoglobin concentrations were assessed by co-oximetry. Control animals were not hemodiluted. Control and anemic rats were recovered for 6,12, 24, 48 hours, 4 and 7 days (n=6 rats/group/time). Animals exposed to hypoxia (10% oxygen) served as positive controls. After sacrifice, cerebral cortical tissue was harvested, snap frozen, and total protein extracted. Western blot analysis for nNOS was performed utilizing a commercially available primary monoclonal antibody (1). Band density was quantified digitally and reported as pixelsμg $protein^{-1}$. A two-way ANOVA and post hoc Tukey test were used to assess data. Significance was assigned at $p< 0.05$ (Mean ± STDEV).
RESULTS: The hemoglobin concentration in anemic rats decreased to 64 ± 11 $g.L^{-1}$ following hemodilution ($p< 0.05$), and then increased steadily toward control values by 7 days (126 ± 11 g.L-1). In hypoxic rats, the hemoglobin concentration increased significantly to 169 ± 10 $g.L^{-1}$ by day 7 ($p< 0.05$). At 12 hours, there was a significant increase in cerebral cortical nNOS protein in both anemic (1,847 ± 195) and hypoxic rats (2,145 ± 138), relative to controls (1,121 ± 295) ($p< 0.05$ for both). At 24 hours, nNOS protein remained significantly elevated in hypoxic rats but returned toward control values in anemic rats (1,643 ± 302).
DISCUSSION: These data demonstrate that acute hemodilutional anemia caused a transient increase in cerebral cortical nNOS protein, which diminished as the hemoglobin concentration recovered toward control values. Hypoxic hypoxia produced a more sustained increase in nNOS, supporting the hypothesis that anemia induced cerebral hypoxia could have triggered the increase in nNOS observed in anemic rats. This increase occurred at a clinically relevant hemoglobin concentration and suggest that nNOS may contribute to endogenous cerebral neuroprotective mechanisms invoked by "anemic hypoxia". (CAS, PSI Support).
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S-138

S(+)-KETAMINE RELAXES ISOLATED BOVINE CEREBRAL ARTERIES BY ACTING AS A CALCIUM ENTRY BLOCKER

AUTHORS: **W. W. Wendling**, I. Kamel, N. Kapur, C. Harakal;
AFFILIATION: Temple University Health Sciences Center, Philadelphia, PA.

INTRODUCTION: The S(+) stereoisomer of ketamine is a more potent anesthetic and has fewer psychotomimetic side effects than its R(-) stereoisomer (1,2). The S(+)-ketamine stereoisomer may come into use as an intravenous anesthetic and N-methyl-D-aspartate (NMDA) receptor antagonist. The purposes of this in vitro study were to examine the direct effects of S(+)-ketamine on cerebrovascular smooth muscle and to elucidate the role of calcium in S(+)-ketamine-induced relaxation. Racemic ketamine relaxes vascular smooth muscle by inhibiting either extracellular calcium influx (3) or intracellular calcium release (4).
METHODS: With the permission of the USDA Meat and Poultry Inspection Program, bovine middle cerebral arteries were obtained from freshly killed animals. The arteries were isolated, immersed in ice-cold physiologic saline solution, transported to the laboratory, and cleaned. Arteries were cut into rings of uniform width to measure isometric tension development in isolated tissue chambers (37 deg C, pH=7.4), or were opened into strips to measure radioactive 45-Calcium (Ca) uptake (3,5).
RESULTS: (i) S(+)-ketamine had little effect on basal arterial tone, in the absence of exogenous vasoconstrictors. (ii) S(+)-ketamine produced dose-related relaxation of arteries pre-constricted with potassium (K+) or the stable thromboxane A2-mimetic U-46,619; half-maximal relaxation was produced by 3 or 5 x 10-4 M S(+)-ketamine respectively. Near-maximal relaxation was produced by 2 x 10-3 M S(+)-ketamine. (iii) Prior endothelial stripping with Triton X-100 had no effect on S(+)-ketamine-induced relaxation of K+-constricted arteries; half-maximal relaxation was produced by 3 x 10-4 M S(+)-ketamine. (iv) In calcium-deficient media containing K+ or U-46,619, S(+)-ketamine produced competitive inhibition of subsequent calcium-induced constriction. (v) S(+)-ketamine (2 x 10-3 M) had no effect on basal 45-Ca uptake (Figure), but inhibited K+-stimulated 45-Ca uptake(** $P<0.01$, ANOVA, Tukey’s test).
DISCUSSION: These results indicate that S(+)-ketamine directly dilates cerebral arteries by acting as a calcium channel blocker. S(+)-ketamine inhibits 45-Ca uptake through potential-operated (K+-stimulated) channels in cerebrovascular smooth muscle.
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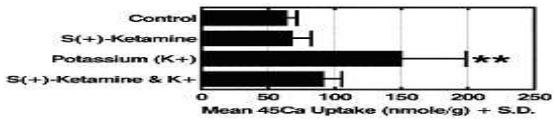

S-139

EFFECT OF DEXMEDETOMIDINE ON BRAIN TISSUE OXYGENATION (PTIO2) IN PATIENTS UNDERGOING CEREBROVASCULAR SURGERY

AUTHORS: **M. K. Sturaitis**, D. Lopez, L. Munoz, S. C. Toleikis, K. J. Tuman;
AFFILIATION: Rush Medical College, Chicago, IL.

INTRODUCTION: Properties favoring Dexmedetomidine (DEX) as a neuroanesthetic adjuvant include anesthetic sparing effect, intraoperative hemodynamic stability and reliable neurophysiologic monitoring (1,2).In animal studies DEX was shown to decrease CBF without affecting global CMRO2 and to increase cerebrovascular resistance in the face of hypoxia and hypercapnia (3,4). Concern remains regarding the clinical consequences of this large reduction in the CBF/CMRO2 ratio or the potential blunting of cerebrovasodilatory responses in brain at risk, however no studies have monitored PtiO2 during DEX administration.
METHODS: With IRB approval, 3 patients were studied during cerebrovascular surgery. (Pnt 1- F 62, Grade 3 SAH, L Sup. Cerebellar artery aneurysm; Pnt 2- F 43, Grade 0, L MCA; Pnt 3- M 36, elective L Frontal AVM). Anesthesia was induced with thiopental (STP) and sufentanil, and maintained with sufentanil infusion, sevoflurane and 50% N2O. After dural opening, brain tissue oxygen and temperature microprobes (Licox, GMS) were directly placed 20-25 mm into brain tissue within the vascular distribution at risk for ischemia, and allowed to stabilize prior to DEX loading (1mcg/kg) and DEX continuous infusion (0.5mcg/kg/hr). PtiO2 and hemodynamic measurements were continuously monitored and recorded q5min. until the start of dural closure. Arterial blood gases were measured and correlated to FIO2 and ETCO2. Bilateral upper and lower extremity SSEP and 4-channel EEG were continuously monitored, and burst suppression was used during temporary occlusion in one case.
RESULTS: After DEX administration, there was a slight immediate increase and overall upward trending of $PtiO_2$, which was maintained except under conditions of surgical stress (Pnt 2). The stability of $PtiO_2$ was evidenced by relatively small standard deviations from baseline (Figure). The standard deviation (SD) were 0.71 and 0.65 for Pnts 1 and 3, respectively. The standard deviation for Pnt 2, who suffered transient surgical stress, was 3.77. In addition, $PtiO_2$ values remained stable throughout burst suppression (STP and DEX). After a transient rise during DEX loading, mean BP returned to baseline and remained constant for all patients (Range: SD = 4-8 mm Hg). Anesthetic concentrations, ETCO2, FIO2, CVP, brain and esophageal temperatures, and hematocrit remained constant throughout the $PtiO_2$ measurement period. SSEP responses remained unchanged. End-procedure immediate awakenings or baseline neurologic status was achieved.
CONCLUSIONS: This preliminary study is the first to evaluate human regional brain oxygenation with DEX administration. Even in circumstances of baseline cerebrovascular compromise, and consistent with studies demonstrating neuroprotection and cognitive improvement with alpha-2 adrenergic agonists, DEX appears to have no detrimental effect (and may reveal an upward trending) for local brain tissue oxygenation.
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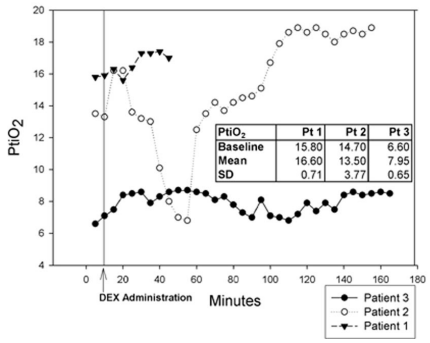

S-140

POSTURE DEPENDENCE OF SPONTANEOUS OSCILLATIONS IN CEREBRAL HAEMODYNAMICS

AUTHORS: **M. Smith**[1], I. Tachtsidis[2], C. E. Elwell[2], T. S. Leung[2], D. T. Delpy[2];
AFFILIATION: [1]The National Hospital for Neurology and Neurosurgery, Centre for Anaesthesia UCL, London, United Kingdom, [2]Department of Medical Physics & Bioengineering, University College London, London, United Kingdom.

INTRODUCTION: Previous studies using near infrared spectroscopy have described spontaneous oscillations in the cerebral circulation [1] that might have a regulatory role [2]. Autonomic reflexes are responsible for maintenance of cardiovascular stability during changes in posture and low frequency oscillations (LFO) in the circulation are believed to be related to the degree of sympathetic stimulation [3]. This study investigates the posture dependence of the magnitude of LFOs in cerebral oxyhaemoglobin concentration (O_2Hb) and blood pressure.
METHODS: 10 young (18-30 years) healthy volunteers underwent three postural changes – 10 minutes in the supine position, 5 minutes standing and a final 10 minute period of sitting. Cerebral O_2Hb and tissue oxygen index (TOI) were continuously monitored using spatially resolved spectroscopy (NIRO 300, Hamamatsu Photonics) and non-invasive blood pressure using a Portapres system (TNO Institute of Applied Physics). Fast Fourier transformation was applied to the O_2Hb and diastolic blood pressure (DBP) signals and the spectral power for the low frequency band (0.04 - 0.15Hz) was calculated from the area under the power spectral density (PSD) curve. Posture-related differences were compared with paired t-tests.
RESULTS: There was no difference in TOI or mean blood pressure between the three postures. In individuals, an increase in the power of the low frequency component in the PSD was associated with an increase in amplitude of the 0.1Hz oscillations observed in the O_2Hb signal. Power spectral analysis of cerebral O_2Hb and DBP from all subjects demonstrated a significant increase in the magnitude of the O_2Hb oscillations between supine and standing ($p<0.005$) and between supine and sitting positions ($p<0.005$) and in the magnitude of the DBP oscillations between supine and standing ($p<0.0005$).
DISCUSSION: This study confirms that the spectral characteristics of spontaneous oscillations in O_2Hb and DBP are posture dependent in normal volunteers. Previous work suggests that LFOs in cerebral haemodynamics might represent periodic fluctuations in the microcirculation, also known as vasomotion, and might be a marker of sympathetic activity [1,2]. In the present study, the identification of synchronous fluctuations in signals from different components of the circulation suggests a common origin. It is therefore likely that the posture dependent LFOs in cerebral O_2Hb are indicative of changes in sympathetic activity associated with changes in posture. It might be possible to use these changes as a diagnostic test to differentiate between different groups of patients with autonomic failure. Our results also suggest that posture dependence should be taken into account when comparing cerebral haemodynamic responses of the resting and activated brain.
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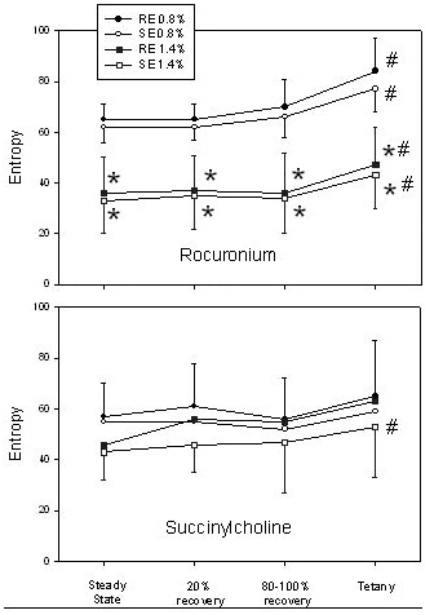
S-141

RESPONSE ENTROPY (RE) AND STATE ENTROPY (SE) DURING RECOVERY FROM PARALYSIS WITH ROCURONIUM OR SUCCINYLCHOLINE

AUTHORS: P. Wheeler, H. M. Koenig, V. L. Baughman, **W. E. Hoffman**;
AFFILIATION: Univ of Illinois at Chicago, Chicago, IL.

BACKGROUND Recovery of Succinylcholine induced paralysis has been reported to activate EEG determined by the bispectral index (BIS). The purpose of this study was to evaluate SE and RE during recovery from rocuronium and succinylcholine induced paralysis.
METHODS After obtaining institutional review board approval, forty adult patients undergoing spinal surgical procedures were recruited and signed informed consent. Awake patients were instrumented for S/5 M-Entropy EEG (Datex Ohmeda Inc, Helsinki, Finland), processed EEG and neuromuscular transmission (NMT) (train of four) measures. Anesthesia was induced with midazolam (2-4 mg), glycopyrolate (0.2 mg), thiopental (2-5 mg/kg), fentanyl (2-3 ug/kg) and isoflurane 0.8% or 1.4%. Paralysis was induced with rocuronium (0.3 mg/kg, n = 20) or succinylcholine (2 mg/kg, n = 20). Measurements were made during awake baseline, anesthetic induction, onset of paralysis with rocuronium or succinylcholine, steady state anesthesia with 0.8% end-tidal isoflurane (n = 20) or 1.4% isoflurane (n = 20), recovery of NMT to 20% and 80% of baseline and tetanic stimulation.
RESULTS SE was 89 ± 1 and RE was 98 ± 1 during baseline with no difference between groups. During steady state with rocuronium, there was a dose related effect of isoflurane (*) on SE and RE (figure 1). During recovery from paralysis with rocuronium, RE and SE did not change significantly but both measures increased during tetanic stimulation (#), suggesting a response to painful stimulation. During succinylcholine induced paralysis there was no dose related difference in RE and SE, primarily because of 3 patients anesthetized with 1.4% isoflurane that showed increases in RE and SE during burst suppression EEG activity. Facial electromyographic (EMG) activity increased before recovery of twitch responses to train of four stimulation in these patients and increases in RE and SE appeared to be related to this activity.
DISCUSSION We conclude that RE and SE can accurately indicate depth of isoflurane anesthesia with minimal interference of facial EMG in patients paralyzed with rocuronium. Succinylcholine treatment is associated with increases in RE and SE during isoflurane induced burst suppression, suggesting EEG activation. These increases appear to be related to facial EMG.



S-142

COMPARISON OF THE EFFECTS OF PROPOFOL AND ISOFLURANE ON CORTICAL SOMATOSENSORY EVOKED POTENTIALS

AUTHORS: **E. H. Liu**, C. P. Chia, H. J. Lim, H. K. Wong, Z. Y. Chen, T. L. Lee;
AFFILIATION: National University Hospital, Singapore, Singapore.

INTRODUCTION: Somatosensory evoked potentials (SSEP) are now widely used to detect intraoperative spinal cord injury and can reduce neurologic deficits during spine surgery. [1] Anesthetic drugs can affect the SSEP, and may cause failure to detect injury. Conflicting results from two studies comparing propofol and sevoflurane may have been due to variations in anesthetic depth, hemodynamics, and nitrous oxide. [2,3] We compared the effects of propofol and isoflurane on the SSEP, while minimizing confounding from these factors. This has not been previously done and we aimed to determine which anesthetic was more suitable for surgery requiring SSEP monitoring.
METHOD: We obtained IRB approval and written consent from 30 patients having elective spine surgery. The patients had no preoperative neurological deficit. They were randomized to receive ether isoflurane or propofol maintenance anaesthesia, after propofol induction. Expiratory isoflurane concentrations and propofol infusions were titrated to maintain the bispectral index (BIS) between 45 and 55.
The right posterior tibial nerve was stimulated at the ankle and the SSEP recorded with scalp electrodes in the medio-central and medio-frontal positions, using a Dantec Keypoint monitor. The P40N50 peak-to-peak amplitude, and latency time to the P40 peak were checked to be normal before induction of anesthesia. These parameters were measured at 20 minutes after induction when the BIS was between 45 to 55 with minimal variation, before the start of surgery. Opioids and nitrous oxide were not used, the patients were supine, normothermic, and blood pressure and heart rate were within 20% of awake baseline values during this period. A neurophysiologist, blinded to the anesthetic allocation, carried out the SSEP measurements.
RESULTS: The groups were similar in age, gender, weight and baseline SSEP measurements. During anesthesia, the P40N50 amplitude was significantly lower with isoflurane (1.2 ± 0.5 vs. 2.2 ± 0.9 μV), and the P40 latency was longer with isoflurane (41.6 ± 3.9 vs. 38.5 ± 2.6 msec).
DISCUSSION: This study showed that propofol caused less depression of the SSEP than isoflurane at moderate depths of anesthesia. We conclude that propofol anesthesia is more suitable when SSEP monitoring is required during surgery.
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S-143

POSITIONAL UPPER EXTREMITY SOMATOSENSORY EVOKED POTENTIAL (SSEP) CHANGES DURING SPINE SURGERY

AUTHORS: **I. R. Kamel**[1], W. W. Wendling[1], E. T. Drum[2], S. A. Koch[1], J. P. Gaughan[3], J. Whitten[3];
AFFILIATION: [1]Temple University Hospital, Philadelphia, PA, [2]Temple University Childrens Medical Center, Philadelphia, PA, [3]Temple University School of Medicine, Philadelphia, PA.

INTRODUCTION: Somatosensory evoked potentials (SSEP's) are monitored during spine surgery to avoid postoperative neurologic injury. The SSEP's may be useful to detect changes in the extremities related to positioning (1, 2). We investigated the incidence of reversible upper extremity positional SSEP changes in different patient positions during spine surgery.
METHODS: We retrospectively reviewed a computerized data base of 996 patients undergoing spine surgeries from 1995 to 2001 in which SSEP monitoring was utilized. Each patient was placed in one or more of five positions: Position A = supine position, arms tucked to the sides in neutral position; Position B = supine position, arms extended on arm boards; Position C = lateral decubitus position, with arms extended on arm boards; Position D = prone "superman" position, shoulders abducted, elbows flexed, arms on arm boards with hands pronated; Position E = prone position, arms are tucked to the side. In addition to age and sex we reviewed 4 temporal events in each position: upper extremity SSEP change, repositioning by the anesthesiologist, the response to repositioning, and occurrence of postoperative neurologic deficits. Median nerve stimulation at the wrist was predominantly performed; ulnar nerve stimulation alone or in conjunction with median nerve was occasionally performed. A reversible positional change was defined as a reduction in SSEP amplitude (50% or greater) or increase in latency (10% or greater), which improved after repositioning.
RESULTS: Patients were placed in a total of 1123 positions during their spine surgeries. Positional upper extremity SSEP changes were identified in 68 of 996 patients (6.8%) and in 80 of 1123 positions (7.1%). Of the 996 patients studied there were 399 males (40%) and 597 females (60%). Mean age was 29 years. The distribution across the 5 positions was significantly different ($P<0.0001$) using the Poisson heterogeneity test. Positions C and D were associated with the highest incidences of positional SSEP changes in the upper extremity during spine surgery compared with positions A, B, and E ($P<0.0001$). No patient with a reversible SSEP change had a subsequent neurologic deficit in the affected limb. The number of identified positions (n) and the % of corresponding upper extremity SSEP changes are shown in the table.

Variable	n	Change n (%)
Total positions	1123	80 (7.1)
Position A	110	2 (1.8)
Position B	28	0 (0)
Position C	377	31 (8.2)
Position D	511	45 (8.8)
Position E	97	2 (2.0)

DISCUSSION: Reversible positional SSEP changes were frequently observed during spine surgery, particularly in the prone " superman" and lateral decubitus positions. Monitoring upper extremity SSEP changes should be of value to prevent position-related nerve injury.
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S-144

REQUIREMENTS FOR TRAIN-OF-FOUR RATIOS WHEN ASSESSING PEDICLE SCREW PLACEMENTS DURING SPINAL SURGERY

AUTHORS: **J. R. Toleikis**, T. W. Starck;
AFFILIATION: Dept. of Anesthesiology, Rush Medical College, Chicago, IL.

INTRODUCTION: A widely utilized monitoring technique for reducing the incidence of nerve root injury resulting from misplacement of pedicle screws during spinal surgery is electrical stimulation of the screws and monitoring of the resulting activity from leg muscles innervated by nerve roots at risk. If activity can be elicited at stimulation intensities below "warning threshold," breaches of the pedicle wall may be present[1]. While muscle relaxation can increase nerve root stimulation thresholds and thus affect pedicle screw testing, only one study to date has objectively measured relaxant levels adequate for pedicle screw measurement[2]. Using a pre (T_0)- and post (T_1)-relaxant single twitch ratio recorded from hand muscles, it was reported that "warning thresholds" may be elevated and may lead to "false negative" results when neuromuscular blockade exceeds 80% (T_1/T_0 ratio < 0.2)[2]. However, acquiring pre-relaxant responses may not be feasible or practical. Train-of-4 (TOF) responses recorded from leg muscles may be more useful since these post-induction responses can easily be obtained from muscles already being utilized for monitoring the nerve roots at risk. The purpose of this study was to determine if a relationship exists between the T_1/T_0 ratio recorded from hand and the T_4/T_1 ratio recorded from leg, that would provide a minimal TOF ratio for assessment of pedicle screw placement.
METHODS: Following IRB approval and patient consent, we evaluated five patients undergoing spinal surgery involving pedicle screw placement. Vecuronium and inhalational-based anesthesia were utilized for all surgical procedures. Adhesive surface electrodes were used to stimulate the ulnar nerve at the wrist and the peroneal nerve at the fibular head. The resulting myogenic responses were recorded from adductor digiti minimi and anterior tibialis muscles, respectively. Baseline twitch responses (T_0) were acquired after the patient was asleep but prior to muscle relaxant administration. TOF responses, consisting of a first twitch (T_1) followed by twitches T_2, T_3 and T_4, were recorded every 3-5 minutes for 1-2 hours after administration of relaxant. T_1/T_0 (hand) and T_4/T_1 (leg) ratios were calculated.
RESULTS: When patients were given intubating doses of relaxant at induction, and the relaxant was allowed to wear off, the response curves for T_1/T_0 and T_4/T_1 twitch ratios recorded from hand and leg muscles highly correlated ($r = 0.78$, $p<0.001$)(Figure). T_1/T_0 twitch ratios measuring 0.2 were comparable to T_4/T_1 ratios measuring 0.1 ± 0.034.
DISCUSSION: This study establishes a relationship between the single twitch amplitude ratios obtained from hand muscles and TOF twitch amplitude ratios obtained from leg. The study shows that T_4/T_1 ratios that exceed 0.2 may be utilized as an effective criteria for assessment of muscle relaxant levels during spinal surgery involving pedicle screw placement.
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1. J. Spin. Disord., 13, 283-289, 2000.
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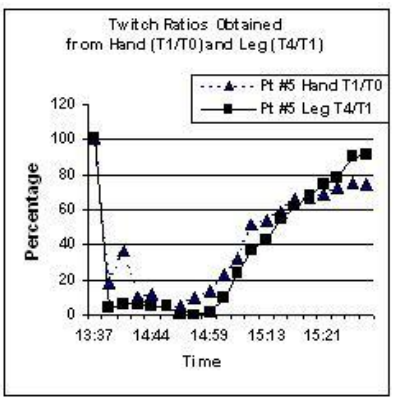


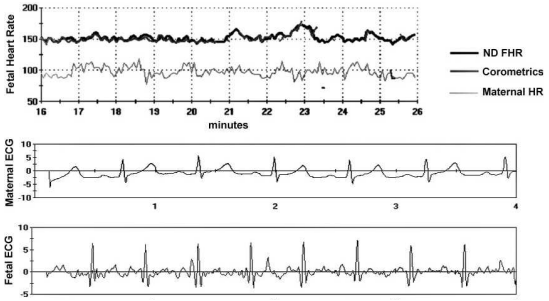
Obstetric Anesthesia

S-145

NON-INVASIVE FETAL ECG: METHOD REFINEMENT AND PILOT DATA

AUTHORS: **T. Y. Euliano**[1], D. E. Marossero[2], N. R. Euliano[3], B. Ingram[1], K. Andersen[1], R. K. Edwards[1];
AFFILIATION: [1]University of Florida College of Medicine, Gainesville, FL, [2]NeuroDimension, Inc, Gainesville, FL, [3]University of Florida College of Medicine and NeuroDimension, Inc, Gainesville, FL.

INTRODUCTION: Despite its limitations, fetal heart rate (FHR) tracing analysis is the best monitor of fetal well being during labor. Transabdominal ultrasound has limitations (tracing loss during fetal movement, potential to confuse maternal for FHR, inability to monitor during cesarean delivery or abdominal surgery). Scalp electrode monitoring (the alternative to ultrasound) has risks including infection and hematoma. There is preliminary evidence that the diagnosis of "fetal distress" can be enhanced with information acquired from the fetal electrocardiogram (FECG), reducing the operative delivery rate by 46%.[1] FECG extraction is a well-known problem of mixed signals – the FECG is hopelessly contaminated by the maternal ECG, maternal electromyograph, and noise.
METHODS: We developed front-end signal processing hardware to enhance the signal/noise ratio of conventional ECG equipment and improve the extraction of FECG. A series of data processing algorithms combined with blind source separation (BSS) was used to extract, in real-time, the FECG, FHR and the electrohysterogram (EHG). A reliability or "trust" factor, based on intrinsic properties of the FECG and FHR, quantifies the separation success from 0 (no separation) to 10. After written, informed consent, 28 laboring patients were enrolled in the study. Abrasive gel was used to reduce skin impedance. Electrode position was varied for the first 11 patients, until an optimal array was identified: 10 electrodes encircling the maternal abdomen, with reference electrodes located centrally and on the right leg. Data, including that from the standard maternal-fetal monitor (Corometrics), were collected on each of the last 17 patients for 12 to 51 minutes (median 45).
RESULTS: The FHR was successfully extracted by FECG for all patients, and correlated well with the standard cardiotocograph-determined rate (RNSE = 2.85 bpm). In this small sample, neither maternal weight (mean 84 +/- 17 kg), membrane status (7/17 ruptured), nor electrode impedance (9.8 +/- 6.8 kΩ) consistently affected the success of FECG extraction. Prematurity (< 37 weeks gestation; n=3) however, had a slight effect, increasing the RMSE to 3.34 bpm.
DISCUSSION: Current methods of assessing fetal well being during labor are inadequate. The FECG may contain additional predictive information. We have developed an improved technique for the non-invasive extraction of FECG where FHR extraction approaches the quality of cardiotocography, with fewer periods of complete signal drop out. The quality of the FECG trace was not quantified but varies significantly over time; this feature requires further improvement. At present, calculation of intervals requires an averaged complex, eliminating measurement of interval variability. Ongoing studies are investigating the utility of the FECG information in labor and antenatal testing. The eventual goal is a sophisticated maternal-fetal monitor that provides enhanced predictive value for the progress of labor and fetal well being.
REFERENCE: 1. Am J Obstet Gynecol 169:1151-60, 1993.



S-146

MATERNAL AND FETAL OUTCOMES AFTER UTERINE RUPTURE/DEHISCENCE

AUTHORS: **K. E. Stack**, R. Y. Gershon;
AFFILIATION: Emory University School of Medicine, Atlanta, GA.

INTRODUCTION: Uterine rupture has been associated with significant maternal and fetal morbidity and mortality. Potential maternal complications include blood transfusion, gravid hysterectomy, visceral injury, and rarely death. Fetal morbidity is not uncommon and death has been reported. Prior uterine surgery is a known major risk factor for uterine rupture. ACOG guidelines (in association with the ASA) provide for close attention to patients attempting a vaginal birth after cesarean section (VBAC), with a recommendation for appropriate personnel and facilities to be "immediately available during active labor to perform an emergency cesarean section."
METHODS: Our institution is a large, tertiary care, inner city hospital serving the indigent with poor prenatal care. Over a one-year period (November 2001 through November 2002), 14 cases of uterine rupture or dehiscence were recorded. Retrospective chart reviews for maternal and fetal outcomes were performed on all cases. The diagnosis was confirmed at cesarean delivery in all 14 patients. The known uterine rupture/dehiscence rate during this time period was 14/4489 (0.3%) live births.
RESULTS: There were no maternal deaths. There was 1 cesarean hysterectomy performed and 13 uterine repairs. 3/14 (21%) patients received blood transfusions, with no more than 2 units per patient required. 10/14 (71%) patients received regional anesthesia, and 5/14 (36%) patients received general anesthesia. One patient had an epidural converted to general anesthesia secondary to inadequate blockade.
There were no fetal deaths. 10/14 (71%) neonates had apgar scores of eight or greater at five minutes of life. 13/14 (93%) neonates had apgar scores of seven or greater at fifteen minutes of life, and by fifty minutes of life, 14/14 (100%) neonates had apgar scores of seven or greater. Currently, there are no known permanent neonatal sequelae.
DISCUSSION: Maternal and fetal outcomes at our institution have been favorable. While we experienced no maternal complications due to general anesthesia, the increased incidence of general anesthesia required while undergoing cesarean delivery in the presence of a uterine rupture or dehiscence may further increase maternal risk for morbidity and mortality secondary to aspiration and/or difficult intubation. Of the 9 cases in which there was fetal distress, 7/9 (78%) patients had existing epidurals in place. Epidural anesthesia was used successfully for cesarean section in 6 (86%) of these cases. Of the 5/14 (36%) cases in which there was no fetal distress, 3/5 (60%) patients received spinal anesthesia for cesarean section. Cesarean delivery, uterine repair, and/or gravid hysterectomy were possible under regional anesthesia in 9/14 patients (64%). Conversion from regional to general anesthesia occurred in 1/10 patients (10%). We believe that early epidural placement in patients undergoing trials for a VBAC (in addition to 24-hour in-house coverage) was essential for good maternal and fetal outcomes.

S-147

EPIDURAL FEVER WITH BUPIVACAINE OR ROPIVACAINE INFUSION FOR LABOR ANALGESIA

AUTHORS: **S. Ramanathan**;
AFFILIATION: Magee-Womens Hospital, Pittsburgh, PA.

INTRODUCTION: Epidural analgesia with continuous infusion is reportedly associated with increase in parturient's and the baby's body temperature (BT). The exact incidence of fever is subject to speculation and it is not known whether the increase is influenced by the local anesthetic used. In this report we provide data on these two issues.
METHODS: A continuous quality improvement database (cqi) was used for data retrieval. The database was reviewed and approved by the IRB for HIPAA compliance.

Variable	Bupi Group	Ropi Group	P Value
n	1129	463	NS
Maternal BL Tempº c	36.62± 0.46	36.62± 0.47	NS
Maternal Temp ºC at 10 cm dilatation	37.03±0.6	37.04±0.6	NS
Maternal Temp ºC at delivery	37.0±0.7	37.0± 0.7	NS
Neonatal Temp ºC at birth	36.6±0.6	36.7 ±0.6	NS
Neonataltemp ºc 6 hrs after birth	36.7±0.3	36.7±0.3	NS
Maternal fever> 38º c	7.3%	8.3%	NS
Neonatal temp º C38º C at delivery	0.44%	2.15%	0.001

Legend: BL – baseline; Temp – temperature. Data are mean±1 SD.
CONCLUSION: Our data show 7-8% of patients will develop a fever during infusion analgesia and the incidence is not statistically different between Bupi and Ropi groups. A higher chance of neonatal fever was seen in the Ropi group. The reason for this is unknown

S-148

DOES THE EPIDURAL SPACE CONTAIN HEMATOPOIETIC CELLS?

AUTHORS: **E. J. Goodman**, H. J. Meyerson, D. J. Zagorski;
AFFILIATION: Case Western Reserve University, Cleveland, OH.

INTRODUCTION: Spinal-epidural abscesses occur so infrequently that it is difficult to determine their incidence with any accuracy. We undertook this study to determine whether there were resident hematopoietic cells in the epidural space that could protect against infection after epidural anesthesia.
METHODS:
After approval from our hospital's IRB was obtained, patients who requested epidural anesthesia for their labor pain were included. The epidural needle was placed using a loss of resistance to saline technique, and the saline that came back out of the needle after being injected into the epidural space was collected. If any blood was visualized on the needle or in the epidural washing fluid, or if less than 1cc of fluid was obtained, the sample was eliminated. The samples were spun onto slides ("cytospins" at 1800 RPM x 5 min.) and stained with Wright-Giemsa stain. Any cells obtained would be characterized further using flow cytometric studies. Spun samples were incubated with fluorescently-conjugated antibodies (to CD19 (B cells), CD3 (T cells), CD16/56 (NK cells) or to CD14 (macrophages)), washed to remove unbound antibody, and analyzed in a flow cytometer.
RESULTS: A total of 6 epidural space washings were analyzed. In two samples, no cells at all were found. In two other samples, we saw only a few elongated, fusiform naked nuclei. From their size and shape, they appeared to come from degenerated, non-hematopoietic mesenchymal cells. In the final two specimens, there was red cell contamination. A few scattered neutrophils could be seen in these samples, evidently as a result of the contamination of the blood.

CONCLUSION: The epidural space does not appear to contain resident hematopoietic cells. The low incidence of epidural abscesses after epidural anesthesia cannot be explained by the presence of these types of cells. However, any blood that is introduced into the epidural space during the placement of the epidural needle or due to the irritation of the epidural catheter might provide protection against infection with the hematopoeitic cells it contains.

S-149

HOW DOES CURRENT OBSTETRICAL ANESTHESIA PRACTICE IN NEW JERSEY COMPARE TO ASA STANDARDS?

AUTHORS: **S. Ginsberg**, A. Solina, S. Cohen, J. Denny, M. Bermann, D. Hall;
AFFILIATION: UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

INTRODUCTION: Clinical Practice Guidelines for OB anesthesia were most recently delineated by the ASA in 1999 (Anesthesiology 1999;90:600-611). These guidelines represent recommendations for clinical practice that are scientifically supported by current literature, & are intended to improve the quality of patient care & satisfaction. The adoption of these guidelines into common clinical practice is predicated upon the strength of the literary support & clinical feasibility of implementation. Our purpose was to delineate common OB practice in NJ & compare it to recognized guidelines.
METHODS: With IRB approval, a questionnaire survey consisting of 52 questions was sent to all practicing anesthesiologists in the State of NJ. 481 questionnaires were mailed: 105 returned-completed; 15 returned-uncompleted-responder did not practice OB anesthesia; & the rest of the surveys were not returned.
RESULTS: Because space limitations do not allow us to present all the survey results, we have selected 7 questions we feel are most important or interesting. Complete survey results are available on our web site at www2.umdnj.edu/anesweb.
#1: Do you allow the pt a liquid diet during labor?
ASA: The task force concluded that oral intake of clear fluids improves maternal comfort but were equivocal about whether this practice increases the risk of pulmonary aspiration.
Survey: 84% of responders do not allow pts a liquid diet during labor.
#2: Do you allow the pt a solid diet during labor?
ASA: Fasting period of at least 6 hrs before elective C/S.
Survey: Less than 1% allowed pts a solid diet during labor.
#3: Do you obtain a platelet count before administration of regional anesthesia for L&D?
ASA: Only recommended routinely for complicated pts including those with pregnancy-induced hypertension.
Survey: 25% of responders perform a platelet count routinely before administering regional anesthesia for L&D.
#4: Do you obtain a PT/PTT before performing regional anesthesia for L&D?
ASA: None cited.
Survey: Less than 1% of responders perform a PT/PTT prior to the administration of regional anesthesia for L&D.
#5: What is the lowest platelet count that you consider safe for the administration of a regional anesthetic for L&D?
ASA: None cited
Survey: 100,000=21%.
#6: Do you routinely use epidurally administered opioid for L&D?
ASA: When a low concentration of epidural local anesthetic is used, the addition of an opioid improves analgesia & maternal satisfaction without increasing maternal, fetal or neonatal complications.
Survey: 73% of responders utilize epidural opioids during L&D.
#7: Do you allow pts to ambulate with an epidural in place?
ASA: none cited.
Survey: 13% of responders allow pts to ambulate with an epidural in place.
SUMMARY: The present survey delineates current OB anesthesia practice in NJ & indicates that it does not importantly differ from ASA guidelines.

S-150

ADDITION OF INTRATHECAL FENTANYL TO LEVOBUPIVACAINE DECREASES THE INCIDENCE OF BREAKTHROUGH PAIN DURING INTRAPARTUM EPIDURAL ANALGESIA

AUTHORS: **Y. Lim**, A. T. Sia, C. E. Ocampo;
AFFILIATION: Kerdang Kerbau Women's and Children's Hospital, Singapore, Singapore.

INTRODUCTION: Intrathecal (IT) levobupivacaine is used recently as an induction agent for combined spinal epidural (CSE) in labor analgesia (1). The addition of fentanyl to levobupivacaine was shown to prolong the duration of epidural analgesia (2) even though the interaction between IT levobupivacaine and fentanyl in prolonging analgesia has not been previously reported in laboring women. The practice of initiating an epidural infusion after IT injection to prolong the duration of analgesia and decrease the incidence of breakthrough pain has gained increasing popularity (3)(4). The effect of a longer duration of analgesia rendered by the IT component on the incidence of breakthrough pain has not been evaluated. We hypothesize that the prolongation of IT component of analgesia rendered by the addition of IT fentanyl 25 mcg to IT levobupivacaine 2.5mg could reduce the incidence of breakthrough pain when an epidural infusion of levobupivacaine 0.125% + fentanyl 2mcg/ml was maintained before the loss of spinal analgesia.
METHODS: We recruited 40 nulliparous, ASA I parturients in early labor who requested for neuraxial analgesia for this randomized, double blinded trial. Twenty received IT levobupivacaine 2.5mg (group L) and twenty received IT levobupivacaine 2.5mg+fentanyl 25mcg (group LF). Fifteen minutes after the IT component was successfully given, an epidural infusion was initiated. Sensory block, motor block, pain scores and post block complications were evaluated. The duration of analgesia was documented as the time from IT injection to the request of additional analgesia. Parturients who delivered without breakthrough pain were classified as 'successful' blocks. The percentage of successful block and duration of analgesia were analysed with X^2 test and Kaplan-Meier technique using log-rank test, respectively. Other data were analysed using one way analysis of variance (ANOVA) and Kruskall Wallis test.
RESULTS: Patients' characteristics in the 2 groups were similar. The percentage of 'successful' blocks in group LF was significantly higher (87.5% *vs* 43.8%, $p<0.05$). The duration of analgesia was also significantly longer in group LF than L (mean 530 min +/-SE65, 95% confidence interval [CI] 403-658min *vs* 361+/-66, CI232-490 min, $p<0.05$). There were no significant differences in systolic blood pressure, sensory block and motor block between the 2 groups. Pruritis was significantly higher in group LF compared with group L (13/20 vs 7/20, $p<0.05$). There was no difference in the satisfaction score and mode of delivery between the groups.
CONCLUSION: Our results showed that IT levobupivacaine+fentanyl resulted in a longer duration of analgesia and a higher rate of 'successful' block without significant side effects. This can potentially decrease the number of top-ups required in labor ward and anesthetists' workload in the delivery suite.
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(1) Anesth Analg 2001; 93:996-1000
(2) Anesth Analg 2001; 92:410-414
(3) Reg Anesth Pain Med 2000; 25:223-7
(4) Anesth Analg 2002; 94:927-932

S-151

COMPARISON BETWEEN INTRATHECAL RACEMIC BUPIVACAINE AND LEVOBUPIVACAINE FOR CSE TECHNIQUE FOR LABOR ANALGESIA

AUTHORS: **N. Sah**, M. C. Vallejo, S. Ramanathan;
AFFILIATION: Magee Womens Hospital, Pittsburgh, PA.

INTRODUCTION: Combined spinal epidural for labor analgesia is commonly performed with a combination of L-R- bupivacaine and an opioid. The purpose of this study was to compare the intensity and duration of motor block and the duration of sensory block with L-R-bupivacaine and levobupivacaine. A human study compared L-R-bupivacaine and levobupivacaine in combination with sufentanil for labor analgesia and showed a similar sensory block with a less intense motor block twenty minutes after administration of the drug.[1] An animal study demonstrated a motor block of shorter duration with levobupivacaine while at the same time had a longer lasting sensory block when compared to L-R- bupivacaine.[2]

METHODS: Patients were randomized into two groups. One group received a mixture of 2.5mg racemic bupivacaine and 25mcg fentanyl into the subarachnoid space and the second group received 2.5mg levobupivacaine and 25mcg of fentanyl. Verbal Analog Scores (VAS) scores and Bromage scores were recorded at 5,15, 30, and every 30 minutes thereafter till the VAS reached >3 at which time the epidural block was activated. Patients' vital signs and fetal heart rate were monitored for 30 minutes after initiating the block. Results were expressed as mean or median and analyzed using Mann-Whitney U tests (VAS scores), X^2 analysis and t-test at $p < 0.05$.

RESULTS: None of the patients in either group had any noticeable motor block. The average duration of sensory block in the two groups was 114.85±26.27 minutes and 101.9±35.20 minutes respectively (p =NS). Median VAS decreased from 7 to 0 in 5 minutes in group1 and from 7.5 to 0 in group 2 (Figure 1).
X-axis = minutes after block, Y-axis = VAS score

DISCUSSION: Despite the earlier studies there is no difference in the intensity and duration of sensory or motor block between racemic bupivacaine and levobupivacaine in our study. In a previous study, levobupivacaine used for spinal anesthesia was shown to have a slightly shorter onset and longer duration as compared to L-R bupivacaine.[3] However our results did not show any difference between the two agents in onset time, duration and sensory and motor block. The question of cardiotoxicity with bupivacaine is irrelevant because of the small dose used. Thus our data do not support the continued use of levobupivacaine for CSE.

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2. Kanai, Y et al. Reg. Anesth. Pain Med. 1999 Sep-Oct; 24(5): 444-52
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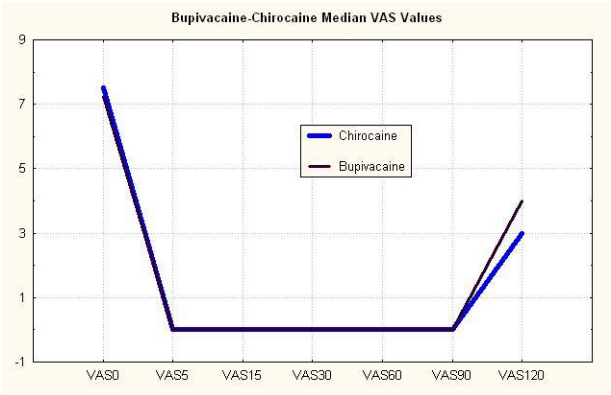


S-152

PROPHYLACTIC INTRAMUSCULAR EPHEDRINE PREVENTS REDUCTION IN MATERNAL BLOOD PRESSURE AFTER COMBINED SPINAL EPIDURAL FOR LABOR ANALGESIA

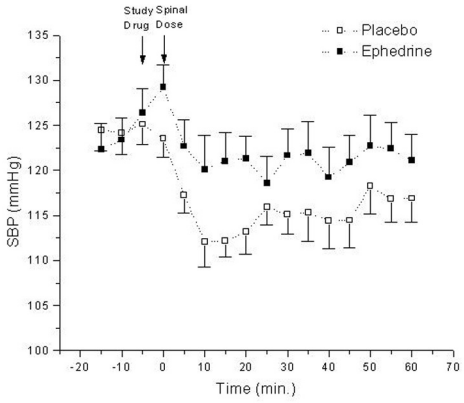
AUTHORS: M. Negron[1], J. Scott[2], **P. Flood**[2];
AFFILIATION: [1]Columbia University, Dept. Anesthesiology, New York, NY, [2]Columbia University, New York, NY.

INTRODUCTION: Maternal hypotension is a known complication after combined spinal epidural (CSE) for labor analgesia.Although this side effect can usually be successfully treated with intravenous ephedrine after the fact, the symptoms of nausea, vomiting and dizziness are unpleasant for the parturient. Hypotension can also result in inadequate uteroplacental perfusion. We hypothesized that a small intramuscular depot of ephedrine would prevent the rapid reduction in maternal catecholamines that occurs after CSE and maintain hemodynamic stability.

METHODS: In a double blind randomized placebo controlled trial, approved by the Columbia University institutional review board, we studied 50 women in active labor who were planning to have CSE for labor analgesia. Women received either an intramuscular injection of ephedrine or placebo at the time of sterile preparation of the back. Maternal heart rate and blood pressure were measured every 5 minutes for the first hour.

RESULTS: There was no difference in demographic variables between groups. 56% of patients in the placebo group had a reduction in systolic blood pressure of 20% or more below their baseline. In contrast, patients who received prophylactic ephedrine had no significant change in their blood pressure after CSE. Mean blood pressure was significantly less in the control group (P less than 0.01). Diastolic blood pressure and heart rate did not differ between the two groups. There were no differences in APGAR scores between groups.

DISCUSSION: A prophylactic dose of 25 mg of ephedrine IM prevented maternal hypotension after CSE. There were no apparent ill effects of this treatment, in this group. However, all patients studied were in good health and care should be used with patients with cardiovascular disorders. Prophylactic ephedrine has had mixed success in the prevention of hypotension after spinal anesthesia and its effectiveness after CSE may be related to the smaller dose of local anesthetic used.



S-153

IS EPIDURAL-PCA ANALGESIA REQUIREMENT FOR LABOR PAIN REDUCED DURING THE NIGHT?

AUTHORS: **S. Cohen**, A. Sakr, C. Pantuck, O. Fadare, E. Sakr, E. Pantuck;
AFFILIATION: UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

INTRODUCTION: We speculated that epidural analgesic requirement is reduced during the night because of reduced patient alertness. Also, it has been reported that cesarean section rate tends to peak in the evening [1]. We compared patients in labor during the day with those in labor at night to determine whether epidural PCA requirement and the incidence of operative delivery are reduced during the night.
METHODS: Following IRB approval and informed consent 210 parturients who requested epidural analgesia for labor pain were randomized to: Group I (n=105): required epidural analgesia during the day from 11:00 to 13 :00 ; Group II (n=105) required epidural analgesia during the night from 23:00 to 01:00. All patients received via the epidural catheter 15 ml solution of epidural ropivacaine (R) 0.1% + sufentanil 1 mcg/ml + epinephrine 2 mcg/ml, followed by an infusion at 6ml/hr, PCA dose 4ml, lockout time 10min (Abbott PCA pump). After loading dose administration (time = 0min), patients were queried with each contraction as to their satisfaction with analgesia. If at time = 20min, VAS>3, patients were given a 5-10ml bolus of the study solution every 10min for a maximum of 20ml as needed until VAS≤3. If analgesia was still inadequate (VAS>3), patients were rescued with 5ml of 0.25% R every 10min as needed to a max of 20ml. At each interval where intervention was required the infusion rate was increased by 2ml/hr to a maximum of 12ml/hr. IV oxytocin was ordered by the obstetricians when needed. Pain, nausea, pruritus, sedation, and motor block were evaluated hourly, or sooner if intervention was required. Patients were asked to rate their satisfaction for 1st stage, 2nd stage, and overall. Data were expressed as mean ± SD. Statistical analysis was performed with Student's unpaired t-test, the Mann-Whitney U test or Fisher's exact test as appropriate at $p<0.05$.
RESULTS: There were no differences among the groups with respect to age, weight, height, initial Cx dilation, 1st stage and ROM to delivery durations, initial pain scores, nausea, vomiting, 2nd stage satisfaction, APGAR scores and baby's weight. There were 54 and 71 ($p<0.03$) primiparae for GI and II respectively. First stage satisfactions were 9.4±1.1 and 9.9±1.2 ($p<0.001$) for GI and II respectively. Overall satisfactions were 9.5±1 and 9.8±0.7 ($p<0.02$) for GI and II respectively.

	Infus Time (hr)	Inf Total Vol (ml/hr)	PCA Vol/Dur (ml/hr)	Extra Bolus Vol (ml)	Resc Ropiv .25% n(%)	Tot Rescue Ropiv 0.25% (mg)	Time to Full Satis (min)	2nd Stage Dur (min)	IV Oxy-tocin n(%)	Pruitus n(%)	Motor Bl <5 n(%)	IV Nalox-one (mg)	Urinary Ret n(%)	Del Type (n) 1=VD 2=Vac 3=Forcep 4=C/S
Gr I N=105 Day	4±3*	13±6	0.05±0.05	9.3±11**	25**(24)	2.5±5**	16±8**	55±60#	75##(71)	54##(51)	14**(13)	0.012±0.03**	41##(39)	1:85 2:5 3:2 4:13
Gr II N=105 Night	8±5	12±14	0.03±0.03	5.2±10	6(6)	0.6±2	12±3	82±93	57(54)	67(66)	53(50.5)	0.004±0.02	61(60)	1:86 2:4 3:1 4:14

*GI<GII, ;<0.001; **GI>GII, p<0.003; #GI<GII, p<0.03; ##GI>GII, p<0.05

CONCLUSION: Despite our expectations, the hourly dose of analgesia required by the Night Group was not different from that of the Day Group.The greater total infusion volume in the Night Group was due to the longer duration of the second stage of labor, which probably resulted from decrease use of oxytocin. The incidence of operative delivery was not greater at night.
REF.: 1.Neuhoff et al., Obstet Gynecol 73:915, 1989

S-154

DOES SALINE INFUSION IMPROVE THE SUCCESS RATE OF PREVIOUSLY INACTIVE EPIDURAL CATHETERS?

AUTHORS: **J. Ranasinghe**, A. Lee, D. J. Birnbach, J. L. Steadman, T. Toyama;
AFFILIATION: University of Miami, Miami, FL.

INTRODUCTION: Several reports have suggested that failure to reactivate inactive labor epidural catheters for postpartum tubal ligation may occur in more than 20 % of cases and increase OR time and cost. Although the likelihood of successful reactivation appears to be inversely related to the period of disuse of the catheter following vaginal delivery the etiology of failure is uncertain, but may be related to loss of patency of the catheter. In our institution, epidurals are routinely placed preemptively in patients diagnosed with severe preeclampsia. Although many of these epidurals are left for prolonged periods prior to use, we still observe a very high success rate of activation of these catheters. Our hypothesis was that infusion of normal saline through inactive catheters would decrease the failure rate when reactivated. The results of a QA investigation are presented.
METHODS: All patients diagnosed with severe preeclampsia with platelet counts greater than 75,000 receive epidurals at this institution. Catheters placed are tested with lidocaine 1.5% with epinephrine and then infused with normal saline at a rate of 3-4 ml per hour. Catheters are activated at the onset of painful contractions with levobupivacaine and/or used for cesarean section as necessary.
RESULTS: For the period January 2002 to March 2003, a review of the QA database revealed 59 patients who had preemptive epidural placement with subsequent infusion of normal saline. Prior to activation, twenty three (39 %) patients had catheters placed for a period of less than 4 hours, seventeen (29 %) patients had catheters placed for between 4 and 8 hours, twelve (20 %) patients had catheters in place for greater than 8 but less than 24 hours and seven (12%) patients had catheters in place for greater than 24 hours. The longest period any of the catheters had been inactive was 67 hours. Successful activation was defined as any catheter which worked well to provide labor analgesia and/or anesthesia for cesarean section. One patient underwent an emergency cesarean section under general anesthesia due to time constraints. That catheter was successfully used later for postoperative pain management. Another catheter was eventually discovered to be intrathecal and was replaced. All other catheters were successfully activated for labor analgesia or for cesarean section.
DISCUSSION: Our experience reveals a 100% rate of successful activation of preemptively placed epidural catheters infused with normal saline. The majority of these catheters were first used more than 4 hours after placement, and in seven cases, after 24 hours. These data suggest that normal saline infusion improves the rate of successful reactivation of dormant epidural catheters, perhaps by ensuring the patency of the catheter.
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Pain - Basic Science

S-155

ROLE OF ANDRENERGIC AND CHOLINERGIC TRANSMISSION IN VOLATILE ANESTHETIC PRONOCICEPTION IN MICE

AUTHORS: T. J. Rowley, D. Daniel, **P. Flood**;
AFFILIATION: Columbia University, New York, NY.

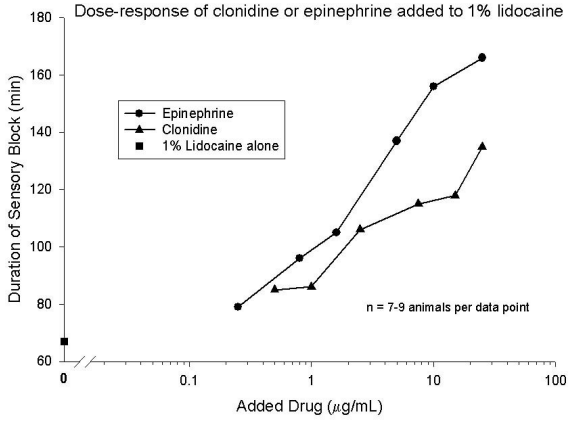
INTRODUCTION: Volatile anesthetic drugs have a biphasic effect on pain transmission. At very low concentrations they enhance pain sensitivity while at higher subanesthetic concentrations they have an analgesic effect. Previous works by the authors have suggested the one potential target of these low concentrations of volatile anesthetic is the neuronal nicotinic receptors. Furthermore, activation of nicotinic receptors is known to facilitate the release of norepinephrine in the spinal cord. It is the aim of the presented work to determine the relationship between the volatile anesthetic, isoflurane, and norepinephrine release in isoflurane's pain enhancing effect.
METHODS: Hind paw withdrawal latency testing coupled with the administration of nicotine via either intrathecal (IT) or intracerebroventricular (ICV) injection was used to determine the location of the nicotinic receptors working in the isoflurane pronociception pathway. To investigate the role of the noradrenergic nervous system, we depleted norepinephrine with adrenergic neurotoxin DSP-4 and inhibited postsynaptic alpha-2 adrenergic receptors with intrathecal injections of yohimbine.
RESULTS: Depleting systemic norepinephrine with DSP-4 caused a reduction in baseline withdrawal latencies and prevented isoflurane pronociception. Baseline latency was also reduced by intrathecal yohimbine and no further decrease was also observed with isoflurane. Nicotine administered through ICV injection increased baseline latency but did not prevent isoflurane pronociception. Conversely, intrathecal applications of nicotine caused a slight reduction in baseline latency; however from this lowered baseline isoflurane did not elicit any further decrease.
DISCUSSION: Isoflurane's effect on pain is separable byconcentration. Pain enhancement comes at low concentrations (as low as 0.1%) while antinociception is observed at higher concentrations. Further, spinal noradrenergic transmission seems to be necessary for isoflurane pronociception to occur. Isoflurane may act by inhibiting tonically active nicotinic receptors that control the release of norepinephrine in the spinal cord.

S-156

DOSE RESPONSE OF CLONIDINE ADDED TO LIDOCAINE FOR SCIATIC NERVE BLOCK IN RATS

AUTHORS: **J. S. Kroin**, D. E. Beck, A. Buvanendran, J. E. Topic, D. E. Watts;
AFFILIATION: Dept. of Anesthesiology, Rush Medical College, Chicago, IL.

INTRODUCTION: Clonidine is increasingly being utilized as an additive to local anesthetics to extend the duration of peripheral nerve blocks. However, the optimal dose of clonidine has not been determined. Inconsistencies are found among reports of the clonidine dose response: 10 µg/mL clonidine added to lidocaine extended the pain free period while 20 µg/mL was no better than lidocaine alone (Anesth Analg 1996;83:760); addition of 30 µg clonidine was more effective than 90 µg clonidine in producing sensory blockade at 10 min after injection (Anesthesiology 1997;87:277). The present study measures the duration of sensory blockade of the sciatic nerve with different doses of clonidine added to 1% lidocaine in intact rats.
METHODS: With animal care committee approval, male Sprague-Dawley rats (400-500 g) were briefly anesthetized with isoflurane and a 25 g needle percutaneously advanced through the sciatic notch until a leg twitch was generated with electrical stimulation via the needle. Then, 0.5 mL of drug solution was injected. Animals were tested for sensory response prior to injection and every 10 min after injection with a pin applied to the plantar midline surface of the ipsilateral hindpaw (tibial nerve distribution). Any foot withdrawal, whether sciatic or femoral nerve mediated, was considered a response. Drug solutions consisted of 1% lidocaine hydrochloride with clonidine hydrochloride or epinephrine hydrochloride added at concentrations of 0-25 µg/mL. In control experiments, clonidine or epinephrine was given intraperitoneally (0.5 mL) 5 min before sciatic nerve injection of lidocaine. Clonidine or epinephrine alone (0.5 mL) was also tested for nerve block. Durations were compared to control values (1% lidocaine) using ANOVA with Dunnett's post hoc test.
RESULTS: The mean duration of sensory block for 1% lidocaine alone was 67 ± 3 min. With either clonidine or epinephrine, the dose response curve is monotonic, with the higher dose always producing a longer duration of blockade (Figure). Clonidine = 2.5 µg/mL or epinephrine = 0.8 µg/mL significantly extended the duration of nerve block. Clonidine or epinephrine 25 µg/mL intraperitonally did not extend the duration of lidocaine blockade. Clonidine or epinephrine 25 µg/mL alone injected into the sciatic notch did not produce any sensory blockade nor did either drug produce sedation (as measured by the animal remaining on the rotarod for 180 sec at 10 rpm).
DISCUSSION: The dose response curve for clonidine or epinephrine added to lidocaine does not demonstrate U-shaped characteristics in which higher doses would be less effective than lower doses. The effect of clonidine or epinephrine appears to be a local effect on the peripheral nerve since systemic injection of these compounds does not extend the blockade of a local lidocaine injection. Neither drug produces sensory blockade in the absence of lidocaine.

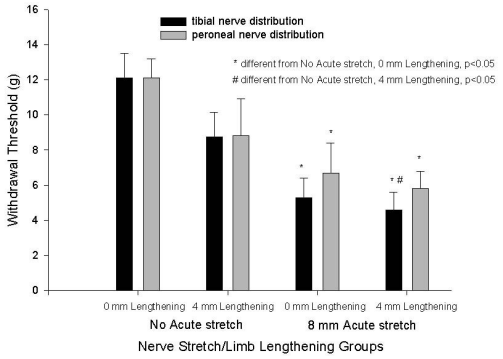


S-157

LONG-TERM ALLODYNIA DUE TO SCIATIC NERVE STRETCH IN RATS

AUTHORS: **J. S. Kroin**[1], J. M. Kerns[2], A. Buvanendran[1], J. E. Topic[1], D. E. Watts[1], K. J. Tuman[1];
AFFILIATION: [1]Dept. of Anesthesiology, Rush Medical College, Chicago, IL, [2]Dept. of Anatomy, Rush Medical College, Chicago, IL.

INTRODUCTION: The incidence of sciatic nerve palsies following total hip arthroplasty (THA) is between 0.5-2%, and it has been hypothesized that nerve stretch may cause not only motor dysfunction (Clin Orthop 1987;218:136), but also neuropathic injury. Pain clinicians are frequently evaluating patients who develop neuropathic pain in the effected limb after THA. However, it is not clear whether it is an increase in limb length or the manipulation of the limb during surgery that contributes to long-term post-surgical pain. The following study in rats investigates the production of allodynia under various conditions of nerve stretch.
METHODS: With animal care committee approval, 350 g male Sprague-Dawley rats (n=42) were anesthetized with isoflurane and the left femur exposed. An osteotomy was performed and 2 mm of femur removed. The proximal and distal ends of the femur were reattached with metal pins and rods under the following conditions: 1) no acute nerve stretch, no final increase in femur length; 2) no acute nerve stretch, 4 mm final increase in femur length; 3) 8 mm acute stretch 1 min, no final increase in femur length; 4) 8 mm acute stretch, 4 mm final increase in femur length. Pre-surgery and starting at Day 2 post-surgery, animals were tested for mechanical allodynia (J Neurosci Meth 1994;53:55) using calibrated von Frey filaments applied to the left hindfoot (dorsal midline skin for peroneal nerve distribution, plantar midline skin for tibial nerve distribution). Before surgery, rats rarely responded to the maximum force applied (15.1 g). Mechanical allodynia in each nerve distribution was compared among the four groups with one-way ANOVA with least significant difference post hoc test.
RESULTS: At Day 2 post-surgery, the mean withdrawal threshold for all groups was >12 g indicating no allodynia. By Day 14, allodynia was pronounced in some groups of animals (Figure). For rats in which the final femur length was unchanged from pre-surgery, withdrawal threshold decreased (greater allodynia) in both the tibial and peroneal nerve distributions when the animals were also subjected to an 8 mm acute stretch during surgery. For rats with a 4 mm increase in final femur length, withdrawal threshold decreased in the tibial nerve distribution when the animals were also subjected to an acute stretch during surgery, although both distributions exhibited greater allodynia than the no acute stretch/no lengthening group.
DISCUSSION: Acute nerve stretch during surgery appears to be the main causative factor for producing long-term allodynia in rats undergoing limb lengthening. This suggests that during THA it is the acute stretching of the nerve during limb manipulation that contributes to long-term pain rather than just the final limb length alone. Future animal studies will explore preemptive peri-operative techniques to potentially lessen the incidence of long-term post-operative pain.



S-158

ASSESSMENT OF VISCERAL PAIN IN A RAT MODEL OF ENDOMETRIOSIS

AUTHORS: **J. S. Kroin**, D. R. Beck, D. E. Watts, J. E. Topic, A. Buvanendran;
AFFILIATION: Dept. of Anesthesiology, Rush Medical College, Chicago, IL.

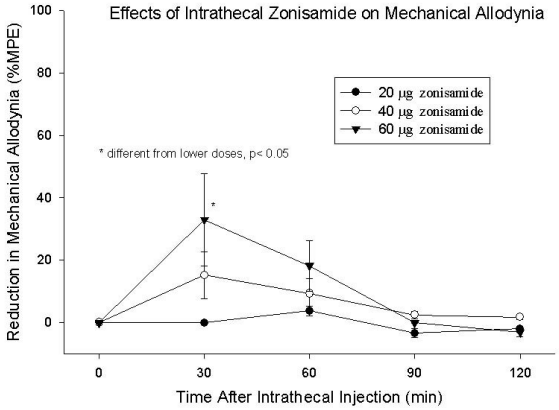
INTRODUCTION: Studies of chronic visceral pain are limited by a lack of simple reproducible animal models. Endometrial cysts can be induced in the rat by autotransplantation of uterine horn tissue onto the mesentery of the small intestines (Fertil Steril 1990;53:921). However, despite the growth of well-defined cysts the animals do not evidence quantifiable pain behaviors (Pain 2002;95:247). The only method currently used to evaluate pain in such animals is assessment of the potentiation by endometriosis of other painful entities such as vaginal stretching (Neurosci Lett 2001;306:185) or ureteral stones (Pain 2002;95:247). The present study investigated whether non-painful stimuli could be used to quantify visceral pain mediated by endometriosis.
METHODS: With animal care committee approval, 220-240 g adult female Sprague-Dawley rats (n=20) were anesthetized with isoflurane, and the peritoneal cavity exposed. Endometriosis was induced using previously described methods (Fertil Steril 1985;44:684; Pain 2002;95:247). A 1-cm section of the left uterine horn was excised, bisected longitudinally, and five 2x2 mm pieces of endometrial tissue isolated. Each piece was sutured to one of the mesentery arteries of the small intestines. All wounds were closed and animals recovered uneventfully. Animals were assessed for mechanical allodynia with von Frey filament testing of lower abdominal skin, or vocalization in response to standardized thumb pressure on the lower abdomen. In addition, substances producing short-term irritability were injected into regions with spinal afferents close to the level of the mesenteric arteries (stomach, 1 mL or colon, 0.5 mL), or intramuscularly (0.2 mL). Statistical comparisons were with the Wilcoxon signed-rank test.
RESULTS: Animals tested prior to surgery demonstrated no mechanical allodynia. When tested from 7-42 days post-transplant, rats still did not evidence allodynia. Intracolonic injections of acetic acid 0.5%, capsaicin 1 mg/mL, substance P 0.05 mg/mL, or PGE2 1 ng/mL did not produce allodynia at the lower abdomen. Delivery of capsaicin 1 mg/mL, glycerol 25%, or bradykinin 12 mg/mL into the stomach by gavage also did not induce allodynia. Intramuscular injection of conjugated estrogens (50 µg) for 10 days likewise did not produce any measurable allodynia. Histologic examination showed that the cysts were characteristic of endometrial tissue: epithelial cells lining cavity, stroma cells underneath epithelial cell layer, and a few endometrial-like glands.
DISCUSSION: Without the use of painful stimuli it is difficult to quantitate the presence of endometriosis in the small intestine region of rats despite histological verification. This may be due to the relatively small number of pain fibers entering the spinal cord from this mesenteric region, so that the addition of other mild stimuli (e.g. colonic capsaicin) projecting to nearby spinal levels could not produce a measurable pain response. Additional studies are needed to identify methods of evaluating visceral pain without the need for confounding painful stimuli.

S-159

EVALUATION OF ANALGESIC EFFECT OF INTRATHECAL ZONISAMIDE IN RATS

AUTHORS: **J. S. Kroin**, A. Buvanendran, D. E. Watts, J. E. Topic;
AFFILIATION: Rush Medical College, Chicago, IL.

INTRODUCTION: Zonisamide (Zonagran®) is an anticonvulsant being considered for the treatment of neuropathic pain. Zonisamide shows some efficacy following systemic administration in neuropathic rats (Anesth Analg 2003;96:1700). Gabapentin, another anticonvulsant, has already been show to reduce hyperalgesia in animal models of pain, with intrathecal as well as systemic administration (JPET 1997;282:1242; Reg Anesth 1997;22:249; Anesth Analg 1999;89:434). The present study investigates the efficacy of zonisamide in several pain models following intrathecal administration.
METHODS: Male Sprague-Dawley rats (300 g) were implanted with intrathecal catheters for bolus drug administration (Physiol Behav 1976;17:1031). Rats were tested for acute pain withdrawal latency with thermal stimulation of the hindpaw using the method of Hargraves (Pain 1988;32:77). Latency of left and right hindpaws was averaged. Animals were tested for post-surgical hyperalgesia with calibrated von Frey hairs applied to the plantar surface of the hindpaw following the foot incision model of Brennan et al (Pain 1996;64:493). Neuropathic pain was evaluated using the spared nerve injury model of Decosterd and Woolf (Pain 2000;87:149) in which calibrated von Frey hairs are applied to the lateral plantar paw (sural nerve territory). Withdrawal force was converted to maximum possible effect (%MPE) = [(postdrug force – predrug force)/(15.1 g – predrug force)] x 100%. Sedation was evaluated by the ability of an animal to ambulate on a rotating rod at 10 rpm for 180 sec. For intrathecal injection, zonisamide sodium salt was dissolved in sterile saline (maximum solubility 7.5 mg/mL limiting maximum delivered dose to 60 µg) and injected in a volume of 8 µL followed by 8 µL saline flush. Withdrawal latency or force at different zonisamide doses was compared over time using repeated measures analysis of variance with least significant difference post hoc test.
RESULTS: Intrathecal zonisamide at doses up to 60 µg did not reduce acute thermal withdrawal latency in the hindpaw of normal rats. Following foot incision, intrathecal zonisamide up to 60 µg did not reduce mechanical hyperalgesia. In animals with neuropathic pain, intrathecal zonisamide at 60 µg had a small antiallodynic effect at 30 min, but lower doses 20-40 µg did not reduce allodynia (Figure). There was no sedation with intrathecal zonisamide up to 60 µg.
DISCUSSION: Intrathecal zonisamide 60 µg was not effective in reducing acute thermal pain in normal rats or alleviating mechanical hyperalgesia in rats with a foot incision. Intrathecal gabapentin at the same dose was also ineffective in acute thermal pain models (Neurosci Lett 1997;222:65), but 10 µg reduced allodynia in the same incision model (Anesthesiology 2002;97:A822). Zonisamide was only minimally effective in reducing mechanical allodynia in the spared nerve injury model following spinal administration. This suggests that observed analgesic effects seen with systemic zonisamide most likely occur at a supraspinal level.

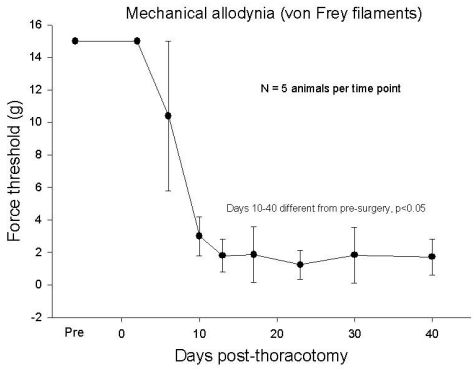


S-160

PERSISTENT PAIN AND HISTOPATHOLOGY FOLLOWING THORACOTOMY WITH RIB RETRACTION IN A RAT MODEL

AUTHORS: **A. Buvanendran**[1], J. S. Kroin[1], J. M. Kerns[2], J. E. Topic[1], D. E. Watts[1], K. J. Tuman[1];
AFFILIATION: [1]Dept. of Anesthesiology, Rush Medical College, Chicago, IL, [2]Dept. of Anatomy, Rush Medical College, Chicago, IL.

INTRODUCTION: The incidence of persistent pain one year after thoracotomy is about 50% (Chest 1991;99:279). A recent clinical study has shown that rib retraction alone caused total conduction block in the intercostal nerves on both sides of the retractor (Eur J Cardiothorac Surg 2002;21:298). A chronic pain syndrome in the thoracic skin can be produced in rats by inducing chronic constriction injury to the intercostal nerves (Can J Anaesth 2001;48:665). Our study characterizes the time course of allodynia produced by thoracotomy/rib retraction in rats and relates allodynia to intercostal nerve histopathology.
METHODS: With animal care committee approval, 350 g male Sprague-Dawley Rats were ventilated with isoflurane. A 3-cm incision was made in the skin of the lateral chest between the right 4th and 5th ribs. The intercostal muscle was exposed and a 1.5-cm incision made in the muscle and pleura above the 5th rib. A self-retaining retractor was placed under the 4th and 5th rib, opened 8 mm and left in place for 60 min. The retractor was removed, air evacuated from the pleural space, and muscles and skin closed. Animals were tested daily for 40 days for mechanical allodynia by measuring the withdrawal force to calibrated von Frey filaments applied to the dorsal skin around the incision. Cold allodynia was tested by placing acetone near the incision and counting scratches/min to the stimulated area. Another group of animals were evaluated for allodynia over a 14-day period and perfused intracardially with fixative for histological examination of intercostal nerves. Withdrawal force thresholds and the scratches/min over days 10-40 were compared to pre-surgery baseline values with the Wilcoxin signed-rank test.
RESULTS: By Day 10, mechanical allodynia post-surgery was either well established in an animal or it did not occur, even up to 40 days. At Day 40, 50% of the animals demonstrated mechanical allodynia (withdrawal force below 4 g). The time course of mechanical allodynia development is shown in the Figure. Prior to surgery, acetone elicited 1.3 ± 1.0 scratches/min. This increased to 9.4 ± 0.8 scratches/min at 40 days post-thoracotomy. Histologic examination demonstrated that in animals with allodynia, the 4th intercostal nerve had almost complete degeneration while in animals without allodynia the 4th intercostal nerve had little degeneration.
DISCUSSION: Thoracotomy and 8 mm rib retraction maintained for 60 min produces persistent allodynia in 50% of the rats, similar to the incidence of long-term post-thoracotomy pain in humans. Histopathology of the intercostal nerves suggests that mild nerve injury is not associated with allodynia but severe nerve degeneration is present in allodynic animals. The above model may be useful to evaluate interventions to reduce nerve injury during surgery as well as other strategies to reduce persistent pain after thoracotomy and rib retraction.



S-161

SKIN LOCATION IS A SIGNIFICANT DETERMINANT OF NEUROSELECTIVE ELECTROCUTANEOUS STIMULATION INDUCED PAIN TOLERANCE THRESHOLDS

AUTHORS: **J. C. Finkel**[1], A. Elrefai[1], K. A. Hummer[2];
AFFILIATION: [1]Children's National Medical Center and George Washington University Medical Center, Washington, DC, [2]Children's National Medical Center, Washington, DC.

INTRODUCTION: Neuroselective electrocutaneous stimulation pain tolerance thresholds (PTT) were used to atraumatically evaluate the efficacy of a new eutectic mixture of lidocaine and tetracaine (70 mg/70 mg) (S-Caine™ topical anesthetic patch) and compared patches containing topical 70 mg lidocaine, 70 mg tetracaine, and placebo. The 3 major sensory nerve fibers; C, Aδ and Aß are stimulated at 5, 250 and 2000Hz, respectively.
METHODS: After IRB approval and informed consent 48 ASA PS I or II volunteers were recruited. Subjects received simultaneous S-Caine™ , lidocaine, tetracaine and placebo patch applications for 30 minutes. Patches were applied in randomized fashion to 2 locations on each forearm. A PTT at each of the three frequencies was performed using the Neurometer CPT/C (Neurotron, Inc. Baltimore, Maryland) at each site. The PTT stimulus was self-administered and stopped by the subject when intolerable.
PTT values were compared by frequency using Mann-Whitney tests. Differences in patch locations were assessed using repeated measures analysis of variance. Overall threshold responses were compared among the 4 treatments using a Friedman's nonparametric analysis.
RESULTS: Each patch location had the same number of each treatment in a randomized order. There were significant differences between the wrist and antecubital locations (Table) but not between treatment groups.

Maximum Tolerated Threshold (mA) by Frequency and Patch Location

Frequency	Site 1 (R wrist) (N=48	Site 2 (R antecub.) (N=48)	Site 3 (L wrist) (N=48)	Site 4 (L antecub.) (N=48)	Left vs. Right	Wrist vs. Antecubital
2000 Hz						
Mean (mA)	4.63	3.79	4.75	3.95	P=0.537	P=0.001
SD	2.78	2.25	2.98	2.56		
250 Hz						
Mean (mA)	2.42	1.83	2.37	1.85	P=0.847	P=0.029
SD	2.77	1.83	2.34	1.68		
5 Hz						
Mean (mA)	2.23	1.66	1.98	1.56	P=0.564	P=0.019
SD	2.67	1.83	2.16	1.49		

DISCUSSION: Neuroselective electrostimulation has been used to evaluate the efficacy of topical anesthetics in terms of onset, duration and intensity of cutaneous analgesia.[2] In this study, however, an analgesic impact was not demonstrated using this methodology. The only significant differences in thresholds occurred between the wrist and antecubital locations regardless of treatment group. This suggests that pain thresholds differ significantly by location. Previous studies have used mirrored-site applications of control and active drug and so this possibility has not previously been examined. Baseline PTTs at each of the testing locations would serve to clarify this issue. Another possibility is that the drug surface area was too small to properly accommodate the electrode diameter and circumference of current spread beyond the electrodes.
CONCLUSIONS: Since the majority of the current travels over the skin, it is possible that non-treated skin was stimulated, thus revealing no difference in drug effect among the treatment groups. It needs to be determined if the neuroselective PTTs derived from different skin locations differ so significantly that topical anesthetic efficacy comparisons should be made using only same or mirrored locations. Additionally, the minimum surface area to be covered in order to accommodate the electrodes used with this technique needs to be determined.
REFERENCES:
1. Pain Digest 1998; 8:219-30
2. Anesth Analg 2002; 94:1259-62

S-162

HERPES VIRUS INDUCED SUBSTANCE P ENABLE C FIBER NOCICEPTIVE RESPONSES IN ANIMALS THAT NATURALLY LACK SP

AUTHORS: **Y. Lu**[1], S. Wilson[2], T. Park[1], C. E. Laurito[1];
AFFILIATION: [1]University of Illinois, Chicago, IL, [2]University of South Carolina School of Medicine, Columbia, SC.

INTRODUCTION: Substance P (SP) and calcitonin gene-related peptide (CGRP) are found in abundance within C fiber nociceptors. African naked mole-rats naturally lack SP and CGRP in their cutaneous nerve fibers and associated dorsal root ganglion cells (Park et al, 2003, J Comp Neurol). Nociceptive behavioral tests on naked mole-rats have shown that these animals lack the typical responses that are thought to be mediated by C fiber nociceptors (eg, sensitization to capsaicin; Lu et al, 2003, IASP). Hence, there is a correlation between the lack of SP/ CGRP and the lack of C fiber mediated nociception response. In the present study we used a virus (Herpes Simplex I) to introduce SP into the C fiber afferents innervating the foot skin and terminating in the dorsal horn. The goal was to determine if SP would enable the animals to exhibit typical C fiber type nociceptive behaviors.
METHODS: Animals were tested in a foot withdrawal to noxious heat stimuli procedure. With the foot withdrawal behavior test, we measure baseline response latencies of hindpaws in response to a high (A-delta fiber mediated) or low (C fiber -mediated) rate of skin heating (Yeomans, 1996, Pain) after anesthetizing naked mole rats with pentobarbital. Then we employed a replication defective herpes simplex virus (HSV type 1) which has been engineered to contain the cDNA for preprotachykinin and a similar recombinant vector containing the Escherichia Coli LacZ gene as a control. One of the hindpaw skin of the mole rats were infected with 8 microliters of 10^7 pfu/microliter of preprotachykinin-encoding HSV vector or LacZ gene HSV vector. Foot withdrawal latencies to the high and low heating rates were measured at 14 days after virus application. We applied 2 mM capsaicin on the virus infected skin area about 10 min. before the measurement of foot withdrawal latencies in approximately 1 hour.
RESULTS: Testing of the treated foot generated typical C fiber type responses that were not different from those of comparison animals (mice). In both cases, application of capsaicin (1-2 mM) sensitized responses to a low heating rate which is selective for C fiber activation. In contrast, testing of the untreated foot showed a lack of C fiber mediated response.
DISCUSSION: These results support a powerful role for SP in C fiber mediated pain, especially since SP appears to activate a pathway that had been naturally disabled through evolutionary adaptation.
REFERENCES: 1) Park et al, 2003, J Comp Neurol. 2) Lu et al, 2003, IASP. 3) Yeomans, 1996 Pain.
Supported by NIH and the Department of Anesthesiology, UIC

S-163

ANALGESIC EFFECTS OF SYSTEMICALLY ADMINISTERED MIDAZOLAM IN RATS

AUTHORS: **T. Nishiyama**, K. Hanaoka;
AFFILIATION: The University of Tokyo, Bunkyo-ku, Tokyo, Japan.

INTRODUCTION: Midazolam is well known to have spinally mediated analgesic effects[1]. However, intrathecal administration of midazolam is not allowed clinically and there are no data to show analgesic effects of systemic administration of midazolam. The purpose of this study was to investigate whether systemically administered midazolam had analgesic effects or not in comparison with intrathecal administration.
METHODS: Male Sprague-Dawley rats (300 - 350 g) with lumbar intrathecal catheters were tested for their thermal tail withdrawal response using the tail flick test or for their paw flinches by subcutaneous formalin injection into the hind paw (formalin test) after intrathecal (IT) (1, 3, 10, 30, and 100 µg / 10 µl) or intraperitoneal (IP) (3, 30, 300, and 3,000µg / 300 µl) administration of midazolam. Saline was used as a control. Behavioral side effects and motor disturbance were also examined. Eight rats were used in each dose group.
RESULTS: In the tail flick test, IP administration induced no dose dependent analgesic effects and even with the highest dose (3,000µg), less than 30% of the maximum possible effect was obtained. IT administration induced dose dependent analgesia in the tail flick test with the 50% effective dose (ED_{50}) of 1.60 µg (95 % confidence interval (CI), 0.45 - 3.02 µg). In the formalin test, both IP and IT administration had dose dependent decreases of the flinches in both phase 1 and 2. The ED_{50}s in the formalin test were 11.6 µg (95% CI, 2.5 - 19.3µg, phase 1) and 52.2 µg (95% CI, 18.3 - 102.7 µg, phase 2) in IP administration and 1.26 µg (95 % CI, 0.35 - 3.18 µg, phase 1) and 1.20 µg (95 % CI, 0.29 - 3.71 µg, phase 2) in IT administration. Motor disturbance and flaccidity were observed with 300 and 3,000µg in IP administration and 30 and 100µg in IT administration. Two rats lost pinna reflex with 3,000µg IT administration.
DISCUSSIONS: If IP midazolam had its effects on the spinal cord, ED_{50}s of both phase 1 and 2 of the formalin test should be similar and analgesic effect should be observed in the tail flick test as seen in IT administration. Therefore, IP midazolam might have analgesic effects on inflammatory induced pain without through the spinal cord. IP midazolam had no effects on thermal induced pain.
REFERENCE: 1. Anesth Analg 93; 1025-1031, 2001

S-164

SPINALLY MEDIATED ANALGESIC INTERACTION BETWEEN N-METHYL-D-ASPARTATE (NMDA) - AND ALPHA-AMINO-3-HYDROXY-5-METHYLISOXAZOLE-4-PROPIONIC ACID (AMPA) – RECEPTOR ANTAGONISTS IN THERMAL OR INFLAMMATORY PAIN IN RATS

AUTHORS: **T. Nishiyama**, K. Hanaoka;
AFFILIATION: The University of Tokyo, Bunkyo-ku, Tokyo, Japan.

INTRODUCTION: N-methyl-D-aspartate (NMDA) receptor is mainly concerned with chronic pain[1] while α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor has some roles in both acute and chronic pain[2]. To elucidate the interaction of these two receptors in pain mechanism, we investigated the analgesic interaction between intrathecally administered AP-5 (NMDA receptor antagonist) and YM 872 (AMPA receptor antagonist) in thermal and inflammatory pain using rats.
METHODS: Sprague-Dawley rats (300 - 350 g) with lumbar intrathecal catheters were tested for their thermal tail withdrawal response using the tail flick test and for their paw flinches by subcutaneous formalin injection into the hind paw after intrathecal administration of AP-5 (1 - 30 µg) or YM 872 (0.3 - 30 µg). Saline was used as a control. The effects of the combination were also tested by an isobolographic analysis using ED_{50} (50% effective dose) values. Behavioral side effects and motor disturbance were also examined. Eight rats were used in each dose group.
RESULTS: ED50 values (µg) are shown. ( ): 95% confidence interval.

	Tail flick	Formalin phase1	Formalin phase2
AP-5	5.4 (2.5-9.7)	7.8 (4.5-12.5)	1.5 (0.2-2.7)
YM 872	1.0 (0.3-2.5)	0.22 (0.07-0.53)	0.20 (0.06-0.61)
Combination (AP-5)	0.55* (0.42-0.71)	0.125* (0.02-1.04)	0.09* (0.04-0.21)
Combination (YM 872)	0.10* (0.08-0.13)	0.021* (0.003-0.18)	0.016* (0.007-0.036)

*: $P < 0.05$ vs. the value of each single agent.
Agitation, allodynia, motor disturbance and/or flaccidity were observed in the rats received AP-5 or YM 872 alone. However, the combination with the doses tested did not induce any observable side effects.
DISCUSSIONS: Intrathecal administration of the combination of AP-5 and YM 872 had significant synergistic analgesia for acute thermal and inflammatory induced pain in comparison with each single agent alone with decreasing motor disturbance and behavioral side effects in rats. In the machnism of pain tested, NMDA- and AMPA- receptors would have strong interaction.
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S-165

ARACHIDONIC ACID PRODUCTS MEDIATE THE STIMULATORY EFFECT OF THE CANNABINOID CP55-940 ON HUMAN WHOLE BLOOD NEUTROPHILS

AUTHORS: **B. Kraft**, H. G. Kress;
AFFILIATION: University of Vienna, Vienna, Austria.

INTRODUCTION: As previously reported, the spontaneous and fMLP-stimulated respiratory burst reaction of human PMN in whole blood was enhanced by the synthetic cannabinoid CP55 940 via a CB2-receptor mediated process. In contrast to this result, the burst of isolated PMN was not stimulated by CP55-940, suggesting an indirectly mediated process by other cells or mediators of the whole blood. The aim of the present study was to further characterize the underlying mechanisms of the whole blood stimulation.
METHODS: Plasma or low and high molecular weight plasma fractions from whole blood samples incubated with CP55-940 (0.1 nM and 1.0 nM) were added to isolated PMN of the same healthy donor. After further incubation, the oxidative bursts of resting and fMLP-stimulated PMN were determined by flowcytometry using the commercial kit Bursttest (Becton Dickinson, USA). In a second approach, the whole blood samples were pre-incubated with the enzyme inhibitors flurbiprofen (cyclooxygenase, COX), MK886 (lipoxygenase, LOX) and meclofenamic acid (COX/LOX) prior to CP55-940 incubation, then the burst reaction was measured.
RESULTS: After incubation with CP55 940 at nanomolar concentrations, only the low molecular weight plasma fraction contained the stimulatory activity for isolated PMN, suggesting the involvement of arachidonic acid metabolites rather than cytokines. After pre-incubation of whole blood samples with meclofenamic acid or flurbiprofen, the CP55-940-induced stimulation was no longer observed. Pre-incubation of the whole blood samples with MK886, an inhibitor of the 5-lipoxygenase activating protein, slightly diminished the stimulatory effect of the CP-conditioned plasma.
CONCLUSION: The CP55 940-induced burst stimulation in whole blood PMN is not a direct drug effect on PMN, but is mediated by arachidonic acid products from other cells of the whole blood, mainly involving the COX pathway.

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MODELS OF MECHANICALLY INDUCED ION CHANNEL ACTIVATION

AUTHORS: **M. A. Schumacher**, H. Eilers;
AFFILIATION: University of California, San Francisco, San Francisco, CA.

INTRODUCTION: Pain arising from mechanical stimuli remains poorly understood and difficult to manage clinically. Mechanically induced activation of small-diameter sensory neurons – nociceptors, is thought to be the first step in the pain pathway. Clues to how mechanical forces, whether by direct physical deformation or by osmotic induced shape change produce nociceptor activation, is only now being revealed. We, and others, hypothesize that specific ion channels exist and are expressed on nociceptor terminals to transduce a physical change in cell membrane shape into an electrochemical signal. Evidence to support this idea has recently come from observations that mice genetically manipulated to lack a subtype of the capsaicin receptor (TRPV4), show impaired detection of noxious "high-threshold" pressure (1). This report is consistent with our previous results showing that TRPV4("SIC") is expressed not only in the tubular epithelium of the kidney, but importantly expressed in a sub-population of nociceptors in sensory ganglion (2). Although TRPV4 is activated under cell stretch (hypotonic) conditions, the ion channel(s) responsible for nociceptor activation in response to cell shrinkage (hypertonic) have not been electrophysiologically characterized nor their cDNAs isolated.
METHODS: To begin to determine the role of shrink activated ion channels in pain transduction, we have initiated the electrophysiologic study of nociceptors under hypertonic (cell shrinkage) conditions. In addition, due to the apparently high abundance of osmotically activated ion channels in kidney, we have initiated an expression-cloning scheme using rat kidney RNA.
RESULTS: Oocytes injected with rat kidney RNA were studied under two-electrode voltage clamp and showed reproducible inward current responses (mean = -37nA, -60mv Vm, n = 61) to hypertonic conditions (450 mOsm). In addition, both inward and outward current responses were observed under hypotonic conditions (80 mOsm). Water injected controls showed minimal current responses.
DISCUSSION: An oocyte model system has been established to isolate a cDNA encoding a mechanosensitive (shrink activated) ion channel. Shrink activated channels are hypothesized to exist in nociceptors and may play an important role in mechanically induced pain.
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S-167

REGULATORY MECHANISMS OF PERIPHERAL OPIOID ANALGESIA

AUTHORS: **M. Schaefer**;
AFFILIATION: Charite - Universitaetsmedizin Berlin, Berlin, Germany.

In studies examining μ-opioid receptor (MOR) binding and G-protein coupling we demonstrated that localized inflammatory pain differentially alters MOR expression and coupling in brain, spinal cord and primary afferent neurons (PAN). While the number and G-protein coupling of MOR was significantly up-regulated in PAN, it remained unaffected in spinal cord and brain. This up-regulation resulted in the analgesic efficacy of the peripherally applied partial MOR agonist buprenorphine which was uneffective under normal conditions. Intrathecal blockade of the sensory input from inflammatory pain prevented the recruitment of endorphin (END) containing immune cells to the injured site. Subsequently, stress-induced intrinsic pain inhibition, normally elicited by a release of END from immune cells, was significantly reduced. An endogenous trigger substance for opioid peptide release is corticotropin-releasing hormone (CRH). We further investigated whether CRH R1 or CRH R2 receptors are expressed on circulating and resident END containing immune cells. Our results demonstrated a high degree of co-expression of CRH R1 and END, CRH R2 and END as well as CRH R1 and CRH R2 both on circulating and resident immune cells. Consistently, analgesic effects of locally applied CRH were antagonized by both CRH R1 and CRH R2 receptor antagonists. Together, these findings improve our understanding of peripheral mechanisms during inflammatory pain both on the regulation of opioid receptor signal transduction and on the modulation of the immigration of opioid containing immune cells. Both mechanisms contribute to fight inflammatory pain by intrinsic control mechanisms.
Supported in part by a grant from the International Anesthesia Research Society.

Pain - Clinical, Acute

S-168

DOES A PREOPERATIVE VIDEO INTERVENTION BEFORE JOINT REPLACEMENT SURGERY IMPROVE PATIENT SATISFACTION WITH POSTOPERATIVE PAIN MANAGEMENT?

AUTHORS: J. M. Klafta, Z. Ford, P. Klock, **J. E. Ellis**;
AFFILIATION: University of Chicago, Chicago, IL.

INTRODUCTION: Postoperative pain remains a significant problem (1), despite anesthesiology-based acute pain services (2).Work has suggested that patient education (3) and patient feelings of control (4) could result in improved satisfaction with postoperative pain relief. We hypothesized that a multimedia preoperative intervention would improve patients' satisfaction with postoperative pain management after hip and knee replacement surgery.
METHODS: 104 patients were interviewed before and after surgery (POD 1-2) after IRB approval and oral consent. Patients were randomized to view (Video) or not view (No Video) a 12-min educational videotape before seeing an anesthesiologist. The videotape was developed specifically for patients undergoing these procedures at our institution. Pain satisfaction was assessed with a VAS. Statistical significance was assessed with Chi-square for categorical values and ordinal logistic regression for continuous variables.
RESULTS: Pain satisfaction tends to be higher for patients with the greatest willingness for regional anesthesia ($p = 0.048$), but the association is not significant after adjustment for multiple testing. No other variables (type anesthesia actually administered, patient demographics, past medical experience, expectation of pain) show a significant relationship with pain satisfaction. While patients found the videotape helpful, their pre-operative assessment of helpfulness of the educational video was greater than their post-operative rating ($p = 0.0008$). Length of stay showed no association with type of anesthesia administered or use of the video.
DISCUSSION: We were unable to show an effect of our educational intervention on pain satisfaction.Neither were we able to confirm the findings of others (4) that gender and age affect pain satisfaction. This might be because our population had uniform surgery (major joint replacement) and had a narrower range of ages than other cohorts (4). The videotape, similar to the findings of others, did not shorten LOS (5). Limitations of our study include a limited pain satisfaction scale, and lack of a standardized anesthetic technique. Strengths include use an institution- and procedure-specific videotape intervention.
REFERENCES: (1) Anesth Analg. 2003;97:534-40 (2) Pain. 1999;80:23-9. (3) Proc AMIA Symp. 1999;780-4. (4) J Pain Symptom Manage. 1998;15:110-6. (5) Eur Heart J. 2002;23:666-74.

Pain Satisfaction

	Regional Anesthesia (%)	Low Pain Satisfaction (%)	Moderate Pain Satisfaction (%)	High Pain Satisfaction (%)
Regional Anesthesia		27%	44%	29%
General Anesthesia		36%	44%	20%
Low Willingness for Regional	14% rec'd regional	41%	41%	18%
Moderate Willingness for Regional	42% rec'd regional	50%	33%	17%
High Willingness for Regional	73% rec'd regional	17%	51%	32%
Preoperative Video	43% rec'd regional	34%	43%	23%
No Preoperative Video	59% rec'd regional	29%	45%	27%

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INDIVIDUAL BASAL PAIN SENSITIVITY AS ASSESSED BY EXPERIMENTAL PAIN TESTING MAY PREDICT ANALGESIC RESPONSE TO OPIOIDS

AUTHORS: O. Detsch[1], **K. Sickmann**[1], M. Hennig[2], S. Jelen-Esselborn[1], E. Kochs[1];
AFFILIATION: [1]Department of Anesthesiology, Technical University of Munich, Munich, Germany, [2]Department of Medical Statistics and Epidemiology, Technical University of Munich, Munich, Germany.

INTRODUCTION: Pain perception shows a large interindividual variability, i.e. some patients seem highly sensitive to noxious stimuli and others seem to be almost insensitive. Likewise, the response to the analgesic effects of opioids displays a large clinical and experimental variability.[1] The present study determined whether assessment of basal pain sensitivity using an experimental pain stimulus could predict the magnitude of the analgesic response to remifentanil.
METHODS: Following IRB approval and written informed consent, 100 patients (19-76 yrs; 71 males) scheduled for various ENT-procedures were enrolled. The experiments took place in the OR before induction of anesthesia. The supra-threshold pain stimulus was provided by an upper arm tourniquet (100 mmHg above systolic blood pressure). Using visual analogue scales (VAS 0-100), basal pain sensitivity was determined after 10 min of tourniquet ischemia for both pain intensity and pain unpleasantness, followed by a 10-min rest. Subsequently, at the end of a 20-min remifentanil infusion (0.15 µg kg-1 min-1), magnitude of pain perception was re-determined (i.e. opioid response). Statistical analysis was performed with parametric tests and linear as well as multiple regression analyses.
RESULTS: There was a large variability in basal pain sensitivity (VASbasal intensity: 43±27, mean±SD; VASbasal unpleasantness: 50±27). Remifentanil caused a mean reduction of VAS scores by 34±25 (intensity) and 35±22 (unpleasantness). Pain perception under remifentanil significantly correlated with basal pain sensitivity for intensity ($r=0.45$; $p<0.0001$) and for unpleasantness ($r=0.59$; $p<0.0001$). Exclusion of patients with maximum remifentanil-induced pain relief (i.e. VAS values of 0 for intensity and/or unpleasantness under remifentanil) from analysis revealed significant correlations of $r=0.43$ ($p<0.0001$; $n=50$) and $r=0.59$ ($p<0.0001$; $n=75$). Multiple regression analysis showed that only basal pain sensitivity had a significant impact on opioid response ($p<0.0001$ for intensity; $p=0.0004$ for unpleasantness), whereas sex, age, alcohol abuse, or smoking had no significant impact.
DISCUSSION: Based on reasonably strong correlations, the results show that the preoperative assessment of a patient's basal pain sensitivity predicts the magnitude of the analgesic response to the prototypic opioid remifentanil (prediction equations: perception of pain intensity under remifentanil equals 0.30 times basal pain sensitivity minus 4.0; perception of pain unpleasantness equals 0.40 times basal pain sensitivity minus 5.6). It has recently been shown that basal pain sensitivity (assessed by an experimental pain stimulus) predicts postoperative pain experience2. Thus, our data suggest that the preoperatively applied ischemic pain test may help tailor the dosing of opioids to achieve an acceptable level of perioperative analgesia.
REFERENCES: 1 Mogill JS: Proc Natl Acad Sci USA, 96: 7744-7751, 1999; 2 Granot M et al.: Anesthesiology, 98: 1422-1426, 2003.

S-170

PREOPERATIVE FENTANYL CHALLENGE IN CHRONIC OPIOID USERS: CORRELATION OF PREOPERATIVE APENEIC THRESHOLDS WITH POSTOPERATIVE ANALGESIC REQUIREMENTS

AUTHORS: J. J. Davis, **R. H. Hall**, K. B. Johnson, J. D. Dillon, T. D. Eagan, J. D. Swenson;
AFFILIATION: University of Utah School of Medicine, Salt Lake City, UT.

INTRODUCTION: Tolerance to the analgesic effects of opioids can occur within 1-2 weeks of therapy (1). For opioid tolerant patients, conventional (PCA) dosing may be ineffective and result in a cycle of escalating doses of opioid administered in the poorly monitored setting of the patient's hospital room. We present a group of opioid tolerant patients who received a preoperative, high dose, fentanyl infusion in the operating room. Using pharmacokinetic simulation, (2) the fentanyl effect site concentration associated with respiratory depression was determined and used to predict postoperative fentanyl requirements. Existing data for fentanyl suggest that the minimum effective plasma concentration providing analgesia is approximately 25–30% of that concentration associated with significant respiratory depression (3,4).
METHODS: After IRB approval and written informed consent, 13 opioid tolerant patients scheduled for posterior spinal instrumentation and fusion were studied. Using pharmacokinetic simulation software (Stanpump, Stanford, CA), the effect site concentration causing severe respiratory depression (RR<5) during an infusion of fentanyl 2ug/kg/min was determined. Postoperatively, a second pharmacokinetic simulation was used to predict an hourly infusion rate that would result in analgesic effect site concentrations. This was achieved by delivering 50% of the total hourly rate as a basal infusion and allowing the patient to deliver the remaining 50% in divided interval doses. At 4 hour intervals, the patient was allowed to increase or decrease the basal rate to maintain a demand dose of 2-3 per hour. Plasma fentanyl concentrations as well as arterial blood gases were measured after the patient had achieved a steady state infusion which resulted in satisfactory analgesia. The predicted effect site concentration causing respiratory depression was compared to the concentration at analgesic steady state using a Pearson's correlation coefficient.
RESULTS: The mean predicted effect site concentration of fentanyl associated with respiratory depression was 22.6±13.8ng/ml. The mean steady-state concentration associated with analgesia was 7.28±5.2 with a range of 2.1–22.3ng/ml. Arterial blood gas analysis at steady state revealed normoxia and normocarbia.
DISCUSSION: The mean predicted effect site concentration of fentanyl associated with respiratory depression was remarkably higher than that previously reported in the opioid naïve population (2ng/ml)(4). Likewise, the mean analgesic concentration measured at steady-state was considerably higher than reported in the opioid naïve populations (0.6ng/ml)(4). Although there was considerable variability among patients with respect to analgesic concentrations (range=2.1–22.3ng/ml), preoperative effect site concentrations associated with respiratory depression correlated well with postoperative analgesic concentrations (r^2 =.92)(figure). Further study is needed to determine whether a preoperative opioid challenge could be a reliable tool in predicting effective analgesic regimens in this population.
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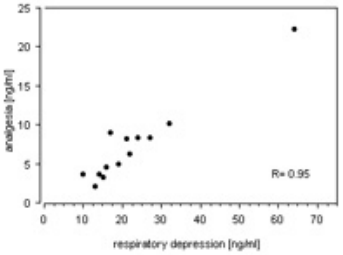

S-171

PREDICTORS OF POSTOPERATIVE ANALGESIC REQUIREMENT AFTER MAJOR LOWER EXTREMITY AMPUTATIONS

AUTHORS: **K. Subramaniam**, E. Holt, K. W. Park;
AFFILIATION: Beth Israel Deaconess Med Center, Boston, MA.

The pathophysiology and treatment of long-term post amputation pain have been evaluated in multiple clinical trials. However, the literature on the characteristics of acute postoperative pain is very scant. In this retrospective chart review at major vascular center, we analyzed the predictors and management strategies of acute post amputation pain.
After institutional board approval, we reviewed the charts of patients who underwent major lower extremity amputations from February 2002 to March 2003. The following informations were obtained ; age, sex, weight and ASA status , comorbid conditions, presence of diabetic neuropathy and nephropathy, hemodialysis , preoperative chronic opioid and non-narcotic analgesic use (e.g neurontin), severity (visual analog scale-VAS) of preoperative pain, type of anesthesia, duration of surgery, intraoperative narcotics, analgesics in PACU, 0-24 & 24-48 hours after surgery and side effects. Statistical analysis was performed using SPSS 11.5 software. Logistic regression was used to identify the risk factors. Comparison of means was also analyzed by independent samples t test. P value less than 0.05 was considered significant.
A total of 52 major amputations (above and below knee) were performed in 49 patients over a period of 14 months. 34 received GA, 11 had SA , 2 each received fem-sciatic block and CSE and one was done with MAC. 14 patients received IVPCA, continuous epidural analgesia was used in 4 and the remaining were managed with nurse controlled intermittent i.v narcotics. Using Logistic regression analysis, none of the following predicted the analgesic requirement in 0-48 hours; sex, preoperative VAS, chronic opioid and use of other analgesics such as neurontin, presence of neuropathy and nephropathy, hemodialysis and intraoperative fentanyl dose.Patients in SA group had lower age group (72± 8.6 years in GA group versus 57±8.9 years, p=0.001) and higher preoperative VAS (4.3±3.2 in GA group versus 6.6± 1.7, p=0.005) compared to patients who received GA. Higher morphine consumption was noted in patients who received SA compared with GA in 0-24 hours (11.9±21 mg in GA versus 68.6 ± 91.5 mg in SA group, p=0.004) and 24-48 hours (10±23 in GA group versus 50±77 in SA group=0.008). Analgesia related side effects were severe nausea and vomiting (n=13), mental status changes (3), deep sedation (4), respiratory depression requiring naloxone (2), respiratory arrest requiring intubation (1), respiratory depression requiring bag and mask ventilation (1), apneic episodes (1) and severe hypotension requiring discontinuing of epidural analgesia(1)
No definitive predictors of acute postoperative pain after major amputations could be identified . Increased analgesic consumption in SA could be due to younger age and higher preoperative VAS. High incidence of opioid related respiratory events was noted , related to increased dose of narcotics required in patients with significant co morbidities. More prospective clinical data is required.

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QUANTITATIVE SENSORY TESTING (QST) IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY: INFLUENCE OF RACE

AUTHORS: **G. E. Larijani**, M. E. Goldberg;
AFFILIATION: Cooper Hospital, Camden, NJ.

INTRODUCTION: Clinicians have long recognized racial differences in postoperative pain experience and expression. There is growing evidence that African Americans (AA) are more sensitive to experimentally induced thermal and pressure pain. Most reported studies of the influence of race on pain have been performed in healthy subjects or patients with chronic pain. In this study we evaluated experimentally induced pain in AA and Caucasian-Americans (CA) who were scheduled to undergo Total Abdominal Hysterectomy under general anesthesia. Relationship between sensory detection thresholds of the abdominal wall and the degree of postoperative pain, as determined by the 24 hr narcotic requirements, were evaluated in these patients.
METHODS: Informed consent was obtained from 29 female patients (18 AA, 11 CA) scheduled for TAH surgery under general anesthesia. Patients were evaluated for thermal (cold and warm) detection limits as well as pain thresholds (cold and warm) while in the surgical holding area, using QST. In addition, subjects were tested for touch detection limit using Von Frey hair filaments. The above tests were done in triplets on the patient's abdomen close to the expected incisional line. Anesthetic management of the patients was at the discretion of the anesthesiologist in charge of the patient. In the post anesthesia care unit patients received morphine according to our institutional criteria and were instructed to use PCA morphine for postoperative pain management. The twenty-four hour morphine dose utilization was determined for each patient. Data was analyzed using un-paired student t-test and is reported as mean (± SD). A $p<0.05$ was considered significant.
RESULTS: There were no significant differences in age (AA 42 ±7 vs. CA 46 ±8 years), height (AA 64 ±3 vs. CA 65± 3 inches), or weight (AA182 ±38 vs. 170±38 lbs) between the two groups. Heat-induced pain was significantly lower in AA (45.6 ±2.8 vs. 48.3 ±1.4 ºC, $p<0.01$). There were no significant differences in cold detection threshold, warm detection threshold, cold-induced pain threshold, or pressure sensation (Von Frey hair) between the two groups. AA used approximately 20% more morphine during the first postoperative day (64± 34 vs. 54 ±25 mg). The difference in postoperative morphine requirements, however, did not reach statistical significance due to the wide variation in morphine requirements among TAH patients.
CONCLUSION: This study confirms greater sensitivity of AA to experimentally induced heat pain in female patients. While the dose of morphine used was higher in AA this difference did not reach statistical significance most likely due to the wide variation in morphine use among patients. The influence of under treatment of postoperative pain on these data needs to be investigated.

S-173

THE MEASUREMENT OF PAIN INTENSITY: A COMPARISON OF EXAMINERS, PHYSICIANS OR CO-MEDICALS

AUTHORS: **K. Kumagai**, M. Kawase, M. Kawanishi;
AFFILIATION: Fujita Health University, Banbuntane-Hotokukai Hospital, Nagoya, Japan.

INTRODUCTION: Pain is recently regarded as "the fifth vital sign." The measurement of pain intensity is essential for the evaluation of treatment outcome. Ease and accuracy of administration of scoring are necessary not only for physicians but also for co-medicals, especially nurses. Generally speaking, the responses of patients to physicians are not always consistent with those to nurses. This study examined the magnitude of the relationship between pain measurement by physicians and those by nurses.
METHODS: 9 chronic pain inpatients (6 males and 3 females) were studied. The average age of the subjects was 62.13 years (S.D. =10.2). The primary pain sites of the subjects include neck, shoulder/arms, low back, and lower extremities. The subjects were asked to rate pain intensity 2 and 10 hours after awakening everyday for 2 weeks. Three scales, the Visual Analogue Scale (VAS), a 101-point Numerical Rating Scale (NRS), and a 4-point Verbal Rating Scale (VRS) were used by physicians and by nurses, respectively. Physicians and nurses asked patients separately. A series of correlation coefficients were computed.
RESULTS: There were significant correlation among VAS, NRS, and VRS, and they were consistent with previous reports. VAS scores asked by physicians and by nurses were correlated significantly in the first week ($r=0.73083$, $p<0.01$) and in the second week ($r=0.81793$, $p<0.01$). NRS were also correlated significantly in the first week ($r=0.52442$, $p<0.05$) and in the second week ($r=0.73804$, $p<0.01$). VRS were not correlated significantly in the first week, but correlated significantly in the second week ($r=0.53132$, $p<0.05$).Discussion: VAS and NRS measured separately by physicians and by nurses were correlated significantly. And the correlation coefficients were greater in the second week than in the first week. VRS was correlated only in the second week. The results indicate that the accuracy of pain intensity measurement can be improved by increasing the number of assessments. Supervision of patients may have produced higher correlation in the second week. Daily and frequent assessments may help to decrease diffidence of patients to answer. Routine and frequent measurement of pain intensity as a vital sign may lead to accurate pain evaluation.

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EPIDURAL DEXMEDETOMIDINE PROVIDES POST-OPERATIVE ANELGESIA

AUTHORS: **M. Maroof**[1], D. Jaine[2], R. M. Khan[2], S. Dogra[1], S. Maroof[2];
AFFILIATION: [1]UNC, Chapel Hill, NC, [2]JN Medical College Aligarh Muslim Universty, Aligarh, India.

INTRODUCTION: To potentiate analgesia of intrathecal Bupivacaine a wide range of opioids have been used epidurally but is associated with delayed respiratory depression. Dexmedetomidine (DXM), a highly selective alpha-2-agonist is known to provide excellent analgesia for 6-8 hours post operatively when injected epidurally during general anesthesia with minimal side effects [1]. We report here the results of a study of the effect of epidurally administered DXM for potentiating perioperative analgesia during the 1st 24 hours in combination with single dose intrathecal bupivacaine.
MATERIAL: The study was undertaken in 42 ASA I and II patients between the age 23-60 yrs, undergoing lower limb (hip and thigh) orthopaedic surgery. These patients did not have any known cardiorespiratory or neuro-muscular disorders. Patients were randomly divided into 2 groups of 21 patients each. Heart rate, Blood pressure, EKG, SaO2 were documented as base before the placement of combined spinal/epidural till the discharge of the patient from recovery room. All patients were preloaded with 10 ml/kg LR immediately prior to procedure. Under aseptic precautions, epidural space was identified by loss of resistance technique in the sitting position: Group (S) received 10 ml of normal saline epidurally. Group (D) received 2 mcg/kg DXM epidurally made up to 10 ml with normal saline. Following this using "Needle through needle technique 2.75 ml of 0.5% bupivacaine was injected intrathecally in both the groups. Patients were placed in supine position. Pain during the 1st 24 hours post operative period was monitored and treated with 2mg/kg Tramadol IM and documented. The patients were discharged from RR as sensory level recovered >2 dermatome of the initial level of sensory loss. Pain free period from spinal injection to the 1st analgesic requirement in the post operative period, the total Analgesic requirements in 1st 24 hours and the level of sedation in 1st 24 hours were monitored and recorded.
RESULTS: Both groups were similar in age, weight and type of surgery and did not show any differences in HR, BP, SaO2 and EKG changes during the study. All of Group S patients complained of pain from 2.5 hour to 4 hrs 40 minutes from the time of spinal injection. All patients in this group required Tramadol 2-4 doses in the first 24 hrs. Only 11 patients in group D required post opereative tramadol during the first 24 hours of surgery, $p > 0.0001$. Patients requiring tramadol in Group D, none was requested before 18 hours of the placement of spinal injection. Following the administration of DXM Group P patients went to rousable sleep lasting 20-30 minutes.
CONCLUSIONS: Epidurally administered Dexmedetomidine may provide post operative analgesia lasting upto 24 hrs.
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* $p > 0.0001$

GROUPS	AGE yrs	WEIGHT kg	ANALGESIC DOSES GIVEN	NO PAIN PATIENTS
S SALINE (21)	40 ± 11.7	52 ± 3.5	3.5 ± 0.9	0
DDexmedetomidine21	43 ± 11.5	51 ± 3.6	1.1 ± 1.3 *	11 *

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NASAL FENTANYL FOR POSTOPERATIVE ANALGESIA IN GYNECOLOGICAL PATIENTS

AUTHORS: **L. Latasch**[1], E. Barrera[2], S. Resch[2], S. Teichmann[2], E. Freye[3];
AFFILIATION: [1]Nordwest Hospital, Dept. of Anesthesia and Pain Therapy, Frankfurt/Main, Germany, [2]Nordwest Hospital, Dep. of Anesthesia and Pain Therapy, Frankfurt/Main, Germany, [3]University Hospital of Düsseldorf, Düsseldorf/Germany, Germany.

INTRODUCTION: Administration of highly lipophilic analgesics through mucous membranes has been advocated in the past [1, 2]. Due to the lack of a standardized dispenser, necessary to guarantee constant and reliable doses of the opioid, the technique has not been developed further. We have tested a new transnasal device which delivered a fixed concentration of 70 µg of fentanyl with droplets size of 80 µm (American Australian Medical Inc, Buffalo, USA).
METHODS: After approval by the local ethical committee, 40 patients following an opioid based balanced anesthesia, were enrolled in the study. After the operation patients self-administered the fentanyl nasal spray whenever they felt this to be necessary. The lockout time for nasal fentanyl was 3 minutes. They were given oxygen (3 l/min) for the first 15 min in the recovery room. VAS (0-10), respiratory rate (RR), transcutaneous oxygen saturation (SpO2), as well as cardiovascular parameters (HR, SYST, DIAST) were attained by an independent observer.
RESULTS AND CONCLUSIOn: Repetitively intranasal fentanyl was used by patients only within the first 3-5 hours after operation. From a mean of 6.2 VAS dropped to a mean of 3.1, using a mean dose of 322 µg (max. 490 µg; min. 120 µg). Having reached a sufficient level of analgesia, all parameters remained within normal values (table 1).
Two patients needed an additional intravenous opioid, another demonstrated a marked decline in SpO2 shortly after the first use of fentanyl. Side effects such as PONV were generally not observed in the first 24 hours. Because of the simple yet effective ease of administration, a fixed dose of intranasal fentanyl presents an attractive alternative for postoperative analgesia in patients.
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Tab. 1: Parameters before and after the use of nasal fentanyl

Parameters	RR (cycles/min)	HR (beats/min)	SYST (mm Hg)	DIAST (mm Hg)	SpO2	VAS (O-10)
Before use	13±2.1	73±14	127±11.7	76±8.9	98±1.3	6.4±1.1
After use	13 ±1.6	72±11	127±17	74±11.6	95±2.7	3.2±1.4

S-176

SELF-ADMINISTRATION OF NASAL SUFENTANIL FOR POSTOPERATIVE ANALGESIA IN GYNECOLOGICAL PATIENTS

AUTHORS: **L. Latasch**[1], D. Piorko[2], V. Lischke[3], E. Freye[4];
AFFILIATION: [1]Nordwest Hospital, Dept. of Anesthesia and Pain Therapy, Frankfurt/Main, Germany, [2]University Hospital Frankfurt, Frankfurt/Main, Germany, [3]Stadtkrankenhaus Bad Homburg, Bad Homburg, Germany, [4]University Hospital Düsseldorf, Düsseldorf/Germany, Germany.

INTRODUCTION: Self-administration of the highly lipophilic sufentanil through mucous membranes is an option which might result in less side effects, faster response to increased pain, side effects, total PACU costs and more convenience for patient and nursing staff (1). Due to the lack of a standardized dispensers in the past (2) which is necessary to guarantee constant and reliable dosing of the opioid, the technique has not been developed further. We have tested a new transnasal device which delivered a concentration of 10 µg of sufentanil, with droplets sizes as small as 80 µm (American Australian Medical Inc, Buffalo, USA) thus guaranteeing a stable reabsorption.
METHODS: After approval by the local ethical committee and informed consent, 40 patients following an opioid based balanced anesthesia took part in the study.
After the operation patients self-administered the sufentanil nasal spray whenever they felt the need. The lockout time for nasal sufentanil was 3 minutes. Patients were given oxygen (3 l/min) for the first 15 min in the recovery room. The pain intensity was measured by visual analogue scale (VAS 0-10), respiratory rate (RR), transcutaneous oxygen saturation (SpO2), cardiovascular parameters (HR, SYST, DIAST) as well as the number of incidences of hypoxemia were attained by an independent observer.
RESULTS AND CONCLUSION: Intranasal sufentanil was self-administered by patients mainly within the first 3-5 hours after operation using a mean dose of 40 µg (max. 60, min 10 µg). VAS dropped from a mean of 6.0 to 2.1 ($p > 0.01$). Having reached a sufficient level analgesia, all parameters remained within normal values (table 1). Approx. 30% of the patients had a drop in SpO2 once during self-administration (max. down to 85%) which was resumed by ordering patients to ventilate. There was no need to top sufentanil with an additional non-opioid analgesic. Because of the high incidence of bouts of insufficient respiration, the concentration of SUF administered by each snuff needs readjustment. Since sufentanil when compared to fentanyl elicits a more potent sedative effect (3) patients may titrate themselves beyond sufficient respiration.

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Tab. 1: Clinical parameters before and after nasal sufentanil

Parameters	RR (cycle/minute)	HR (beats/min)	SYST (mmHg)	DIAST (mm Hg)	SpO2	VAS (0 - 10)
Before Use	14,4	89,4	131,9	77,0	97,6	6,0
After Use	10,7	75,3	118,1	72,3	95,1	2,3

S-177

THE INCIDENCE OF POST-OPERATIVE NAUSEA AND VOMITING IN THE 48 HOURS FOLLOWING MAJOR JOINT SURGERY

AUTHORS: **S. M. Shah**[1], E. R. Viscusi[2];
AFFILIATION: [1]Thomas Jefferson University Hospital, Philadelphia, PA, [2]Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA.

INTRODUCTION: Post-operative nausea and vomiting (PONV) remains a challenge for inpatient care. PONV is not only distressing for the patient, but often leads to delayed patient recovery and activity. These issues as well as the costs of treatment, may add significantly to the cost of select patient populations. Although the overall risk of PONV and that of certain populations (GYN, breast surgery, elderly) is well documented, specific "at risk" groups and duration of symptoms in many populations remain unknown. In general, elderly individuals have a low incidence of PONV. Our clinical impression with elderly individuals undergoing major joint surgery suggests PONV is a major consideration for up to 48 hours post-op. The purpose of this study was to examine the incidence of PONV for up to 48 hours following major joint surgery.
METHODS: Following IRB approval of this retrospective study, a total of 90 patients undergoing major joint replacement surgery (hip or knee replacement) were reviewed for their incidence of nausea/vomiting for 48 hours following surgery. Anesthesia consisted of intrathecal (IT) local anesthetic plus IT morphine for hip replacement and IT local anesthetic with postoperative local anesthetic epidural for knee replacement surgery. In addition, postoperative pain was supplmented using 48 hours of IV patient controlled analgesia (PCA) for both groups. Pain therapy was titrated to patient comfort. The incidence was defined as patients requiring approved therapy for PONV (ondansetron, promethazine, metoclopramide) after complaining of symptoms.
RESULTS: see Table
DISCUSSION: In our incidence study, approximately 42% of individuals undergoing major joint surgery suffered from PONV. This incidence is higher than expected with an average population age of 63 years. Interestingly, the incidence remains remarkably consistent over gender biases to PONV. Overall, the incidence of PONV was higher in patients undergoing total knee replacement surgery (52% vs. 39%).
PONV requiring treatment following major joint surgery may be significantly higher than expected based on these findings, and of longer duration (up to 48 hours). This population may warrant consideration as "at risk" for PONV, and require special consideration for prophylaxis and treatment.

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Table

Procedure	Subjects	Incidence	Incidence (males)	Incidence (females)	Total Incidence MJS (males)	Total Incidence MJS (females)	Total Incidence MJS	Average Age
Hip Replacement	N=57 M=31 F=26	39%	35%	35%	37%	46%	42%	61
Knee Replacement	N=33 M=7 F-26	52%	43%	58%				65

S-178

REDUCTION IN POSTOPERATIVE NAUSEA AND VOMITING FOLLOWING PREOPERATIVE AND POSTOPERATIVE ADMINISTRATION OF ROFECOXIB FOR TOTAL KNEE ARTHROPLASTY (TKA)

AUTHORS: **A. Buvanendran**, D. Elmofty, M. Moric, J. S. Kroin, K. J. Tuman;
AFFILIATION: Dept. of Anesthesiology, Rush Medical College, Chicago, IL.

INTRODUCTION: Postoperative nausea and vomiting (PONV) have been associated with decreased patient satisfaction, delayed discharge and patient discomfort (*Acta Anaesth Scand* 2001; 45, 4-13). We examined whether administering a cyclooxygenase-2 (COX-2) inhibitor preoperatively and postoperatively decrease PONV after TKA performed with regional anesthesia.
METHODS: Following IRB approval and informed consent, 68 patients scheduled for primary TKA were randomized into two groups and entered into the study. In the rofecoxib group (n = 34), patients received a dose of rofecoxib 50 mg both 2 hrs and 24 hrs before surgery. This group also received 50 mg of rofecoxib daily for next 3 days postoperatively in the hospital. The control group (n = 34) received placebo preoperatively and postoperatively. All patients had a combined spinal (11.25 mg hyperbaric bupivacaine and 25 µg fentanyl)- epidural anesthetic for the surgery and had a standardized surgical technique including limb tourniquet. In the recovery room an epidural infusion of bupivacaine 1 mg/ml and fentanyl 10 µg/ml at 6 ml /hr with a PCA mode of 1 ml every 15 minutes was commenced to titrate to VAS 3-4 for 2 days. After 48 hrs the epidural patients were transitioned to oral hydrocodone. Evaluation of PONV included direct questioning of the patients after surgery. The criterion for classification as nauseous is defined as a self-reported acknowledgment in response to direct questioning by a researcher. Vomiting was defined as at least one instance of vomiting during the same time period. As a correlated secondary measure, prescriptions of antiemetics were also recorded. Results were evaluated using the Mann-Whitney U Test.
RESULTS: Demographics did not differ between the groups. Both nausea and vomiting were lower for the rofecoxib group than the placebo group, with vomiting reaching statistical significance (Table). The administration of antiemetics was also significantly lower in the rofecoxib group. Results demonstrate that 41% of the patients in the control group required rescue medication vs. 18% in the rofecoxib group ($p < 0.038$).
Discussion: Results of this prospective randomized trial comparison SHOWS the efficacy of preoperative and postoperative administration of rofecoxib in reduction of postoperative vomiting and anti-emetic consumption. While factors such as reduced opioid consumption and improved analgesia may be responsible for reduced PONV, it has been shown that COX-2 inhibition alone can prevent pharmacologically induced emesis in animals (Neuropharmacology 2000; 39: 2329-35).

Table. Postoperative Nausea and Vomiting

	Placebo		Rofecoxib		P-Value
	# of patients	Percent	# of patients	Percent	
Outcome					
Nausea	15	(44%)	8	(24%)	0.083
Vomiting	9	(26%)	2	(6%)	0.047
Antiemetic use	14	(41%)	6	(18%)	0.038

Values are number (%).

S-179

PREVALENCE OF PAIN AT HOME AFTER DAY CARE SURGERY

AUTHORS: **F. Raps**, H. Gramke, M. De Rijke, M. Van Kleef, M. Marcus;
AFFILIATION: University Hospital Maastricht, Maastricht, Netherlands.

INTRODUCTION: Because of the development of better anaesthetic and surgical techniques, day care surgery has grown rapidly in many European and North-American countries. However, little is known how patients experience pain at home, the days after surgery. The purpose of our study was to assess the prevalence and intensity of post-operative pain in the 4 days following the operation.
METHODS: From October 2002 till February 2003, 650 patients who underwent a surgical procedure at the day care unit of the University Hospital Maastricht, were included. Exclusion criteria were: age < 18 years, acute surgery, limitations of self-expression or visual dysfunction. Patients treated according our current post-operative pain protocol, were asked to rate their pain by filling in Visual Analogue Scales (VAS) before, 1 and 2 hours after surgery. A diary was given to the patients to further score their pain 3 times a day, the following 4 days at home.
RESULTS: The patients were 19-89 years (mean 50 years). Male-female distribution was 44-55%. 61% received general and 39% regional anaesthesia. 84% Of the patients experienced no or mild pain (VAS < 5) on the day of surgery. 16% reported to have moderate to severe pain (VAS >=5). On day 1 this was respectively 86% and 14%, day 2 92% and 8%, day 3 93% and 7%, day 4 94% and 6%. Highest VAS scores were found for abdominal surgery (among which inguinal hernia), breast surgery, orthopaedic surgery of the upper extremities and gynaecological laparoscopic procedures.
CONCLUSION: Although a significant amount of patients was pain free after the operation, attention should be given to those interventions that caused moderate and severe pain.

S-180

PREEMPTIVE ANALGESIC EFFECTS OF ETORICOXIB IN MINOR GYNECOLOGICAL DAY-CASE SURGERY

AUTHORS: **W. Liu**[1], C. Loo[2], J. Chiu[3], H. Tan[3], H. Ren[1];
AFFILIATION: [1]Peking Union Medical College Hospital, Beijing, China, [2]KK Women's And Children's Hospital, Singapore, Singapore, [3]KK Women's and Children's Hospital, Singapore, Singapore.

INTRODUCTION: Nonsteroidal anti-inflammatory drugs (NSAIDS) play an important role in postoperative analgesia. The selective COX-2 inhibitors have been increasingly used in place of NSAIDS due to fewer side effects. This prospective, randomized, double blinded and placebo controlled study was designed to evaluate the preemptive analgesic effects of a new selective COX-2 inhibitor, etoricoxib in day-case uterine evacuation patients.
METHODS: A total of 40 day-case patients undergoing evacuation of uterus for missed or incomplete spontaneous abortion were randomized to 2 groups receiving either placebo or etoricoxib 120mg 30-60 min before operation. Pain score (VAS 0-100) was recorded postoperatively at 15min, 30min, 60min and at home ready time. If pain score were more than 50, rescue analgesia of i.v. 25µ g fentanyl would be given. Recovery time like feeding time, step-down time (time in PACU) and home ready time were also recorded. Follow-up evaluation via telephone was performed at 24 hours after surgery to assess post-discharge pain, analgesic requirements (oral paracetamol 1g) and patients' satisfaction with their overall pain management.
RESULTS: There were no significant differences in patients' age, weight and surgical duration between the two groups. For postoperative pain assessment, there was no difference in the proportion of patients complaining of pain in both groups (placebo group 70% and etoricoxib group 60%). Table 1 showed the average pain score at 15min, 30min, 60min, home ready time, 6 hours and 24 hours in both groups. Etoricoxib provided better pain relief at home ready time (P<0.05) and 6 hours after operation (P<0.01). 60% of patients in the placebo group and 35% of patients in etoricoxib group required analgesic rescue in PACU. After discharge, there were 3 patients in placebo group and only 1 patient in etoricoxib group needed oral paracetamol. The results, however, was not significant. There were no differences in the feeding time, step-down time and home readiness time (65.70±18.41min[mean± SD] vs 63.50±15.30; 78.60±19.86 vs 82.60±16.93 and 79.30± 18.99 vs 83.80±18.21 respectively) . No patients complained of pain at 24 hours and all could perform normal activities. The overall pain management satisfaction score didn't show any difference either (93.22± 8.67 vs 95.75± 7.30; P=0.144).
DISCUSSION: Etoricoxib 120mg administered orally for preemptive analgesia decreased pain intensity at home ready time and 6 hour postoperatively in the day-case uterine evacuation patients. However, there was no difference in the home ready time and overall pain management satisfaction between two study groups.

Table 1: Postoperative pain score

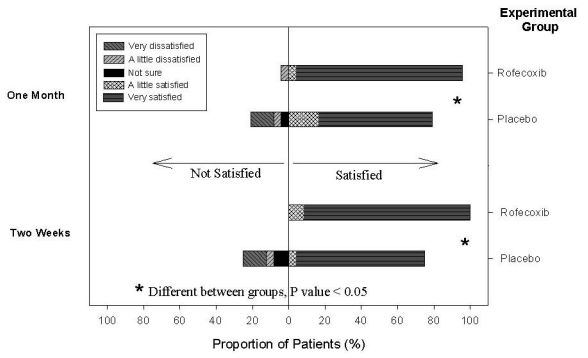
	placebo	etoicoxib	Significance
15 min post operation	36.95± 29.18 (mean±SD)	25.50± 27.38	NS(not signifi-cant)
30 min post operation	27.75± 22.97	24.75± 18.39	NS
60 min post operation	14.50± 21.83	9.25± 16.96	NS
Home ready time	7.50± 10.45	0.85± 2.46	P<0.05
6 h post operation	7.50± 12.39	0.00± 0.00	P<0.01
24h post operation	0.00± 0.00	0.00± 0.00	NS

S-181

PATIENT SATISFACTION WITH ANALGESIA AFTER PREOPERATIVE AND POSTOPERATIVE ADMINISTRATION OF ROFECOXIB

AUTHORS: **A. Buvanendran**, M. Moric, D. Elmofty, J. S. Kroin, K. J. Tuman;
AFFILIATION: Dept. of Anesthesiology, Rush Medical College, Chicago, IL.

INTRODUCTION: Recently there is great interest in the perception of health care provided to patients that are presenting to our competitive hospital medical care. We examined whether administering a cyclooxygenase-2 (COX-2) inhibitor preoperatively and postoperatively effects subjective perception (satisfaction) of analgesia treatment adequacy, after total knee arthroplasty (TKA) performed with regional anesthesia.
METHODS: Following IRB approval and informed consent, 66 patients scheduled for primary TKA were randomized into two groups. In the rofecoxib group (n = 33), patients received a dose of rofecoxib 50 mg both 2 hrs and 24 hrs before surgery. This group also received 50 mg for the next 3 days and later, 25 mg of rofecoxib daily for 14 days postoperatively. The other group (n = 33) received placebo preoperatively and postoperatively. All patients had a combined spinal (11.25 mg hyperbaric bupivacaine and 25 µg fentanyl)- epidural anesthetic for the surgery and had a standardized surgical technique. In the recovery room an epidural infusion of bupivacaine 1 mg/ml and fentanyl 10 µg/ml at 6 ml /hr with a PCA mode of 1 ml every 15 minutes was commenced to titrate to VAS 3-4 for 2 days. After 48 hrs the patients were transitioned to oral hydrocodone. Patients were interviewed by telephone at home at 2 and 4 weeks by research personnel and asked to rate their satisfaction with the analgesia provided for their postoperative pain control. They were asked to classify their response into one of five categories: Very dissatisfied, A little dissatisfied, Not Sure, A little satisfied, Very satisfied. Comparison was made using the Mantel-Haenszel Chi-Square Test.
RESULTS: Demographics did not differ between the groups and all of the patients had the surgery due to degenerative arthritic joints. There was little variation between the one month and two week responses, indicating a relatively stable measure (Figure). The rofecoxib group responded significantly more positively to the analgesia than did the placebo group during both the two-week (P-value=0.0257) and the one-month (P-value=0.0326) phone interview.
DISCUSSION: We conclude that patients have greater satisfaction with analgesia when rofecoxib is included as part of a multimodel pain management approach after TKA. Greater satisfaction with analgesia for the patients in the rofecoxib group may be related to pain relief provided by the COX-2 inhibitor for other arthritic joints in the body.



S-182

DOES SUBLINGUAL PIROXICAM PROVIDE PREEMPTIVE ANALGESIA?

AUTHORS: **T. Visser**[1], J. Petry[1], H. Gramke[1], J. Mustaki[2], M. Vercauteren[3], M. Marcus[1];
AFFILIATION: [1]University Hospital Maastricht, Maastricht, Netherlands, [2]Hopital de Zone Morges, Service d'anesthesiologie, Morges, Switzerland, [3]Universitair Ziekenhuis Antwerpen, dpt. anaesthesiology, Edegem, Belgium.

INTRODUCTION: The use of NSAID's for preemptive analgesia is controversial. O'Hanlon (1) found clinically important effects of preemptive NSAID's, but this is contradictory tot the majority of studies that have used NSAID's to preemp postoperative pain. In these studies the routes of administration included oral, rectal, intramuscular and intravenous. Another route, which could be used, is the sublingual one, which can have advantages. We investigated this sublingual route for preemptive analgesia.
METHODS: After approval of the Ethical Committee and written informed consent, 44 ASA I or II patients (18-65 years laparoscopic intervention for bilateral inguinal hernia) were enrolled in this randomised, double blind, double dummy prospective study. One group of patients (P.pre) received 2 hour before the operation sublingual Piroxicam 40mg and 10 minutes postoperative a placebo. The other group (P.post) received first a placebo and 10 minutes postoperative Piroxicam 40mg sublingual.
General anesthesia was induced and a bolus of 100mg tramadol was given. Postoperative analgesia was supplied by patient controlled intravenous tramadol.
One day postoperatively, the patients received 40mg Piroxicam sublingual. Postoperatively, visual analog pain scores (VAS) and the cumulative PCA Tramadol were recorded for each subject
Statistical significance was defined as $P < 0.05$.
RESULTS: Only at T1 (6 h) the VAS was significantly lower between P.pre group (1.76) and P post group (3.4). A significant difference for consumption of Tramadol was shown between the groups at T2 (20 hours)(P.pre 114+78, P.post 151mg+80) and T3 (30 hours))(P.pre 147mg+88, P.post 205mg+115).
DISCUSSION: The combination of preoperative Piroxicam sublingual with tramadol PCA decreased the use of analgesics with superior analgesia postoperatively which points in the direction of preemptive analgesia.
1.O'Hanlon et al (2001). Can J Anesth **48**: 162-166.

S-183

PRE-EMPTIVE ANALGESIA IN LAPAROSCOPIC CHOLECYSTECTOMY PATIENTS SIMPLIFIES THEIR POST-OPERATIVE PAIN MANAGEMENT

AUTHORS: **O. P. Maslovsky**;
AFFILIATION: Khmelnitsky Regional Clinic Hospital, Khmelnitsky, Ukraine.

INTRODUCTION: The goal of our study was to determine an analgesia quality after laparoscopic cholecystectomy (LC) with pre-emptive analgesia (PEA).
METHODS: In this blind-controlled study 115 informed healthy European women (age 35±8 yr.) divided into 2 groups underwent LC under combined general anesthesia. Groups were composed without significant differences for BMI, lab data, risk factors, etc. The 1st group (PEA, 64 pt.) received trometamine ketorolac (TK) 45 mg im and ketamine (K) 25 mg besides standard premedication (SP) 30 min prior induction of anesthesia. The 2nd group (SP, 51 pt.) was given SP only. The anesthesia protocols were identical for both groups – general combined endotracheal anesthesia, PRVC ventilation after paralysis with 12 mm Hg carboperitoneum. Postoperative analgesia protocols were the same in both groups and simplified. The first TK 45 mg im patient received at the pain onset about 2 points (Wong Baker FACES Pain Rating Scale, 1991) following TK 45 mg im every 12 hours. An additional analgesia was available with morphine 5-10 mg im on demand.
RESULTS: Postoperative analgesia requirements were studied in both groups as shown in table below (Mean±SD)

	SP only	PEA+SP	p
First p/op demand, min	58±37	172±53	<0.01
Morphine at the I day, mg	21.5±8.4	6.1±5.7	<0.01
Morphine at the II day, mg	25.3±9.3	6.5±8.5	<0.01
Overall Morphine, mg	51±20.3	13.9±9.8	<0.01
Morphine IM, times	4.9±2.2	1.3±1.1	<0.01
First walk, hours p/op	20.1±6.3	12.4±5.2	<0.01

DISCUSSIONS: Pre-op administration of TK 45 mg im and K 25 mg im in patients 30 min prior laparoscopic cholecystectomy results in significant threefold post-op analgesia prolongation and decreases analgesics consumption in post-op patients. Such kind of pre-emptive analgesia makes economical benefits for medical service.
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S-184

COX-2 INHIBITOR MELOXICAM PREMEDICATION REDUCED POSTOPERATIVE ANALGESIC COMSUMPTION IN PATIENTS AFTER DENTAL SURGERY

AUTHORS: **T. Aoki**[1], H. Yamaguchi[2], H. Naito[3], K. Shiiki[3], Y. Ota[1], A. Kaneko[1];
AFFILIATION: [1]Tokai University Hospital, Isehara, Japan, [2]Ryugasaki Saiseikai Hospital, Ryugasaki, Japan, [3]Iwaki Kyoritsu General Hospital, Iwaki, Japan.

INTRODUCTION: COX-2 activation is reported to be involved in the generation of the centrally-mediated inflammatory pain hypersensitivity process (1). And a preoperative COX-2 inhibitor may have a preferable effect in terms of preventing post-traumatic pain accompanying surgery (2), and which effect is called pre-emptive analgesia. Meloxicam is one of COX-2 inhibitors available in practice. It has not been reported if meloxicam premedication has a pre-emptive analgesic effect when used in a dental surgery under local anesthesia. In this study, we tested if meloxicam premedication might produce pre-emptive analgesic effect in patients undergoing unilateral mandibular third molar extraction under inferior alveolar nerve block using a local anesthetic.
METHODS: The study protocol was approved by the local ethical committees of the institutions. Ninety-two consecutive ASA physical status I or II patients undergoing unilateral mandibular third molar extraction surgery were enrolled in this study, and were allocated into one of the 3 groups using randomizing method. Group A (n=32), B (n=30), and C (n=30) patients were given meloxicam, 10 mg, ampiroxicam, 27 mg, and placebo orally 90 min. prior to surgery, respectively. In all patients the surgery was completed within 30 min under inferior alveolar nerve block using 1.0% lidocaaine containing 0.001% epinephrine. Postoperatively the patients were allowed to take oral loxoprofen, 60 mg, each when they needed for the postoperative wound pain relief. Postoperative pain was evaluated at the clinic on the first, 7th, and 14th day after surgery, respectively, using visual analog scale (VAS) and verbal rating scale (VRS), and the number of loxoprofen per a day they took. These parameters were compared among the 3 groups using Kruskal-Wallis rank test with statistical significance of $p<0.05$.
RESULTS: VAS and VRS scores tended to be lower in Group A compared with those in Group B or C, but they were without statistical significance. The analgesic consumption on the day of surgery was significantly lower in Group A than in Group C. The analgesic consumption on the first postoperative day after surgery was significantly lower in Groups A and B than in Group C. The total postoperative analgesic consumption during the study period was significantly less in Group A than in Group C.
DISCUSSIONS: The results of this study indicate that meloxicam premedication showed pre-emptive analgesic effect after the dental surgery. The reduced postoperative analgesic consumption brings patients major benefits in terms of the reduced incidence of the analgesic-induced adverse effects and the reduced cost.
Conclusions: COX-2 inhibitor meloxicam, 10 mg, premedication did not improve VAS and VRS scores, but reduced the analgesic consumption compared with the control group.
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S-185

COMPARISON OF SUBCUTANEOUS VERSUS INTRAVENOUS MORPHINE IN RENAL TRANSPLANTATION BY PCA

AUTHORS: **C. Chandralekha**, S. Krishnan, L. Kashyap, V. Mohan;
AFFILIATION: All India Institute of Medical Sciences, New Delhi, India.

Postoperative pain is not adequately treated for fear of sedation in end stage renal disease. PCA allows patients to self-administer analgesic medications to control postoperative pain.
This study was undertaken to compare the i.v. SOS, i.v. PCA and s.c. PCA requirement of morphine for postoperative analgesia in post renal transplant patients.
MATERIALS AND METHODS: Sixty five patients of age 20-50 years with end stage renal disease scheduled for live or cadaveric renal transplantation were studied. They were randomized into three groups on the basis of route of administration of postoperative analgesia:
Group1 : intermittent intravenous (i.v.) 3 mg morphine SOS.
Group2: intravenous PCA morphine with 0.5 mg boluses and a lockout interval of 15 minutes, 1mg/ml morphine in normal saline.
Group3: subcutaneous PCA morphine with 0.5 mg boluses and a lockout interval of 15 minutes using 1mg/ml morphine in normal saline.
Patients were anesthetised with general anesthesia on controlled respiration. A subcutaneous cannula was placed in the pectoral region before reversal of neuromuscular blockade in patients of group 3.
All patients received bolus of 3 mg i.v. morphine in the ICU. Subsequently, postoperative analgesia was according to the group randomly selected earlier. Parameters were recorded at 1,2,6,12,18 and 24 hours after extubation:
1.Pain score at rest, cough and at movement, assessed by the standard 10 cm VAS.
2.Total Morphine requirement in the first 24 hour postoperatively
3.Monitoring of vital parameters, SpO_2 and any side effects.
Sedation scores were noted at the same intervals and graded as: 0=no sedation, 1=sedated but awake, 2=asleep but waking up easily, 3=drowsy (needs shaking), 4=responds only to pain, 5=comatose.
Data was analyzed using the statistical package for social sciences (SPSS v 11.0). A p value of <0.05 was considered statistically significant.
RESULTS :
1.Total morphine requirement was statistically similar in all the groups.
2.patients in the s.c. PCA group had lower VAS scores for pain at rest, coughing and movement.
3.Morphine consumption did not correlate with postoperative blood urea and serum creatinine levels of the patient.
4.There was an increase in respiratory rate with an increase in pain scores in all three groups. Heart rate and systolic blood pressure did not correlate well with pain scores.
5.s.c. PCA group had a statistically lower incidence of sedation and PONV.
6.Supplementary bolus of i.v. morphine increases the incidence of side effects.
We conclude that in patients with end-stage renal disease undergoing renal transplantation-
1.s.c. PCA morphine is a safe and effective method for postoperative analgesia and is associated with less sedation and PONV.
2.Change in respiratory rate is important parameter to assess pain in-patients on beta-blockers.

S-186

EVALUATION OF THE BRACHIAL PLEXUS BLOCK AT THE HUMERAL CANAL USING A NEUROSTIMULATOR

AUTHORS: **Q. Fan**[1], X. Xu[2], F. Jin[1], B. Yu[1];
AFFILIATION: [1]Department of Anesthesiology, Rui Jin Hospital, Shanghai Second Medical University, Shanghai, China, [2]Department of Anesthesiology, Tai Zhou Center Hospital, Zhe Jian, China.

INTRODUCTION: To evaluate the efficacy and safety of the multiple peripheral nerve block technique at the humeral canal with the use of a neurostimulator.
METHODS: 128 ASA I-II patients aged 18-65 years undergoing upper limb surgery with a brachial plexus block at the humeral canal were included in the study. All patients were in a supine position. Upper limbs were positioned in abduction (90°), and external rotation and the course of the brachial artery on the medial side of the arm was marked. A BraunTM neurostimulator with a 22-gauge 50-mm needle was used for all patients. The puncture site was at the junction between the upper and middle thirds of the arm, above the brachial artery. The needle was introduced following the direction of the brachial artery, toward the axilla. After crossing the brachial fascia, the neurostimulator was started. The initial current was 2 mA, rapidly decreased when motor response was noted. Nerve location was performed in the following order: median, ulnar, radial and musculocutaneous.
RESULTS: The success rate was 96 %. The threshold of minimal stimulation used to locate each nerve before injecting the anesthetic solution was the unique predictive factor for identified failure. For the median nerve, the threshold was 0.7 mA with a relative risk of failure (RRF) 1.45 (P=0.04). For the radial nerve the threshold was 0.5 mA with a RRF 1.35 (P=0.03), 0.6 for the ulnar nerve with a RRF 1.34 (P=0.04), and 0.5 mA for the musculocutaneous nerve with a RRF 1.48 (P=0.03). For any equal or higher stimulation level, the risk of failure of the humeral block increased. Adverse events occurred in 3 % of all cases and were usually minor.
DISCUSSION: The study provides supplementary information on the efficacy and safety of this technique. Stimulation thresholds are clinically identified for the first time as the main factor linked to the failure of a technique using neurostimulator. The humeral block is a reliable peripheral block allowing good success rates results with minor complications, which can be used as an alternative to the axillary block.
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FASCIAL COMPARTMENT INJECTION IN THE PROXIMAL POPLITEAL FOSSA FOR ANALGESIA OF THE LOWER EXTREMITY

AUTHORS: J. D. Swenson, **M. Sutherland**, S. P. Richardson;
AFFILIATION: University of Utah School of Medicine, Salt Lake City, UT.

INTRODUCTION: Current techniques for sciatic nerve blockade at the level of the popliteal fossa describe correct positioning of the needle or catheter by eliciting a motor or sensory stimulation (1, 2). The sciatic nerve is contained within a discrete fascial compartment bordered laterally by the biceps femoris (BF) muscle and medially by the semimembranosus/semitendinosus (SM/ST) muscles. This study evaluates the effectiveness of sciatic nerve blockade by simple injection of local anesthetic into this fascial compartment without motor or sensory stimulation from the patient.
METHODS: After IRB approval and written informed consent, 10 patients undergoing elective foot and ankle reconstruction were studied. Height (cm) and weight (kg) were recorded for each patient. Using only surface anatomy landmarks, the groove between the SM/ST and the BF muscles was identified 10 cm above the popliteal crease. This area was prepped and draped in a sterile fashion. An 18G, 4.8 cm intravenous catheter was inserted 4cm into this groove. No attempt was made to elicit a paresthesia or motor stimulation. After careful aspiration, 25cc of 0.5% bupivicaine with epinephrine (5 mcg/ml) were injected in 5ml increments through the 18G catheter. A 20G epidural catheter was then inserted through the 18G catheter to 15 cm at the skin. Temperature sensation and motor strength (scale 0-5) were assessed at 10 minute intervals. Correct catheter placement within the fascial compartment was confirmed by injection of iopamidol contrast under fluoroscopy. The duration of analgesia was determined by recording the time to first request by the patient for reinjection of the indwelling catheter.
RESULTS: Loss of temperature sensation was noted at 11.7 $\pm$ 0.4 and 15.0 $\pm$ 5.5 minutes in the peroneal and tibial nerves. The mean maximal decrease in motor function was 2.6$\pm$ 1.1/5 for dorsiflexion and 2.8$\pm$ 1.3/5 for plantar flexion. The mean duration of analgesia after initial injection was 19.3 $\pm$ 9.7 hours. Contrast injection into the fascial compartment between the SM/ST and BF muscles showed even distribution of injectate in the fascial compartment. All patients reported return of analgesia with reinjection of the indwelling catheter. There were no complications.
DISCUSSION: Simple injection into the fascial compartment between the SM/ST and the BF muscles in the proximal popliteal fossa produces analgesia and sensory loss but not complete motor block of the tibial and peroneal nerves. Contrast injection into this compartment confirms consistent distribution of injectate. This procedure is technically easy to perform and does not require immediate proximity of the needle to the nerve.
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ULTRASOUND GUIDED FASCIA ILIACA BLOCK

AUTHORS: J. D. Swenson, **M. A. Sutherland**, S. P. Richardson;
AFFILIATION: University of Utah School of Medicine, Salt Lake City, UT.

INTRODUCTION: The original technique for fascia iliaca block (1) relies on the ability to detect a loss of resistance in two distinct fascial planes (fascia lata, fascia iliaca). Despite excellent results achieved with this technique, femoral nerve blocks are typically performed using paresthesia or motor stimulation. The limited application of the fascia iliaca technique may be related to difficulty identifying these distinct fascial planes. We describe a technique for catheter placement deep to the fascia iliaca using ultrasound guidance.
METHODS: After IRB approval and written informed consent, 10 patients undergoing elective total knee arthroplasty were studied. A 7.5 MHz ultrasound probe was used to determine the position and depth of the femoral artery at a level immediately caudal to the inguinal ligament. Using sterile technique, an 18 G, 4.8 cm intravenous catheter was advanced 1cm lateral and 1cm deep to the posterior border of the femoral artery. A 20 ml syringe containing 0.5% bupivicaine with epinephrine 5 mcg/ml was attached to the catheter using IV extension tubing. The catheter was then withdrawn at 1mm intervals until there was no resistance to injection. Local anesthetic was injected in 5ml increments after careful aspiration. A 20G epidural catheter was inserted through the 18G IV catheter to a distance of 15 cm at the skin. Following local anesthetic injection, motor strength (scale of 1-5) for the quadriceps muscles and hip adductors was assessed at 10 minute intervals. Temperature sensation in the anterior, lateral,and medial aspects of the thigh was also assessed at ten minute intervals. The duration of analgesia was determined by noting the time of the patient's request for re-injection of the indwelling catheter.
RESULTS: Sensory blockade in the anterior, lateral, and medial aspects of the thigh occurred at 11.3 $\pm$ 3.5, 13.8 $\pm$ 5.2, and 15.0 $\pm$ 5.3 minutes respectively. Motor strength in the quadriceps muscle decreased to 1.6 $\pm$ 1.2/5. No motor block was detected with hip adduction. The duration of analgesia after initial injection was 17.5 $\pm$ 8.0 hours. All patients reported return of satisfactory analgesia on subsequent catheter injections.
DISCUSSION: Ultrasound of the femoral artery can be a reliable tool to perform fascia iliaca block without the use of motor or sensory stimulation. Injection at a point 1cm lateral and deep to the artery produced consistent femoral and lateral femoral cutaneous nerve block. There was no evidence of motor block in the distribution of the obturator nerve, although loss of sensation over the medial thigh suggests possible sensory block of this nerve as well. Precise location of the femoral artery using ultrasound is also useful to avoid inadvertent puncture of the vessel.
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COMBINED USE OF PARAVERTEBRAL BLOCK AND GENERAL ANESTHESIA IN BREAST CANCER SURGERY

AUTHORS: **K. Ono**, C. Hirayama, K. Ishii, Y. Okamoto, H. Hidaka;
AFFILIATION: Fukuyama City Hospital, Fukuyama, Japan.

INTRODUCTION: It has been reported that paravertebral block (PVB) can be used as an alternative to general anesthesia (GA) for patients undergoing major breast surgery1. To provide surgical anesthesia by PVB alone, however, it requires injection of local anesthetic at multi-level cervical and thoracic paravertebral spaces in the majority of cases2. This is associated with not a little patient discomfort during neural block and during surgery in awake, which has made PVB an uncommon choice of anesthesia. On the other hand, increasing the volume of local anesthetic injection at single site was reportedly as effective as multi-site injection3. If such single-injection PVB is performed prior to GA, its long-lasting analgesic effect seems likely to improve postoperative pain relief as well. This study was undertaken to investigate if the single-injection PVB adds to patient satisfaction when combined with GA for breast cancer surgery.
METHOD: Twenty-six women (ASA I-II) undergoing modified radical mastectomy with axillary dissection were investigated. PVB was performed as described by Karmakar2 at T1 level using 22G spinal needle and 15 ml of 0.5 % ropivacaine was injected. Thereafter, GA was induced with propofol and fentanyl, followed by a continuous infusion of propofol. Patients were given vecuronium to facilitate tracheal intubation and ventilated with nitrous oxide in oxygen. After surgery, they were transferred to recovery room and held there overnight. The visual analogue scale (VAS) pain scores were recorded on a 100 mm scale and postoperative medication were also recorded. These data with PVB were compared with those of 17 patients previously undergone similar surgical procedure under GA without PVB in our hospital.
RESULTS: The VAS score in patients with PVB was 34+9 (mean+SE) on admission to the recovery room and it significantly decreased to 13+1 next morning (Paired t-test). Frequency of postoperative administration of analgesics in patients with PVB was significantly fewer than those without PVB (Chi-Square test, see Table 1).
DISCUSSION: As expected, the single-injection PVB performed prior to GA improved postoperative pain relief in breast cancer surgery. In contrast to patients without PVB, few patients with PVB needed analgesics more than twice postoperatively. Because of unilateral somatic and sympathetic nerve blockade, it is also conceivable that the hemodynamic and respiratory effects of PVB are to a lesser degree than those of epidural block. Above findings suggest that combined use of PVB and GA may be a preferable choice of anesthesia for patients undergoing major breast cancer surgery.
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Table 1. Postoperative administration of analgesics

Frequency of administration	PVB+GA (n=26)	GA alone (n=17)
0	11	4
1	13	2
2 or more	2	11

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PATIENT-CONTROLLED ANALGESIA WITH REMIFENTANIL TCI COMPARED WITH PIRITRAMIDE BOLUS THERAPY FOR EXTRACORPORAL SHOCK WAVE LITHOTRYPSY

AUTHORS: **S. Schraag**;
AFFILIATION: University of Ulm, Ulm, Germany.

INTRODUCTION. Patient-controlled analgesia (PCA) and sedation with remifentanil has been used for extracorporal shock wave lithotripsy (ESWL) because it allows for rapid individualized titration [1, 2]. However, an increased incidence of respiratory adverse events is frequently observed with remifentanil when given as a bolus [3]. We tested whether patient-controlled Remifentanil target controlled infusion (TCI) would influence the efficacy of analgesia, and the respiratory safety margin compared to standard practice during ESWL.
METHODS. After obtained institutional ethic`s committee approval and written informed consent, 60 patients with ureter and calix lithiasis undergoing ESWL were studied. They were allocated randomly to receive either Remifentanil-TCI PCA (Group 1) or Piritramide bolus doses, with an initial of 7.5 mg, followed by 3.75 mg thereafter (Group 2) in a double-blind, double-dummy study design. Respiratory depression (SaO2 <91% over 5 minutes, requiring supplementary oxygen), efficacy of analgesia (11-point VAS), patient satisfaction (PS), and the quality of recovery score (QRS) [4] were obtained three hours and 1 days after the procedure. Statistical analysis was performed using Wilcoxon signed ranks test with a significance level of $\alpha<0.05$.
RESULTS. Patient characteristics and gender distribution were comparable between both groups. Patient ratings and incidence of adverse events (median, range) are listed in the table below (*denotes significance):

Time	Criteria	Remifentanil (n=30)	Piritramide (n=30)	p-value
Day 1	VAS (0-10)	1 (0-6)	3 (0-7)	0.003*
	PS (0-10)	9 (2-10)	9 (1-10)	0.361
	QRS (0-18)	16 (12-18)	15.(11-18)	0.607
Day 2	VAS (0-10)	2 (0-9)	3 (0-9)	0.019*
	PS (0-10)	9 (2-10)	9 (2-10)	0.384
	QRS (0-18)	16 (9-18)	14.5 (8-18)	0.250
Overall	Resp. event (%)	43 (13 of 30)	3 (1 of 30)	n.a.
Overall	Nausea (%)	40 (12 of 30)	47 (14 of 30)	n.a.

Episodes of respiratory depression were more frequent with remifentanil (group 1) but all were moderate and easily reversed with supplementary oxygen, whereas 17% (5 of 30) of patients in group 2 required prolonged supervision in PACU.
DISCUSSION. Remifentanil administered as a patient-controlled TCI significantly improved efficacy of analgesia during ESWL compared to standard practice. However, overall patient satisfaction and quality of recovery was equally good with a trend in favour of remifentanil, despite a high percentage of mild to moderate nausea in both groups.
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INTERPLEURAL MORPHINE ANALGESIA AFTER THORACOTOMY

AUTHORS: **S. Dabir**, B. Radpay, T. Parsa, L. Saliminejad, M. Kazempour;
AFFILIATION: National Research Institute of Tuberculosis and Lung Disease-Dr.Masih Daneshvari Hospital, Tehran, Iran (Islamic Republic of).

INTRODUCTION: The value of interpleural analgesia with morphine after thoracotomy is still contraversial. Interpleurally injected morphine may occupy receptors on intercostal nerves and produce analgesia (1-3). This randomized, double–blind trial was designed: 1) to evaluate the effect of interpleural morphine in the treatment of postthoracotomy pain, 2) compare this to a commonly used intravenous analgesic dose of morphine.
METHODS: 36 ASA class I - II patients, scheduled for lateral thoracotomy under general anesthesia were entered into the study after ethics committee approval, and informed patient consents. An epidural type catheter was placed in the pleural space under direct vision before closure of the chest. At the end of the surgery, with patient supine, the chest tubes were clamped for 15 minutes and the following solutions were randomly injected: 18 patients received morphine sulfate 0.2 mg/kg in normal saline 40 ml interpleurally(ip)and normal saline 10 ml intravenously(iv) [interpleural morphine group = ipm] ; 18 patients received normal saline 40 ml ip, and morphine sulfate 0.05 mg/kg in normal saline 10 ml iv [interpleural saline group = ips]. Then every 4 hours, regardless of degree of pain, patients were given trial solution for the first 24 hours postoperatively. Patients received supplementary doses of iv morphine upon request. Pain, supplemental analgesic consumption and side effects were recorded by a blinded observer during 24 hours. Sedation was evaluated using a five point scale (4). Before each trial injection and 30 minutes after that, postoperative pain was assessed during rest and deep breathing, by using a Faces Pain Scale (5) .
RESULTS: Results were available for 15 patients in ips and 16 patients in ipm groups. There were no significant differences in patient characteristics, length and type of surgery. Pain scores obtained after intervention were significantly lower than those before the intervention at all times in two groups. All pain scores were significantly lower in the ipm group than in the ips group at all times. Supplementary morphine requirements were significantly lower in the ipm group. Sedation scores were significantly higher in the ips group.
DISCUSSION: Interpleural morphine, in the studied dose, is safe and produces effective analgesia with minimal adverse systemic effects after thoracotomy. Effective analgesia may be related to the higher dose of morphine given interpleurally. This probably results from the need to anesthetize higher intercostal nerves and from the more rapid dilution of drugs within the pleural cavity and from the more rapid removal of the morphine from the pleural space through the chest drainage tube (6).
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COMPARISON OF PAIN RELIEF EFFECT BETWEEN EPIDURAL MORPHINE AND RECTALLY ADMINISTERED MORPHINE AFTER VATS LOBECTOMY IN PATIENTS WITH LUNG CANCER

AUTHORS: **K. Yamaguchi**[1], N. Akamatsu[2], T. Sugita[2], Y. Sekiguchi[2], T. Miyazaki[1];
AFFILIATION: [1]Juntendo University School of Medicine, Tokyo, Japan, [2]Saiseikai Central Hospital, Tokyo, Japan.

BACKGROUND; To evaluate the pain relief effect of morphine chloride after video-assisted thoracoscopic surgery (VATS) lobectomy in patients with lung cancer, pain severity based on the visual analog scale (VAS) and additional analgesic requirements were compared between patients given epidural morphine and those given rectally administered morphine until 4 postoperative days (POD) in the present study.
METHODS; Twenty-five patients undergoing elective VATS lobectomy due to lung cancer were randomized to the following two groups; 1) Group E (n=15consisted of the patients given epidural morphine, and 2) Group R (n=10) of those given rectal administration of morphine. Prior to the induction of general anesthesia, a thoracic epidural catheter was placed at the level of the T4-6 interspaces in Group E , and the patients were provided with an infusion pump allowing allowing continuous infusion of morphine chloride as a 10mg/100ml solution at a rate of 2 ml/hour for 48 hours prior to incision.. The patients in Group R received a rectal administration of 20 mg of morphine chloride after introduction of general anesthesia. Pain severity was evaluated by recording a pain score and needs of additional analgesic (15 mg of pentazocine and 25 mg of hydroxyzine were injected intramuscularly 24hour after surgery and 50 mg of indometacin suppository was administered from 1-POD). The observation period included 4-POD.
RESULTS; The two groups were matched by sex and ages. Pain severity based on VAS from 0-POD to 4-POD in Group E was lower than that in Group R, but the difference was not significant. The analgesic requirements on 0-POD in Group E were significantly smaller than those in Group R ($p < 0.05$), but no significant difference in the requirements between the groups was observed from 1-POD to 4-POD. There was no postoperative mortality or morbidity including prolonged air leakage.
CONCLUSION; Although there was no significant difference in pain severity based on VAS after surgery between Groups R and E, epidural morphine provided superior analgesia and reduced additional drug requirements on 0-POD. Our results suggested that epidural morphine was superior to rectally administered morphine in terms of additional analgesic requirements.

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EFFECTIVE DISCOGENIC PAIN RELIEF IN PATIENTS WITH PULSED RADIOFREQUENCY OF THE DORSAL ROOT GANGLIA (DRG'S)

AUTHORS: **D. K. Cope**, M. Loomba, H. K. Dhadha, N. N. Rizk;
AFFILIATION: University of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: Past studies describing pulsed radiofrequency in the lumbar dorsal root ganglia to treat patients with radicular pain have not demonstrated significant long term benefits(1). However the pulsed modality radiofrequency preferentially affects small pain fibers, such as the sinoverterbral nerve which innervates the dorsal lumbar discs, rather than large motor or sensory fibers implicated in radicular pain. Therefore we conducted this study in patients with degenerative lumbar disc disease in which the main pain pattern was non-radicular to determine the effects of pulsed radiofrequency at bilateral L_2, L_3 and L_4 DRG's.
METHODS: Six patients seen at our clinic from June 2002 through December 2002 were selected based on the following criteria:
1. Chronic low-back pain on weight bearing for at least six months, not attributable to radiculopathy or sacroilitis.
2. Unsuccessful physical therapy.
3. Unsuccessful series of either epidural or selective nerve injections.
4. Failed relief from NSAIDs and adjuvants.
5. Continued pain despite high opioid doses.
Patients gave informed consent, were given IV sedation and MAC.Procedure was done sterilely in the prone position under fluoroscopic guidance. At the DRG's sensory and motor stimulation confirmed needle positioning. Pulsed RF for 42° c for 120 sec.
RESULTS: Table I summarizes the results. Improvement in function at six mos. ranged from 50% improvement to 90%. Activity level improved with 3/6 requiring no ambulation assistance device. Opioid use decreased (4/6) and nonsteroidal and adjuvant medication use either remained stable (4/6) or decreased (2/6). No patient reported increased medication use. The only reported side effect was transient neuritis (1/6) that resolved in 15 days.
Pain decreased for all patients (Mean: baseline 7.5/10, post-procedure 5.0/10, one mo 2.0/10, four mo 2.2/10, six mo 3.0/10) but returned to baseline in one patient after six months.
DISCUSSION: Discogenic low back pain is a very common condition with limited treatment options. Previously it was thought that the disc annulus was not innervated, but recent neuroanatomical studies have shown rich innervation by the sinovertebral nerves, branches of the lumbar ventral rami, the gray rami communicans and even the sympathetic chain. By pulsed RF at the DRG's we have shown improvement in pain scores, function in daily activities, ability to ambulate without assistant devises, opioid, NSAID and adjuvant medication requirement that this therapy can provide sustained relief at six months follow up with minimal risk or side effects. These patients had failed physical therapy, other neuroaxial injections, medical management, and even sustained opioid therapy. We have demonstrated a safe and efficacious procedure to treat disc pain and are currently collecting outcome data on a much larger patient population to see if indeed this is a therapy that offers significant patient benefit.
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Patients	Pain Score (1-10)	Function	Medications: Opioids	NSAIDs	Adjuvants	Side Effects (motor, sensory, sympathetic symptoms and function, neuritis, infection, and systemic effects)
1	BL 7; Post 4; 1 mo 2; 4 mo 2; 6 mo 2	Able to climb stairs; Able to do household activity; Overall 60% better	N / A	Decreased	Decreased	None
2	BL 9; Post 7; 1 mo 5; 4 mo 5; 6 mo 2	Able to walk and climb steps; Discontinued assist device; Overall 80% better; Sleep and mood improved	Decreased methadone	N / A	Same	None
3	BL 6; Post 5; 1 mo 0; 4 mo 0; 6 mo 0	No longer using cane; Able to do yard work; Able to return to hunting; Greater than 80% better	Decreased	Decreased	Decreased	Transient neuritis
4	BL 8; Post 6; 1 mo 0; 4 mo 0; 6 mo 1	Overall 90% better	Decreased	N / A	Same	None
5	BL 7; Post 4; 1 mo 1; 4 mo 2; 6 mo 2	No use of assist device; Able to stand and walk for longer periods; Mood and sleep 80% better	Decreased	Same	Same	None
6	BL 8; Post 4; 1 mo 4; 4 mo 4; 6 mo 8	Function initial improvement 50%	Same	Same	Same	None

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EPIDURAL STEROID INJECTION FOR POST LAMINECTOMY SYNDROME: TRANSFORAMINAL VERSUS CAUDAL

AUTHORS: **J. J. Huang**;
AFFILIATION: Anesthesiologists of Greater Orlando, Orlando, FL.

INTRODUCTION: Pain treatment for post laminectomy syndrome patients is a challenge. It remained questionable whether scar tissue can explain the post laminectomy pain syndrome. Epidural steroid injection is a well accepted therapeutic modality used in the management of lumbar radicular pain. Transluminar, transforaminal, and caudal approach had been widely applied for post laminectomy syndrome patients. It is unknown whether different injection techniques have different outcome. We performed this observations and cross-over study to compare transforaminal epidural injection with caudal injection for patients with post laminectomy syndrome.
METHODS:The patients with recurrent low back pain after having had one or two lumbar laminectomies and having diagnosed by either neurosurgeon or an orthopedic surgeon as having postlaminectomy syndrome were included in the study. The pain duration was at least 6 months, the pain intensity (VAS) was > 7, and the pain was unilateral radicular pain. The pain did not response to physical therapy, antiinflammatories, or analgesics. All epidural injections were performed at an ambulatory surgery center by one anesthesiologist. All patient initially received caudal epidural steroid injection after evaluation. Two weeks later, patient was reevaluated. If patient had significant pain relief from caudal injection, then caudal epidural steroid injection was repeated. If patient had no significant pain relief from caudal injection, then transforaminal epidural injection was performed.
Caudal epidural injection: a 22-gauge spinal needle was radiographically guided to the caudal spinal canal. The needle position was verified by contrast spread into the caudal spinal canal. Then 80 mg triamcinolone with 15 mg lidocaine (15ml in total) was injected into the caudal spinal canal. Transforaminal epidural injection: a 25-gauge 10-cm spinal needle was radiographically guided to the dorsal/ventral aspect of the neural foramina at the suspected symptomatic radicular level. Once an epiduralgram was obtained, 40 mg triamcinolone with 15 mg lidocaine (2ml in total) was injected into the epidural space. A quality of pain relief of 50% or greater was considered as significant. Data was analyzed with Fisher's exact test. A P value of < 0.05 was considered significant.
RESULTS: There were total 12 patients in the study. Three patients had significant pain relief from caudal epidural injection. Eight patients had no pain relief from initial caudal epidural injection, however, they subsequently had 50% pain relief from transforaminal epidural injection. One patient had no relief from either caudal or transforaminal epidural injections. The difference in pain relief effect between transforaminal epidural injection and caudal epidural injection was statistically significant (8/1 vs. 3/9) ($P < 0.05$).
CONCLUSION: Transforaminal epidural steroid injections had better pain relief for post laminectomy syndrome patients than caudal epidural injection.

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INCIDENCE OF LOWER THORACIC LIGAMENTUM FLAVUM MIDLINE GAPS

AUTHORS: **P. Lirk**[1], C. Kolbitsch[2], J. Rieder[2], C. Keller[2], B. Moriggl[2];
AFFILIATION: [1]Medical College of Wisconsin, Milwaukee, WI, [2]University of Innsbruck, Innsbruck, Austria.

INTRODUCTION Lower thoracic epidural anesthesia and analgesia (EDA) has gained increasing importance in perioperative pain therapy for abdominal surgery. The loss-of-resistance technique used to identify the epidural space is thought to rely on the penetration of the ligamentum flavum. However, the exact morphology of the ligamentum flavum at different vertebral levels remains controversial. Therefore, the aim of this study was to directly investigate the incidence of lower thoracic ligamentum flavum midline gaps in embalmed cadavers.
METHODS Vertebral column specimens were obtained from 47 human cadavers. On each dissected level, ligamentum flavum midline gaps were recorded.
RESULTS The incidence of midline gaps / number of viable specimens at the following levels was: T_{6-7}: 2 / 45 (4.4 %), T_{7-8}: 1/47 (2.1 %), T_{8-9}: 2 / 45 (4.4 %), T_{9-10}: 7/39 (17.9 %), T_{10-11}: 12 / 34 (35.2 %), T_{11-12}: 10 / 35 (28.5 %), T_{12} / L_1: 6 / 38 (15.8 %).
DISCUSSION In conclusion, the present study could determine the frequency of lower thoracic ligamentum flavum midline gaps. Previous investigations have shown that the ligamentum flavum frequently fails to fuse in the midline at cervical and high thoracic levels (1). In contrast, gaps are rarer at the lumbar levels (2). Gaps in the thoracic ligamentum flavum are most frequent between T_{10} and T_{12}, Using the midline approach, one cannot therefore rely on the ligamentum flavum to impede entering the epidural space in all patients.
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ANALGESIC USE FOR TREATMENT OF CANCER PAIN AMONG HOSPICE PATIENTS

AUTHORS: **P. A. Sloan**[1], P. LaFountaine[2], K. Samba[1], C. Alexander[3], S. Connor[4], B. Ferrell[5];
AFFILIATION: [1]University of Kentucky, Lexington, KY, [2]Hospice of the Bluegrass, Lexington, KY, [3]University of Maryland, Baltimore, MD, [4]NHPCO, Alexandria, VA, [5]City of Hope, Duarte, CA.

INTRODUCTION: Pain control for cancer patients remains a significant problem in health care.[1] Recent studies have shown that pain associated with advanced cancer can usually be treated using standard analgesics and adjuvant analgesics.[2] The purpose of this study was to document the analgesic and adjuvant analgesic use among patients from a sample of hospices across the United States.
METHODS: With IRB approval, 141 home hospice patients from 7 hospices across the USA with cancer pain were followed for a minimum of 7d, and a maximum of 90d . At each hospice nurse visit, NSAID use, opioid analgesic use and dosage, adjuvant analgesic use, and non-drug methods of analgesia were recorded. Mean overall opioid use was calculated as oral morphine equivalents for all patients.
RESULTS: During a 21 month data collection period, 141 home hospice patients (68M, 73F) with a mean (S.D.) age of 68.9 (12.2) yrs were followed for 42.4 (30) days. 133 patients (94%) used an opioid for pain control. The most prevalent opioids used were morphine (41%), oxycodone (35%), fentanyl patch (20%), and hydrocodone (16%). Twenty-four % of patients were using 2 or more opioids. Of patients using morphine, 93% used the oral route of administration; 80% of patients required 180 mg daily or less; and 86% of patients required 300 mg daily or less. The overall initial mean oral morphine equivalent daily dose was 193.7 mg for all patients. 94 patients (67%) used NSAIDs, with acetaminophen being the most prevalent (36%). Adjuvant analgesics were used by 78 (55%) of patients: antidepressants (47%), steroids (37%), and tranquillisers (22%) being the most common. Nondrug methods of analgesia were used by a minority of patients with heat (14%) and message (14%) being the most common methods.
CONCLUSIONS: 1) Almost all patients (94%) with cancer pain required opioids for analgesia. 2) Morphine by the oral route was the most common opioid prescribed. 3) Most patients (86%) required modest doses of morphine (<240 mg daily) for pain relief. 4) Most patients required concomitant NSAID analgesics (67%) and adjuvant analgesics (55%). 5) Nondrug methods of analgesia were used in a minority of cancer pain patients.
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EFFICACY OF CANCER PAIN RELIEF AMONG HOME HOSPICE PATIENTS

AUTHORS: **P. A. Sloan**[1], P. LaFountaine[2], K. Samba[1], C. Alexander[3], S. Connor[4], B. Ferrell[5];
AFFILIATION: [1]University of Kentucky, Lexington, KY, [2]Hospice of the Bluegrass, Lexington, KY, [3]University of Maryland, Baltimore, MD, [4]NHCPO, Alexandria, VA, [5]City of Hope, Duarte, CA.

INTRODUCTION: Pain control for cancer patients remains a significant problem in health care even though standard analgesic regimens provide adequate pain relief in the majority of patients.[1] In spite of the obvious commitment of hospice programs to control cancer pain, few studies have documented the efficacy of the hospice community in managing cancer pain.[2] The purpose of this study was to assess the prevalence and management of pain among patients from a sample of hospices across the United States.
METHODS: With IRB approval, 141 home hospice patients from 7 hospices across the USA with cancer pain were followed for a minimum of 7d, and a maximum of 90d, with self-evaluation of pain and pain satisfaction at each hospice nurse visit. Tumor type, pain location and pain etiology were recorded. Patients recorded pain intensity using a numeric pain rating scale (0=no pain; 10=worst pain).[3] Patients rated the interference of pain with mood, relationships, activity, and sleep using the pain satisfaction instrument (0=does not interfere; 10=completely interferes).[3]
RESULTS: During a 21 month data collection period, 141 home hospice patients (68M, 73F) with a mean (S.D.) age of 68.9 (12.2) yrs were followed for 42.4 (30) days. The most prevalent tumors were lung (26%) and colon (13%) with most patients (74%) having local or widespread metastases. On the pain intensity scale, mean (S.D.) pain scores on study entry were current pain 3.3 (2.9) and 24-hr average pain 4.4 (2.4). These scores dropped by the final evaluation to 2.5 (2.6) and 3.0 (2.2) respectively, with significant differences of $p<01$ compared with study entry. The cancer pain interfered with mean (S.D.) scores on mood, relations, activity, and sleep of 4.0 (3.3), 2.8 (3.0), 5.5 (3.8), and 4.3 (3.9) at study entry compared with 2.7 (3.0), 2.2 (2.7), 3.8 (3.7), and 2.3 (2.9) at final evaluation, respectively, with significant differences each of $p<.05$ compared with study entry.
CONCLUSIONS: 1) Patients entering hospice had good pain control, with a mean pain score of 3.3. 2) Home hospice care further significantly reduced pain reporting (to 2.5) over the study period. 3) Home hospice care significantly reduced interference of cancer pain on patients reported mood, relations, activity and sleep.
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FACTOR STRUCTURE OF THE BRIEF SYMPTOM INVENTORY(BSI) USING A LARGE SAMPLE OF CHRONIC PAIN PATIENTS

AUTHORS: L. A. Rokicki, **M. Moric**, A. Buvanendran, A. D. Ivankovich, T. R. Lubenow;
AFFILIATION: Rush Medical College, Chicago, IL.

INTRODUCTION: There is widespread agreement that psychological distress should be assessed during an initial psychological pain evaluation (Turk & Melzack, 2002).The Symptom Checklist-90 (Derogatis, 1983; SCL-90) and a shortened version, titled the Brief Symptom Inventory (Derogatis, 1983; BSI), have often been used to screen for psychological distress during the pain evaluation. However, both measures were developed and factor analyzed using psychiatric and control populations. It is unclear whether the derived factors (i.e., subscales) are valid when used with chronic pain patients. Shutty, DeGood, and Schwartz (1986) found that different SCL-90 factors emerged using a sample of chronic pain patients. The validity of the factor structure of the BSI for chronic pain patients has not been evaluated.
METHODS: Following IRB approval, a convenience sample of 1233 patients who attended a university pain center from October, 1994 to January, 2003 and completed all 53 items of the BSI was used. Items were subjected to an exploratory factor analysis (FA) and then first and second order confirmatory factor analyses (CFA). To evaluate the stability of the factor solutions, a split-half design was utilized. In order to compare results from the confirmatory factor analyses, the factor structure of the SCL-90 reported by Shutty, DeGood, and Schwartz was used as a reference. All analyses were performed using SAS.
RESULTS: The initial exploratory FA using all patients suggested a 9-factor solution. A comparison of current results to those reported by Shutty et al. for the SCL-90 revealed that eight of the nine factors were rather consistent. Six of the BSI factors replicated those reported for the SCL-90; two BSI factors presented slightly different than those reported for the SCL-90. A new factor found with the BSI seemed to be representative of irritability, and two factors reported for the SCL-90 (Interpersonal Sensitivity and Sleep) were not replicated using the BSI. A second-order CFA using the BSI items replicated the three-factor model found for the SCL-90. The second order factors appeared to represent distrust in others, cognitive distress, and somatic distress.
DISCUSSION: Results from the current study suggest that the use of the original subscales of the BSI may not be valid for chronic pain patients and support results obtained by Shutty, DeGood, & Schwartz following empirical validation of the SCL-90 subscales. Further replication is warranted, but clinicians may want to consider using the current factor solution as an alternative interpretation of psychological distress when evaluating chronic pain patients.

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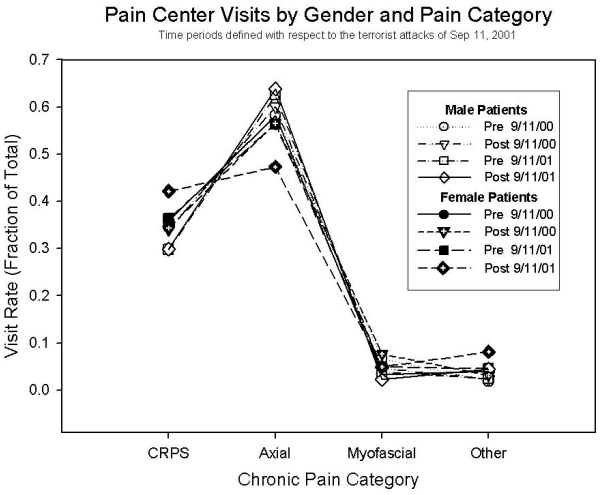
GENDER AND PAIN CATEGORIZATION DIFFERENCES AMONG CHRONIC PAIN PATIENTS DURING PAIN CENTER VISITS AFTER THE SEPTEMBER 11 TERRORIST ATTACK

AUTHORS: **A. Buvanendran**, M. Moric, A. Mehta, J. S. Kroin, K. J. Tuman;
AFFILIATION: Dept. of Anesthesiology, Rush Medical College, Chicago, IL.

INTRODUCTION: Chronic pain is often a source of great psychological distress, and may be more susceptible to influence by other psychological and/or psychosomatic sequala. To investigate such a relationship we examined the effect of the terrorist attacks of 9/11/01 on the clinic visits rates of chronic pain patients categorized by gender and pain etiology.
METHODS: Following IRB approval we investigated 968 patients attending a university pain center, across four time periods to identify possible variances among visit rates resulting from the terrorist attacks of Sep 11th. In addition to gender, patients were also categorized according to chronic pain etiology: Complex Regional Pain Syndrome (CRPS), axial pain, myofascial and others. Time periods were defined as one month before (Pre 9/11/01) and one month after the attacks (Post 9/11/01), as well as the same two time periods one year prior (Pre 9/11/00 and Post 9/11/00). The results were evaluated using Fishers' exact test.
RESULTS: Demographics did not differ between the groups. Profiles of visit rates (Figure) are stable across gender and pain categories, except for the category representing females after the attacks of Sep11, 2001. Females' visits Post 9/11/01 had a decrease in the proportion of axial patients with a corresponding small increase in the CRPS percentage. The most pertinent comparison is the Post 9/11/01 period with the same time period a year earlier (Post 9/11/00). There were more female patients with CRPS (P-value=0.040), lower Axial (P-value= 0.017), and higher "Other" category visits (P-value=0.009), while the myofascial category remained the same (P-Value= 1.000). Male patients showed little change over the same categories: CRPS (P-value=0.379), Axial (P-value= 0.400), Other (P-value=0.225), and Myofascial (P-Value= 0.200) category visits.
DISCUSSION: Although the distribution of visits to the pain center remains stable across time, we have shown that external forces may have a selective impact on certain chronic pain patients. In this case, the terrorist attacks have lead to an increase in the visit rate for female CRPS patients, which may be an indication of psychosomatic or psychological distress. In addition to providing insight into the vulnerability of this patient population, these results should lead us to re-evaluate their psychological treatment plan.



S-200

MULTI-DAY LOW DOSE KETAMINE INFUSION FOR THE TREATMENT OF COMPLEX REGIONAL PAIN SYNDROME (CRPS)

AUTHORS: **M. E. Goldberg**[1], R. J. Schwartzman[2], G. E. Larijani[1], J. Dotson[1], R. Domsky[1];
AFFILIATION: [1]Cooper Hospital, Camden, NJ, [2]Drexel University, Philadelphia, PA.

INTRODUCTION: CRPS is often quite debilitating and difficult to treat. Recent evidence suggests that allodynia and hyperalgesia associated with this syndrome can be related to central sensitization and increased N-methyl-D-aspartate (NMDA) receptor activity. Previous study has suggested that high dose ketamine infusion (an NMDA receptor antagonist) is useful in treating patients with CRPS. We hypothesized that a low dose infusion is beneficial with reduced associated risk in the treatment of CRPS.
METHODS: After IRB approval we evaluated the pain journals of patients with a primary diagnosis of CRPS who were referred for outpatient ketamine infusion. All patients were diagnosed by the same physician (RJS), and each patient had failed conservative treatment. Patients were admitted to our short procedure unit, monitored with continuous EKG, pulse oximetry and blood pressure q 15. Ketamine was mixed in 500cc of NSS to a dose of 40-80 mg. The infusion was performed over a 4-hour period, each day for 10 days. Journal entries were made daily prior to infusion until completion of treatment, which occurred for 10 days, over a 2-week period. The patients were asked to rate the intensity as well as the quality of their pain using verbal (0-4) and visual (0-10) analog scales. Data was analyzed utilizing paired student t-test. A $p < 0.05$ was considered statistically significant.
RESULTS: Data was obtained for 9 patients over the 10-day infusion course. Patients reported significant reduction in the sensations of throbbing pain (2.56 ± 0.46 vs 1.83 ± 1.2), burning pain (2.33 ± 1.0 vs 1.61 ± 1.05), and described their pain as significantly less "fearful and cruel" (1.39 ± 1.27 vs 0.67 ± 0.87) by the 5th day of therapy. They also reported significant improvements in color (7.20 ± 1.92 vs 4.93 ± 3.32) and temperature (7.92 ± 1.36 vs 5.92 ± 2.54) of the affected extremity with a significant decrease in the incidence of muscle spasm. They also reported significant improvement in the posture of the affected extremity. By the 10th day, the visceral component of pain had improved significantly and the percentage of patients reporting relief had increased significantly. The overall maximum pain reduction was 55% occurring on approximately day 7 of treatment. The mean VAS score at this time was 4.89. There were no significant side effects reported requiring treatment.
DISCUSSION: Hyper-excitability or central sensitization of the NMDA receptor has been suggested as one factor for the maintenance of chronic pain. Ketamine has been utilized to treat CRPS, although the effects have been short lived. High dose infusion has been utilized to treat CRPS, but has associated high costs, risks and necessary intensive care utilization. Multi-day low dose outpatient infusion appears to be a useful adjunct and should be further explored.

S-201

EFFECTS OF CORYDALIS YANHUSUO AND ANGELICAE DAHURICAE ON COLD-INDUCED PAIN: A CLINICAL TRAIL

AUTHORS: **C. Yuan**, S. Mehendale, J. T. Xie, T. Jiang;
AFFILIATION: The University of Chicago, Chicago, IL.

INTRODUCTION: Pain is the most common clinical complaint and causes significant human suffering. Since use of currently available analgesics is associated with different degree of adverse effects, newer analgesic agents continue to be investigated, including those derived from botanical sources. In this study, we evaluated the efficacy and safety of a Chinese herbal pain-relieving formulation (1), consisting of Rhizoma Corydalis Yanhusuo and Radix Angelicae Dahuricae (or YHP capsule, Corydalis Yanhusuo:Angelicae Dahuricae = 2:1).
METHODS: With approval from the local ethics committee, five healthy subjects participated in this two-session pilot study. Their mean age ± SD was 25.3 ± 3.9 years. In each session, a cold-pressor test (2, 3) was performed, in which subject's forearm was immersed into ice-cold water (1.5°C ± 0.5°C) for approximately 180 sec. Pain score ratings were collected at four time points from 30-170 sec during the test. In the morning of Day 1, the cold-pressor test was performed to obtain the baseline value. Subjects were then instructed to ingest five YHP capsules three times (equivalent to 9.75 g of raw herbs): at noon and 7 PM on Day 1 and 8 AM on Day 2. In the second session at 9 AM of Day 2, the cold-pressor test was repeated. Results were analyzed using repeated measures analysis of variance (ANOVA).
RESULTS: Fig. 1 shows effect of YHP on pain intensity rating as a function of immersion time at 30, 70, 110 and 170 sec. Data is expressed as mean pain rating ± SEM. There was a significant reduction in the overall pain score rating after three doses of YHP compared to baseline level ($P < 0.05$), suggesting an analgesic effect of YHP. No adverse effects were observed.
DISCUSSION: The cold-pressor test requires immersion of a limb in ice-cold water, which results in cold-induced tonic pain. The advantage of the cold-pressor method is its simplicity and high validity (2). The analgesic effect of YHP observed in this trial will be confirmed in future controlled studies. In addition, constituents in YHP herbs will be investigated to determine their mechanisms of analgesic effects.
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S-202

LYSIS OF EPIDURAL ADHESIONS USING RACZ-CATHETER

AUTHORS: **A. Spacek**, M. Oehmke, F. X. Neiger;
AFFILIATION: Dept. of Anesthesiology and Intensive Care, AKH, University of Vienna, Vienna, Austria.

INTRODUCTION: The so-called Racz-catheter is a special, stainless steel fluoropolymer-coated spiral-tipped epidural catheter, which has been developed several years ago by Dr. Racz for the nonsurgical lysis of epidural adhesions in treatment of a variety of painful conditions (1, 2). This procedure is indicated in chronic, therapy resistant low back pain and radiculopathy due to epidural adhesions after surgical interventions, infections or herniated discs. Unfortunately there are only few reports on the pain relief after the nonsurgical lysis of epidural adhesions using Racz-catheter and the duration of this effect.
METHODS: Therefore, up to now we have performed 25 such procedures in patients with failed back surgery syndrome. The Racz-catheter was placed within the epidural adhesions under fluoroscopy via hiatus sacralis. According to the procedure protocol, local anaesthetic (10 ml 0.25% bupivacaine), steroid (80 mg triamcinolone) and 10 ml 10% saline were injected via catheter. The application of local anaesthetic and hypertonic saline was repeated twice within 48 hours. Patients were discharged after removal of the catheter. The potential side effects and complications of treatment via Racz-catheter include unintended intrathecal injection of local anaesthetic or hypertonic saline which can lead to cardiac arrhythmias, paraparesis or paraplegia, bowel and/or bladder dysfunction, sexual dysfunction, and infection. To prevent infections patients received antibiotic therapy intravenously during the hospitalisation and orally after the discharge for 5 days. Pain was measured on visual analogue scale (VAS, 0-10). Pain relief and duration of pain relief were recorded.
RESULTS: No side effects or complications have occurred. Out of 25 performed procedures, 24 provided at least 20 % pain relief for at least one week. Moreover, 18 these procedures provided more than 50% pain relief for at least one week. The duration of this effect in dependence of the extension of pain relief is shown in the table.

DISCUSSION: Patients with failed back surgery syndrome very often suffer from therapy resistant pain. The lysis of existent epidural adhesions can provide pain relief. The nonsurgical lysis of epidural adhesions in these patients can be performed using the so-called Racz-catheter. This interventional pain management technique provides a good pain relief, however, this effect seems not to be long-lasting.
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Duration and Extent of Pain Relief

	Pain Relief of 20%	Pain Relief of > 50%
Duration of Effect:1 Week	24 (96%)	18 (72%)
Duration of Effect: 2-6 Weeks	3 (12%)	12 (48%)
Duration of Effect: 7-14 Weeks	2 (8%)	-
Duration of Effect:12-20 Weeks	-	3 (12%)

Pediatric Anesthesia

S-203

INCIDENCE OF ALLERGIES IN THE PEDIATRIC SURGICAL POPULATION AND THE RISK OF ADVERSE REACTIONS TO ANESTHETICS

AUTHORS: E. Cerboni, N. A. Mallavaram, J. C. Schwarzenberger, **L. S. Sun**;
AFFILIATION: Columbia University, New York, NY.

INTRODUCTION: The prevalence of allergies in children is increasing.[1, 2] While the occurrence of allergic reactions to anesthetic agents among adult surgical patients is well documented, these reactions are not as well described in the pediatric surgical population.[3, 4, 5] We aim to document the incidence of allergies in a pediatric surgical population and determine if the presence of allergies increases the risk of allergic reaction to anesthetic agents.
METHODS: Following IRB approval, we performed a retrospective review of anesthetic records in 7737 (male = 4754, female = 2983) children who underwent surgery in 2002 at our institution to document the incidence of allergies. In those patients who had a documented history of allergies, we reviewed the intra-operative medications used, any adverse events (laryngospasm, bronchospasm, airway constriction) in the operating room and the post-anesthesia care unit, and the use of any medications to abort an anaphylactic reaction. We included drug, latex, food, and other allergies such as pollen and dust. Differences between males and females were analyzed using the chi-square test, and $p \leq 0.01$ was deemed significant.
RESULTS: 936 patients had allergies (incidence = 12.1%). 694 were drug, latex, and other non-food allergies, and 242 were food allergies. The most frequently reported allergies were: penicillin (244), sulfa (95), cephalosporin (79), nuts (60), egg (56) and latex (52). Thirty-one patients (incidence = 0.4%) reported allergies to agents used during anesthesia: opioids (28), local anesthetics (2), and propofol (1). Also, 14 patients reported allergy to NSAIDS. There were no documented adverse reactions to the anesthetic drugs administered. These drugs included midazolam, fentanyl, morphine, rocuronium, propofol, and inhalational anesthetics. Of the 56 patients with egg allergy, 12 of them received propofol without any adverse reaction. In addition, there was no significant gender difference observed.
DISCUSSION: The incidence of allergies in this pediatric surgical population is 12%. Based on our results, adverse reactions to anesthetic agents secondary to allergies are extremely rare. Furthermore, there appears to be no additional risk of allergic reaction to anesthetic agents in pediatric surgical patients who have allergies. There were no adverse reactions to propofol in children with egg allergy. Also, there was no significant gender difference observed.
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S-204

A CENTRAL REGION OF THE TYPE I RYANODINE RECEPTOR GENE SERVES AS THE PRIMARY TARGET FOR THE INITIAL GENETIC SCREENING FOR MALIGNANT HYPERTHERMIA IN NORTH AMERICA

AUTHORS: **Y. Sei**[1], N. Sambuughin[2], H. Rosenberg[3], T. Tautz[4], T. Nelson[5], S. M. Muldoon[1];
AFFILIATION: [1]Uniformed Services University of the Health Sciences, Bethesda, MD, [2]Barrows Neurological Institute, Phoenix, AZ, [3]Saint Barnabas Medical Center, Livingston, NJ, [4]University of California, Davis, Davis, CA, [5]Wake Forest University, Winston-Salem, NC.

INTRODUCTION: Malignant Hyperthermia (MH) is a pharmacogenetic disorder of skeletal muscle manifested as a life threatening hypermetabolic crisis following exposure to inhalational anesthetics and depolarizing muscle relaxant. Genetic studies have shown the ryanodine receptor 1 (RYR1) on chromosome 19q13.1 (MHS1 locus;OMIM 145600) is the primary gene for susceptibility to malignant hyperthermia (MHS).To date, over 40 mutations associated with MHS and central core disease (CCD) have been identified in the RYR1. CCD is a congenital myopathy that is also caused by mutations in the RYR1 gene and usually predisposes to MH. The mutations in the RYR1 gene are localized in three clusters: N-terminus region (MH/CCD1), central region (MH/CCD2) and C-terminus region (MH/CCD3). Previously we have screened the first two regions and found mutations in 22% of MHS families[1]. The objective of this study is to evaluate the frequency of mutations in all three regions in our North American MH population to elucidate an effective strategy for initial genetic screening.
METHODS: 124 unrelated individuals, diagnosed as MHS according to North American MH caffeine/halothane contracture test (CHCT), were studied. We performed polymerase chain reaction (PCR)-based restriction fragment length polymorphism (RFLP), a single strand conformation polymorphism (SSCP) and denaturing HPLC (DHPLC) methods to test for the presence of known mutations in MH1 (exons 2, 6, 9, 11, 12 and 17), MH2 (exons 39, 40, 44, 45 and 46), and MH3 (exons 95, 100, 101 and 102) regions.
RESULTS: A total of 29 out of 124 MHS families (23%) have been identified to have 14 different mutations in this North American population. Approximately 70% of mutations, which include a novel mutation, originated from the MH2 region. In 8 families (28%), mutations were identified in MH/CCD1 region. Screening MH/CCD3 region yielded a novel mutation in a single family diagnosed as CCD.
DISCUSSION: Detection rate for the selected RYR1 regions is 23% in MHS families in our North American population. The majority of the mutations were found in the central MH2 region. The low frequency of each mutation in such a large gene (15Kbp cDNA) makes screening time consuming and difficult. These results suggest that testing the MH2 region first may be the most effective screening strategy for North American MH patients except for patients with CCD.
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S-205

THE EFFECTS OF PROPOFOL AND SEVOFLURANE ON ECG INDICES OF TRANSMURAL DISPERSION OF REPOLARISATION IN CHILDREN - A RANDOMISED CONTROLLED TRIAL

AUTHORS: **S. D. Whyte**, P. D. Booker, D. G. Buckley;
AFFILIATION: Royal Liverpool Children's Hospital, Liverpool, United Kingdom.

INTRODUCTION: Prolongation of the QT interval is associated with torsades de pointes, classically in children or young adults with long QT syndromes (LQTS). Any overt or covert predisposition to torsades may be unmasked by perioperative stress. Which anaesthetic drugs are safest to use in these patients? Susceptibility to torsades arises from increased transmural dispersion of repolarisation (TDR) across the myocardial wall, rather than QT interval prolongation *per se* [1]. Agents that don't increase TDR would be useful in minimising any perioperative increased risk of torsades. Several anaesthetic drugs prolong the QT interval, but their effect on TDR is unknown. TDR can be measured on the ECG as the time interval between the peak and end of the T wave (Tp-e) [2]. We have investigated the effects of propofol and sevoflurane on the QT and Tp-e intervals in children.
METHODS: 50 ASA I-II children, aged 1-14, received propofol (group P – target plasma concentration 3 µg/ml) or sevoflurane (group S - 8% for induction followed by 3%) for 15 mins prior to elective surgery. No premedication was given. Both groups breathed 40% oxygen in air. We recorded a 12 lead ECG on each patient pre-induction and 15 minutes post-induction. RR, QT and Tp-e intervals were measured by investigators blinded to the anaesthetic received and to the pre-induction/post-induction status of the recording. Corrected QT interval (QTc) was calculated as QT/√RR. Paired t-tests were used to compare QTc and Tp-e before and after propofol and sevoflurane anaesthesia; unpaired t-tests were used for between-patient comparisons of QTc and Tp-e after propofol or sevoflurane anaesthesia.
RESULTS: Age and weight were similar between groups P (n = 22) and S (n = 28). Interobserver variation was least in leads I, II and V5. Sevoflurane significantly prolonged the pre-induction QTc (see table); propofol did so less consistently (p also <0.05 in aVR, V1-3; data not shown) and to a lesser extent (lead I: 430 vs 445 msec, $p < 0.02$; lead II: 432 vs 449 msec, $p < 0.01$; lead V5: 442 vs 456 msec, $p < 0.02$). Neither agent had any significant effect on the pre-induction Tp-e.

ECG Lead	I	II	V5
Propofol			
QTc pre	418	423	436
QTc post	430	432	442
p	0.012	0.06	NS
Sevoflurane			
QTc pre	406	413	423
QTc post	445	449	456
p	<0.0001	<0.0001	<0.0001
Propofol			
Tp-e pre	71	75	80
Tp-e post	74	74	83
p	NS	NS	NS
Sevoflurane			
Tp-e pre	71	71	77
Tp-e post	66	70	80
p	NS	NS	NS

QTc = corrected QT interval (msec)
Tp-e = T wave peak-end interval (msec)
Pre = pre-induction
Post = post-induction
p = p value for paired t-test

DISCUSSION: Sevoflurane increases the duration of myocardial repolarisation in children to a greater extent than propofol. As the dispersion of repolarisation appears unaffected, the risk of torsades de pointes is likely to be minimal with either agent. Overall, propofol causes less electrophysiological disturbance & should be used in preference in high risk children, such as those with long QT syndromes.
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S-206

THE EFFECTS OF LIDOCAINE OR DILUTION ON WITHDRAWAL MOVEMENT DUE TO ROCURONIUM INJECTION IN PEDIATRIC PATIENTS

AUTHORS: **W. Choi**, Y. Lee, H. Yang;
AFFILIATION: Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Republic of Korea.

BACKGROUND: Rocuronium is a nondepolarizing muscle relaxant of rapid onset and of intermediate duration. It is useful for short operation and for rapid control of the airway in pediatric patients. However the intravenous injection of rocuronium cause pain and a withdrawal movement. The purpose of this study was to evaluate the effect of lidocaine pretreatment in pediatric patients receiving rocuronium(10 mg/Ml) and diluted rocuronium (1 mg/Ml) on withdrawal movement.
METHODS: The study was approved by our institutional review board, and informed consent was obtained from all parents. One hundred and twenty five patients, aged from 4 months to 10 years, ASA physical status 1-2 undergoing general anesthesia for elective surgery were randomly enrolled in the study. Allergy history to a trial drug, pediatric patients on analgesics, difficult vein access and severely crying pediatric patients on arrival were excluded. All patients were non-premedicated and had a 22G i.v. catheter inserted into the dorsum of hand before operation. On arrival in the operation room, routine non invasive monitors were placed and a free flow of intravenous fluid without edema, redness, hardness or pain was confirmed. After the administration of glycopyrrolate 0.004 mg/kg, inhalational induction was performed with 4~8 vol% of sevoflurane by face mask fitting. One group received rocuronium 0.3 mg/kg or vecuronium 0.05 mg/kg was administered after 0.5 Ml of 0.9% NaCl. A second group received rocuronium 0.3 mg/kg or vecuronium 0.5 mg/kg after lidocaine 1 mg/kg. A third group received rocuronium 1 mg/Ml diluted with 0.9% NaCl (1:9). Muscle relaxant-induced withdrawal movements were assessed by using a 4-grade scale (0-3). We also observed pulse rate alterations. Vein redness was evaluated just after administration and vein hardness was measured five minutes after intubation by using 4-grade scale (0-3).
RESULTS: Withdrawal movements were more intense in the rocuronium group (3.8 times, $P < 0.01$) than in the vecuronium group. Lidocaine pretreatment (1.8 times, $P < 0.01$) or diluted rocuronium (1.9 times, $P < 0.01$) decreased withdrawal movement incidence. Withdrawal movement incidence was positive correlated with a change in pulse rate (Spearman's rho = 0.36, $P < 0.01$).
CONCLUSIONS: Lidocaine pretreatment in patients receiving rocuronium or diluted rocuronium effectively reduces withdrawal movement during the administration of rocuronium.

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ISOFLURANE AND NEURODGENERATION IN THE DEVELOPING RAT BRAIN: IS IT A FUNCTION OF AGE

AUTHORS: **L. W. Faberowski**, R. Pearlstein, D. S. Warner;
AFFILIATION: Duke University, Durham, NC.

INTRODUCTION: In an *in vivo* postnatal day 7(PND) rat pup model, isoflurane elicited widespread neurodegeneration (1). Using organotypic hippocampal slices, thus eliminating the physiologic variables inherent in an *in vivo* model, we studied the effects of isoflurane in rat pups of *differing* postnatal age. *We hypothesized that there are age related differences in isoflurane effects on neurodegeneration in the developing brain.*
METHODS: Organotypic hippocampal slices were prepared from Sprague-Dawley rats (PND 4, 7 and 14) as described by Stoppini et al. with some modification and maintained in culture for 7-14 days. Isoflurane (1.5%) was administered using an agent specific vaporizer with air (21% O_2, 5% CO_2 and 70% N_2) for 5hrs. All conditions were maintained within 37 +/-3 ^{0}C. Control conditions were exposed to fresh gas flow as per above in the absence of isoflurane. Neuronal cell death was assessed 3 days after exposure to isoflurane using Sytox staining and expressed as mean optical density.
RESULTS: There was not a significant difference in neuronal cell loss in slices prepared from PND4 pups after a 5 hr exposure to 1.5% isoflurane as compared to controls exposed to air (p=0.077). A similar absence of effect was also noted in slices prepared from PND14 rat pups (p= 0.075). However, a significant effect on neuronal cell death was noted in PND7 slices exposed to 1.5% isoflurane for 5 hours (p<0.0001) (*Figure 1*).
DISCUSSION: Neurogenesis in the brain during ontogeny, as distinguished from the mature state, may either diminish or enhance its vulnerability to anesthetic exposure. This is likely attributable to developmental differences in receptor subunit composition (2, 3). Thus, the effect of 1.5% isoflurane on neuronal cell death seems dependent on the *postnatal age* of the rat pup used and may be related to developmental differences in NMDA and $GABA_A$ receptor subtypes that occur during normal brain development. For example, agonism of the $GABA_A$ receptor causes depolarization in *younger* rat brain, but inhibition in *mature* rat brain (3). Similarly, agonism of the NMDA receptor causes a minimal depolarization response at PND0 but normal adult function by PND21 (2). As a result, conclusions drawn from adult brain regarding responses to isoflurane may be different from responses of developing neural tissue.
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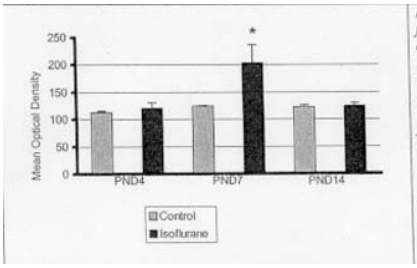

*Figure 1: Hippocampal slices from postnatal day (PND) 4, 7 and 14 rat pups were exposed to 1.5% isoflurane for 5 hours. Cell death in CA1 was determined using Sytox staining (0.5uM) and imaged using fluorescent microscopy. Data below show an age related effect on cell death. Control represents exposure to fresh gas flow alone. Data are displayed as mean optical density+/- SD. *denotes statistical significance p<0.05.*

S-208

FACTORS THAT INFLUENCE PARENT'S DECISIONS TO THEIR CHILDREN PARTICIPATE FOR PEDIATRIC ANESTHESIA RESEARCH

AUTHORS: **P. P. Nicolcescu**, F. O. Purcaru, I. P. Georgescu, A. I. Georgescu, I. M. Sosea, V. C. Calina;
AFFILIATION: University of Medicine, Craiova, Craiova, Romania.

INTRODUCTION: We examinated factors that influence parents to consent or decline participation in pediatric anesthesia study related to their children.
METHODS. After approval by ethics committee 387 parents including physicians, medical students and nurses were subsequently asked to complete a questionnaire detailing the reason for their decision for consenting or declining their children participation for anesthesia research. The questionnaires were designed to be completed anonymously in house at their leisure. Parents were a asked whether they "strongly considered", "considered somewhat" or "did not considered" certain factors when deciding to participate or not. Statistical analysis was performed by student t test for parametric data and chi^2 test for qualitative data p<0,05was considerate significant.
RESULTS: 387 completed questionnaires were returned 301 (77%) from those who consented to their children participation in pediatric anesthesia research and 86 (23%) from those who declined. There were no demographic differences among the consenters and not consenters. The most important factors in the parents decision to consent were related to their understanding and perceived importance of the study (fully explained), very little risk for children and the potential benefit to other children. Nonconsenters strongly considered the fear for children safety (89%) fear of the unknown (6%) fear for the study's effect on children outcome (5%). Financial benefit was not an "strongly considered factors. in their decision.

CONCLUSIONS. A large percent (77%) of our hospital medical staff consented their children participation in pediatric anesthesia research. The most important factor that influence parent's decision was the children safety.
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S-209

HEART RATE RESPONSE TO SKIN INCISION AS A TEST OF THE EFFECTIVENESS OF CAUDAL ANALGESIA IN CHILDREN

AUTHORS: B. C. Weldon;
AFFILIATION: University of Florida, Gainesville, FL.

INTRODUCTION: It is sometimes difficult to predict the adequacy of postoperative analgesia with a caudal block placed in children under general anesthesia. Two recent reports have used anal sphincter tone and skin temperature variation to test the efficacy of caudal analgesia (1, 2). This prospective study was designed to evaluate the ability of heart rate response to surgical incision to predict the effectiveness of postoperative caudal analgesia.
METHODS: After obtaining parental informed consent, eighty children undergoing inguinal surgery were enrolled to recieve a standardized anesthetic with either halothane or sevoflurane. Following induction of anesthesia, a caudal block was performed using 1ml/kg of a mixture of equal volumes of 0.25% bupivicaine and 1% lidocaine with 1:200,000 epinephrine. The inhalational anesthetic was adjusted to 1 MAC prior to skin incision. The time interval between block placement and incision and the child's heart rate response to incision were documented. The caudal block was considered to be ineffective if there was a heart rate increase of >20% within 60 seconds of skin incision. In the PACU the block was determined to be effective if the child had lower extremity weakness and did not respond to toe pinch but withdrew to finger pinch. The specificity, sensitivity, positive predictive value and negative predictive value were calculated for heart rate response as a predictor of a postoperative caudal block effectiveness.
RESULTS: Seventy seven (96%) children were found to have a functioning block in the PACU. The mean time from caudal block placement to skin incision was 11.5 ± 1.8 minutes. The Table displays the distribution of children into four groups based on their heart rate response and the effectiveness of their caudal block. Heart rate response to incision as a predictor of a functioning caudal block in the PACU was found to have a Sensitivity of 88%, Specificity of 100%, Positive Predictive Value of 100% and Negative Predictive Value of 25%.
DISCUSSION: The absence of a heart rate response to incision guaranteed that children would have effective postoperative analgesia. The fact that some children had a heart rate response to incision and a functioning block in the PACU is likely due to the short interval between block placement and surgical incision in our study. This method of evaluating the adequacy of a caudal block will be useful to clinicians who want to be confident that their patients will emerge from anesthesia without pain.
REFERENCES: 1. Anesth Analg 2002;94:1161 2. J Ped Surg 2003;38:386

Table for Calculating Accuracy of Heart Rate Increase as a Predictor of Postoperative Analgesia

	Functional Caudal Block in PACU	Absent Caudal Block in PACU	TOTALS
No Heart Rate Response	68	0	68
>20% Increase in Heart Rate	9	3	12
TOTALS	77	3	80

S-210

STEEP AND DEEP; TARGETED ANTERIOR CAUDAL EPIDURAL CATHETERS

AUTHORS: C. J. Frandrup, D. Siker;
AFFILIATION: Medical College of Wisconsin, Wauwatosa, WI.

BACKGROUND: Anteriorly placed caudal epidural catheters placed via the caudal approach have the advantage of targeted lumbar/thoracic analgesia with decreased total local anesthetic dosing.[1,2] Catheter placement has been confirmed radiographically with minimal coiling or knotting of catheters using this approach[3]. We expand this knowledge by demonstrating catheter placement in the anterior epidural space with intra-operative visualization during surgical exploration of the spinal canal. We demonstrate that using a steep and deep needle placement, catheter placement is reliably in the anterior epidural space and is easily advanced to a mid-incision dermatome.
METHODS: 60 consecutive pediatric patients (1-6 years old) scheduled for dorsal rhizotomy were enrolled in the acute pain service. Once the epidural space was opened by the neurosurgeon, an 18g Tuohy epidural needle was placed at >60 degrees and advanced deeply into the sacral canal. A stiff PVC epidural catheter was advanced to mid-incision and identified as anteriorly placed by the neurosurgeon. Analgesia was provided with a solution of 0.0625% bupivicaine, fentanyl 2 mcg/cc, and clonidine 1 mcg/cc at a rate of 0.1 cc/kg/h.
RESULTS: In all patients the catheter tip was within one vertebrae of the predicted position. In 6 patients the catheter was inadvertently displaced intra-operatively and replaced. However, in all patients adequate peri-operative analgesia was provided. There were no complications. Catheters were used for two days with excellent pain relief noted in all cases.
DISCUSSION: A continuous infusion using an anteriorly placed epidural catheter via the caudal route allows for a targeted epidural analgesic. We show that caudally placed epidural catheters are directed to the anterior epidural space and stay midline. Posterior or paramedian approaches invariably become unilateral or coiled when advanced deeply[4]. It was previously thought anterior catheter placement was the most common cause of unilateral block,[5] occurring in 21% of patients with traditional lumbar epidurals[6] secondary to foraminal placement of the epidural catheter.[7] We had no cases of unilateral block in our study.
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S-211

ANAESTHETIC MANAGEMENT OF CHILDREN WITH TEMPOROMANDIBULAR JOINT ANKYLOSIS

AUTHORS: **D. K. Sreevastava**;
AFFILIATION: Armed Forces Medical college, Pune, India.

INTRODUCTION: Children with temporo- mandibular joint (TMJ) ankylosis need careful airway assessment and specialized techniques may be needed to gain safe control of the upper airway. The paper would discuss the typical problems associated with TMJ ankylosis against the backdrop of our set up, our institutional experience and the changing practices in airway management.
METHODS: Anaesthesia records of 20 patients with severe degree of TMJ ankylosis of bony variety only, over three year period were reviewed. Special emphasis was laid upon preoperative airway assessment, anaesthetic agents and technique used, choice of intubation methods, complications during the airway management, intraoperative events and postoperative sequel if any.
RESULTS: The youngest patient was 3 yrs old. There were 12 male patients as against 8 females. All cases had fixed restriction to mouth opening which was less than 2.5 cm. 9 patients had no or negligible mouth opening. Facial asymmetry and mandibular deviation were the commonest features amongst all the patients. Surgery resulted in mouth opening of more than 2.5 cm in all the cases. Nasotracheal intubation was done in all the cases. 2 patients were subjected to blind nasal intubation without using any aid where as in the rest fibreoptic bronchoscope (FOB) assisted nasal intubation was done. All cases were done under anaesthesia which was maintained with the help of nasal airway connected to a T-piece circuit till the time tube was placed. There were three cases of trigeminovagal reflex. Extubation related problems were uncommon in our study.
CONCLUSION: TMJ ankylosis is one of the most difficult types of airways to secure. In these patients , various intubation techniques include trans nasal Fibreoptic bronchoscope assisted intubation, blind nasal intubation, nasal guided intubation, intubation with radiographic C-arm assistance, retrograde intubation , use of special instruments and lastly surgical airway. The role of blind nasal intubation or retrograde intubation in management of an anticipated airway difficulty appears to be diminishing now. Our experience underscores the importance of FOB aided intubation which should be the first choice in these cases and can eliminate the morbidity associated with surgical airway with reasonable experience.

S-212

NEUROBLASTOMA WITH EXCESSIVE CATECHOLAMINE SECRETION: PERIOPERATIVE MANAGEMENT IN A CHILD

AUTHORS: **J. W. Sparks**, C. Seefelder;
AFFILIATION: Department of Anesthesiology, Perioperative Medicine and Pain Treatment; Harvard Medical School, Children's Hospital Boston, Boston, MA.

INTRODUCTION: A 5 year old female with an abdominal mass suspected to be neuroblastoma presented for biopsy and central line placement. Intraoperatively, severe hypertension required nitroprusside infusion, mechanical ventilation and unanticipated admission to the ICU. Diagnostic work up revealed stage III neuroblastoma with dramatically elevated catecholamine levels [norepinephrine (serum: 22,610pg/ml urine: 3280 mcg/g Cr.) and dopamine (serum: 3744pg/ml urine: 3430 mcg/g Cr.)]. Treatment with phenoxybenzamine was started. During her first two cycles of chemotherapy, severe hypertension occurred with systolic blood pressures above 240 mm. Hg and diastolic blood pressures above 110 mm. Hg. As a result, enalapril was added for blood pressure stabilization. The following two cycles were tolerated without hemodynamic perturbations and the patient was scheduled for surgical resection.
METHODS: The patient was admitted 3 days preoperatively to transition from phenoxybenzamine, enalapril and diamox to doxazosin therapy. Doxazosin was initiated at 0.5 mg and titrated to 1.5 mg bid prior to surgery. Preoperative echocardiogram revealed asymmetric LVH with normal biventricular function and an EKG demonstrated a prolonged QTc of 510 msec. without arrhythmia. Following pre-medication with midazolam, an uneventful induction with propofol, fentanyl and cisatracurim was performed and the patient was intubated. Maintenance of anesthesia was achieved with isoflurane in an air/oxygen mixture along with bupivicaine and hydromorphone continuous epidural infusion. Fenoldopam, magnesium and nitroprusside infusions were used to control intermittent catecholamine induced hypertension during tumor manipulation. With removal of the tumor, all vasodilator infusions, including the epidural infusion, were discontinued and phenylephrine, along with dopamine, infusion was initiated to treat the anticipated reduction in heart rate and blood pressure.
RESULTS: The patient transported to the ICU intubated and in stable condition with dopamine @ 5 mcg/kg/min and phenylephrine @ 0.5 mcg/kg/min. Postoperative analgesia was provided via bupivicaine and hydromorphone continuous epidural infusion. Extubation occurred the following morning and vasoactive infusions were discontinued on the second postoperative day. She was discharged home on postoperative day seven without antihypertensives and urine catecholamine levels returned to normal. Her prolonged QTc on EKG normalized prior to discharge.
DISCUSSION: Neuroblastomas may be associated with elevated catecholamine levels and increased blood pressure. Massively increased catecholamine levels, as in this patient, are unusual and require perioperative management according to guidelines for pheochromocytomas to avoid perioperative morbidity and mortality. Because its non-competitive nature allows direct alpha-agonist therapy for management of hypotension, doxazosin has been recommended over phenoxybenzamine for preoperative alpha adrenergic receptor blocker in cases of pheochromocytoma resection [1]. Doxazosin's selective alpha-1 adrenoceptor antagonism reduces risk of arrhythmias, and its shorter duration reduces risk of postoperative hypotension[1]. Considering the longstanding catecholamine storm in our patient, her rapid discontinuation from vasopressors and stable perioperative course following preoperative management with doxazosin was remarkable.
REFERENCE: [1] *BrJ.Anaesthesia* 2000;85:44-57

S-213

WHOLE LUNG LAVAGE FOR PULMONARY ALVEOLAR LAVAGE IN A 7 YEAR-OLD GIRL

AUTHORS: **B. Radpay**;
AFFILIATION: Shaheed Beheshti University of Medical Scienses, Tehran, Iran (Islamic Republic of).

Pulmonary alveolar proteinosis (PAP) is a rare pulmonary disease and rarer in children with a slight predominace in males.In this disease abnormal accumulation of surfactant in alveoli causes dyspnea, non - productive cough and recurrent pneumonia. PAP may be primary (Idiopathic or hereditary) or secondary (as a result of HIV infection, lymphoproliferative disorders, tuberculosis or contact with insecticides).
We present a 7year old girl who had symptoms and signs of progressive dyspnea (on exertion and at rest), non productive cough, intermitant fever and cyanosis at rest from 14 months ago. She was disabled, oxygen dependent and had a critical condition. She had no clinical significance before that time. At presentation she was cyanotic, had clubbing, tachypnea and coarse cracles in chest examinaion. She had no remarkable lab findings except for an ESR of 27. Chest x-Ray revieled bilateral infiltrations with a granular appearance and CT Scan of the chest showed a crazy-paring appearance. Lung biopsy confirmed the diognosis of PAP.
After induction of general anesthesia a 3.5 mm I.D. bronchial blocker (univent TM) tube and a 8 Fr. nasogastric tube was inserted into the left main bronchus by guidance of a pediatric fibroptic bronchoscope, the cuff of univent tube inflated and one lung ventilation of the right lung intiated well after sealing of the left lung. The left lung lavage began with 250 ml of 37 0C normal saline solution each time for the total amount of 2.5 liters (10 times) so that the drained fluid at the end of procedure was quite clean. Then the univent tube changed with a conventional 5.5 mm I.D. single lumen tracheal tube.
The patient was admitted to the intensive care untit with stable vital signs and acceptable arterial blood gas analysis and monitored for 24 hours.She was discharged two days later with good general conditions(acceptable Pao2, Paco2 and PH without need for supplemental oxygen).
She was admitted for contralateral lung lavage 3 weeks later.
The main factors for presentation of this case are as follows: 1) Due to short stature of this child and lack of standard techniques and instruments suitable for this age group this procedure was unique and important as a teaching case. 2) as far as the search that we have done there is no report in the childhood group by such a method. 3) The most important aspect of this procedure is insertion of two instruments (univent tube and nasogastric tube) simultanously in one main stem bronchus successfully So that we recommend this technique for such conditions.
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S-214

THE USE OF MIVACURIUM FOR PEDIATRIC ECT

AUTHORS: **D. B. Glick**, S. Dinwiddie, G. Gautam, Y. Bryan;
AFFILIATION: University of Chicago, Chicago, IL.

INTRODUCTION: Methohexital is usually chosen as the induction agent for electroconvulsive therapy (ECT) because it does not raise the seizure threshold. Succinylcholine is given to keep the patient paralyzed during the seizures. In this case, two different agents were chosen because of the unavailability of methohexital and the restraints the FDA places on the use of succinylcholine in pediatric patients.
CASE REPORT: An 11-year-old girl became catatonic following treatment with haloperidol for schizophrenia. Catatonia was attributed to neuroleptic malignant syndrome, which proved resistant to treatment with bromocriptine. She was, therefore, referred for ECT. Her medical history was otherwise unremarkable, and there was no family history of malignant hyperpyrexia.
Because methohexital has been unavailable at our institution for almost a year, we use propofol for our adult patients receiving ECT. The acceptability of propofol for use in ECT has been previously reviewed[1]. This case added the novel challenge of avoiding the use of succinylcholine since according to an FDA warning "the use of succinylcholine in pediatric patients should be reserved for emergency intubation or instances where immediate securing of the airway is necessary, e.g., laryngospasm, difficult airway, full stomach . . ." to avoid the risk of hyperkalemia in a child with previously unsuspected muscular dystrophy[2]. In adults who need ECT but have contraindications to the use of succinylcholine, case reports suggest that mivacurium at a dose of 0.2 mg/kg is an effective alternative[3,4]. Because the effects of mivacurium last approximately twice as long as those of succinylcholine, we gave doses of propofol to our patient every 7 minutes to cover the interval of paralysis. This dosing regimen also allowed us to minimize the peak propofol levels, which we hoped would minimize the effect on seizure threshold.
The seizures achieved using this approach were acceptable in duration and character by EEG criteria, there was minimal muscular contraction during the seizures, and the child's catatonia was completely resolved after the treatment cycle. She did, however, suffer persistent short-term memory loss.
CONCLUSION: In children who require ECT, using a combination of repeat doses of propofol and 0.2 mg/kg of mivacurium is an acceptable alternative to the use of methohexital and succinylcholine.
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S-215

ANESTHETIC MANAGEMENT OF PEDIATRIC PATIENTS UNDERGOING VIDEO-ASSISTED THORACOSCOPIC SURGERY

AUTHORS: **J. M. Walz**[1], P. Foley[1], M. P. Hirsh[2], F. E. Habib[1];
AFFILIATION: [1]Dept. of Anesthesiology, University of Massachusetts Medical Center, Worcester, MA, [2]Dept. of Pediatric Surgery, University of Massachusetts Medical Center, Worcester, MA.

INTRODUCTION: Single lung ventilation (SLV) is essential during Video-assisted thoracoscopic surgery (VATS) (1). We present a retrospective analysis of the anesthetic management of 8 pediatric patients ages 13 months to 16 years undergoing VATS. The techniques utilized to obtain adequate SLV are discussed.
METHODS: After Institutional Review Board approval, we conducted a retrospective analysis of pediatric patients undergoing VATS at the University of Massachusetts Medical Center between March and August 2003. Patients up to 16 years of age who required single lung ventilation were included. Anesthetic management including technique utilized to obtain SLV and method to verify correct positioning of the tube is presented. All patients received a general anesthetic.
RESULTS: In the 5 patients who were younger than 10 years old, single lung ventilation was achieved by selective mainstem intubation with cuffed or uncuffed single lumen endotracheal tubes (SLT). In the 3 patients who were 10 years or older, left sided 28- or 32 French (F) double lumen endotracheal tubes (DLT) were placed. No bronchial blockers were utilized for any of the studied patients. Correct positioning of SLTs was verified using fiberoptic bronchoscopy (FOB) or fluoroscopy in patients who underwent concomitant central line placement. DLTs were placed under fiberoptic guidance. Adequate single lung ventilation was achieved in all patients. Among the patients with DLTs**,** maintenance of adequate SpO2 necessitated CPAP in one patient**;** while in another, single lung ventilation had to be abandoned after one hour. There were no anesthesia related complications in any of the patients. (Table 1).

Table 1. Anesthetic characteristics.

Patient	Age	Indication for Surgery	Site of Surgery	Type of ETT	Verification of tube position
1	13mo	Parapneumonic effusion. RT MS bronchus obstruction.	RT.	4 uncuffed SL ETT, LT MS.	FOB.
2	18mo	Pneumonia, Empyema.	LT.	4.5 cuffed SL ETT, RT MS.	Fluoroscopy.
3	2.5y	Parapneumonic effusion.	RT.	5 uncuffed SL ETT, LT MS.	Fluoroscopy.
4	5y	Parapneumonic effusion.	LT.	4.5 cuffed SL ETT, RT MS.	FOB. Fluoroscopy.
5	6y	Parapneumonic effusion.	RT.	4.5 cuffed SL ETT, LT MS.	FOB.
6	10y	Biopsy of RT lung mass.	RT.	28 F LT DLT.	FOB.
7	12y	Biopsy of LT lung mass.	LT.	32 F LT DLT.	FOB.
8	15y	Necrotizing pneumonia with BIL effusions.	BIL.	32 F LT DLT.	FOB.

Key: MS=mainstem, LT=left, RT=right, BIL=bilateral, SL=single lumen.
DISCUSSION: The advantages of VATS over open thoracotomy are well established (2). It has been successfully utilized in children as small as 3kg (3). We present a series of eight patients ages 13 months to 15 years undergoing VATS with SLV, who were managed with SLTs or DLTs. While some authors suggest using FOB to assess positioning (4), we provide evidence that auscultation in conjunction with fluoroscopy is sufficient in patients with SLTs. Although the use of selective bronchial blocking has been advocated for VATS in children 5 years or older (5), this can be cumbersome and time consuming. In our small study population, the surgeons concluded that the exposure afforded by SLV with selective endobronchial intubation with SLT was excellent. Therefore, based on our experience, we conclude that SLV for VATS can be safely and easily accomplished with either SLT or DLT. In addition, confirmation of endobronchial SLT placement can be done using fluoroscopy and auscultation.
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S-216

CAN HEARING THE PULSE SAVE ON CUTTING DOWN ON THE INFANT'S ARTERY WHEN YOU CAN'T FEEL IT? - A PILOT STUDY USING PERCUTANEOUS DOPPLER (PD) ACCESS SYSTEM™

AUTHORS: **S. T. Verghese**, B. L. O'Neill, G. B. DiRusso, F. M. Midgley, G. R. Martin, K. M. Patel;
AFFILIATION: Children's National Medical Center and George Washington University Medical Center, Washington, DC.

INTRODUCTION: We evaluated the use of percutaneous Doppler (PD) access system™ in infants under 10kg who had nonpalpable pulses after multiple unsuccessful percutaneous attempts in obtaining arterial line access.
METHODS: We prospectively studied 18 infants, ASA PS 3-4 undergoing cardiac surgery. Anesthesia fellows under the supervision of the attending cardiac anesthesiologists attempted percutaneous (PC) arterial line access by palpation method. When PC was not successful, and the pulses were nonpalpable due to hematoma- normally indicating the need to proceed with a cutdown (CD), percutaneous PD access™ (Escalon Vascular Access™, Inc.) was used. PD access system utilizes a hand held monitor and a Doppler transducer located at the tip of the access needle to enable the clinician to hear the arterial flow as the tip of the needle approaches the vessel. The increase in the signal intensity as the vessel is contacted enables successful localization and entry.
RESULTS: There were 18 infants including 5 neonates (5.83 ± 4.42 mo; 6.77 ± 2.17kg) and 8 of them had cyanotic heart disease with high hematocrit. Use of PD access system avoided the usual practice of surgical cut down in 12 (66.7%) out of 18 infants who had non-palpable pulses. The time needed for successful PD access in infants was 5.75 ± 3.70 min vs. 18.83 ± 3.76 min for cut down (P=0. 0002). A smaller 24-gauge Doppler catheter was more successful in infants than the larger 22-gauge needle (P=0.013).
DISCUSSION: PC arterial line access in newborns and infants is technically more difficult than in the older child even when the pulses are palpable. PC success rate for infants under 10kg by palpation alone has been reported to be 63%.(1) In children with cyanotic heart disease with high hematocrit there was a higher failure rate. Hyperviscosity of blood in the polycythemic patients results in sluggish flow and delayed flashback even when the catheter is intraluminal. This may explain the high failure rate by palpation method. There is an initial learning curve in using the PD access system. Our successful cannulations were performed by the same pediatric anesthesiologist, and showed better success as the study progressed. In conclusion, our preliminary study shows that the PD access system™ is a useful technique for percutaneous accessing of arteries in small neonates and infants less than 10kg especially after failed percutaneous attempts resulting in non-palpable pulses. Surgical cutdown, which usually was standard after encountering nonpalpable pulses, was avoided in more than 60% of patients by the use of the PD access system. It remains to be seen if routine use of this system would increase the success rate and decrease the morbidity of arterial cannulation in small infants.
REFERENCE: (1) Anesth Analg 200; 92:S64.

S-217

OPTIMAL INSERTION LENGTH OF CENTRAL VENOUS (CV) LINES VIA THE FEMORAL VEIN IN INFANTS AND CHILDREN

AUTHORS: **Y. Shinohara**, T. Arai, J. Shiono, M. Yamashita;
AFFILIATION: Ibaraki Children's Hospital, MIto, Japan.

INTRODUCTION: Insertion of CV lines is essential in anesthesia for pediatric open–heart surgery. The recommended insertion length of CV lines via the internal jugular or subclavian vein has been determined in infants and children (1-2), however the insertion length via the femoral vein has not been well studied. This study determined the optimal insertion length of CV lines via the femoral vein.
METHODS: Infants and children, who had undergone cardiac catheterization via the right femoral vein, were the subjects of the study. After routine cardiac catheterization, an angiographic catheter tip was placed at the level of the third lumbar vertebral body (L3). At that point, a marker was placed on the catheter at the insertion site. Then, the catheter was fully removed, and the distance from the marker to the tip of the catheter, i.e. the distance from the femoral insertion site to the L3 level, was measured and recorded. The femoral-L3 length was termed as "the optimal insertion length".
RESULTS: This length was measured in 42 infants and children (age: 1 month - 94 months, weight: 3.6 kg - 26.7 kg). The weight of the patient and the length correlated well (Fig.1): Y=0.45X+8.13, r^2 (coefficient of determination)=0.84, X: body weight in kg, Y: optimal length of catheter insertion in centimeters.
DISCUSSION: Malposition of CV catheters may cause severe complications such as thrombosis, perforation of the vessel, cardiac tamponade, arrhythmia, catheter migration and discontinuity. The inferior vena cava (IVC) connects to the right atrium (RA) at the T8 or T9 level and branches to the common iliac veins around L5. The hepatic veins and renal veins merge with IVC just below the IVC-RA junction and at L1 level, respectively. The catheter has to be placed between the L1 and L5 to avoid blocking free flow of those veins. Therefore, we chose the L3 level as the optimal tip position of the femoral venous lines. The length derived from the above formula could be used as a guideline for CV line insertion via the femoral vein in infants and children.

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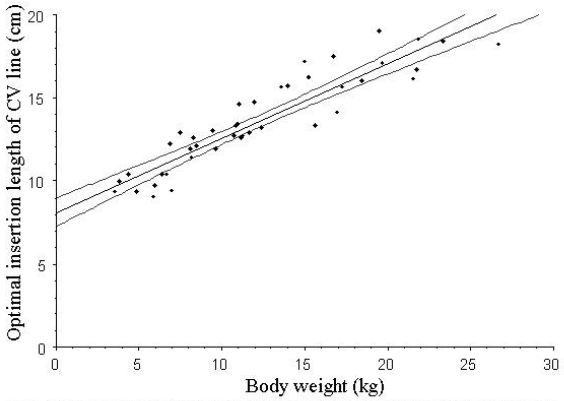

Fig.1 Correlation between the distance from the femoral insertion site to the L3 level and □ the body weight of patients. Regression line & 95% confidence intervals.

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DIFFERENCES IN THE TYMPANIC AND RECTAL TEMPERATURE CHANGES OF CHILDREN UNDERGOING MRI OF THE EXTREMITIES

AUTHORS: **Y. F. Bryan**, M. Szafran, G. Gautum, T. Templeton, A. Tung;
AFFILIATION: University of Chicago, Chicago, IL.

INTRODUCTION: Children undergoing brain MRI experience a greater difference in their mean core body temperature change measured at the rectum than the tympanic membrane. (1) Heating of the head occurs from the absorption of radiofrequency radiation of the coils encircling the head during brain scans. (2) Since coils used for MRI of the extremities are limited to an appendage, we sought to determine if there was a difference in the core body temperature changes measured at the tympanic membrane and rectum.
METHODS: With IRB approval, we prospectively studied 7 children who underwent upper or lower extremity MRI studies under general anesthesia. The mean age was 4 ± 1.6 years (range, 1 to 6 years), and the mean weight was 18 ± 4.2 kg (range, 9 to 21 kg). The induction and emergence occurred adjacent to the magnet room were the ambient temperature was 22-24ºC. All the patients were induced with sevoflurane in oxygen and had an LMA placed. Three patients received propofol at induction. Maintenance was with sevoflurane and all patients breathed spontaneously. The patients were covered with a hospital gown and a single cotton blanket. No heating device was used. The tympanic and rectal temperatures were measured immediately after induction prior to the MRI and upon completion of the scan prior to emergence. The ambient temperature of the magnet room was 19-20°C. The MRI studies were 5 upper extremity and 2 lower extremity.
RESULTS: The mean differences in the tympanic and rectal temperature changes from pre to post-MRI scan were -2.1ºC and -1.7ºC respectively. The mean tympanic temperatures pre and post-scan were 37.0 ± 0.5°C and 34.9 ± 0.9°C. The mean rectal temperatures pre and post-scan were 37.2 ± 0.4ºC and 35.5 ± 1.0ºC. The mean time of the MRI was 83 ± 42 min and the mean time spent in the magnet room was 100 ± 45 min.

DISCUSSION: Our findings reveal a greater mean temperature change measured at the tympanic membrane than in the rectum for extremity MRI scans. This observation contrasts earlier findings in brain scans of lesser temperature changes at the tympanic membrane. Potential reasons may be due to a lack of heating of the head using extremity coils or the lag in the rectal temperature. (3) Further studies of temperature monitoring during MRI are required to determine the differences measured at core and peripheral sites.
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S-219

MRI OF ENTIRE SPINE MINIMIZES CORE BODY TEMPERATURE CHANGES IN CHILDREN UNDER GENERAL ANESTHESIA

AUTHORS: **Y. F. Bryan**, M. Szafran, G. Gautum, T. Templeton, A. Tung;
AFFILIATION: University of Chicago, Chicago, IL.

INTRODUCTION: Recent findings reveal that not all children who undergo MRI of the brain under general anesthesia become hypothermic. (1) In addition, awake and sedated children experience increases in their tympanic temperatures after MRI. (2,3) Awake adults who undergo MRI of the spine also have increases in their core body temperature from the absorption of energy during the scan. (4) We sought to determine the core body temperature changes in children who underwent MRI of their entire spine.
METHODS: With IRB approval, we prospectively studied 11 children who underwent MRI scans of their entire cervical, thoracic and lumbar spine under general anesthesia. The mean age was 4.5 ± 2.2 yr (range, 1.5 to 7 years), and the mean weight was 18.4 ± 6.3 kg (range, 9 to 23 kg). All the patients were induced with sevoflurane in oxygen and had and an LMA placed. The patients were covered with a hospital gown and a single cotton blanket .No heating device was used. The tympanic and rectal temperatures were taken post-induction pre-scan and pre-emergence post-scan. The ambient temperature of the magnet room was 19-20°C and of the control room adjacent to the magnet room was 22-24ºC. ASA physical status scores were 1, n = 1; 2, n = 10.
RESULTS: The mean tympanic temperatures pre and post-scan were 37.0 ± 0.5°C and 36.1 ± 0.8°C and the mean rectal temperature pre and post-scan scan were 37.2 ± 0.3 ºC and 36.2 ± 0.6 ºC. The mean tympanic and rectal temperature differences were –0.9 ± 1.0 ºC and –1.1 ± 0.7ºC. The mean time of the MRI was 77 ± 37 min and the mean time spent in the magnet room was 90 ± 38 min.
DISCUSSION: Our study indicates that both the mean tympanic and rectal temperatures post-scan were greater than 36 ºC despite exposure of the anesthetized children to prolonged periods in the cool environment of the magnet rooms. Potential reasons may be due to the absorption of radiofrequency radiation during the scan offsetting the heat loss to the cool environment. Further studies are required to understand the effects of the MRI on the thermoregulation of anesthetized children.
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S-220

COMBINED BRAIN AND SPINE MRI REDUCES CORE BODY TEMPERATURE DROP IN CHILDREN

AUTHORS: **Y. F. Bryan**, M. Szafran, G. Gautum, T. Templeton, A. Tung;
AFFILIATION: University of Chicago, Chicago, IL.

INTRODUCTION: Certain children require lengthy MRI studies of their brain and spine. This simultaneously exposes anesthetized children to cool environments of the magnet room and heating from the introduction of radiofrequency radiation during scanning. (1) Not all children undergoing MRI under general anesthesia become hypothermic. (2) Awake and sedated children experience increases in their core body temperature after MRI of the brain. (3,4) We sought to determine the magnitude of the core body temperature changes in children undergoing combined brain and spine MRI scans.
METHODS: With IRB approval, we prospectively studied 5 patients who underwent 9 complete MRI scans of the brain and spine. The mean age was 7.5 ± 2.5 years (range, 3 to 11 years), and the mean weight was 30 ± 10 kg (range, 20 to 43 kg). The induction and emergence occurred adjacent to the magnet room were the ambient temperature was kept between 22-24 ºC. All the patients were induced with sevoflurane in oxygen and had an LMA placed except one who had a tracheostomy; one patient received propofol at induction. Maintenance was with sevoflurane and all patients breathed spontaneously. The patients were covered with a hospital gown and a single cotton blanket. No heating device was used. The tympanic and rectal temperatures were measured immediately after induction prior to the MRI and upon completion prior to emergence. The ambient temperature of the magnet room was 19-20°C. ASA physical status scores were as follows: 2, n = 4; 3 n = 1.
RESULTS: The mean tympanic temperature pre and post-scan were 37.0 ± 0.5°C and 36.0 ± 0.8°C. The mean rectal temperature pre and post-scan were 37.1 ± 0.3ºC and 35.6 ± 0.7 ºC. The mean time of the MRI was 125 ± 54 min and the mean time spent in the magnet room was 137 ± 53 min. The change in tympanic and rectal temperature per hour of scan time was – 0.4 ± 0.4 ºC and -0.66 ± 0.3 ºC respectively.
DISCUSSION: Our findings indicate a decrease in the core body temperature change despite the lengthy scans and a decline in the magnitude of temperature change per hour of MRI. This may be due to the activation of thermoregulatory responses in the children decreasing heat loss and also from the absorption of energy during the scan partially replacing the heat loss to the environment. The use of two different coils may have influenced the temperature changes as well. Further studies are needed using MRI-compatible temperature monitoring equipment in order to understand the mechanism of heat exchange during MRI in children.
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S-221

BIS SPEEDS AWAKENING OF PEDIATRIC PATIENTS HAVING DENTAL RESTORATIONS UNDER GENERAL ANESTHESIA

AUTHORS: Z. S. Messieha, R. C. Ananda, W. E. Hoffman, I. Punwani, H. M. Koenig;
AFFILIATION: Univ of Illinois at Chicago, Chicago, IL.

INTRODUCTION: Occasionally, pediatric patients who have oral rehabilitation procedures under general anesthesia experience prolonged sedation and delayed discharge from recovery. This is a problem as all these cases are performed as day surgeries. We compared the effect of not monitoring the BIS to monitoring the BIS on time from discontinuation of general anesthesia to extubation and to discharge from the post anesthesia care unit.
METHODS: After IRB approval of the protocol, 19 patients were enrolled. Written informed consent was obtained from the parent or guardian and assent was obtained from children 7 years and older. Each study subject received 0.7 mg/kg oral versed. After adequate sedation was established, the patient was transferred from the preop area to the OR. General anesthesia proceeded with sevoflurane, rocuronium 1 mg/kg and fentanyl 1 ug/kg intravenous. Ondansetron 0.15 mg/kg was administered near the end of the case. The BIS was recorded continuously from admission until discharge. In Group I, the anesthesiologist knew and maintained the BIS at 60-70 during the dental procedure. In Group II, the anesthesiologist did not know or use the BIS. Time from discontinuation of the sevoflurane to extubation, time from discontinuation of sevoflurane to discharge from post anesthesia care unit (PACU), and the duration of the PACU stay were noted and compared.
RESULTS: The two groups were comparable with regard to age, weight, ASAPS, and gender. Time from discontinuation of sevoflurane to extubation: Group I = 4±2minutes, Group II = 7±4 minutes ($P < 0.05$). Time from discontinuation of sevoflurane to discharge: Group I = 55±21 minutes, Group II = 70±15 minutes. Duration of PACU stay: Group I = 47±20 minutes, Group II = 58±14 minutes.
DISCUSSION: The patients in Group I where BIS was known and used were extubated in a shorter time after general anesthesia. Patients in group I also showed a trend for a shorter PACU stay, 12 minutes sooner than the patients in Group II. Based on our results the use of BIS speeds extubation and may facilitate faster discharge of pediatric dental patients from the PACU after oral midazolam and general anesthesia.

S-222

VALIDITY OF AN EMERGENCE DELIRIUM SCORING SYSTEM

AUTHORS: S. S. Pai, N. A. Mallavaram, **L. S. Sun**;
AFFILIATION: Columbia University, New York, NY.

INTRODUCTION: Emergence delirium is the state of disorientation, agitation and confusion described during emergence from anesthesia. Almost all emergence delirium studies in children have employed a simple scoring system to evaluate delirium or agitation during emergence [1-7]. However, these simple scoring systems do not accommodate the wide range of behavior children experience during emergence. The aim of this study was to construct a more detailed scoring system for children's behavior to evaluate emergence delirium/agitation following short surgical procedures and to test the validity of this scoring system.
METHODS: Following IRB approval, we recruited 30 patients older than 6 months and 25 patients between 2 and 6 months of age. We used a four point scale to assess five different categories of behavior: state, vocalization, orientation, activity and facial expression (see table). For children older than 6 months, speech was used as a substitute for vocalization and demeanor for facial expression. The investigator (Observer 1) and the nurse in the recovery room (Observer 2) evaluated each patient in the immediate post-operative period. The five behavioral variables were totaled to obtain a score between 4 and 20. The scores were normally distributed so we analyzed the data using Pearson product-moment patient correlation coefficient.
RESULTS: The data was analyzed separately for the two different ages. The mean scores for Observer 1 for children between 2 and 6 months (n = 25) were 13.12±4.78 compared to the mean score of 13.24±4.9 for Observer 2. For children older than 6 months (n = 30) Observer 1 had a mean score of 9.97±15.1 and Observer 2 had a mean score of 9.83±5.2. The Pearson product-moment correlation was compared for both age groups (r = 0.985 and r = 0.978 for younger and older children respectively)
DISCUSSION: The preliminary results suggest that our scoring system can be used as a means to evaluate emergence characteristics in all children above 2 months of age.

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2-6months

SIGNS	1	2	3	4	Score
State	Sleepy,eyes closed	Arousable, quiet alert	Active alert	Agitated	
Vocalization	None	Minimal	Whimpering	Crying	
Orientation	None	Responsive	Consolable	Unconsolable	
Activity	Minimal	Purposeful	All 4 extremities	Uncontrolled thrashing	
Facial expression	Flaccid,eyes closed	Visual tracking	Grimace	Contorted	

6 months and above

SIGNS	1	2	3	4	Score
State	Sleepy,eyes closed	Arousable	Active alert	Agitated	
Speech	Clear	Understand w/effort	Incoherent	Shouting	
Orientation	Quiet	Consolable/responds to name	Unconsolable by nurse/parents	Does not recognize	
Activity	Minimal movement	Purposeful	Excited-all 4 extremities	Thrashing	
Demeanor	Calm	Grimace	Whimpering	Crying agitatedly	

S-223

EARLY EXTUBATION AFTER TETRALOGY FALLOT REPAIR

AUTHORS: **G. Leyvi**, E. Reith, A. Stock, D. G. Taylor, J. D. Wasnick, A. J. Saubermann;
AFFILIATION: Montefiore MC / AECOM, Bronx, NY.

INTRODUCTION: New surgical techniques and anesthetics may reduce the cost of pediatric cardiac surgery (1, 2, 3). Regional anesthesia and analgesia may facilitate early extubation and it is postulated reduce hospital length of stay. So called fast-track management has been suggested as a cost-savings maneuver; however, definitive studies are lacking in consensus as to its efficacy. This retrospective study examines the role of one approach to fast track management in the care of patients undergoing repair of simple and complex tetrology of Fallot.

METHODS: 55 patients who underwent repair of tetrology of Fallot between July, 1999 and July, 2002 were retrospectively reviewed. Two management approaches were employed in this patient population. 18 of 55 patients were identified as belonging to the caudal anesthesia group. These patients were administered a single caudal epidural injection of preservative–free morphine (70 - 110 mcg/kg) mixed with 0.25% bupivicaine (1 mg/kg) following the induction of anesthesia. The remaining patients were administered general anesthesia without caudal placement. General anesthesia consisted of fentanyl, a non-depolarizing muscle relaxant, and inhalational agents titrated to effect. With approval of the institutional review demographic data was collected for both groups including: age, sex, weight, days ICU stay, days hospital stay, and time to extubation. Statistical analyses were performed by two group's t test.

RESULTS: There were no statistical differences between the groups regarding age, weight, anesthesia time, surgical time, bypass time, and aortic cross clamp time. There was no statistical difference between the groups regarding hospital length of stay. Borderline significant differences were discerned between the caudal and the non-caudal groups (p=0.1) for pediatric ICU length of stay (3.5 days range 2 - 9 days, caudal group vs. 5.0 days range 1 - 76 days, non-caudal group) and median time to extubation; for the caudal group was 3.8 hours (range 0 - 144 hours) and 21 hours (range 1 - 1176 hours) for the non-caudal group. Table 1 shows the percent of patients extubated at specific time points.

Table 1. Time to extubation for "caudal" and "non-caudal groups".

	Percent of patients extubated by specific time					
	In OR	0 to 2 hours	2 to 8 hours	8 to 16 hours	16 to 24 hours	24 to 48 hours
Caudal group	17%	28%	61%	72%	89%	89%
Non-caudal group	0%	8%	30%	51%	70%	76%

CONCLUSION: This albeit small retrospective study demonstrated small reductions in ICU stay and time requiring mechanical ventilation in patients managed with fast-track approaches utilizing caudal analgesia. Clearly, a randomized, prospective study is needed to confirm this result. Moreover, cost-benefit analysis needs to be completed to discern the overall efficacy of this technique in the management of the tetrology of Fallot patient.

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Pharmacology-Basic Science

S-224

ANESTHETIC PRECONDITIONING PRESERVES MITOCHONDRIAL RESTING MEMBRANE POTENTIAL AFTER ISCHEMIA IN GUINEA PIG HEARTS

AUTHORS: **E. Novalija**, L. G. Kevin, M. M. Henry, J. T. Eells, D. F. Stowe;
AFFILIATION: Medical College of Wisconsin, Milwaukee, WI.

BACKGROUND: As mitochondrial activity is a key determinant of cardiac cellular function, and by extension global cardiac function, it is likely that the mechanism of anesthetic preconditioning (APC) involves preservation of mitochondrial function. We have previously shown that ATP synthesis is preserved and reactive oxygen species formation is attenuated in mitochondria isolated form hearts that were exposed briefly to sevoflurane prior to ischemia/reperfusion.[1] Changes in mitochondrial membrane potential ($\Delta\psi_m$) that characterize the heart after APC and ischemia/reperfusion injury are unknown. We hypothesized that APC stabilizes mitochondrial resting $\Delta\psi_m$ and initiates preservation of mitochondrial structure and function to permit continued oxidative phosphorylation during early reperfusion.
METHODS: Isolated guinea pig hearts were treated with two 2-min pulses of sevoflurane (APC, 0.37 mM), with or without the putative mitochondrial ATP-sensitive potassium (mK_{ATP}) channel antagonist 5-hydroxydecanoate (APC+5-HD, 5-HD) before 30 min ischemia and 120 min reperfusion. Control (CON) hearts were neither subjected to ischemia nor pharmacological treatments and ischemic (ISC) hearts underwent no pharmacological treatment. Global cardiac function and tissue damage were measured (n=34). In another series of experiments, using the same protocol, hearts were reperfused for only 5 min and mitochondria were isolated by differential centrifugation (n=24). Changes in the resting $\Delta\psi_m$ were estimated using the fluorescent cationic dye Rhodamine 123 (0.2 μM) which accumulates electrophoretically in mitochondria as a direct function of the $\Delta\psi_m$ and is released upon membrane depolarization. The maximal depolarization capacity of mitochondria was determined after a challenge with carbonylcyanide-p-trifluoro-methoxylphenol hydrazone (CCCP, 2 μM) and Antimycin A (AA, 3 μM), a combination of mitochondrial uncouplers.
RESULTS: Resting $\Delta\psi_m$ in mitochondria isolated from ISC hearts (–140±22 mV) was significantly depolarized relative to resting $\Delta\psi_m$ measured in mitochondria from CON hearts (–200±8 mV). In contrast, mitochondrial resting $\Delta\psi_m$ in APC hearts (–190±10 mV) was not significantly different from mitochondrial resting $\Delta\psi_m$ measured in CON hearts. This was accompanied by induced global cardiac protection manifested by improved contractile, vascular and electrical function, and decreased infarction on reperfusion. Inhibition of the mK_{ATP} channel by 5-HD abolished each of these protective effects.
DISCUSSION: The results indicate that preservation of the resting $\Delta\psi_m$ afforded by APC plays an important role in protection of cardiac function and cellular integrity during early reperfusion.
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S-225

HALOTHANE AND PROPOFOL MODULATION OF GABAA RECEPTOR-MEDIATED INHIBITORY POSRSYNAPTIC CURRENTS IN RAT CORTICAL NEURONS

AUTHORS: **A. Kitamura**[1], R. Sato[2], R. Ogawa[1], T. Narahashi[2];
AFFILIATION: [1]Nippon Medical School, Tokyo, Japan, [2]Northwestern Medical School, Chicago, IL.

INTRODUCTION: Type A gamma-aminobutyric acid (GABAA) receptors are a site of action for a variety of general anesthetics1),2), and there are both similarities and differences about clinical characteristics between each anesthetics. The present study was aimed at comparing the effects produced by two types of anesthetics on GABAA receptor function.
METHODS: Pharmacologically isolated GABAA receptor-mediated miniature inhibitory postsynaptic currents (mIPSCs) were recorded with whole-cell and cell-attached patch-clamp techniques in rat cortical neurons that had established synaptic networks in culture. Effects of clinically relevant concentrations of halothane and propofol were compared concerning kinetics of both spontaneous GABAA receptor-mediated IPSCs and single-channel currents in interneurons.
RESULTS: In whole-cell recordings, mIPSC duration was prolonged by application of 0.6 mM halothane or 3 microM propofol, without important effects on amplitude or frequency. The each effect of halothane and propofol on mIPSC duration enhanced total charge transfer by 140 and 160% during each spontaneous synaptic event. Cell-attached patch-clamp recordings showed no differences in single-channel conductance upon application of either drug. Either drug made a given channel 4 to 5 times more likely to be open at a given time point. Halothane accomplished this by increasing the mean open life time (time constant of the component for open time distributions), while propofol acted by decreasing the interburst interval (time constant for the component of closed time distributions).
DISCUSSION: Halothane and propofol similarly enhanced GABAA receptor-mediated inhibitory synaptic transmission in rat cortical interneurons by increasing the probability that GABA-activated Cl- channels would be open3),4). However, we concluded that the drugs differed in their mechanisms for increasing the net time for which a channel would be open, from the analysis of single channel recording of GABA-current.
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S-226

PENTOBARBITAL AND MIDAZOLAM ENHANCE EXCITATORY GABAA-MEDIATED DEPOLARIZING POTENTIALS IN RAT HIPPOCAMPAL NEURONS

AUTHORS: D. P. Archer, N. Samanani, S. H. Roth;
AFFILIATION: University of Calgary, Calgary, AB, Canada.

INTRODUCTION: High concentrations of anesthetics enhance γ-aminobutyric acid ($GABA_A$) receptor-mediated depolarizing potentials (DPSPA's)(1). It is not known whether enhancement of DPSPA's occurs at the lower concentrations of drug (approximately 1/10 of the anesthetizing concentration) that occur during the excitement phase of anesthesia(2). Here we have examined the influence of low concentrations of pentobarbital and midazolam on excitatory postsynaptic potentials (EPSP's) and DPSPA's in pyramidal neurons in rat hippocampus *in vitro*.
METHODS: Protocols were approved by the Faculty of Medicine Animal Care Committee. All experiments were on 400 µm hippocampal slices prepared from 20-30 day old male Sprague-Dawley rats performed in an interface tissue chamber as previously described(3). Intracellular recordings were obtained from CA1 pyramidal neurons whose cell bodies were impaled with sharp microelectrodes (resistance 50-100 MΩ) filled with 3 M potassium acetate. EPSP's were evoked by single pulse stimulation with a bipolar tungsten electrode inserted into the Schaffer collateral pathway. We generated DPSPA's with trains of 8 stimuli at a frequency of 100 Hz applied in the stratum radiatum close (<0.5mm) to the impaled cell. In the latter experiments excitatory transmission was blocked by the addition of 50 µM 2-amino-5-phosphonopentanoic acid (AP-5), 10 µM 2, 3-dihydro-6-nitro-7-sulfamoyl-benzo(f)-quinoxaline (NBQX) and 50 µM ketamine to the artificial CSF (aCSF) perfusing the chamber. Effects of pentobarbital (5 µM) and midazolam (0.1 µM) were evaluated by measuring intracellular responses before and after 30 minutes of application of drugs.
RESULTS: Pentobarbital and midazolam increased the amplitudes of the EPSP and the DPSPA and increased the number of neurons spiking during a $DPSP_A$. DPSPA's were abolished by the addition of 10 µM picrotoxin to the perfusate (4 slices) or when bicarbonate in the aCSF was replaced with the organic buffer HEPES (3 slices).

Condition	EPSP amplitude, mV	$DPSP_A$ amplitude, mV	Spiking
Control	10 ± 4 (n=7)	11 ± 5 (n=7)	2/7
Pentobarbital 5 M	15 ± 5 (n=7)*	16 ± 4* (n=7)	6/7*
Control	6 ± 3 (n=4)	8 ± 3 (n=15)	2/15
Midazolam 0.1 M	12 ± 9 (n=4)*	10 ± 4 (n=15)*	8/15*

Mean values ±standard deviations; * indicates $P<0.05$ for paired t-test against control.
DISCUSSION: The results show that the low concentrations of pentobarbital and midazolam that have excitatory behavioral effects *in vivo* are associated with neuronal excitation *in vitro*. Both drugs increase the amplitude of the DPSPA response and the EPSP. These findings are consistent with the hypothesis that midazolam and pentobarbital can have direct excitatory effects on hippocampal neurons, possibly through GABAA receptor-dependent, bicarbonate mediated mechanisms(4).
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S-227

TIME-DEPENDENT INHIBITION OF MUSCARINIC M1 AND M3 SIGNALING BY LOCAL ANESTHETICS IN *XENOPUS* OOCYTES

AUTHORS: S. Herroeder[1], S. Pecher[1], G. Kaulitz[1], E. Martin[1], M. E. Durieux[2], M. W. Hollmann[1];
AFFILIATION: [1]University Hospital Heidelberg, Heidelberg, Germany, [2]University of Virginia, Charlottesville, VA.

INTRODUCTION: We have previously shown that signaling of G protein-coupled receptors (GPCRs) induced by several lipidmediators (e.g. lysophosphatidic acid (LPA) or thromboxane (TXA_2)) is time-dependently inhibited by local anesthetics (LA) in *Xenopus* oocytes and human neutrophils (hPMNs) [1,2]. This study aimed to determine whether GPCRs known to be LA-sensitive and stimulated by more hydrophil agonists (muscarinic receptors) are also inhibited in a time-dependent manner. Since time-dependent inhibition of GPCRs was shown to be critically dependent on the G_q protein and muscarinic receptors have been demonstrated to be mediated by G_q, we anticipated a similar characteristic for LA-induced decrease in signaling.
METHODS: We expressed muscarinic m1 and m3 receptors in *Xenopus* oocytes. Using two-electrode voltage clamp, we measured, at different time points (10 min - 48 h) after LA-application, the effects of prolonged incubation with lidocaine (at $^1/_{10}$ of IC_{50}, 1.8 or 37 nM) or intracellularly injected QX314 (at $^1/_{10}$ of IC_{50}, 42 nM) on Ca^{2+}-activated Cl^-currents ($I_{Cl(Ca)}$), elicited by methylcholine (MCh) at EC_{50}. To define the mechanism of action in more detail, the effects of prolonged extracellularly application of lidocaine (37 nM) on G_q-depleted (DNA antisense-knock down) *Xenopus* oocytes have also been studied. Data are normalized to corresponding control responses and shown as mean±SD (n>25).
RESULTS: To our great surprise, muscarinic m1 and m3 signaling was not time-dependently inhibited by extracellularly applied lidocaine. Prolonged incubation in lidocaine revealed a biphasic response curve. Whereas signaling was significantly inhibited by 33 % (38 %) after 120 min, muscarinic responses increased significantly to 114 % (121 %) after 8 hours. In contrast, intracellular QX314 exerted the expected time-dependent inhibition as previously observed for LPA and thromboxane signaling. Conversely, prolonged (more than 8 hours) incubation of G_q-depleted oocytes with lidocaine showed even more enhanced MCh-evoked responses.
DISCUSSION: Unexpectedly our study has shown that muscarinic m1 and m3 signaling is not time-dependently inhibited by extracellularly applied lidocaine. Despite reduced signaling for the first 2 hours of LA administration, muscarinic responses seemed to be upregulated by the presence of lidocaine. Since intracellularly injected QX314 exerted the expected time-dependent inhibiton, we hypothesize that for muscarinic signaling two opposite effects counteract each other. G_q-mediated time-dependent inhibition on the one and extracellularly-mediated increase in response size on the other hand. The exact site and mechanism of action of this upregulation of muscarinic signaling by prolonged incubation with LA requires further investigation.
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MUSCARINIC RECEPTORS MODULATE THE RELEASE OF [^{3}H]-NORADRENALINE FROM RAT SPINAL CORD

AUTHORS: **E. Umeda**, Y. Aramaki, T. Mori, T. Kazama;
AFFILIATION: National Defense Medical College, Tokorozawa, Japan.

INTRODUCTION: Spinal muscarinic receptors are involved in mediating antinociceptive effects.[1] There is evidence that stimulation of the noradrenergic neurons of spinal cord is associated with antinociception. The effect of the cholinesterase inhibitor neostigmine on noradrenaline(NA) release from rat spinal cord was investigated using in vitro perfusion experiments.
METHODS: The investigation was approved by the Institutional Animal Use and Care Committee.After the SD-rat spinal cord slices were preincubated for 30 min at 37°C in 1 ml oxygenated medium containing 0.1 microM[^{3}H]NA, the slices were superfused at 37°C with oxygenated medium. After an initial perfusion of 90 min, 5-min fractions were collected with a fraction collector. Noradrenaline release was induced by electrical stimulation (3 Hz, 2 ms, 40 V, for 3 min). The slices were field stimulated for 3 min during the 4th (S1) and 11th (S2) 5-min superfusion collection period. Perfusion of drugs was started at the 8th collection period (15 min before S2) and was maintained until the 14th collection period. Radioactivity of the fraction and of the tissue was measured with liquid scintillation spectrometry. Fractional release (FR in %) was calculated as a percentage of the radioactivity present in the slices at the beginning of the stimulation period. The effect of drugs on evoked release was expressed as the ratio of the fractional release (FR) values for the second (S2) and first (S1) stimulation (FRS2/FRS1). Drugs were administered between S2 and S1 and kept in the perfusion fluid until the end of experiments. The following drugs were used [^{3}H]NA, neostigmine, pirenzepine(M1 antagonist), AFDX116(M2 antagonist), atropine(muscarinic antagonist). Results are expressed as mean ± SD. Data were analyzed using one-way ANOVA followed by Dunnett's test. Statistical significance was set at $p < 0.05$.
RESULTS: Neostigmine significantly increased the release of [^{3}H]NA in a concentration-dependent manner. The FRS2/FRS1 was increased from 0.99 ± 0.10(control) to 1.30 ± 0.07(0.01microM), 1.53 ± 0.37(0.1microM , $p<0.05$), 1.63 ± 0.03(1microM , $p<0.05$), and 2.20 ± 0.50(10microM , $p<0.05$) respectively. Pirenzepine(1microM) and atropine(0.3microM) significantly reduced the release of [3H]NA, but AFDX116 did not significantly reduced the release [^{3}H]NA in the presence of neostigmine(1microM).
DISCUSSION: Neostigmine enhanced the release of NA in response to neuronal stimulation and pirenzepine and atropine inhibited the release of NA in the presence of neostigmine.The results obtained from this investigation indicate that muscarinic receptors are involved in the modulation of NA release from rat spinal cord, neostigmine is able to enhance noradrenergic neurotransmission and acetylcholine can stimulate the spinal cord NA release via M1 muscarinic receptors.Our findings are of broad relevance to our understanding of spinal noradrenergic mechanisms underlying the control of nociception.
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S-229

EFFECTS OF LOW CONCENTRATIONS OF PENTOBARBITAL ON EXCITATION-SPIKE (E-S) COUPLING IN THE CA1 PATHWAY IN RAT HIPPOCAMPUS

AUTHORS: **D. P. Archer**, K. Nguyen, S. H. Roth;
AFFILIATION: University of Calgary, Calgary, AB, Canada.

INTRODUCTION: Low concentrations of pentobarbital enhance synaptic transmission in rat hippocampus(1). Specifically, population spike (PS) amplitude, in response to paired-pulse stimulation of the CA3-CA1 pathway, increased during application and washout of 5 μM pentobarbital(1). These findings could be due to an increase in synaptic strength as shown by an increase in the excitatory postsynaptic potential (EPSP) or to an increase in the ability of the EPSP to evoke an action potential in the postsynaptic cell(2). This study examined the contribution of these two mechanisms by concurrent recording of field EPSP's (fEPSP's) and PS responses during and after perfusate application of 5 μM pentobarbital.
METHODS: Protocols were approved by the institutional Animal Care Committee. Experiments were performed on 400μm hippocampal slices prepared from 20-30 day old male Sprague-Dawley rats in an interface tissue chamber as previously described(1). Paired-pulse stimulation was applied to the stratum radiatum at a frequency of 0.1 Hz with a bipolar tungsten electrode. Interpulse interval (40-60 msec) was adjusted to produce enhancement of the second evoked response (paired-pulse facilitation). Sufficient stimulus intensity was set to produce a half-maximal amplitude of the second of the evoke population spikes (PS_2). Glass microelectrodes were placed in the stratum radiatum and stratum pyramidale to record of fEPSP's and PS responses respectively and analyzed with Labview®-based customized software. Effects of pentobarbital (5 μM) were evaluated by measuring fEPSP slopes and PS_2 amplitudes, before, after 30 minutes of drug application, and after 90 minutes of drug washout. Values averaged over a 10-minute epoch prior to the three time endpoints were compared using repeated measures ANOVA.
RESULTS: Both the fEPSP slope and the PS_2 amplitude remained unchanged during perfusion with drug-free aCSF (7 slices, $P>0.5$, $P>0.8$ respectively). Exposure to 5 μM pentobarbital for 30 minutes followed by 90 minutes of drug washout resulted in a 100% increase in PS_2 amplitude; the fEPSP slope remained unchanged.

Measurement	n	Control	Pentobarbital, 30 min.	Washout, 90 min
PS_2 amplitude, mV	9	2.0 ± 0.8	2.3 ± 1.0	4.1 ± 1.4*
fEPSP slope, mV / sec	9	2.0 ± 0.6	2.2 ± 0.7	2.7 ± 0.13

Mean values ± standard deviations; n = # of slices, * indicates P=0.001 in comparison with the other measurement times.
DISCUSSION: These results suggest that enhancement of synaptic transmission induced by pentobarbital is produced mainly by an increase in E-S coupling, one of the components of long term potentiation (LTP)(2). The present findings are consistent with the hypothesis that exposure to pentobarbital during stimulation of hippocampal pathways may facilitate synaptic plasticity in these circuits(3).
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S-230

PROPOFOL INCREASES EXTRACELLULAR SEROTONIN LEVELS IN THE MOUSE HIPPOCAMPUS

AUTHORS: **R. A. Whittington**, L. Virag;
AFFILIATION: Columbia University, New York, NY.

INTRODUCTION: It has been implied that the serotonergic system may play a role during the state of general anesthesia.[1] Previously, it has been suggested that propofol can increase serotonergic activity in the cortex of rats.[2] However, these studies were limited by the fact that serotonergic activity was indirectly determined by measuring the serotonin (5-HT) metabolite, 5-hydroxy indole acetic acid (5-HIAA), instead of 5-HT itself. Thus, it is unclear if what was measured was a true change in the neuronal 5-HT pool or a propofol-induced change in 5-HT metabolism. Moreover, the measurement of 5-HIAA levels was performed shortly after the administration of pentobarbital anesthesia, a drug previously demonstrated to alter extracellular 5-HT levels in the brain.[3] The purpose of this study was to examine the CNS extracellular 5-HT response to propofol in pharmacologically naive mice.
METHODS: Adult, male mice with a pure 129/SV genetic background were used in these experiments. Forty-eight hours prior to the study, each mouse had a cerebral microdialysis guide cannula placed in the ventral hippocampus (VHC) region, under pentobarbital and ketamine anesthesia. On the day of the experiment, a cerebral microdialysis probe was inserted into the VHC of the awake mouse and the probe was perfused with artificial CSF at a rate of 0.5 ul/min. Dialysates were obtained throughout the study at 20 min intervals for the determination of extracellular 5-HT levels via high performance liquid chromatography. Once a stable baseline was achieved, the mice received either an intraperitoneal injection of propofol 100 mg/kg (n=5) or an equal volume of intralipid (control, n=3). 5-HT levels were then subsequently measured for another 120 min. Dialysates for each group were compared to their respective baseline via ANOVA and Dunnett's post-hoc test was applied when appropriate. Between-group comparisons were performed via means of an unpaired t-test. Data are expressed as mean ± SD and $p < 0.05$ was considered statistically significant.
RESULTS: Within 20 min of administration, propofol produced a significant increase in hippocampal 5-HT which lasted approximately 80-100 min (Fig. 1). The peak increase in extracellular 5-HT occurred 40-60 min after propofol administration, 388 ± 153% of the baseline 5-HT level. Throughout the study, there were no changes in hippocampal 5-HT levels in the intralipid group.
DISCUSSION: These data demonstrate that a sedative-hypnotic dose of propofol can significantly increase extracellular 5-HT concentrations in the mammalian brain. Furthermore, the previously reported changes in serotonergic activity following propofol administration[2] were most likely due to changes in the neuronal 5-HT pool. It remains to be seen if these increases in extracellular 5-HT play a role in mediating propofol's mood elevating and antiemetic effects.
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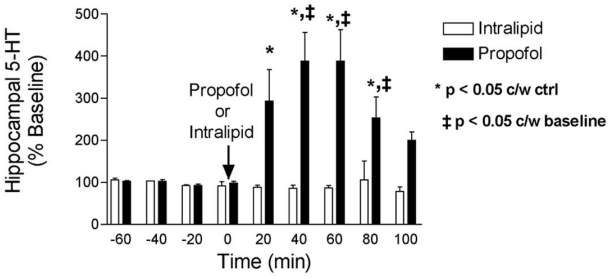

Fig. 1

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LIDOCAINE BLOCKADE OF OPEN CHANNELS INVOLVES THE PERMEATION LOOP IN RAT SKELETAL MUSCLE MU1 NA+ CHANNELS

AUTHORS: **K. J. Gingrich**[1], L. Wagner[2];
AFFILIATION: [1]Thomas Jefferson University, Philadelphia, PA, [2]University of Rochester, Rochester, NY.

INTRODUCTION: A cytoplasmic loop of Domain III contributes to the permeation pathway in voltage-gated Na+ channels (P-loop). The mutation K1237S in this region potentiates local anesthetic (LA) blockade (1).We previously reported that LAs induce dual (rapid and discrete) interacting modes of open channel blockade in single inactivation-deficient channels (2) pointing to two distinct LA binding reactions involving the aromatic tail and charged head of the LA molecule within the permeation pathway. We have also shown that the pore-lining F1579 residue contributes to a binding site underlying discrete block (3). The objective of this study was to determine whether the P-loop residue K1237 plays a role in either discrete or rapid open channel blockade by LAs and hence gain mechanistic insight into its potential involvement in LA inhibition of Na+ channels.
METHODS: Open channel LA blockade can be more readily observed when fast inactivation is absent. We therefore performed the QQQ mutation (I1303Q, F1304Q, M1305Q) in the III-IV inter-domain that eliminates fast inactivation in rat skeletal muscle alpha-subunit sodium channels (RSkM1). Mutagenesis was performed using PCR techniques. To gauge open channel interactions, we studied LA-induced changes in the timecourse of non-inactivating macroscopic QQQ and QQQ-K1237S Na+ currents expressed in *Xenopus* oocytes using two-electrode voltage clamp.
RESULTS: The *Figure* shows that depolarization (–10mV) triggered a Na^+ current (baseline designated by solid horizontal line) marked by the downward current deflection (solid line, Control) in a oocyte expressing QQQ channels. The response manifests little reduction over the 50 millisecond pulse confirming elimination of fast inactivation. A response with 500μM lidocaine (*L*) and normalized to peak amplitude is plotted on the same axes. *L* induced a time-dependent reduction of QQQ currents consistent with the onset of open channel blockade. The timecourse obeyed a monoexponential timecourse (fitted function extrapolated to start of depolarization is indicated by smooth dashed line: time constant, τ_B; magnitude, M). Greater [*L*] increased the rate ($R=1/\tau_B$) and M of block until both reached a plateau near 2mM (R=0.4[1/ms], M=0.6, N=5), consistent with interacting rapid and discrete block (data not shown). *L* (500μM) also produced monoexponential reduction of QQQ-K1237S current (dashed line) but with greater R and M compared to QQQ. QQQ-K1237S concentration relationships for R and M were shifted leftward nearly ten-fold relative to those of QQQ without alteration of plateau values (N=5).
CONCLUSIONS: These macroscopic results accord with dual interacting modes (discrete and rapid) of LA pore blockade observed previously in single Na+ channels. In addition, the results suggest that rapid block is influenced by K1237 and that this residue contributes to a distinct binding domain mediating rapid block.
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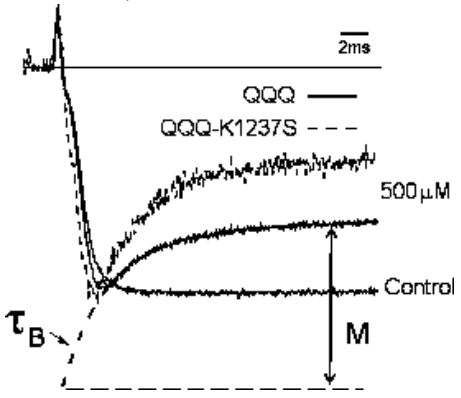

S-232

SENSITIVITIES TO HALOTHANE AND PROPOFOL IN MICE LACKING THE N-TYPE CALCIUM CHANNEL

AUTHORS: **T. Takei**, K. Makita, T. Tanabe;
AFFILIATION: Tokyo Medical and Dental University, Tokyo, Japan.

INTRODUCTION: Volatile anesthetics at clinically relevant concentrations are known to depress excitatory synaptic transmission in the central nervous system (CNS) [1] and have been shown to inhibit several subtypes of VDCCs in vitro [2]. The N-type VDCC which, as well as the P/Q-type, is widely expressed in neurons and a major contributor of neurotransmitter release has been suggested to be more sensitive to volatile anesthetics than the P/Q-type [3]. To clarify that the inhibition of the N-type channel contributes to the mechanisms underlying actions of volatile anesthetics, we examined sensitivity to halothane in vivo and in the hippocampal slice preparation using mice lacking the N-type channel. We also examined sensitivity to propofol that unlikely affects excitatory synaptic transmission.
METHODS: Halothane EC50s for the loss of the righting reflex (MACRR) and for the loss of the tail pinch/withdrawal response (MAC) were assessed in null mutant (-/-) for the N-type VDCC, heterozygous mutant (+/-), and wild-type (+/+) littermates [4]. We also measured propofol-induced sleep time defined as the duration for which the righting reflex was lost after intravenous injection (26 mg/kg). We further recorded field excitatory postsynaptic potentials (fEPSPs) under halothane administration at the Schaffer collateral-CA1 synapses in hippocampal slices from these mice [5].
RESULTS: Both MACRR and MAC for halothane was significantly lower in -/- mice than in +/+ mice (MACRR: 1.00 ± 0.04 vs. 1.16 ± 0.04 vol%, p = 0.019; MAC: 1.46 ± 0.04 vs. 1.70 ± 0.05 vol%, p = 0.005). Propofol-induced sleep time was significantly shorter in -/- mice than in +/+ mice (303.2 ± 13.1 vs. 356.7 ± 16.8 s, p = 0.024). Halothane depressed fEPSPs recorded from hippocampal slices more greatly in -/- mice than in +/+ mice at both 1 vol% (90.5 ± 4.3 vs. 106.0 ± 3.9 %control, p = 0.023) and 2 vol% (65.5 ± 5.5 vs. 80.2 ± 3.1 %control, p = 0.049).
DISCUSSION: Our results indicate that disruption of the N-type VDCC increases sensitivity to halothane likely because reduced glutamate release in excitatory synapses lacking the N-type channel accelerates depressing effect of halothane on excitatory transmission. On the other hand, disruption of this channel decreases sensitivity to propofol possibly because reduced gamma-aminobutyric acid (GABA) release in inhibitory synapses obtunds potentiating effect of propofol on inhibitory transmission. The current study implies that agents that block the N-type VDCC may augment potency of volatile anesthetics such as halothane, whereas they may counteract many intravenous anesthetics that mainly act on GABA-A receptor such as propofol.
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S-233

SEROTONERGIC INPUTS MODULATE MEMORY CONSOLIDATION AT DISCRETE TIME POINTS POST TRAINING IN THE RAT MODEL

AUTHORS: **P. M. Murphy**[1], K. J. Murphy[2], D. C. Moriarty[1], C. M. Regan[2];
AFFILIATION: [1]Mater Misericordiae Hospital, Dublin, Ireland, [2]The Conway Institute, Dublin, Ireland.

BACKGROUND: The hippocampus is an important constituent of the 'intrinsic memory pathway', and plays a key role in the process of memory consolidation. Sertonergic neuronal feeds to the hippocampus from the raphe nuclei[1] appear to modulate this process of memory formation[2] although the exact time interval at which this occurs has not previously been elucidated. This study aims to identify the time period during which serotonin exerts a modulatory effect via the 5-HT_3 receptor.
METHOD: P80 Male Wistar rats (200-300g) were trained in a Passive Avoidance Paradigm. 5-HT_3 receptor agonists and antagonists were administered by intra-peritoneal injection at increasing intervals post-training (0, 3, 6, 9 hours):
a) 1ml/kg NACL 0.9% (Control Group).
b) 2-Me-5HT (10 mg/kg).
c) 2-Me-5HT plus Ondansetron 0.1 mg/kg.
Recall for the learned event (step through latencies) were recorded at 24 and 48 hours post-training. Immunohistochemistry for polysialylated neural cell adhesion molecule (PSA-NCAM) in the dentate gyrus was performed on animals culled 12 hours post training.
RESULTS: The 5-HT_3 receptor agonist 2-Me-5HT induced a significant amnesia when administered at the 6-hour post-training time point. This was not seen at any other time point. PSA-NCAM expression in the dentate gyrus was seen to correlate closely with this finding.
CONCLUSION: Serotonergic inputs to the hippocampus act to impair memory consolidation during a discrete time point 6 hours post training.
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S-234

MECHANISM OF AGE DEPENDENCY OF MAC: MULTI-UNIT AND MULTI-PATH SYSTEM (MUMPS) OF ANESTHESIA

AUTHORS: Y. Kaminoh[1], H. Kamaya[2], C. Tashiro[1], I. Ueda[2];
AFFILIATION: [1]Hyogo College of Medicine, Nishinomiya City, Japan, [2]University of Utah, Salt Lake City, UT.

INTRODUCTION: General anesthesia follows a steep slope of the dose-response curve around the MAC values. We suspected that the network of the nerve system was related to the steepness, and proposed a mathematical model, Multi-Unit Multi-Path System (MUMPS)(1). According to the MUMPS, at least 10^6 conduction pathways construct a nerve network, and each pathway contains more than 100 conduction units. The MUMPS also indicated that a whole system is blocked by lower anesthetic concentration than that required to block the conduction units, depending on the number of units and pathways. Patients are anesthetized at far lower concentrations, at which anesthetic effect on each unit would be negligible. It is known that MACtics decreases as age advances by 6-7 % per decade, and the variation of the age dependency among anesthetics is negligible(2). The conventional pharmacokinetic parameters failed to explain the age-dependency of MAC. In this presentation, we revealed the mechanism of age-dependency of MAC using the MUMPS model of the anesthesia mechanism.
METHODS: We hypothesized that the anesthetic potency on each conduction unit was constant at every age group. We calculated MAC by changing the number of conduction pathways (m) and conduction units (n). We also calculated MAC_{95}/MAC, because the values of m and n define the steepness of the dose-response curve. We compared our theoretical values of MAC and MAC_{95}/MAC to those of sevoflurane on humans which were reported from a single institute to ensure the consistency of the data.
RESULTS: MAC and MAC_{95}/MAC of sevoflurane were reported to be 2.49 % and 1.16 (at age 4.31 years) (3), 1.71 % and 1.21 (47.5 years) (4), and 1.48 % and 1.34 (71.4 years) (5), respectively. Thus, MAC decreased and MAC_{95}/MAC increased by aging. The MUMPS model expected that MAC increased and MAC_{95}/MAC decreased by increasing m, although MAC and MAC_{95}/MAC decreased by increasing n. The effects of aging are related to the m decrease. The figure showed the relation between the relative MAC (rMAC) and MAC_{95}/MAC of *in vivo* results (symbols) and theoretical values of MUMPS (line). The rMAC values of *in vivo* results and MUMPS were 1, when age was 4.31 years , and when $m=10^7$ and $n=10^3$, respectively. The age effects on rMAC were calculated by changing m, keeping n constant. Theoretical values of MUMPS are comparable to the *in vivo* results of sevoflurane.
DISCUSSION: The Influence of age to MAC is well known, and is important in the clinical practice(2). Our MUMPS model of the anesthesia mechanism successfully revealed that a reduction of the conduction pathway accounts for the age-dependency of MAC.
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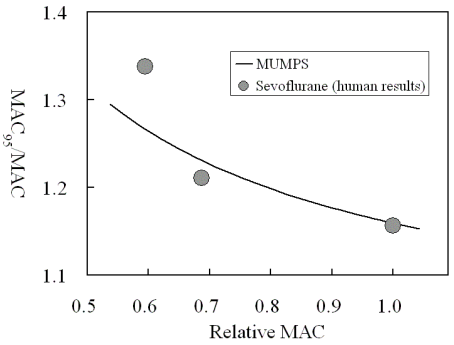
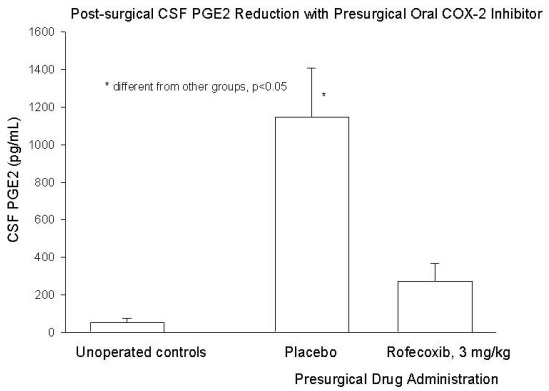


S-235

COX-2 INHIBITOR SUPPRESSION OF CENTRAL PGE2 UPREGULATION IN A POST-SURGICAL RAT MODEL

AUTHORS: A. Buvanendran, J. S. Kroin, D. E. Watts, J. E. Topic, K. J. Tuman;
AFFILIATION: Dept. of Anesthesiolgy, Rush Medical College, Chicago, IL.

INTRODUCTION: Injection of an inflammatory agent into the rat hindpaw produces both COX-2 upregulation in the lumbar spinal cord and a large PGE2 increase in the cisternal CSF (Nature 2001;410:471). Surgical incision in rats (bilateral arthrotomy) also produces a large increase in central PGE2 (Kroin et al., Anesthesiology 2003;98:A952). The present study evaluates central PGE2 upregulation following thoracic incisions in rats, and examines if pre-surgical oral COX-2 inhibitor (rofecoxib) administration suppresses any central PGE2 increase.
METHODS: With animal care committee approval, 300 g male Sprague-Dawley rats (n=12) were anesthetized with isoflurane and lateral incisions 2 cm-long were made in the superficial muscles above the 3rd, 5th, and 7th rib on both sides. Muscles were closed with 2-0 silk sutures and skin with 4-0 nylon sutures, and all animals were active after recovery from anesthesia. At 1 h before surgery, 6 of the 12 animals had been given a 3 mg/kg rofecoxib dose (oral suspension) while the other 6 received an oral placebo suspension. Another group of animals (n=6) served as unoperated controls. At 6 h post-surgery, animals were re-anesthetized with isoflurane, the membranes covering the cisterna magna rapidly exposed, and 100 µL CSF collected for central PGE2 measurement. PGE2 was assayed by enzyme immunoassay. CSF PGE2 concentrations between the rofecoxib, placebo, and unoperated control groups were compared with ANOVA with Tukey B post hoc testing.
RESULTS: CSF PGE2 in unoperated controls was 52 ± 22 pg/mL. Bilateral thoracic incision induced a large increase in cisternal PGE2 concentration at 6 h post-surgery (1148 ± 261 pg/mL). Administration of rofecoxib 1 h before surgery, reduced the CSF PGE2 to 24% of the value of placebo-treated animals (Figure).
DISCUSSION: Extensive surgical incision in the rat causes a large upregulation of spinal PGE2. This central PGE2 increase can be greatly reduced by prior oral administration of a COX-2 inhibitor. Further investigations are needed to determine if this reduction of central PGE2 can have a role in the management of postoperative pain.

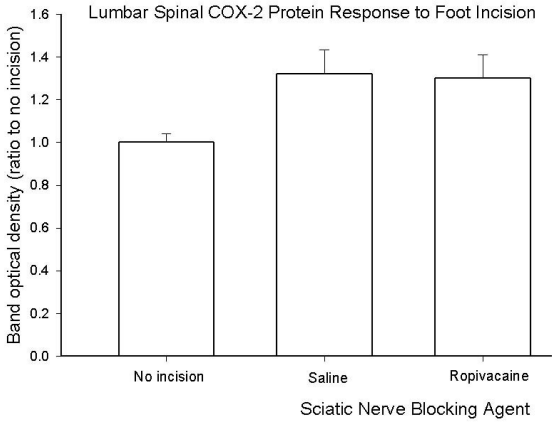


S-236

SPINAL CYCLOOXYGENASE-2 (COX-2) UPREGULATION FOLLOWING FOOT INCISION DOES NOT DEPEND ON AFFERENT NERVE ACTIVITY

AUTHORS: **J. S. Kroin**[1], Z. D. Ling[2], D. E. Watts[1], J. E. Topic[1], A. Buvanendran[1], K. J. Tuman[1];
AFFILIATION: [1]Dept. of Anesthesiology, Rush Medical College, Chicago, IL, [2]Dept. of Pharmacology, Rush Medical College, Chicago, IL.

INTRODUCTION: Following peripheral inflammation, there is an increase in spinal cord cyclooxygenase-2 (COX-2) protein and mRNA (FEBS Let 1996;390:165; Br J Pharm 1997;120:71P), which could be mediated by either an afferent nerve barrage from the traumatized nerve endings or from humoral factors released from the site of inflammation. In a recent study, we demonstrated that there was also an increase in COX-2 protein in the lumbar spinal cord following bilateral foot incision that was maximal at 3 h (32% increase over control) (Kroin, et al, Anesthesiology 2003;98:A953). In another study, the increase in lumbar spinal COX-2 mRNA level caused by an inflammatory irritant injected into the rat hindpaw was only moderately decreased with local anesthetic blockade of the sciatic nerve (Nature 2001;410:471). In the present study, we examined whether the upregulation of lumbar COX-2 protein following foot incision would be prevented by nerve blockage.
METHODS: With animal care committee approval, 350 g male Sprague-Dawley rats were injected bilaterally in each sciatic notch with 0.5 mL ropivacaine hydrochloride 0.5% (n=9), or normal saline (n=9) to block the sciatic nerves. Ten minutes later, animals were anesthetized with isoflurane and received a bilateral foot incision to the plantar surface of each hindpaw. In unblocked rats, these incisions produced mechanical hypersensitivity in each hindpaw similar to that seen by Brennan et al (Pain 1996;64:493) with unilateral foot incision. Ninety minutes later, animals were given a repeat injection in each sciatic notch (to extend the duration of the ropivacaine nerve block to 3 h). At 3 h after foot incision, animals were rapidly sacrificed and the lumbar spinal cord removed by ejection. Spinal cord sections were processed and analyzed for COX-2 protein using Western blot analysis. The effect of nerve block was compared with a 2-sample t-test.
RESULTS: Local anesthetic blockade of the sciatic nerve prior to incision and during a 3 h post-operative period did not decrease lumbar COX-2 protein compared to incisional animals with saline control injections (Figure). Sensory nerve block was confirmed by von Frey filament testing of mechanical hyperalgesia, which demonstrated an elevation of withdrawal force threshold to 144 mN or greater in rats receiving ropivacaine versus a hypersensitive 20 mN threshold in saline injected incision animals.
DISCUSSION: Afferent nerve input from foot incision does not contribute significantly to spinal cord COX-2 upregulation. This is consistent with the results of Samad et al (Nature 2001;410:471) based on an inflammatory pain model. Other biochemical and neurohumoral mechanisms must be interrogated to determine the mechanism(s) by which surgery upregulates spinal cyclooxygenase-2.



S-237

SAFETY OF THE NOVEL DELTA-OPIOID AGONIST MYFADOL IN MICE

AUTHORS: **J. S. Kroin**, M. Shulman, J. E. Topic, D. E. Watts, A. D. Ivankovich;
AFFILIATION: Dept. of Anesthesiology, Rush Medical College, Chicago, IL.

INTRODUCTION: Myfadol is a non-peptide opioid (MW 360) which has recently been characterized as a delta-opioid receptor agonist in rodents (Anesthesiology 2003;98:A907). Following oral administration, myfadol at doses < 200 mg/kg produces maximal analgesic effect, like other full agonists such as morphine, in the rodent thermal foot withdrawal test of Hargraves et al (Pain 1988;32:77). However, motor side effects and safety following oral administration of higher doses of myfadol have not yet been determined. This study examines the effects of oral myfadol up to 2000 mg/kg on ambulation, sedation, and toxicity in mice.
METHODS: With animal care committee approval, experiments were performed on 22 g adult female CD-1 mice (Charles River). Ambulation was assessed by the animal's performance on the rotarod (20 rpm, 60 sec). Animals were accommodated to the device for two days before any testing. The mean latency (average of 2 trials) before falling off the rotarod was recorded. Sedation was assessed with the righting reflex by measuring the time required for an animal to return to the upright position when placed supine. Any deaths at higher doses (up to 2000 mg/kg) will be converted to an LD_{50}. On the testing day, baseline ambulation and righting times were measured, and then myfadol (in a commercial oral suspension) was administered by gavage (0.4 mL volume) into the stomach with a blunt 20 g feeding needle at doses of 0, 200, 400, 800, 1200, 1600, or 2000 mg/kg. The righting reflex latency was evaluated at 30 min post-dosing. Mice were evaluated on the rotarod at 35 min after drug administration. Six mice were injected at each dose. Ambulation or sedation latency at different doses was compared with the Kruskal-Wallis test with post hoc comparison with the Mann-Whitney U test. LD_{50} was calculated by probit analysis.
RESULTS: There were no deficits in ambulation or in the righting reflex at myfadol doses up to 1600 mg/kg. At 2000 mg/kg, one of the six mice could not ambulate, lost the righting reflex, and died. The estimated LD_{50} is greater than 2000 mg/kg.
DISCUSSION: Oral myfadol produced motor deficits and sedation only at doses above 1600 mg/kg. As a comparison, greater than 90% analgesic efficacy was reached below 200 mg/kg in rodents (Anesthesiology 2003;98:A907). No animal died at myfadol doses ≤1600 mg/kg. Studies in primates have shown that non-peptide delta-opioid agonists produce little or no dependence with chronic administration (JPET 2001;299:629). If future studies with oral myfadol also demonstrate no physical dependence with chronic use, then the above primate study and results of this safety study, along with myfadol's full analgesic efficacy, suggest the benefit of further testing for the treatment of chronic pain.

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CENTRAL NERVOUS AND CARDIOVASCULAR TOXIC EFFECTS OF CO-ADMINISTERED LIDOCAINE AND ROPIVACAINE IN RATS

AUTHORS: D. Li, Q. Wan, W. Li;
AFFILIATION: 2nd Hospital, Harbin Medical University, Harbin, China.

INTRODUCTION: The use of mixtures of local anesthetics for regional anesthesia has become more popular recently[1]. However, there is a lack of data evaluating the systemic toxicity after the mixtures of lidocaine and ropivacaine up to now. We designed the present study to evaluate the systemic toxicity induced by administered intravenously co-administered two local anesthetics.
METHODS: Forty-eight Wistar rats were anesthetized with 3% isoflurane in oxygen, tracheotomized and mechanically ventilated. Electrocardiogram, electroencephalogram, and arterial blood pressure were continuously recorded and body temperature was maintained at 37° to 38°. Then anesthesia was maintained with 1% isoflurane, the animals were left undisturbed for 20 min. After blood-gas values were confirmed to be normal, the animals were randomly divided into four groups (n=12 for each group), an intravenous infusion of local anesthetics were begun as the follows: the animals in the group A received 0.5% ropivacaine 2.0 $mg \cdot kg^{-1} \cdot min^{-1}$; the group B received 0.5% ropivacaine 2.0 $mg \cdot kg^{-1} \cdot min^{-1}$+0.5% lidocaine 2.0 $mg \cdot kg^{-1} \cdot min^{-1}$; the group C received 0.5% ropivacaine 2.0 $mg \cdot kg^{-1} \cdot min^{-1}$+1.0% lidocaine 4.0 $mg \cdot kg^{-1} \cdot min^{-1}$; and the group D received 1.0%lidocaine 4.0 $mg \cdot kg^{-1} \cdot min^{-1}$. The following toxic end points were recorded and the cumulative doses of local anesthetics calculated: first seizure activity (SZ), first dysrhythmia (DYS), and asystole (ASYS). Arterial blood was drawn at the onset of SZ, DYS and ASYS. Plasma concentrations of local anesthetics were determined by high-performance liquid chromatography.
RESULTS: The cumulative doses of ropivacaine that produced SZ and ASYS in the group C were smaller than the corresponding doses in the group A (P=0.017, P=0.009), but no significant difference was seen at the onset of DYS (P=0.415). Between group B and A, the corresponding cumulative doses of ropivacaine were no significant difference at the onset of SZ, DYS and ASYS (P=0.943, P=0.428, P=0.58). Among group A, B and C, the corresponding plasma concentrations of ropivacaine were no significant difference at the onset of SZ, DYS and ASYS (P>0.05). The time of the occurrence of lidocaine-induced toxic events (SZ, DYS, ASYS) in the group D were longer than those of ropivacaine-induced toxic events in the group A (P<0.0001).
DISCUSSION: The systemic toxicity of 0.5% ropivacaine with 1.0% lidocaine under conditions of this study is more than that of the 0.5% ropivacaine, but there is no significant difference between 0.5% ropivacaine with 0.5 % lidocaine and 0.5% ropivacaine .
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S-239

IMPROVING MUSCLE RELAXANT STUDIES WITH POTENTIATION MODELLING

AUTHORS: D. J. Eleveld;
AFFILIATION: University Hospital Groningen, Groningen, Netherlands.

INTRODUCTION: In pharmacokinetic-pharmacodynamic (PK-PD) modeling studies neuromuscular block is estimated by comparing the evoked peak twitch to a control value measured in the absence of neuromuscular block. In practice this control value is often difficult to determine because repeated motor nerve stimulation enhances the evoked mechanical response of the corresponding muscle resulting in an increased twitch response. This is known as twitch potentiation or the staircase phenomenon and is the result of myosin light chain phosphorylation creating an increased twitch force production for a given amount of Ca2+ released at each action potential. Proper modeling of potentiation may reduce twitch prediction error and improve PD parameter estimations.
METHODS: We used an exponential model to describe the degree myosin light chain phosphorylation and associated twitch potentiation and combined it with a standard PK-PD model to predict mechanomyographic twitch measurements during muscle relaxation. The resulting fit model parameters were compared to those resulting from a standard PK-PD model and standard practice of normalising twitches to recovery values and assuming potentiation remains constant.
RESULTS: The use of a combined PK-PD-Potentiation model increases twitch prediction accuracy and allows twitch prediction to include data measured during twitch stabilisation. Standard deviation of the residuals for the combined PK-PD-Potentiation model is lower than for standard PK-PD modelling practice even though it predicts a larger data set. PD parameter ec50 and standard deviation of residuals were found to be significantly different. Figure 1 shows a representative fitting using a combined PK-PD-Potentiation model. The degree of potentiation (P) is clearly not constant throughout the course of muscle relaxation.

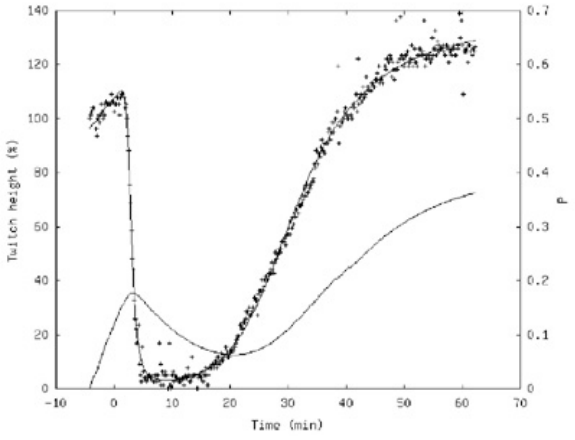

Figure 1: Measured and predicted twitch values and estimated potentiation using a combined PK-PD-Potentiation model.
DISCUSSION: We conclude a combined PK-PD-Potentiation model can predict twitch response during neuromuscular monitoring more accurately and more completely than standard PK-PD modelling practice and leads to slightly different estimations for some PD parameters.

S-240

EFFECTS OF CARBAMAZEPINE AND PHENYTOIN ON ROCURONIUM-INDUCED NEUROMUSCULAR BLOCKADE ON THE RAT PHRENIC NERVE-DIAPHRAGMATIC PREPARATION

AUTHORS: **Y. Lee**, H. Yang;
AFFILIATION: Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Republic of Korea.

BACKGROUND: Phenytoin and carbamazepine are useful anticonvulsants perioperatively. It may augment a neuromuscular block from nondepolarizing muscle relaxants. The potency of rocuronium is increased after an acute high dose of phenytoin. Rocuronium is a non depolarizing muscle relaxant of rapid onset and intermediate duration of action. This study was designed to investigate the effects of phenytoin and carbamazepine on rocuronium-induced neuromuscular blockade using rat phrenic nerve-diaphragm preparation.
METHODS: This study was approved by the institutional animal care committee of the Asna Medical center. Eighty male Sprague-Dawley rats were randomly allocated into 8 groups. Animals were anesthetized with 40 mg/kg of thiopental sodium intraperitoneally and the diaphragm with phrenic nerve was dissected and the phrenic nerve-diaphragm preparation was suspended in 100 ml of Krebs solution in organ bath. The bath was aerated with 95% O_2 and 5% CO_2 at 32°C. The phrenic nerve was stimulated with the supramaximal intensity by stimulator through isolation unit and twitch responses were measured by precalibrated force displacement transducer and recorded. The interactions of rocuronium and phenytoin and carbamazepine were determined. After one hour's stabilization period, rocuronium 300 μg was added to the bath initially. After 10 minutes, in pheytoin group, phenytoin was administered to make the phenytoin concentration of 1, 10, and 100μg/ml in Krebs solutio. In carbamazepine group, carbamazepine was administered to make the carbamazepine concentration of 0.5, 5, and 50 μg/ml in Krebs solution. In phenytoin with carbamazepine group, phenytoin simultaneously with carbamazepine was administered to make the phenytoin concentration of 10 μg/ml and the carbamazepine concentration of 5 μg/ml in Krebs solution. We measured twitch responses at 10 minutes after rocuronium administration and 10 minutes after anticonvulsants administration.
RESULTS: There were significant depressions in the twitch response of rocuronium in phenytoin 100 μg/ml group compared with control group. And there were significant depressions in the twitch response of rocuronium in carbamazepine 5 μg/ml and 50 μg/ml group compared with control group. In addition, there were significant depressions in the twitch response of rocuronium in phenytoin 10 μg/ml with carbamazepine 5 μg/ml group compared with control group.
CONCLUSIONS: The potency of rocuronium was increased in phenytoin and carbamazepine administration. Phenytoin and carbamazepine could be caused the recurarization perioperatively.

S-241

MOLECULAR LENGTH AND MECHANISM OF NEUROMUSCULAR BLOCKING ACTION OF GW280430A

AUTHORS: **C. Lee**;
AFFILIATION: Harbor-UCLA Medical Center, Torrance, CA.

GW280430A (GW), the new tetrahydroisoquinolinium neuromuscular blocking (NMB) agent, has superior activity profile in human [1]. Like its predecessors, it presumably blocks by binding to both receptive sites of the endplate acetylcholine receptor [1,2]. To do so, these long-chain NMB agents must bend to fit into the inter-site free space, which has been estimated to span 20-30 Angstrom (A), closer to 20 A [2]. For example, the lowest energy conformer of mivacurium has a preferred molecular length of 15.9 A [3]. However, GW is unique with asymmetric onium heads and asymmetric chlorofumarate connecting chain [1]. The author examined the molecular conformation of GW to test the hypothesis that GW likewise prefers a bent short conformation to permit a bisquaternary mechanism of action, notwithstanding its unique molecular structure.
METHODS: The Sybyl6.9 software package ran on an Octane workstation (Silicon Graphics, Inc.) equipped with dual processors [3]. GW was first modeled as straight molecule and subjected to extensive searches for low-energy conformers using the method of simulated annealing (SA) [2,3]. One thousand cycles of SA were run, and the product of each cycle was energy minimized to 0.05 kcal/mol/A convergence, using the MMFF94s force field. The molecular conformation of these1000 low energy conformers was analyzed. Their molecular length and distance between the two N atoms (*N-N*) were computed. The lowest energy conformer was identified as the most credible representative of the molecule. Preliminary studies [3] had shown that molecules of similar complexity required such extensive SA runs to yield credible conformers.
RESULTS: Among the 1000 conformers, energy decreased with reduced molecular length (Energy = 270 + 0.7 x Length, $P < 0.0001$). The lowest energy conformer measured 20.3 A in length, and 9.5 A *N-N*. Among 17 lower energy conformers (within 5 kcal/mol of the lowest), the length was 17.8-22.5 A (9.5-11.9 A, *N-N*). The straight conformer was 16.6 kcal/mol higher in energy, and much longer (30.4 A long, 15.8 A, *N-N*).
DISCUSSION: With a most preferred molecular length of 20.3 A, GW is no exception to the rule that potent long-chain diester bisquaternary NMB agents exist as bent molecules in order to fit into the inter-site free space [2,3]. The bulky onium heads shield the N atoms, so that an *N-N* distance of 9.5 A does not mean strong ganglionic block as it does in hexamethonium (9.0 A). The straight conformer practically does not exist (because of high energy penalty), and cannot fit inter-site to function as NMB agent. Conformational pre-screening may aid future drug design.
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S-242

TIME TO PEAK SUBMAXIMAL NEUROMUSCULAR BLOCK USING TWO NONDEPOLARIZING MUSCLE RELAXANTS

AUTHORS: **S. B. Bhatt**[1], V. Nigrovic[1], A. Amann[2], J. Kohl[1];
AFFILIATION: [1]Medical College of Ohio, Toledo, OH, [2]University of Innsbruck, Innsbruck, Austria.

INTRODUCTION: Our simulations of the neuromuscular block (NMB) using an effect compartment containing a constant amount of the postsynaptic receptors (~ $1.3 \bullet 10^{-10}$ mol $\bullet$ kg^{-1}), but of variable volume, demonstrated that the time to peak but submaximal NMB (onset time) is negatively related to the magnitude of the NMB, if a small volume ($V_E < 10^{-3}$ L $\bullet$ kg^{-1}) is assigned to the effect compartment. No such relationship is evident for a large assigned volume ($V_E > 3 \bullet 10^{-3}$ L $\bullet$ kg^{-1}). The goal of our study was to test the relationship between the onset times and the magnitudes of the NMB produced by two nondepolarizing muscle relaxants: rocuronium and cisatracurium.
METHODS: The study was approved by the local IRB. Fifty three adult non-obese patients consented to participate. Following iv administration of 1 - 2 mg midazolam and fentanyl 3 - 5 μg $\bullet$ kg^{-1}, anesthesia was induced with propofol 2 - 3 mg $\bullet$ kg^{-1}. Oral endotracheal intubation was performed following the application of topical lidocaine (4%, 3 ml). Anesthesia was maintained with propofol 100 - 150 μg $\bullet$ kg^{-1} $\bullet$ min^{-1} and 66% N_2O in oxygen. Ventilation was controlled to maintain normocapnia (E_tCO_2 36 - 40 mmHg). A thumb on one hand was abducted (preload between 250 and 300 g) and connected to a force transducer (FT10). Supramaximal stimuli to the ulnar nerve at the wrist were applied at 0.1 Hz. The elicited contractions of the thumb were recorded continuously. Following a stabilization period of 10 min, rocuronium was injected intravenously as a bolus to 30 patients (doses: 150, 200, 250, 275, 300, and 375 μg $\bullet$ kg^{-1}) and cisatracurium to 23 patients (doses: 30, 35, 40, and 45 μg $\bullet$ kg^{-1}). The records of thumb contractions were subsequently quantified by denoting the twitch strength before injection of a muscle relaxant as 1.0. Onset time was obtained by visual inspection of the recorded twitches; NMB was defined as NMB = 1 - twitch.
RESULTS: With rocuronium, onset times increased linearly from 3.5 to 6.5 min when NMB increased from 15% to 90% demonstrating a significant positive correlation ($P << 0.01$). For cisatracurium, onset times did not corelate with the magnitude of NMB (5% to 90%). On the average, the peak submaximal NMB was produced at 7.8 min. The sigmoid relationship between NMB and the injected doses was confirmed for both drugs.
DISCUSSION: Lack of correlation between the onset time and the magnitude of NMB as observed with cisatracurium is compatible with the postulated large volume of the effect compartment. The positive correlation between the onset time and NMB produced by rocuronium also appears to exclude the possibility of a small volume of the effect compartment.

S-243

NEW TRIAL OF INTRATRACHEAL ADMINISTRATION OF ROCURONIUM IN RATS

AUTHORS: **H. Sunaga**, M. Kaneko, H. Hajiri, Y. Amaki;
AFFILIATION: The Jikei University School of Medicine, Tokyo, Japan.

INTRODUCTION: Neuromuscular blocking agents are usually administered intravenously or intramuscularly.We investigated the pharmacodynamics study of rocuronium administered via intratracheal route to evaluate its efficiency.
METHODS: Sprague-Dawley rats were anesthetized intraperitoneally with pentobarbital, urethane, and atropine, then endotracheal tubes were intubated. Mechanical ventilation was done by an animal ventilator. Carotid artery cannulation was done for blood gas analysis. Mechanical twitch responses of the tibialis anterior muscle to sciatic nerve stimulation (supramaximal stimulation, duration 0.3msec, frequency 0.1Hz) delivered by an electric stimulator were amplified by a force transducer and recorded on a mini polygraph. After 10min stable baseline period in mechanical twitch responses, a thin tube was inserted into the trachea above 2cm from carina through an endotracheal tube, and a bolus of rocuronium (0.65mg/ 200g body wt.) was instillated into the trachea. The onset time (from administration of rocuronium to maximum block), duration time (from administration to T25), and recovery time (T25 toT75) were observed.
RESULTS: Blood gas analysis was stable throughout the experiment. The maximum onset time, duration time, and recovery time were approximately 240sec., 400sec., and 170sec. respectively.
CONCLUSIONS: This study is the first trial of finding new administration rout of rocuronium in rats. From our experiment shorter onset, duration, and recovery time was shown under the administration of rocuronium via the intratracheal route in comparison with intramuscular administration. The effiency of new intratracheal administration route was demonstrated.

Pharmacology-Clinical

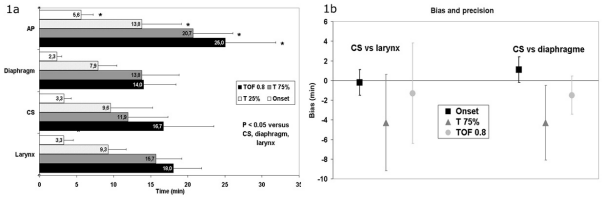
S-244

AGREEMENT BETWEEN THE ADDUCTING LARYNGEAL MUSCLES AND THE CORRUGATOR SUPERCILII MUSCLE IS INSUFFICIENT FOR CLINICAL MONITORING

AUTHORS: **G. Michaud**, G. Trager, S. Deschamps, F. Donati, T. M. Hemmerling;
AFFILIATION: Univeristé de Montréal, Montréal, PQ, Canada.

INTRODUCTION: Phonomyography (PMG) consists of recording low frequency sounds created during muscle contraction and has been validated to show good agreement with mechanomyography (1,2). In this study, phonomyography was used to measure neuromuscular block (NMB) simultaneously at four muscles.
METHODS: In 15 patients, PMG was recorded via small condenser microphones taped over the thenar mass (adductor pollicis), over the eyebrow (corrugator supercilii), at the paravertebral region at T12/L1 (diaphragm) and beside the vocal cords (adducting laryngeal muscles). After induction of anesthesia, the corresponding motor nerves were stimulated supramaximally using train-of-four (TOF) stimulation every 12 seconds. Onset, peak effect and offset of NMB after mivacurium 0.1 mg/kg were measured and compared using ANOVA, followed by *t*-test and the Bland-Altman method to determine agreement and bias between diaphragm, larynx and the corrugator supercilii muscle.
RESULTS: Onset and offset of NMB was significantly longest at the adductor pollicis muscle; the significantly lowest peak effect was reached at the corrugator supercilii muscle. Peak effect was not significantly different between the adductor pollicis muscle and either the adducting laryngeal muscles or the diaphragm (figure 1 a). Whereas there was a significantly shorter onset of NMB at the diaphragm than at the corrugator supercilii muscle, recovery of NMB was not significantly different between the corrugator supercilii muscle and either the adducting laryngeal muscles or the diaphragm. The peak effect of the corrugator supercilii muscle was significantly less pronounced than at the adducting laryngeal muscles, using the Bland Altman method, there was a considerable bias of – 0.2 min and – 1.3 min with wide limits of agreement of 2.6 min and 10.2 min for onset and recovery to TOF 0.8, respectively (cs – larynx) (figure 1 b).

DISCUSSION: We present the first study where simultaneous monitoring of NMB at the corrugator supercilii muscle, adductor pollicis muscle, laryngeal adducting muscles and diaphragm was performed using the same method, phonomyography. Recent enthusiasm about the good correlation of the corrugator supercilii muscle with the adducting laryngeal muscles (3) cannot be supported by our study. Considering a mean tof 0.8 of 16 min, limits of agreement as determined in our study between corrugator supercilii and adducting laryngeal muscles are not acceptable neither for scientific nor for clinical measurements.
REFERENCES: 1 Anesthesiology. 2003 Feb;98(2):359-63; 2 Br J Anaesth. 2002 Mar;88(3):389-93. 3. Anesthesiology. 2001 Jul;95(1):96-101

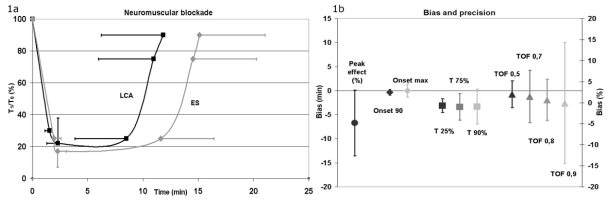


S-245

A NOVEL SITE FOR EXTERNAL MONITORING OF THE NMB AT THE LARYNX?

AUTHORS: **G. Trager**, G. Michaud, S. Deschamps, F. Donati, T. M. Hemmerling;
AFFILIATION: Université de Montréal, Montréal, PQ, Canada.

INTRODUCTION: Phonomyography (PMG) consists of recording low frequency sounds created during muscle contraction and has been validated to show good agreement with mechanomyography (1,2). In this study, phonomyography was used to compare interior monitoring of the adducting laryngeal muscles with an external monitoring site at the neck.
METHODS: In 12 patients, PMG was recorded via small condenser microphones taped at the surface of the larynx, externally at the neck and beside the vocal cords (adducting laryngeal muscles). After induction of anesthesia, the recurrent laryngeal nerve was stimulated supramaximally using train-of-four (TOF) stimulation every 12 seconds. Onset, peak effect and offset of NMB after mivacurium 0.1 mg/kg were measured and compared using *t*-test and the Bland-Altman method to determine agreement and bias between those two monitoring sites.
RESULTS: Onset time and recovery to TOF of 0.8 were not statistically different between the two monitoring sites. However, peak effect, recovery to 25%, 75%, 90% of control twitch height were significantly longer at the external monitoring site than at the adducting laryngeal muscles (Figure 1 a, LCA = adducting laryngeal muscles; ES = external site). Bland Altman method determined significant bias and wide limits of agreement between the two monitoring sites for all onset, peak effect and recovery times (Figure 1 b, bias = LCA - ES).



DISCUSSION: A new external monitoring site at the neck cannot be used interchangeably with internal laryngeal monitoring, wide limits of agreement being not sufficient even for clinical purposes. External monitoring might reflect simply NMB at strap muscles of the neck but not relaxation of the larynx. This contradicts an earlier study where good correlation was found between this external monitoring site and conditions of intubation (3).
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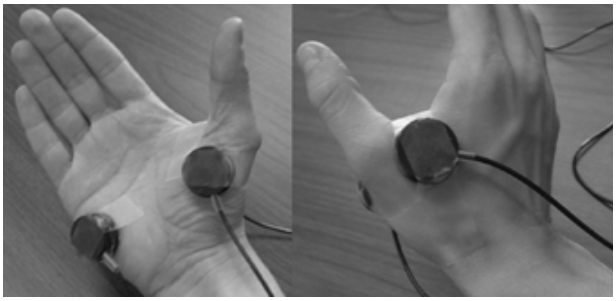
S-246

PHONOMYOGRAPHY OF THE HAND

AUTHORS: **G. Michaud**, G. Trager, F. Donati, S. Deschamps, T. M. Hemmerling;
AFFILIATION: Université de Montréal, Montréal, PQ, Canada.



INTRODUCTION: Phonomyography (PMG) consists of recording low frequency sounds created during muscle contraction (1,2) . In this study, phonomyography of three regions of the hand (adductor pollicis (AP), hypothenar (HT) and first dorsal interosseous (FDI) muscles) was compared to mechanomyography of the adductor pollicis.
METHODS: In 14 patients, PMG was recorded via small condenser microphones taped over the thenar mass, the hypothenar eminence and the dorsal groove between the first and second metacarpal bones to record the acoustic signals of AP, HT and FDI.(Figure) Mechanomyography of the AP was simultaneously recorded using a force transducer. After induction of anesthesia, the ulnar nerve was stimulated supramaximally using train-of-four (TOF) stimulation every 12 seconds. Onset, peak effect and offset of neuromuscular block after rocuronium 0,6 mg/kg were measured using PMG and compared to MMG using t-test and the Bland-Altman test.
RESULTS: Onset and peak effect of the AP, HT and FDI measured using PMG and compared to MMG were not significantly different. Offset (T 25%, T75 %, TOF 0.8) of the MMG AP, PMG AP and PMG FDI were of 33.9 (10.8) and 45.0 (11.9) and 61.1 (23.4) min, 35.3 (11.8) and 48.6 (13.8) and 59.6 (22.0) min and 35.9 (11.6) and 48.8 (15.6) and 60.2 (23.2) min, without being significantly different. Only T 25%, T 50%, T 75% and T 90% at hypothenar muscles were significantly shorter than at any other muscle sites. Smallest bias and shortest limits of agreement were found at the thenar region with a bias of 1.5 min and limits of agreement of 4.8 min (MMG - PMG).
DISCUSSION: Best agreement between MMG of the AP and PMG of the hand was found for the FDI and AP muscles. Phonomyography of those two muscles could be used interchangeably with mechanomyography of adductor pollicis.
REFERENCES: 1 anesthesiology. 2003 feb;98(2):359-63; 2 br j anaesth. 2002 mar;88(3):389-93.

S-247

DOES CHRONIC THERAPY WITH COMBINATION OF ANTICONVULSANTS AFFECT NEUROMUSCULAR BLOCK (NB) BY ROCURONIUM STRONGER THAN CARBAMAZEPINE ALONE?

AUTHORS: **A. Spacek**, F. X. Neiger;
AFFILIATION: Dept. of Anesthesiology and Intensive Care, AKH, University of Vienna, Vienna, Austria.

INTRODUCTION: Patients chronically receiving carbamazepine are known to be resistant to some nondepolarizing muscle relaxants such as vecuronium or rocuronium (1).We have investigated if the chronic therapy with the combination of anticonvulsants affects the rocuronium-induced NB stronger than carbamazepine alone.
METHODS: After IRB approval and informed consent, until now a total of 28 patients with ASA physical scores I-III and normal cardiac, renal, pulmonary and hepatic function scheduled for a variety of neurosurgical procedures could be included in the study. Group I (n=11) patients received carbamazepine for at least 4 weeks (plasma drug levels were verified by radioimmunoassay prior to surgery and were within the therapeutic range). Group II (n=6) patients also were on chronic therapy with carbamazepine, phenytoin and valproic acid for at least 4 weeks. Group III (n=11) patients served as controls. Anesthesia was induced with 3-5 mg/kg thiopental and 3 mcg/kg fentanyl and maintained by moderate hyperventilation (Et CO2 at 30-35 mmHg) with N2O 70% and isoflurane 0.5% in 02, supplemented with repeated doses of fentanyl. Rocuronium (0.6mg/kg) was administered for muscle relaxation. Skin temperature was maintained above 36°C. All patients were monitored with ECG, blood pressure monitor, pulse oximeter, end-tidal CO2 and temperature probe. The ulnar nerve was stimulated supramaximally at the wrist with train-of-four stimuli (square wave 100 ms 2 Hz for 2 s at 20 s intervals). The compound electromyography (EMG) from the hypothenar eminence was recorded using a Datex NMT monitor. The following parameters were determined: lag time, onset, 10%, 25%, 50%, 75% recovery of baseline response and recovery index (RI: 25-75%). Statistical analysis were made using the two tailed t-test for unpaired data and ANOVA. P<0.05 was considered statistically significant.
RESULTS: There was no significant difference in demographic data between all groups. The times of recovery to 10%, 25%, 50%, 75% of the baseline response as well as the recovery index (RI 25%-75%) were significantly shorter both in patients on chronic carbamazepine therapy and on the theqapy witi the combination of anticonvulsants than in control group patients.
DISCUSSION. Our results demonstrate that patients on chronic carbamazepine therapy and on combination of various anticonvulants are resistant to rocuronium-induced NB. The combination of several anticonvulsants does not affect NB of rocuronium stronger than carbamazepine alone.
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1 Anesthesiology 1999; 90: 109-112

Results ((* p<0.05 vs control) (Table: mean±SD in min.).

	Carbamazepine (n=11)	Mixed (n= 6)	Control (n=11)
Lag time	0.9±0.2	0.8±0.16	0.9± 0.3
Onset	2.8±1.2	2.8±1.1	2.6±1.0
10% Recovery	19.8±6.9 *	19.0±5.9*	29.2±13.5
25% Recovery	25.7±7.6 *	23.7±6.1*	36.1±13.1
50% Recovery	30.4±8.2 *	28.1±6.9*	43.5±15.6
75% Recovery	36.5±10.6 *	32.8±7.5*	57.0±23.8
Recovery Index	10.9±4.6 *	9.1±3.5*	20.8±12.5

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OTHER FACTORS BUT NOT BLOOD IONIZED CALCIUM LEVEL DID AFFECT VECURONIUM ACTION ON SECONDARY HYPERPARATHYROIDISM

AUTHORS: **S. Takagi**, T. Aoki, O. Nagata, M. Ikeda, M. Ozaki;
AFFILIATION: Tokyo Women's Medical University, Tokyo, Japan.

INTRODUCTION: Neuromuscular blocking action of vecuronium on secondary hyperparathyroidism (2HPT) is different from usual manner of its effect. The mechanism of this phenomenon has not been known. We therefore studied the time course of action with vecuronium in patients with primary hyperparathyroidism (1HPT) and 2HPT during total intravenous anesthesia.
METHODS: With IRB approval and informed consent, twenty two patients were enrolled in this study. Eight patients were 1HPT, another eight patients were 2HPT and six patients were normal parathyroid and renal function (Cont). The ratio of height for the first twitch (T1) to the baseline value before vecuronium (0.1mg/kg) administration was measured by an electromyogram during total intravenous anesthesia with propofol and fentanyl. The time to maximum block (Onset Time: OT), duration of action until 25% recovery of T1 (Duration Time: DT) and the recovery time between 25 and 75% (RT) after administration of vecuronium were measured. The results were analyzed using the unpaired t-test. Differences were considered significant at $P<0.05$.
RESULTS:

Pharmacodynamic data and blood ionized Calcium level

	Cont	1HPT	1HPT
OT (mean ± SEM; sec)	136 ± 15	128 ± 14	233 ± 27*
DT (mean ± SEM; sec)	1959 ± 154	2060 ± 182	1889 ± 215
RT (mean ± SEM; sec)	570 ± 82	764 ± 73	1261 ± 220*
Calcium (mmol/L)	1.17 ± 0.02	1.54 ± 0.06*	1.31 ± 0.04*

Both OT and RT were prolonged significantly in 2HPT. Ionized calcium level in 1HPT and 2HPT was significantly higher in comparison with control. However, pH and total protein in the blood was not different significantly among group
DISCUSSION: The influence of renal failure upon the effect of vecuronium is pharmacodynamic prolongation. Although blood ionized calcium level was high in 1HPT, the time course of neuromuscular blocking effect of vecuronium was similar to control in our results. Nonetheless, OT and RT were prolonged significantly in 2HPT with high blood ionized calcium level same as 1HPT. Accordingly it is considered that renal insufficiency was stronger factor than ionized calcium upon the effect of vecuronium. Those results indicated that influence of uremic toxin for neuromuscular junction, elimination of metabolites of vecuronium and a tissue blood flow disorder could be the cause for pharmacodynamic prolongation of vecuronium in 2HPT.
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DEVELOPMENT OF A MECHANISM-BASED PK-PD MODEL OF THE REVERSAL OF ROCURONIUM-INDUCED NEUROMUSCULAR BLOCK BY ORG 25969

AUTHORS: **G. S. Ruigt**[1], B. Ploeger[2], M. Danhof[2], A. Bom[3], M. P. van Iersel[1];
AFFILIATION: [1]NV Organon, Oss, Netherlands, [2]LAP&P, Leiden, Netherlands, [3]NV Organon, Newhouse, United Kingdom.

INTRODUCTION: Org 25969 is a cyclodextrin, which has been chemically optimized for complexation with rocuronium. By this chelation Org 25969 effectively and rapidly inactivates rocuronium, which makes it a useful compound for the reversal of rocuronium-induced neuromuscular block (1). This paper describes the development of a PK model for Org 25969 and rocuronium and the development of a mechanism-based PK-PD model for the effect of the complexation of rocuronium by Org 25969 on rocuronium-induced neuromuscular block. One of the objectives was to determine whether the affinity constants determined in vitro by microcalorimetry are a suitable descriptor of the complexation process in-vivo.
METHODS: A mechanism-based PK-PD model was developed using data from a clinical phase-I study evaluating the kinetics of Org 25969 and rocuronium as well as the effect of Org 25969, administered either alone or 3 minutes after 0.6 mg/kg rocuronium, on rocuronium-induced NMB, as determined by AMG-derived TOF ratio. Population PK models for Org 25969 and rocuronium were developed first and were subsequently used to predict the effect of the complex formation on the PK of rocuronium. A sigmoid E_{max} model with a hypothetical effect-compartment (2) was used to estimate the parameters of the PK/PD model for rocuronium without Org 25969 on the basis of the clinical data. To validate the models a Posterior Predictive Check (PPC) was performed, involving Monte Carlo simulations. The PK and PK/PD models were fitted to the data by means of non-linear mixed effect modeling with NONMEM.
RESULTS: The PK characteristics of rocuronium and Org 25969 alone could be adequately described with a three-compartmental model with first-order elimination from the central compartment, which was validated by PPC. The PK interaction model, in which the PK parameters of both compounds were fixed to those derived from the individual models, adequately predicted the observed increase in the total rocuronium concentration after administration of Org 25969. The PK of rocuronium after administration of Org 25969 was simulated using the PK interaction model, in which the PK parameters were again fixed to the parameters of the individual models. When the K_d was optimized on the data using the PK interaction model, the estimated value of 0.21 μM was very close to the value of 0.1 μM obtained by microcalorimetry. As determined by PPC, the PK/PD interaction model also adequately predicted the observed effect of Org 25969 administration on rocuronium-induced NMB.
DISCUSSION: The microcalorimetrically determined K_d value appears to be a good predictor of the affinity constant, which in the PK/PD model best fits the clinical data. This indicates that the risk of potential interactions of 25969 with other compounds may effectively be probed with simulations using these in vitro K_d values.
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S-250

THE IMPACT OF MIVACURIUM AND ROCURONIUM ON RECOVERY TIMES IN AMBULATORY ANESTHETIC PROCEDURES

AUTHORS: **J. L. Apfelbaum**[1], C. A. Walawander[2];
AFFILIATION: [1]The University of Chicago Hospitals and Clinics, Chicago, IL, [2]Cognigen Corporation, Buffalo, NY.

INTRODUCTION: This study was designed to evaluate the recovery times of patients undergoing ambulatory surgery with the short-acting, fast-emergence anesthetic agents, mivacurium, and rocuronium.
METHODS: After IRB approval, patients who received either mivacurium or rocuronium at five surgical centers were included in the analysis. The primary outcome was total time spent in the post anesthesia care unit (PACU) and/or second stage recovery unit. The ability to bypass the PACU was also evaluated.[1] The Wilcoxon rank sum test and chi-square test were used for comparisons. The interrelationships between patient characteristics, neuromuscular blocking agents, bypass of the PACU, surgery duration, surgical procedure, and use of reversal agent and inhalation agent were explored with a linear regression model. Statistical significance was defined as $p<0.05$.
RESULTS: A total of 344 patients received mivacurium and 190 patients received rocuronium. Recovery times and surgical times, stratified by type of neuromuscular blocking agent and by PACU requirements, are presented in Table 1. Patients who received mivacurium had a shorter recovery time than patients who received rocuronium, $p < 0.0001$. In both groups, if a patient bypassed the PACU, the total recovery time was significantly shorter than if a patient needed care in the PACU, $p < 0.0001$. Surgical duration was statistically different between the mivacurium and rocuronium groups. Bypass rates for the PACU were 29.1% and 21.6% for the mivacurium and rocuronium groups, respectively, $p = 0.06$. The factors statistically related to total recovery time with a baseline duration of 144 minutes were mivacurium use (-18 minutes), bypass ability (-41 minutes), females (+19 minutes), ENT procedures (+21 minutes), and surgery duration > 1 hour (+24 minutes), $p < 0.05$.

Table 1:

	Mivacurium		Rocuronium	
	Did Not Bypass	Bypassed PACU	Did Not Bypass	Bypassed PACU
	Mean (sd) min-med-max	Mean (sd) min-med-max	Mean (sd) min-med-max	Mean (sd) min-med-max
Total Recovery Time (min)	151.0 (79) 14-139-455	94.8 (56) 25-89-360	224.7 (120) 40-205-660	148 (77) 25-142-310
Total Surgery Time (min)	70.6 (49) 3–59–410	51.3 (28) 5–45–155	81.2 (42) 20–73–280	74.4 (36) 29–65–176

DISCUSSION: In ambulatory surgical procedures, total recovery time depends on multiple factors. The linear regression model demonstrated that recovery times were shorter with mivacurium than with rocuronium when patient characteristics, length of surgery, type of surgical procedure, and site effect were considered.
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1. Anesthesiology 2002; 97(1):66-74.

S-251

ASSESMENT AND PREVENTION OF SUCCINYLCHOLINE INDUCED FASCICULATIONS

AUTHORS: **D. Steinberg**;
AFFILIATION: Hospital Clinicas Caracas & Policlinica Mendez Gimon, Caracas, Venezuela.

INTRODUCTION: Visible rating of fasciculations is difficult to perform since it is subjectively scored, consequently several allegedly objective methods have been introduced with relative success. Clinically a most often four-step rating system is used (1, 2, 3). We recently demonstrated by regional monitoring that rapacuronium (RAP) almost completely suppress succinylcholine (SCH) induced fasciculations (4). In order to further demonstrate both the advantage of such a method and compare that pretreatment with a lesser effective defasciculating agent as mivacurium (MIV), the following clinical trial was undertaken.
METHODS: After consenting, 60 elective patients with no obvious clinical contraindication for SCH, were anesthetized with intravenous agents and nitrous oxide and randomly allocated to three groups (n= 20). Group 1 received SCH 1 $mg.Kg^{-1}$, to those in group 2, 100 $\mu g.Kg^{-1}$ RAP (¶) was used as a pretreatment 3 minutes before SCH 1 $mg.Kg^{-1}$, and MIV 10 $\mu g.Kg^{-1}$ with the same timing and sequence was administered to group 3. Four blinded independent observers looked for fasciculations in six anatomical regions (two upper extremities: left (UL) and right (UR), two lower extremities: left (LL) and right (LR), trunk (TK): including thorax and abdominal wall and the head (HD): including face and neck). A 0 to 3 scale was used for an individual score related to increased fasciculation intensity. Mean average for each region and patient was used for comparison by Kurskall-Wallis and Tukey methods, analysis of variance and Student-Neuman Keuls tests.
RESULTS: Right lower limb resulted with the lower score and left upper extremity and the trunk showed the highest scores. Statisticall differences disappeared after pretreatment. Consistently in every single region rating was significantly higher in the absence of defasciculating drugs, and RAP scored the lower (Table No. 1).
DISCUSSION: Increased accuracy with the present method could be found in comparison to the traditional on which a number of patients classified by a global score are pooled into a certain group. As unaware referees were included, subjectively scores should be reduced, something considered as mandatory for this kind of studies. This is a non-invasive method without any other devices added, that could be difficult to adjust and with a wide range of individual variation (1, 2). In conclusion: RAP seems to be the new golden standard for defasciculating drugs. Although MIV significantly reduced fasciculations, RAP resulted statistically better. The proposed method is considered to be consistent, practical and accurate.
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(¶) *Rapacuronium data was collected before its withdrawal from the market*.

Table 1	1) UL	2) UR	3) LL	4) LR	5) TK	6) HD	SIG	total
1) SCH	2.35±1	1.75±1	1.8±0.8	1.45±0.9	2.6±0.5	1.95±0.7	4)vs=1-5	11.8±3.4
2) RAP	0	0	0.05±0.2	0.05±0.2	0	0	N.S.	0.1±0.3
3) MIV	1.2±1	1.15±1	1.1±0.9	1.1±0.9	1.6±1.3	1.05±0.9	N.S.	7.2±5.4
SIG	1) vs=2-3 2)vs=3	1) vs=2-3 2)vs=3	1) vs=2-3 2)=3	2) vs=1-3	1) vs=2-3 2)vs=3	1) vs=2-3 2)vs=3		1) vs=2-3 2)vs=3

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PRIMING ROCURONIUM - MIVACURIUM MIXTURES

AUTHORS: D. Steinberg;
AFFILIATION: Hospital Clinicas Caracas & Policlinica Mendez Gimon, Caracas, Venezuela.

INTRODUCTION: Rocuronium (ROC) and mivacurium (MIV) mixtures have already been studied (1), but priming muscle relaxants mixtures have not. Mixtures as well as priming have been intended with the main purpose to reduce time for tracheal intubation, by increasing speed of action, but confusing terminology is used to describe speed and onset time (1, 2). Employing properly derivative parameters, the aim of this study is to find an even faster action of these drugs.
METHODS: Consenting adult elective patients were anesthetized with intravenous agents and nitrous oxide and randomly allocated to receive a mixture of ROC (200 $\mu g.Kg^{-1}$) + MIV (50 $\mu g.Kg^{-1}$) either by bolus (n= 20) or priming (n= 24) with 10% of this dose 3 minutes before the remaining amount. Using electromyography, time to 80% block, onset time, maximal effect, train of four (TOF) fade and clinical duration were assessed. Velocity was calculated as the ratio between time and fractional blockade at the initial (up to 80%), final stage (between 80% and maximal effect) and the overall onset period. After maximal block was achieved an airway was inserted and anesthesia continued with sevoflurane (1 MAC_{ET}). Analysis of variance, Student-Neuman-Keuls and T test with a 0.05 level of significance were used for statistical comparison.
RESULTS: Neuromuscular action significantly increased after priming (Table 1). No significant difference was found in clinical duration and TOF fade measured at approximately 80% block. The second stage of onset time (final) was statistically slower (more time taken to produce each % of blockade) than the other two.
DISCUSSION: Actual ratio for the mixture (4:1) is the same but the total amount of drugs are intermediate in comparison to that used in other investigations (1). Monitoring method (electromyography vs mecanomyography) could account for possible differences. Present doses were purposely chosen to avoid excessive shortening of onset and reduction of data that biased and variated estimates (3). A faster action (sec / %) was noticed with priming during the entire onset time, in good agreement with similar findings already described for ROC (2, 4). As significant more speed was added by priming during the initial stage of onset in comparison to the final period, some advantage may be taken if an early intubation is considered (4). In conclusion, priming ROC + MIV mixture is a reliable and consistent method to obtain a faster action of muscle relaxants drugs. Poor contribution of a more presynaptic action (TOF fade) by priming is clinically demonstrated and any change is introduced to clinical duration.
REFERENCES: 1) Anesthesiology (1994) 81: 388.- 2) Can J Anaesth (2003) 50: A.60.- 3) Anesthesiology (2002) 96: 711.- 4) Anaesthesia (1991) 46: 341.-

Table1	80% (sec)	MAX (%)	ONSET	INITIAL	FINAL	OVERALL
BOLUS	185±59	97±2	314±84	2.35±0.74	7.64±3.24	3.24±0.95
PRIMING	131±51	99±1	232±70	1.64±0.64	5.35±1.98	2.35±0.75
.p	0.0001	0.006	0.0001	0.0001	0.003	0.0001

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ROCURONIUM-MIVACURIUM INTERACTION COMPARED TO THAT OF ATRACURIUM-MIVACURIUM

AUTHORS: D. Steinberg;
AFFILIATION: Hospital Clinicas Caracas & Policlinica Mendez Gimon, Caracas, Venezuela.

INTRODUCTION: Great contradiction arises when mivacurium (MIV) (m) and atracurium (ATR) (a) interaction, with similar molecular structure, was studied previously (1, 2). Although MIV and rocuronium (ROC) (r) interaction, from a different family was also analyzed (3), close potency for ROC and ATR deserves a further conclusive trial under very similar clinical conditions.
METHODS: Dose-response relationships for the three agents were performed first. To adult, elective and consenting patients, anesthetized with intravenous agents and nitrous oxide, MIV (n= 45) 20, 30 or 40 $\mu g.Kg^{-1}$ or either ROC and ATR (n= 45 e/a) 50, 100 or 200 $\mu g.Kg^{-1}$ was administered, and ED_{50} was calculated by an alternate method (4) using the depression of the first response to a train of four stimulation during electromyographic monitoring. In the second part of the study, a combination of 0.2, 0.3 or 0.4 x ED_{50} just obtained for the three drugs (n= 45 e/a), was used by the same methodology to estimate the experimental and theoretical ED_{50} for each component in a given additive mixture and then a fractional algebraic sum was used to identify the type of interaction (dm/(ED)m+dr-a//ED)r-a).
RESULTS: Algebraic sum for the MIV+ATR combination was near one denoting additivism, meanwhile, for the MIV+ROC mixture was less than one pointing to synergism (Table No. 1).
DISCUSSION: Essential features for a valid comparison are the same clinical and methodological analysis for every included drug. This is accomplished in the present study, but is not so in previous trials. ED_{50} for MIV changed from some studies due to many factors: introduction of a volatile agent, use of different amounts for the same drug during the dose-response curve construction, differences in dosage and number of combinations (1, 3). Regarding some results for the combination MIV+ATR coming from two groups of investigators, different systems for neuromuscular monitoring and age of the patients are decisive to arrive to a valid comparison (1, 2). In conclusion, when clinical conditions and methods for analysis are maintained constant, MIV-ATR interaction is definitively of the additive type. On the other hand MIV-ROC interaction gives rise to synergism. Due to the close potency of ATR and ROC, structural chemical differences may account in part to explain synergistic combination.
REFERENCES: 1) Br J Anaesth (1994) 73: 484.- 2) Anesth Analg (1994) 79: 998.- 3) Anesthesiology (1994) 81: 388.- 4) Anesth Analg (2000) 90: 1191.-

Table No. 1	MIV $\mu g.Kg^{-1}$	theor	expr	FRACTION (exp/ED)	ATR ROC	theor	expr	FRACT
ED_{50}	43±10	65±11*	20±5*	0.3	144±62	219±39*	67±15*	0.3
ED_{50}	43±10	28±5*	19±5*	0.44	143±61	93±19*	63±17*	0.44
	(theor/ED)	ATR	(expr/theor)	ATR	.dm/(ED)m+			
	MIV	ROC	MIV	ROC	.da-r/(ED)a-r			
ED_{50}	1.51	1.52	0.3	0.3	0.93			
ED_{50}	0.65	0.66	0.67	0.67	0.88			

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ONSET TIME AND SPEED OF ACTION: VECURONIUM AND ATRACURIUM REVISITED

AUTHORS: D. Steinberg;
AFFILIATION: Hospital Clinicas Caracas & Policlinica Mendez Gimon, Caracas, Venezuela.

INTRODUCTION: Velocity for some muscle relaxants varied during onset time (1). It is assured that after vecuronium (VEC) and atracurium (ATR), depression of the twitch contraction is more gradual than rocuronium meaning that the initial rapid decrease is followed by slower depression, but no supporting data is offered (2). Some reviewers state that VEC and ATR have a similar onset time (3), but any delay can be detected during onset when paralysis is complete as after 3 or 4 x ED_{95}, preventing comparisons (2, 3). The aim of the present study is to compare onset time and speed of action for VEC and ATR by the use of adequate parameters and doses.
METHODS: During induction with intravenous, narcotics and nitrous oxide anesthesia, two groups of adult, elective and consenting patients received either VEC 40 $\mu g.Kg^{-1}$ (0.88 x ED_{95}) (n= 38) or ATR 250 $\mu g.Kg^{-1}$ (0.9 x ED_{95}, according to our previous dose response relationship) (n= 26). Using electromyography, time to 80% blockade (sec), maximum effect (%) and onset time (sec) were assessed. Speed of action was derived as the ratio between time and fractional blockade (sec / %) during the ***initial*** phase of onset (up to 80%), the ***final*** period (between 80% and maximal block) and the ***overall*** velocity (from drug administration until maximal block). Results are expressed as mean ± standard deviation. Analysis of variance, Student-Neuman-Keuls and T test and $p<0.05$ level for significance were used for statistical comparisons.
RESULTS: No significant differences were noticed for pharmacodynamic and velocity data (Table No. 1).
DISCUSSION: During the development of dose-response curves, doses of 20 to 50 $\mu g.Kg^{-1}$ of VEC or 100 to 250 $\mu g.Kg^{-1}$ of ATR took a similar onset time of 6.7 to 4.5 and 6.6 to 5.9 minutes respectively to attain the maximum effect (4, 5). In another investigation, equipotent doses (1 x ED_{90}: 43 and 188 $\mu g.Kg^{-1}$) showed a statistical difference in onset time (4.7 vs 6.7 minutes) (6), but monitoring systems and final blockade may account for differences with present results. Using appropriate parameters, both VEC and ATR showed a faster initial than a very slower final period during onset of action. Although this trend resembles that of rocuronium, figures for the latter are faster (1). In conclusion: velocity during the onset period is not uniform, been faster at the beginning and slower at the end, both for VEC and ATR, without any significant difference among drugs.
REFERENCES: 1) Can J Anesth (2003) 50: A60.- 2) Anaesthesia (1991) 46: 341.- 3) Anesthesiology (1984) 61: 444.- 3) Br J Anaesth (1985) 57: 1060.- 4) Anesthesiology (1985) 62: 657.- 5) Br J Anaesth (1983) 55: 125.- 6) Anesthesiology (1984) 61: 444.-

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ROCURONIUM AND ATRACURIUM: ARE THEY EQUIPOTENTIAL?

AUTHORS: D. Steinberg;
AFFILIATION: Hospital Clinicas Caracas & Policlinica Mendez Gimon, Caracas, Venezuela.

INTRODUCTION: Data for atracurium (ATR) and rocuronium (ROC) potency yield to somehow similar near figures (1, 2, 3). Methodology during the construction of dose-response curves, sample size, clinical conditions, and chronology could account for differences. In order to clarify similarities or not between potencies of these two agents, the following trial was undertaken.
METHODS: During induction with intravenous agents and nitrous oxide, two groups of elective and consenting patients received randomly either ATR (n= 45) or ROC (n= 45). Similar single doses (50, 100 and 200 $\mu g.Kg^{-1}$) were administered to three subgroups (n= 15 e/a). Using depression of the first response after a train of four stimulation obtained by electromyography $ED_{50, 90}$ and $_{95}$ were calculated by an alternate method (4). Two additional subgroups received 1 x ED_{50} just calculated for both ATR (n= 15) or ROC (n= 15) and maximum effect and onset time assessed by the same monitoring system. Analysis of variance, Student-Neuman-Keuls and T test were used for statistical comparisons and $p<0.05$ level considered for significance.
RESULTS: No statistical difference was noticed between neither $ED_{50, 90, 95}$ or maximal effect and onset time for 1 x ED_{50}. for both ATR and ROC (Table 1).
DISCUSSION: Reviewing data from the same institution, although more than 10 years apart, showed 14 to 15% difference among ED_{50}'s for ATR and ROC probably related to a small sample sizes for groups and differences in fractional doses between drugs used to build a dose-response curve (1, 2). An even smaller difference was found for ED_{95}'s in another contemporary study, once again dissimilar and small groups were assigned to different fractional doses for developing the same relationship (3). Values for the effect compartment concentrations corresponding to 50% block have been reported in the same range with about 20% differences between ATR and ROC, a decade apart (5, 6). In conclusion, when potency and other pharmacodynamic features of muscle relaxants have to be compared, efforts must be excerted to use identical clinical and methodological conditions for calculations. As a lack in these conditions may account for differences, some clinical comparisons already published may deserve to be further revisited.
REFERENCES: 1) Anesthesiology (1985) 62: 657.- 2) Can J Anaesth (1992) 39: 139.- 3) Anaesthesia (1998) 53: 872.- 4) Can J Anesth (2003) 50: A61.- 5) Can J Anaesth (2003) 49: 353.- 6) Clin Pharmacol Ther (1991) 49: 515.-

Table 1

$g.Kg^{-1}$	ED_{50}	ED_{90}	ED_{95}	50 $g.Kg^{-}$	100	200	*(%)	*onset
ATR	144±62	234±101	277±120	8.6±4	17±8	60±26	25±18	302±91
ROC	143±61	227±97	265±114	13.4±7	16±6	46±23	21±8	290±52
.p=	0.933	0.642	0.715	0.041	0.729	0.125	0.440	0.678

***maximal blockade (%) and onset time (sec) for 1 x ED_{50}**

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2004; 98; S-1–S-282

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EFFECTS OF ROCURONIUM IN MYASTHENIA GRAVIS UNDERGOING THYMECTOMY

AUTHORS: **Y. Lim**, Y. Lee, H. Yang;
AFFILIATION: Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Republic of Korea.

BACKGROUND: Myasthenia gravis is an autoimmune disease caused by antibodies to the acetylcholine receptors at the neuromuscular junction. Loss of these receptors leads to a defect in neuromuscular transmission with muscle weakness and fatigue. Rocuronium is a monoquaternary steroid analogue of vecuronium and provides a rapid onset of action. The onset and duration of rocuronium in patients undergoing thymectomy due to myasthenia gravis was investigated.
METHODS: Eighteen patients undergoing thymectomy due to myasthenia gravis were allocated in myasthenia group. Eighteen patients of ASA physical status class I, II without hepatic, renal or neuromuscular disease undergoing orthopedic surgery were allocated in control group. Anesthesia was induced with thiopental 4-5 mg/kg and maintained with isoflurane (1.0 - 1.2 vol%) and 50% N2O. Rocuronium 0.5 mg/kg in myasthenia gravis group and 0.6 mg/kg in control group was given. Tracheal intubation was performed after the twitch response was depressed more than 95%. Neuromuscular relaxation was assessed at the adductor pollicis with supramaximal stimulation of the ulnar nerve at 2 Hz every 12 sec. The onset and recovery time for T1, T2, T3, and T4 to appear from maximal blockade was recorded. And the recovery time from T1 to T4 was measured.
RESULTS: The onset time to maximal block was shortened and the time for T1, T2, T3, and T4 to appear from maximal blockade was prolonged in patients with myasthenia gravis. The recovery time from T1 to T4 was prolonged in patients with myasthenia gravis.
CONCLUSIONS: Rocuronium induced neuromuscular blockade more rapidly and prolonged the recovery time.

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REDUCING PAIN FROM PROPOFOL ADMINISTRATION: A SIMPLIFIED METHOD USING XYLOCAINE AND A TOURNIQUET

AUTHORS: **P. E. Horowitz**[1], D. L. Kline[2], D. Mangar[2];
AFFILIATION: [1]Univ. of South Florida, Tampa, FL, [2]Tampa General Hospital, Tampa, FL.

INTRODUCTION: Pre-treatment with a 60 second tourniquet and I.V. xylocaine to markedly reduce the incidence and severity of painful propofol injection was described in 1992.[1] A review of randomized studies of methods to reduce pain with propofol found the xylocaine with tourniquet method to be the most effective compared with other measures including mixing xylocaine and propofol in a syringe, injection into a rapidly flowing carrier infusion or using a larger vein and intravenous cannula.[2] Other tourniquet with xylocaine protocols have utilized exsanguination of the extremity or administration of sub anesthetic amounts of propofol. We report a randomized study of the incidence and severity of propofol injection pain using a visual analog scale (VAS) of 0-100mm to document the analgesic effect of the prior injection of lidocaine 30mg with a tourniquet followed by a full induction dose of propofol. We have simplified the original xylocaine with tourniquet technique by not relying upon exsanguination of the extremity, reducing the amount of xylocaine and injecting directly into the IV cannula without a carrier intravenous infusion.
METHODS: Fifty unpremedicated ASA 1-2 patients received a 20 gauge IV cannula in the dorsum of the hand and were randomized into one of 2 groups. The first group received propofol 2mg/kg via a one way injection valve attached directly to the cannula hub. In the second group, a tourniquet was inflated to 50mmHg and lidocaine 30mg was injected through the cannula. After 60 seconds the tourniquet was released and propofol 2mg/kg was injected. In both groups, the patients verbally reported a VAS score for pain based upon a 0-100mm scale immediately after completion of each lidocaine and propofol administration.
RESULTS: The mean VAS pain score for the propofol group (25 patients) was 30 (range 10-100) and 100% of these patients reported pain upon injection. In the xylocaine with tourniquet group (25 patients), the mean VAS score after lidocaine 30mg injection with an inflated tourniquet was 1.7 (range 0-10); 56% of these patients had no pain. The mean VAS score for the subsequent injection of propofol 2mg/kg after deflation of the tourniquet was 1.4 (range 0-10); 76% of these patients had no injection pain.
DISCUSSION: Prior injection of lidocaine 30mg into an IV cannula in the dorsum of the hand after forearm tourniquet inflation reduces the incidence and severity of pain from a full induction dose of propofol. This simplified method to reduce propofol injection pain without performing exsanguination of the extremity or using a rapidly flowing carrier IV fluid is superior to other reported methods such as mixing lidocaine and propofol before injection.
REFERENCES: 1. Anesth Analg 1992;74:250-2
2. Anesth Analg 2000; 90:963-969

S-258

COMPARISON OF A LOWER-LIPID EMULSION OF PROPOFOL WITH THE STANDARD PROPOFOL EMULSION FOR SEDATION DURING MONITORED ANESTHESIA CARE

AUTHORS: **D. Song**, M. A. Hamza, P. F. White;
AFFILIATION: UT Southwestern Medical School, Dallas, TX.

INTRODUCTION: The currently used formulations of 1% propofol (e.g., Diprivan®) contain 10% soybean oil emulsion. However, a new emulsion of 1% propofol (Ampofol®) which contains 50% less lipid has recently become available for clinical investigation. This study was designed to compare the pharmacodynamic properties of Ampofol® to Diprivan® when administered for intraoperative sedation.
METHODS: Sixty-three healthy consenting outpatients undergoing superficial operations with local anesthesia were randomly assigned to receive either Ampofol® or Diprivan® for intravenous sedation. The sedation was initiated with a propofol loading dose of 0.75 $mg \cdot kg^{-1}$ IV bolus followed by an initial infusion rate of 50 $\mu g \cdot kg^{-1} \cdot min^{-1}$ to achieve an Observer's Assessment of Alertness/Sedation's score (1) of 3. The desired level of sedation was maintained with a variable-rate propofol infusion during the operation. The onset times to achieving a sedation score of 3 (or induction time), the severity of pain (scale 0=none, 1=mild, 2=moderate, 3= severe) on injection of the loading dose, intraoperative hemodynamic variables and EEG bispectral index (BIS) values were recorded at specific intervals. In addition, recovery times, postoperative pain and nausea scores (verbal rating 0=none to 10=worst imaginable), as well as patient satisfaction (0=highly dissatisfied, 100=completely satisfied) with their intraoperative sedation were assessed. Data were analyzed using Student t-test, with $p<0.05$ considered statistically significant. Values are expressed as mean±SD, numbers and percentages.
RESULTS: There were no significant differences between Ampofol® and Diprivan® with respect to the demographic data, intraoperative hemodynamic variables and BIS values.

	Ampofol	Diprivan
Age (yr)	52±15	51±12
Weight (kg)	75±28	73±20
Duration of sedation (min)	44±19	39±17
Propofol infusion rate (mg/kg/min)	101±28	98±29
Induction time (sec)	65±17	67±36
Mild pain on injection (n, %)	8, 26	6, 21
Moderate pain on injection (n, %)	8, 26 *	2, 7
Home readiness (min)	68±84	52±21
Satisfaction score	99±4	100±1

* = P <0.05
DISCUSSION: Ampofol® was equipotent to Diprivan® with respect to its sedative properties during monitored anesthesia care. Ampofol® was associated with an increased incidence of pain on injection.
REFERENCES: 1) Chernik, et al. J Clin Psychopharmacol 1990; 10: 244-51

S-259

INITIAL CLINICAL EVALUATION OF AMPOFOL, A NOVEL FORMULATION OF PROPOFOL-A RANDOMIZED, DOUBLE-BLINDED COMPARISON WITH DIPRIVAN

AUTHORS: **D. Song**, P. F. White, K. W. Klein, M. A. Hamza;
AFFILIATION: UT Southwestern Medical School, Dallas, TX.

INTRODUCTION: The high lipid content of existing propofol formulations has raised concerns regarding potential side effects, including increased plasma triglyceride levels and microbial contamination with long-term use (1, 2). Recently, a new lower-lipid emulsion formulation of propofol, Ampofol (Amphastar Pharmaceuticals, Inc, CA), containing propofol 1%, soybean oil 5% and egg lecithin 0.6% has been introduced into clinical trials. The new formulation of propofol, Ampofol processes intrinsic antimicrobial activity and does not require a preservative. This study was designed to compare the efficacy and recovery profiles of Ampofol and Diprivan (AstraZeneca, Wilmington, DL) when used for induction and maintenance of general anesthesia as part of a balanced anesthetic technique.
METHODS: Following IRB approval and informed consent, 63 healthy outpatients undergoing ENT procedures were randomly assigned to either the Diprivan or Ampofol group. All patients were premedicated with rofecoxib, 50 mg po, and midazolam, 20 mcg/kg iv. Anesthesia was induced with sufentanil, 0.1 mcg/kg iv, lidocaine, 0.5 mg/kg iv, and propofol, 2 mg/kg iv (injected over 15-18 sec). Since the physical appearances of Diprivan and Ampofol are identical, both the anesthesiologists and the investigators were blinded with respect to the formulation of propofol. After tracheal intubation, anesthesia was maintained with a propofol infusion, 100-200 mcg/kg/min, and N_2O 67%. The EEG-BIS monitor was used to assess the effect of propofol on the brain and BIS values were recorded at 10-min intervals. Onset times from injection of propofol to loss of the eyelash reflex and dropping a syringe, and recovery times from discontinuation of propofol infusion to opening eyes and orientation, as well as an assessment of quality of induction were recorded. Postoperative pain and nausea scores were recorded on an 11-point verbal scale and patients satisfaction with their anesthesia was evaluated on a 100-point scale at specific intervals. Data were analyzed using t-test, Kruskal-Wallis test and chi-square test, with $p<0.05$ considered statistically significant (mean ±SD).
RESULTS: The Ampofol and Diprivan groups were similar with respect to demographic data, duration of anesthesia and total dosage of propofol. Induction and recovery variables are summarized below:

	Ampofol	Diprivan
Loss of eye reflex (sec)	41±9	41±6
Dropping of syringe (sec)	39±8	40±6
Intraoperative BIS value	36±10	34±10
Pain on injection (%)	39	9 *
MAP depression (>25%) (%)	16	31
Excellent quality of induction (%)	80	77
Awakening (min)	15±9	13±6
Home readiness (min)	171±58	166±57
Satisfaction score (0-100)	97±5	97±5

* = P<0.05
DISCUSSION: Ampofol 1% is equipotent to Diprivan 1% with respect to its anesthetic (hypnotic) properties during general anesthesia. However, Ampofol was associated with a higher incidence of mild pain on injection. The effects of the lower lipid content on patient outcome will require further studies involving longer-term administration (e.g., ICU sedation and TIVA).
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S-260

PROPOFOL AND METHOHEXITAL ARE ADDITIVE DURING BIS-GUIDED TIVA

AUTHORS: **D. M. Mathews**, S. Kumar, Z. Said, M. Klewicka, G. G. Neuman;
AFFILIATION: St Vincent Catholic Medical Center, New York, NY.

INTRODUCTION: Propofol or methohexital may be used for total intravenous anesthesia (TIVA). Studies comparing their interaction and outcome were conducted before the availability of "depth of hypnosis" monitors such as the BIS monitor (Aspect Medical Systems, Newton MA). [1] The primary goal of this study was to describe the interaction between these two agents during BIS-titrated TIVA. The secondary goal was to compare the emergence and recovery parameters in three groups: propofol, methohexital or a combination of the two.
METHODS: Using double-blinded protocol, 135 patients undergoing ambulatory orthopedic surgery were randomized to receive one of three hypnotic infusions: propofol 10 mg/cc + saline sham (PROP), methohexital 6.67 mg/cc + intralipid sham (METH) or propofol 5 mg/cc + methohexital 3.34 mg/cc (COMBO). Anesthesia was induced with 0.1cc/kg of each solution and repeated boluses of 0.02 cc/kg given until the BIS reached 50. An infusion of each solution was started at 0.6 cc/kg/hr. A 20 mcg/kg alfentanil bolus was given and an infusion started at 0.35 mcg/kg/min. Rocuronium 0.5 mg/kg was given and an LMA was inserted. No nitrous oxide was used. The hypnotic infusions were adjusted to maintain the BIS at 50. Alfentanil 2 mcg/kg bolus with an increase in infusion by 0.05 mcg/kg/min was given for HR or BP > 20% over baseline or patient movement. At the end of the procedure, the hypnotic agents and the alfentanil were discontinued simultaneously. Time to eye opening, LMA removal and orientation were determined. The average infusion rate of each hypnotic and alfentanil were determined. Groups were compared using t-testing with Bonferroni correction. Emergence times were compared with Dunn's test of nonparametric multiple comparisons.
RESULTS: 45 PROP, 44 METH, and 43 COMBO patients completed the study. Demographic data, average BIS values and alfentanil infusion rates were not different among the groups. Average surgical time was longer in the PROP group compared to METH or COMBO patients, 87.0 compared to 73.8 and 78.7 minutes, respectively. The isobologram of the hypnotic infusion rates (mean ± S.D.) is shown in the figure and is clearly an additive relationship. All emergence measures patients were longer in the METH than the PROP or COMBO patients, and were significantly different for orientation time: 16.7 compared to 11.6 and 10.5 minutes, respectively.
DISCUSSION: The relationship between propofol and methohexital infusion rates during BIS-guided TIVA is additive. Emergence from a combination of the two agents is not different from propofol alone: this is perhaps due to the longer surgical time in the PROP patients. The combination of propofol and methohexital is stable for up to 48 hours,[2] and, depending on acquisition costs and wastage,[3] may be more cost effective than propofol alone.

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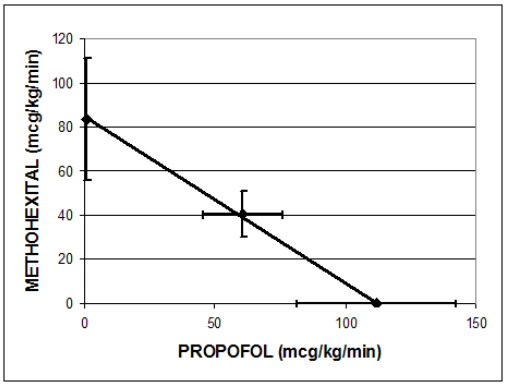
[2]Anesth Prog 2001;48:61-5
[3]Anesth Analg 1999;88:723-8



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PROPOFOL SEDATION REQUIREMENTS AND COGNITIVE FUNCTION TESTING FOLLOWING SELECTIVE PHOSPHODIESTERASE 5 INHIBITION IN HEALTHY VOLUNTEERS

AUTHORS: **T. Engelhardt**[1], J. MacDonald[1], J. Cleland[2], H. F. Galley[1], P. Maruff[3], A. Collie[3], N. R. Webster[1];
AFFILIATION: [1]Anaesthesia and Intensive Care, Aberdeen University, Aberdeen, United Kingdom, [2]Department of Clinical Psychology, Grampian University Hospital Trust, Aberdeen, United Kingdom, [3]CogState Ltd, Charlton, Australia.

INTRODUCTION: The nitric oxide – cyclic GMP pathway has been implicated in modulating the effects of general anesthesia and we have previously shown a change of salivary cyclic GMP during anesthesia during minor surgery (1,2). We postulated that limiting the breakdown of cyclic GMP through selective phosphodiesterase inhibition with sildenafil would influence the propofol sedation requirements, plasma cyclic GMP concentrations and recovery profile in healthy individuals.
METHODS: Following local ethics committee approval and written informed consent 10 male and female volunteers, aged 22-46 years and ASA 1 or 2 were recruited for this prospective placebo-controlled, double-blind, randomised cross-over study. Following baseline cognitive function tests using the CogState^{R} program, volunteers received either 100mg sildenafil or placebo orally. Propofol sedation was started after 45 min at 0.5 µg/ml predicted plasma concentration using a target controlled infusion system and increased by 0.1 µg/ml every 3 min until loss of verbal contact (LVC) when the propofol infusion was stopped. Cognitive function testing was repeated 30 min after LVC. Plasma cyclic GMP levels were determined at baseline, prior to sedation, at LVC and 30 min after LVC using enzyme immunoassay. The study was repeated after 1 week using the opposite sildenafil or placebo.
RESULTS: There was no difference in the total amount of propofol used, predicted propofol plasma concentration or duration of sedation between the 2 groups. The time for return of spontaneous verbal contact was significantly reduced with sildenafil pre-treatment when compared with placebo (4 [3-8] min versus 6 [3-5] min, p=0.019). The cyclic GMP concentrations were significantly reduced in the placebo group at LVC (8.76 [4.7-23.8] nmol/l) and 30 min after LVC (9.04 [1.8-28.1] nmol/l) when compared to baseline cyclic GMP concentrations (16.58 [5.2-34.4] nmol/l, p=0.004). Cyclic GMP concentrations were significantly increased after administration of sildenafil when compared to baseline concentrations and remained above baseline throughout the experiment (13.52 [10.8-61] nmol/l before sedation, 15.43 [10.8-62.1] nmol/l at LVC and 14.2 [3.6-46.9] nmol/l 30 min after LVC). Simple reaction times and choice reaction times were significantly increased after sedation in the sildenafil pre-treated group (p=0.013) whereas no difference was observed in the placebo treated group.
DISCUSSION: We have shown that selective phosphodiesterase inhibition does not change propofol sedation requirements in healthy volunteers but influences the recovery profile as assessed by changes in cognitive function. Propofol sedation also changes the plasma cyclic GMP concentrations, which are affected by pre-treatment with sildenafil. Further studies into the changes of cyclic GMP during anesthesia and recovery from anesthesia are warranted.
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S-262

PROPOFOL TIOPENTAL MIXTURE ANESTHESIA AND THE PRESSOR RESPONSE TO INTRAVENOUS EPHEDRINE

AUTHORS: **P. P. Nicolcescu**, F. O. Purcaru, I. P. Georgescu, A. O. Georgescu, V. C. Calina, I. N. Sosea;
AFFILIATION: University Hospital no1 Craiova, Craiova, Romania.

INTRODUCTION: We studied the effects of Propofol Thiopental mixture on pressor response to intravenous Ephedrine.
METHODS: We studied 20 patients (15 females) ASA physical status I scheduled for elective laparoscopic cholecistectomy. The patients were not premedicated and all received ephedrine 0,1 mg/kg i.v. before and after anesthesic induction. For the induction of general anesthesia the patients received 5 ml Propofol-Tiopental mixture (1 g Thiopental diluted in 20 ml Propofol 10% in the same syringe). Heart rate (HR), systolic arterial blood pressure (SBP) mean arterial blood pressure (MBP) and diastolic arterial blood pressure (DBP) where made at 1 minute intervals for 10 minutes after the injection of ephedrine in awake and anesthesiated patients. The chi2 test was used for qualitative (descriptive) variables and student test for quantitative (continuos) variables in order to performed biostatistical analysis . Data are expressed as mean ± SD p values <o,o5 were considered statistically significant
RESULTS. HR increased significantly after the administration of ephedrine 0,1 mg/kgc i.v. while the patients were awake ($p<0,05$) but there was no increase in HR after the ephedrine administration under propofol thiopental mixture anesthesia. SBP, MBP and DBP increase after intravenous ephedrine in awake patients but after induction of hypnosis with Propofol Tiopental mixture the level of the pressor responses to ephedrine were significantly greater ($p<0,05$) than during the awake state. The MPP increased by 18 ± 8% and 5 ± 5% during propofol tiopental mixture anesthesia and the awake state respectively.
CONCLUSION. The pressor response to intravenous ephedrine 0,1 mg/kg was significant increased after Propofol Tiopental mixture anesthesia as compared with the awake patients. Intravenous ephedrine is effective for intraoperative hypotension after Propofol Tiopental mixture induction.
REFERENCE Anesth Analg 2002; 94: 1207-11 Anesthesiology 2001; 94: 833-9

S-263

GENDER DOES NOT ALTER THE ACCURACY OF TARGET-CONTROLLED INFUSION OF FENTANYL

AUTHORS: **D. H. Moller**[1], A. Bicker[1], P. Passier[2], N. Houwing[2], I. Rampil[1], P. Glass[1];
AFFILIATION: [1]SUNY Stony Brook, Stony Brook, NY, [2]Organon Inc, Oss, Netherlands.

INTRODUCTION: The pharmacokinetics of fentanyl has been well established for more than ten years. However, the initial studies used to assess pharmacokinetic parameters from McClain(1) and Scott(2) are based solely on male subjects. The impact of gender on pharmacokinetics can be determined either by deriving the pharmacokinetic parameters in a group of patients that include males and females and determining if gender is a covariate in the model. Alternatively one can use a predetermined pharmacokinetic set to predict drug concentration and assess if the measured concentrations are different between genders. We used this latter approach to deliver fentanyl via a target-controlled infusion (TCI) device to provide increasing levels of concentration to a group of mixed gender.
METHODS: Nineteen subjects (ten male and nine female) were enrolled in this study. An intra-arterial catheter was placed to obtain plasma samples for assay via Liquid Chromatography/Mass Spectroscopy. A TCI system was used to target Fentanyl levels based on the pharmacokinetics of McClain for a three compartment model with a fixed V_1 as modified by Shafer for patients weighing 40 to 90 kg.(3) (V_1=26.91, K_{10}=0.041, K_{12}=0.185, K_{21}=0.103, K_{13}=0.141, K_{31}=0.02) Each infusion step lasted thirty minutes with samples at t=19 and 26 minutes. For each subject the Percent Performance Error (PPE)[100x(target level – actual level)/(target level)] was then calculated.
RESULTS: A t-test reveals there was no difference in Body Mass Index between genders (24.7 for males and 24.8 for females P = .91) whereas body weight was different (76.4 males vs 65.4 female $P<0.016$). The weighted average (SumProduct corrected for number of data points) of PPE for females was -61.2% (95% CI -15.4 to -107.3) vs -45.7 (95% CI -9.4 to -81.9) for males. Figure 1 shows the PPE by infusion step for both males and females. Horizontal lines represent 95% confidence intervals for respective genders.
DISCUSSION: For both genders, the plasma concentrations were higher than targeted, but not statistically different despite differences in body weight. There was no difference between groups over increasing infusion steps, indicating that the pharmacokinetic rate constants incorporated in the TCI device can be used equally well for either gender, despite both theoretical and measured differences in compartment size. The overlap of 95% CI demonstrates that a pharmacokinetic set that does not include differences based on gender produces equally accurate results for both genders.
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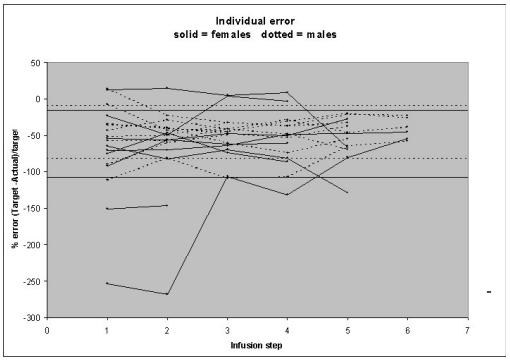

S-264

GENDER DOES NOT EFFECT THE RESPIRATORY DEPRESSANT EFFECT OF FENTANYL

AUTHORS: **D. H. Moller**[1], A. Bicker[1], P. Passier[2], N. Houwing[2], P. Glass[1];
AFFILIATION: [1]SUNY Stony Brook, Stony Brook, NY, [2]Organon Inc, Oss, Netherlands.

INTRODUCTION: Although there have been numerous animal studies comparing opioid based analgesia between genders, little is known about the respiratory depressant effects of the mu opioids in males and female. One of the few studies looking at gender effects of the opioids have shown that the hypercapnic ventilatory response to a dose of morphine is different between genders with males having a significantly blunted response to hypercapnic increases in minute ventilation (1) However, the effects of the more selective phenylpiperdine mu agonists (fentanyl being the prototype) remains uninvestigated. We designed a study where potential gender differences in pharmacokinetics would be minimized and minute ventilation could be assessed at several different concentrations of Fentanyl.
METHODS: Nineteen subjects (10 male and 9 female) were enrolled in this study. An intra-arterial catheter was placed for sampling Fentanyl concentration and assayed by Liquid Chromatography/Mass Spectroscopy. Baseline minute ventilation was assessed in a hyperoxic, hypercarbic environment (7.5% Carbon Dioxide, 92.5% oxygen) with a re-breathing system where CO2 was held constant. Minute ventilation was assessed for one minute after four minutes of breathing the above mixture. A computer controlled infusion device was used to target plasma Fentanyl levels in response to minute ventilation. Each infusion step was 30 minutes in duration with Fentanyl levels assessed at 19 minutes after the start of infusion and MV assessed between minutes 20-25. Increases in plasma concentration of Fentanyl were based on minute ventilation response with a goal of three to six steps per patient to achieve a maximum of 70% depression in minute ventilation.
RESULTS: A Scatter plot of the raw data for the entire population is seen in figure 1. Percent depression in minute ventilation is defined as 100 X (Baseline-experimental)/baseline. Fentanyl concentration is the measured concentration from plasma.
DISCUSSION: Previous investigators have found gender related differences in both respiration and analgesic effect of opiates based on dose(2). Dose only studies do not differentiate pharmacokinetic from pharmacodynamic differences. In this study we exclude potential pharmacokinetic gender differences. In a raw scatter plot of the population data, it does not appear that there are differences between males and females in minute ventilation response to Fentanyl. This study also confirms the large variation in the ventilatory depressant effects of Fentanyl across the population.

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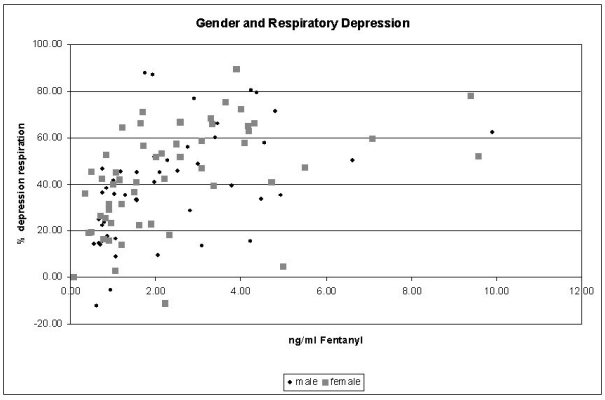

S-265

EFFECT OF THE BETA-ADRENERGIC BLOCKER ATENOLOL ON VOLATILE ANESTHETIC INDUCTION WITH SEVOFLURANE IN ADULTS

AUTHORS: **M. Yamakage**, H. Sasaki, S. Iwasaki, M. Mizuuchi, A. Namiki;
AFFILIATION: Sapporo Medical University School of Medicine, Sapporo, Japan.

INTRODUCTION: Induction of anesthesia can be achieved rapidly with sevoflurane and N2O. Appropriate hypnotic premedication should be used for smoother induction of anesthesia and for the patients comfort. Beta-blocker not only reduces the anesthetic requirement for skin incision during anesthesia but also reduces the bispectral (BIS) index during anesthesia. We hypothesized that premedication with beta-blocker would induce more rapid and smoother induction of anesthesia by sevoflurane.
METHODS: Ttwenty-four ASA physical status I or II adult patients were enrolled in this study. The patients were randomly divided into two groups: a control group (n = 12) and beta-blocker group (n = 12). Each patient in the beta-blocker group was orally premedicated with 25 mg atenolol 1 hr before the anesthesia. Cardiac output and BIS index were monitored. The anesthetic circuit was circulated with 3 L/min O2, 6 L/min N2O and 5% sevoflurane. The patients were instructed to breathe out to residual volume, and then the anesthetic mask was fitted tightly. They were then told to take repeated vital capacity breaths through the mouth. After loss of consciousness had been confirmed, the fresh gas flow rates of O2 and N2O were decreased to 2 L/min and 4 L/min, respectively, and the patients breathing was assisted thereafter. The trachea was intubated 5 min after sevoflurane exposure. Induction time and specific side effects of induction were recorded. Heart rate and mean blood pressure were also recorded. BIS changes during the study were fitted to sigmoid curves, and the amplitude and slope of each curve were calculated. Statistical analyses were performed using the unpaired t-test or one-way ANOVA with Fishers test. A P value less than 0.05 was statistically significant.
RESULTS: Cardiac output before the induction of anesthesia was significantly lower in the beta-blocker group than in the control group. There were no significant differences in the induction time and specific side effects during induction between the groups. The downward sloping part of the BIS index curve in the beta-blocker group was significantly sharper than that in the control group, and the amplitude of the BIS index after induction of anesthesia was significantly lower in the beta-blocker group than in the control group. Hemodynamic changes caused by endotracheal intubation were significantly inhibited in the beta-blocker group but not in the control group.
DISCUSSION: The decrease in the BIS index curve in the beta-blocker group was significantly faster than that in the control group, and the hemodynamic changes caused by endotracheal intubation was significantly inhibited in the beta-blocker group. Oral premedication of 25 mg atenolol is recommended to use for smoother and stable induction of anesthesia using sevoflurane without troublesome hemodynamic suppression.

S-266

THE EFFECT OF SEVOFLURANE ON THE POSTOPERATIVE FUNCTION OF TRANSPLANTED RENAL ALLOGRAFT

AUTHORS: **Y. Takasaki**, T. Fujikawa, K. Takechi, C. Yamashita, K. Nitta;
AFFILIATION: Uwajima Municipal hospital, Uwajima, Ehime, Japan.

INTRODUCTION: Sevoflurane has become widely utilized in clinical anesthesia despite the potential to induce nephrotoxicity. Although clinically significant renal injury has not been reported in association with sevoflurane (1), it remains unclear whether the use of sevoflurane is relatively safe for a specific procedure such as kidney transplantation. Therefore, we conducted this retrospective study in order to compare the effect of sevoflurane on the postoperative function of the renal allograft with that of isoflurane in patients who underwent living kidney transplantation.
METHODS: From 1998 to 2001, 101 adult patients experiencing chronic renal failure underwent living kidney transplantation at Uwajima Municipal hospital. Among these recipients, 22 with multiple kidney transplantations, 14 with ABO mismatching to donors, and 2 with moderate hepatic dysfunction were excluded. We then reviewed the medical and anesthesia records of 63 recipients and corresponding donors enrolled in this study. Because all recipients received either isoflurane or sevoflurane for maintenance of anesthesia, they were divided into either the isoflurane (Iso, n=31) or the sevoflurane (Sev, n=32) group. Each volatile anesthetic was administered at a fresh gas flow of 4-6 l/min with mixture of N_2O (50%) and O_2 (50%) via partial rebreathing anesthesia circuit with soda lime.
RESULTS: There were no differences regarding age (Iso 44.5 ± 2.8 vs. Sev 48.4 ± 2.4 year), body weight (53.6 ± 2.0 vs. 55.2 ± 1.5 kg), preoperative blood urea nitrogen (BUN) and serum creatinine (Cr) values, duration of anesthesia (248.9 ± 8.5 vs. 246.1 ± 8.3 min), and minimum alveolar concentration hour exposure (2.9 ± 0.1 vs. 3.3 ± 0.2) in recipients between the Iso and the Sev groups. There were also no differences regarding age, body weight, preoperative BUN and Cr values in donors between the groups. The period required for the procedure from removal of the renal allograft to the completion of transplantation was not different between the Iso and the Sev groups (53.4 ± 2.9 vs. 56.2 ± 3.0 min). BUN and Cr values measured on the 1st, 2nd, 3rd, and 7th postoperative day significantly decreased compared with the preoperative values in each group, whereas these values on the same postoperative days were not significantly different between the groups. All recipients were postoperatively managed in a similar way in terms of fluid therapy, and the administration of antibiotics and immunosuppressants.

	Group	Preoperation	POD1	POD2	POD3	POD7
BUN (mg/dl)	Iso	58.6 ± 4.6	30.2 ± 1.9*	25.0 ± 2.0*	24.0 ± 2.0*	25.4 ± 2.5*
	Sev	55.9 ± 4.0	30.5 ± 1.8*	26.5 ± 2.6*	25.6 ± 2.9*	30.0 ± 3.1*
Cr (mg/dl)	Iso	8.0 ± 0.57	2.4 ± 0.19*	1.5 ± 0.14*	1.3 ± 0.09*	1.1 ± 0.09*
	Sev	7.4 ± 0.51	2.4 ± 0.20*	1.5 ± 0.15*	1.3 ± 0.14*	1.2 ± 0.12*

Values are expressed as means ± SEM. *P<0.05 compared with preoperative values in both groups
DISCUSSION: This study showed that sevoflurane had no detrimental effects on the function of the transplanted renal allograft during the early postoperative days. In clinical anesthesia for recipients undergoing living kidney transplantation, sevoflurane is safely available without causing adverse renal effect.
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S-267

EFFECT OF NICARDIPINE ON THE ACUTE HEMODYNAMIC RESPONSE TO ELECTROCONVULSIVE THERAPY: A DOSE-RANGING STUDY

AUTHORS: **Y. Zhang**, P. F. White, D. Song;
AFFILIATION: UT Southwestern Medical Cen, Dallas, TX.

INTRODUCTION: Nicardipine is a dihydropyridine calcium antagonist which was introduced into clinical practice for use by intravenous (IV) infusion. Although nicardipine has been used during electroconvulsive therapy (ECT)(1), the optimal dose for controlling the acute hemodynamic responses during ECT has not been previously studied. The object of this study was to evaluate the safety and efficacy of three different doses of nicardipine for preventing acute hypertensive responses during ECT when administered immediately prior to the ECT stimulus.
METHODS: After IRB approval, 20 ASA I-III patients (age 33~87) undergoing ECT procedures (≥ 4 times) were involved in this study. According to a cross-over randomization scheme, each patient was given saline (control), nicardipine 1.25 mg, 2.5 mg or 5 mg IV bolus injection 1-2 min prior to the ECT stimulus at different ECT treatment session. All patients were premedicated with glycopyrrolate 3μg/kg IV, and anesthesia was induced with methohexital, 1 mg/kg IV followed by succinylcholine, 1 mg/kg IV. Rescue treatment for increases in MAP and/or HR >35% of the pre-anesthesia baseline value was labetolol, 5-10 mg IV boluses. Mean blood pressure (MAP) and heart rate (HR) were recorded at 1-2 min interval. Data were expressed as mean±SD. A p-value < 0.05 was considered statistically significant.
RESULTS: In the Control group, the MAP and HR were increased significantly after ECT stimulus (97 vs126 mmHg, 81vs 126 bpm, P<0.05). In the nicardipine 2.5 mg group, the MAP and HR did not increase significantly after the ECT stimulus (P>0.05); In the nicardipine 5 mg group, the HR increased significantly after ECT and the MAP was significantly decreased on awakening (P<0.05). The rescue labetalol dosage in the Control group was significantly greater than in the nicardipine treatment groups (22±10 mg vs11±8 mg, 7±3 mg and 5±0 mg, P<0.05).

	Control (n=19)	Nicardipine 1.25 mg (n=19)	Nicardipine 2.5 mg (n=20)	Nicardipine 5 mg (n=18)
MAP (mmHg) Baseline	97±9	99±10	99±9	102±8
Pre-ECT	102±10	109±11	103±12	108±13
ECT Stimulus	126±23*	120±12	106±10	108±12
Awake	97±12	93±10	95±12	91±12*
HR (bpm) Baseline	81±12	78±8	76±13	74±9
Pre-ECT	96±18	99±14	93±15	98±12
ECT Stimulus	126±23*	120±15	105±20	125±18*
Awake	95±14	94±12	96±14	101±14
Labetolol Dose(mg)	22±10*	11±8	7±3	5±0

CONCLUSION: Nicardipine 1.25 to 5 mg IV boluses produced dose-dependent effects on the hemodynamic response to the ECT stimulus. Nicardipine 2.5 mg was most effective in controlling the acute hemodynamic responses to ECT stimulus. When the nicardipine IV bolus dose was increased to 5 mg, the HR was significantly increased after ECT, and a lower MAP value was observed upon awakening. In order to prevent the acute hemodynamic responses to ECT, nicardipine 2.5 mg IV bolus would appear to be optimal choice dose.
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S-268

THE INFLUENCE OF PRE-ADMINISTRATION OF FLURBIPROFEN ON PLASMA PROSTAGLANDIN E2, CATECHOLAMINES AND HEMODYNAMIC RESPONSES BEFORE AND AFTER TOURNIQUET INFLATION

AUTHORS: **M. Takada**[1], M. Fukusaki[1], Y. Terao[1], K. Yamashita[1], C. Inadomi[1], K. Sumikawa[2];
AFFILIATION: [1]Nagasaki Rosai Hospital, Sasebo, Japan, [2]Nagasaki univ. School of Med., Nagasaki, Japan.

INTRODUCTION: Tourniquet inflation during limb surgery often causes a tourniquet pain and a progressive increase in systemic arterial pressure. This study was designed to evaluate the effect of pre-administration of flurbiprofen, a non-selective cycloxygenase inhibitor, on plasma prostaglandin E2 (PGE2), catecholamines and hemodynamic responses under general anesthesia during knee surgery.
METHODS: Sixteen patients undergoing knee surgery were randomly assigned into two groups. Five min before tourniquet inflation (350mmHg), a placebo (Group A;n=8) or flurbiprofen,1mg/kg (Group B;n=8), was given intravenously in a double blind fashion. Intralipid® was used as a placebo. Anesthesia was maintained with N2O-02-Sevoflurane. Catheters were placed in the ipsilateral femoral vein for collection of local blood and in a vein of the arm for sampling of systemic blood. Measurements included systolic arterial pressure (SAP), plasma concentrations of PGE2 (femoral vein) and norepinephrine (NE), which were measured before tourniquet inflation (T1), 60 to 90 min after starting tourniquet inflation (T2), and immediately after tourniquet deflation (T3). Statistical differences ($P<0.05$)were determined using ANOVA and Student's t test . Data were shown in mean±SD.
RESULTS: Plasma concentrations of PGE2 were 212±63 pg/ml in Group A and 211±51pg/ml in Group B at T1. PGE2 increased significantly at T2 (334±99 pg/ml) in Group A, while it showed no change in Group B. SAP (96±9mmHg in Group A and 107±7mmHg in Group B at T1) significantly increased at T2(127±9mmHg in Group A, $P<0.01$, 134±21mmHg in Group B, $P<0.01$) and significantly decreased at T3 (105±17 mmHg in Group A,110±17mmHg in Group B) as compared with those at T2. Plasma concentration of NE showed no change throughout the time course in either group.
CONCLUSIONS: The results suggest that the pre-administration of flurbiprofen suppressed the increased prostaglandin formation due to tourniquet ischemia, whereas it could not suppress the tourniquet-induced hypertension resulting from continuous stimulation of C-fibers enhanced by the increased prostaglandin formation.
REFERENCES: (1)Pain 2001;89:117-25 (2)Anesthesiology 2001;94:599-603

S-269

EVALUATION OF QT PROLONGATION WITH LOW-DOSE DROPERIDOL ADMINISTRATION FOR ANTIEMETIC PROPHYLAXIS

AUTHORS: **D. Song**, B. Navarette, P. F. White, K. W. Klein;
AFFILIATION: UT Southwestern Medical School, Dallas, TX.

INTRODUCTION: Droperidol has been reported to be highly cost-effective if used in small doses for the prevention of PONV (1). However, a recent FDA "Black box" warning on droperidol indicating its potential of producing QT prolongation has lead to a marked reduction in its us (2). We hypothesized that use of low-dose droperidol for antiemetic prophylaxis is not associated with clinically-significant QT prolongation.
METHODS: Following institutional approval and informed consent, 24 ASA 1-2 outpatients undergoing ear, nose or throat operations were enrolled in this study. Patient with clinically-significant heart disease were excluded from the participation in this study. General anesthesia was induced with propofol, 1.5-2 mg/kg and sufentanil 0.2 mcg/kg IV. Rocuronium 0.6 mg/kg IV was used to facilitate tracheal intubation. After intubation, anesthesia was maintained with desflurane 4% inspired and a sufentanil IV infusion 0.15 mcg/kg/hr. Prior to the surgical incision, patients were randomly assigned to receive a blinded IV study medication consisting of either saline 2 ml or droperidol 0.625 or 1.25 mg for antiemetic prophylaxis. At the end of surgery, all patients received dolasetron 12.5 mg IV. In addition to continuous on-screen ECG monitoring throughout the operation, the standard lead II ECG was recorded before injection of the study medication and every minute after the injection for 10 min. The QTc (i.e., QT corrected for heart rate) was calculated using Bazett formula ($QT/RR^{0.5}$) from the recorded ECG strips. Data were analyzed using ANOVA, with $p<0.05$ considered statistically significant (mean ±SD)
RESULTS: The three treatment groups were similar with respect to demographic data, duration of anesthesia. The changes in the ECG QTc after administration of study medication are summarized below:

	Saline (n=8)	Droperidol 0.625 mg (n=8)	Droperidol 1.25 mg (n=8)
Age (yr)	48±11	42±15	43±15
Weight (kg)	79±18	81±15	84±24
Time of surgery (min)	115±30	97±40	151±113
Baseline QTc (msec)	428±24	431±28	435±38
QTc at 5 min (msec)	430±53	429±67	435±59
QTc at 10 min (msec)	430±33	430±47	440±61
QTc > 440 msec at 10 min (n)	0	1	1
QTc >450 msec at 10 min (n)	0	0	1
ECG abnormalities (n)	0	0	0

DISCUSSION: Use of small dose of droperidol (0.625-1.25 mg IV) for antiemetic prophylaxis was not associated with a clinically-significant prolongation of the QT interval.
REFERENCES: 1) Tang, et al. Anesth Analg 1996; 83:304-13. 2) Gan, et al. Anesthesiology 2002; 97: 287.

S-270

ASSESSING MORPHINE INTERACTIONS WITH ITS GLUCURONIDE METABOLITES- A PRELIMINARY ANALYSIS

AUTHORS: **S. E. Kern**, J. White, E. Wittwer, A. Ratka, T. Egan;
AFFILIATION: University of Utah, Salt Lake City, UT.

INTRODUCTION: Morphine is primarily metabolized to morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G). M6G is considered to be a potent agonist and a significant contributor to the analgesic effect produced by morphine while M3G is considered to be inactive in humans. Since M6G contributes to the analgesic effect after morphine administration, the primary hypothesis of this study is that alterations of the relative amount of M6G produced in an individual will result in alterations in analgesia.
METHODS: After IRB approval, 5 male subjects have been enrolled out of a planned 20 total subjects (10 male/ 10 female) within the age range of 18-40 in this two-period crossover study. During one study session, subjects receive 50 mg of ranitidine IV 30 minutes before the study session. Ranitidine has been shown in both in vitro and in vivo studies to inhibit the formation of M3G and to enhance the production of M6G.[1] A target controlled infusion of morphine is used to achieve a plasma concentration of 10 ng/mL of morphine, which is maintained for a period of 1 hour while assessments of subjects response to a noxious stimulus (pressure algometry) are made. The target concentration of morphine was then increased to 50 ng/mL and held for 1 hour while the measurements were repeated. At the end of this session, measurements of response to stimuli and morphine and metabolite concentrations were made during the washout period. In the crossover session, each subject receives a saline infusion at the beginning of the study rather than the ranitidine dose.
RESULTS: The area under the algometry response curve (AUEC) for the five subjects is shown in Table 1. Four subjects showed an increased level of analgesia (greater AUEC) when ranitidine was administered prior to the morphine infusions. This is likely to be due to increased M6G produced when ranitidine competes for the metabolic enzymes that glucuronidate morphine. One subject did not show this result but had a very low initial baseline algometry reading, which may have elevated his AUEC for the control period. Paired t-test between the ranitidine and placebo results currents shows a p value = 0.16 but the analysis is underpowered.
DISCUSSION: The results indicate that administration of ranitidine produces a increase in morphine effect presumably by increasing the production of M6G. This will be confirmed by plasma concentration measurements which will also allow for the interaction modeling between morphine and its metabolites.
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Supported in part by a grant from the International Anesthesia Research Society.

Impact of ranitidine on the analgesic AUEC of Morphine.

Subject #	AUEC with Ranitidine	AUEC with Saline Placebo
1	1210 lbs-in^{-2}-min	1900 lbs-in^{-2}-min
2	4213 lbs-in^{-2}-min	2628 lbs-in^{-2}-min
3	2638 lbs-in^{-2}-min	1790 lbs-in^{-2}-min
4	5180 lbs-in^{-2}-min	2195 lbs-in^{-2}-min
5	1570 lbs-in^{-2}-min	1200 lbs-in^{-2}-min

Regional

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2-CHLOROPROCAINE VERSUS LIDOCAINE FOR INJECTION PAIN

AUTHORS: **C. T. Grubb**, P. J. Balestrieri, J. J. McAllister, M. C. Bivens, L. R. Goldhar;
AFFILIATION: University of Virginia, Charlottesville, VA.

INTRODUCTION: Local anesthetics are generally painful on skin infiltration. A prior study conducted on volunteers found that 2-chloroprocaine was less painful on injection than both lidocaine and lidocaine with sodium bicarbonate.(1) An inherent flaw in volunteer studies is the introduction of selection bias. We thus sought to determine whether these findings could be generalized to actual patients. To our knowledge, pain on injection of 2-chloroprocaine in a clinical context has not been studied. We conducted a prospective, double-blinded, randomized trial to evaluate the pain on injection of lidocaine versus 2-chloroprocaine.
METHODS: Laboring parturients were prospectively randomized to receive either lidocaine 1% or 2-chloroprocaine 2% for local anesthesia prior to epidural placement. A standardized injection technique with 3 ml of non-carbonated local anesthetic was used for each subject. The anesthetic was injected over 10 seconds using a 1.5-inch, 25-gauge needle without raising a skin wheal. Patients rated their pain during local infiltration using a 100 mm visual analogue scale (VAS, 0-100). A similar VAS score was later obtained to rate the pain from epidural placement alone.
RESULTS: A total of 27 patients were enrolled – 13 in the lidocaine group and 14 in the chloroprocaine group. There were no differences in demographic data between the two groups. Mean VAS +/- SD was 19.5 +/- 15.4 for lidocaine, and 8.6 +/- 8.8 for chloroprocaine (P=0.014). There was no difference between the groups for pain with epidural placement: lidocaine, 27.8 +/- 22.4; chloroprocaine, 28.1 +/- 22.5 (P=NS).
DISCUSSION: The preliminary data from our ongoing study suggests that 2-chloroprocaine is clinically less painful on injection than lidocaine. Furthermore, 2-chloroprocaine is preferable in pregnant patients since no active metabolites reach the fetus.(2) We used lidocaine 1% for our comparison, as it is included in many procedure kits for local anesthesia. Our subjects demonstrated greater than 50% less injection pain with 2-chloroprocaine; yet pain associated with epidural placement did not differ between groups. We have thus found that 2-chloroprocaine is both better tolerated and equally efficacious when compared to 1% lidocaine for local anesthesia prior to epidural placement. Future studies should address the use of 2-chloroprocaine in other patient groups and clinical settings.
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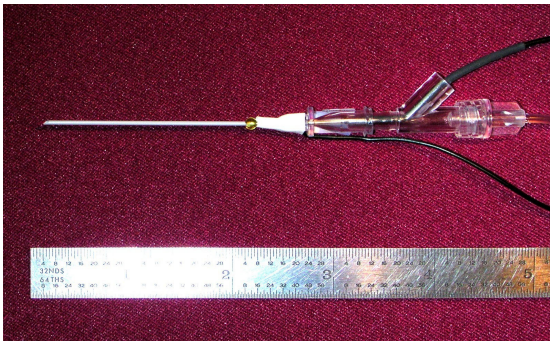
ULTRASOUND GUIDED REGIONAL ANESTHESIA TO TARGET VASCULAR SOURCE-EVALUATION OF CW ULTRASOUND MOUNTED WITHIN A STIMULATING REGIONAL NEEDLE

AUTHORS: **R. A. Greengrass**[1], C. Nightengale[2], N. Feinglass[1], L. Gambino[1], D. Wang[1], S. Trigg[1];
AFFILIATION: [1]Mayo Clinic Jacksonville, Jacksonville, FL, [2]Austin Medical, Austin, TX.

INTRODUCTION: Surface ultrasound guided regional anesthesia has recently been utilized in an effort to enhance performance of regional anesthetic techniques. (1,2). Unfortunately, performance of surface guided ultrasound techniques often requires extra personnel to coordinate the ultrasound probe with the regional anesthetic needle. Recently a device has been developed (Escalon vascular) which contains a piezoelectric crystal mounted within the tip of a 19 gauge insulated needle which allows ultrasound guided direction of a regional needle with the ability to utilize concurrent nerve stimulation if necessary.



(Figure1). We report our initial evaluation of this device compared to a standard nerve stimulating technique.

METHODS: Forty patients undergoing peripheral upper extremity surgery were randomized to receive either ultrasound guided or standard nerve stimulated axillary brachial plexus anesthesia. Patients randomized to the ultrasound guided group had the needle inserted just lateral to the coracobrachialis muscle in the upper axilla following which the tip was directed medial or lateral to detect a vascular source. The needle was then directed toward the source until a clear signal at a low gain was obtained following which 50 ml of 1 % mepivacaine with one in 400,000 epinephrine was injected in increments. The nerve stimulator technique was performed in a standard manner utilizing a 50mm Simuplex (B.Braun) needle following which local anesthetic was incrementally injected. Time from preparation of skin until injection of local anesthetic was determined. Evaluations of block of the sensory and motor components of the ulnar medial, radial and musculocutaneous nerves were performed at 10 minute intervals for 30 minutes.
RESULTS: To date 16 patients have been evaluated. Time for block performance did not differ between the two methods (approximately 8 minutes) The time for onset of hypalgesia and anesthesia in the sensory and motor distributions of the peripheral nerves was similar.
DISCUSSION: Although this trial is in an early phase it appears that the ultrasound guided technique is easy to perform and has a similar success rate compared with a conventional nerve stimulator technique. Although not tested, the combination of ultrasound with nerve stimulation together might provide enhanced success rates compared to utilization of either entity alone. The next phase of the study will be evaluation of a PW-crystal with the capability of even more accurate information regarding the distance of the needle tip from the vascular source. This system should theoretically further enhance success rates as accurately placing the needle within the neurovascular bundle should be possible.
Supported in part by NIH grant. R44GM57750
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S-273

FENTANYL DOES NOT DECREASE THE EFFICACY OF HEMODYNAMIC AND T-WAVE CRITERIA FOR DETECTING INTRAVASCULAR INJECTION OF THE EPINEPHRINE TEST DOSE DURING PROPOFOL ANESTHESIA: A DOSE-RESPONSE STUDY

AUTHORS: **S. Takahashi**[1], H. Toyooka[1], M. Tanaka[2];
AFFILIATION: [1]Dept. of Anesthesiology, Institute of Clinical Medicine, University of Tsukuba, Tsukuba, Japan, [2]Dept. of Anesthesia, Akita University School of Medicine, Akita, Japan.

INTRODUCTION: During propofol and nitrous oxide (N2O) anesthesia, heart rate (HR) (positive if >10 bpm increase), and systolic blood pressure (SBP) criteria (positive if >15 mmHg increase) are reliable indicator for detecting an IV injection of a test dose containing 15 mg epinephrine(1,2). Whether the additional fentanyl during propofol and N2O anesthesia affects the reliability of epidural test dose is still unclear.
METHODS: Following IRB approval and informed consents, 60 ASA I adult patients undergoing elective surgeries were studied. After induction of general anesthesia and tracheal intubation using propofol 2 mg/kg and vecuronium 0.2 mg/kg IV, ventilation was mechanically controlled to obtain normocapnia. Anesthesia was maintained with propofol and 67% N2O in O2. Propofol was administered at the rate of 8 mg/kg/h to maintain plasma concentration at 3 µg/ml. All patients were assigned randomly to 3 groups (n = 20 each)- (1) Control group (normal saline), (2) fentanyl-2 group (fentanyl 2µg/kg), and fentanyl-4 group (fentanyl 4µg/kg)- according to the dose of pretreatment of fentanyl injection IV. Five minutes after pretreatment, the simulated epidural test dose (epinephrine 15µg) was injected IV into a peripheral catheter, and SBP, HR and T-wave amplitude were continuously monitored for 5 min.
RESULTS: In all groups, significant increases in both SBP and HR were observed. All patients developed maximum HR increases >10 bpm and maximum SBP increases >15 mmHg. All patients showed absolute T-wave amplitude decreases by >=25% or >=0.1 mV.
CONCLUSION: Our results suggest that fentanyl <=4 µg/kg does not decrease the reliability of simulated epidural test dose containing epinephrine 15 µg. T-wave amplitude may not be related to the does of fentanyl.
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S-274

OUTCOMES AFTER ACL RECONSTRUCTION: THE EFFECT OF FEMORAL NERVE BLOCK ANALGESIA

AUTHORS: **B. A. Williams**, M. T. Vogt, C. M. Figallo, J. J. Irrgang, M. L. Kentor, C. D. Harner;
AFFILIATION: University of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: We are studying the influence of femoral nerve block analgesia (FNBA) on outcomes after anterior cruciate ligament (ACL) reconstruction. Our hypothesis is that patients undergoing FNBA (versus not) will manifest better self-reported recovery outcomes, physical function outcomes, and objective measures of neuromuscular function. The specific aim is to determine the quality of immediate recovery and extent of reported pain, and to determine whether the use of FNBA is associated with impairment of quadriceps femoris torque output. Comparisons were performed among following 3 treatment groups: (i) single-shot FNB and infusion with levo-bupivacaine, (ii) single-shot FNB with levo-bupivacaine and infusion with saline, and (iii) single-shot sham FNB and infusion with saline.
METHODS: Consented patients (n=89) undergoing ACL reconstruction received spinal anesthesia and were randomized to receive one of the 3 FNBA treatments.A standardized multimodal analgesic technique was used for all patients perioperatively (IV ketamine, intra-articular neostigmine-meperidine-ketorolac, and po rofecoxib and oxycodone). Outcomes throughout the first week after surgery were compared across treatment groups using Verbal Pain Score, SF-8, and the Quality of Recovery [QoR-40] Score [1]. Goniometry with electromyography data were collected 1,3,7, and 12 weeks after surgery, to test postoperative range of motion in extension and flexion, and to determine quadriceps femoris torque output. Assessments at 3, 7, and 12 weeks were performed with SF-36 and Knee Outcome Survey.
RESULTS: Oxycodone consumption differed at POD#1-2. Verbal pain scores with activity differed among treatment groups on POD#1-3. SF-8 scores differed among treatment groups at POD#2-7 for patients undergoing ACL autograft. QoR-40 scores and ability to perform straight leg raise during the first week did not differ. At weeks 1-12, Verbal Pain Scores, SF-36 outcomes, Knee Outcome Survey results, incidence of quadriceps lag, quadriceps torque output, and degrees of knee flexion did not differ among treatment groups.
DISCUSSION: Reflex neuromuscular inhibition is a theoretical risk of temporarily abolishing afferent discharge in a peripheral nerve. Reflex inhibition can lead to muscle weakness, atrophy, immobilization, and joint damage, [2] all of which may lead to gait abnormalities and impede physical therapy progress. These may occur, in theory, despite satisfactory pain relief and patient-reported outcome survey scores. At this time, there is no evidence to indicate any trends toward these adverse sequelae, but further enrollment is required to confirm. During the first week after surgery, there are consistent trends of differences in patient reported outcomes (verbal pain scores, SF-8 scores), and in opioid consumption, based on nerve block treatment group, these trends are accentuated in patients undergoing the more-painful ACL autografts. The differences between treatment groups may be attenuated as a result of the multimodal analgesia techniques incorporated into the protocol for all patients.
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Outcomes after ACL Reconstruction Based On Nerve Block Treatment Group

Treatment Group	POD#1 Oxycodone mg consumption	POD#1 VPS with Movement	POD#4 Straight Leg Raise (%)	POD#4 SF-8 PCS(Autografts)	POD#7 SF-8 MCS(Autografts)	Wk#1 KOS-ADLS (scale 0-100)
A	46	4.3	92	30	55	39
B	38	4.1	94	35	53	44
C	35	2.8	100	34	60	48
Sample Size	n=88	n=88	n=85	n=63	n=58	n=80
P value	0.085	0.047	0.364	0.038	0.012	0.087

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OUTCOMES IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY WITH POSTOPERATIVE CONTINUOUS FEMORAL NERVE CATHETER ANALGESIA

AUTHORS: **M. L. De Ruyter**, K. E. Brueilly, B. L. Howe, A. K. O'Brien, B. A. Harrison, R. A. Greengrass;
AFFILIATION: Mayo Clinic Jacksonville, Jacksonville, FL.

INTRODUCTION. Continuous peripheral nerve catheter infusions for postoperative analgesia in patients undergoing total knee arthroplasty (TKA) may be advantageous (1,2). We hypothesized that a femoral nerve block followed by a continuous femoral nerve catheter infusion in patients undergoing elective TKA would lead to improved physical therapy performance and shortened hospital stay.
METHODS. We retrospectively studied 50 patients who underwent elective, unilateral, primary TKA between June 2001 and September 2002. Patients were divided into one of two groups; those that had received a femoral block and catheter (FNC group) (n=24) and those that had not (non-FNC group) (n=26). Postoperatively, all patients had equal access to intravenous patient controlled narcotic analgesia (PCA). In each group, patients received either a general, epidural or spinal anesthetic; epidural catheters were removed in the a.m. of POD#1.
In the FNC group, patients received their block and catheters via a nerve stimulator technique prior to undergoing anesthesia. The initial bolus was 30 ml 0.5% ropivacaine with epinephrine followed by a postoperative infusion of 0.2% ropivacaine (8-12 ml/hr). Patients were assessed by physical therapists on postoperative day (POD) #1 and #2 with twice daily rehabilitation sessions (four sessions total). The self-reported pain scores (scale 1-10, with 10 = maximum) were recorded at the first physical therapy session. Parameters measured at the first session and at the concluding fourth session included knee range of motion (flexion), physical assistance required to go from the supine to the sitting position (Supine-Sit), and gait assistance. Length of stay (LOS) was recorded.
RESULTS. There was no difference between the two groups in gender, age, or ASA classification. The average pain score at the first POD#1 session for the FNC group = 4.8 and for the non-FNC Group = 4.9 (N.S.). The mean duration of the continuous infusion was 2.6 days. Knee flexion in the FNC group was superior at initial evaluation (76.5 vs. 67.0 degrees ($p<0.05$)) and at the fourth session (101.8 vs. 87.7 degrees ($p<0.05$)). The Supine-Sit score was significantly less (patients were more independent) after the fourth session in the FNC group ($p<0.05$). There was no significant difference in the amount of gait assistance required between the two groups, however there was a trend towards more independence in the FNC group. The mean LOS for FNC group = 3.6 days vs. non-FNC group = 4.2 days ($p<0.05$).
DISCUSSION. Despite no difference in pain scores at initial physical therapy evaluation, the FNC group had better goniometric testing and advanced further in ambulation skills compared to the non-FNC group. Femoral nerve block with continuous femoral nerve infusion for postoperative analgesia following TKA facilitates rehabilitation and clinically and statistically decreases hospital stay.
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2. Anesthesiology 91(1):8-15, 1999

S-276

THE TIP STIFFNESS OF THREE TYPES OF EPIDURAL CATHETERS: AN IN VITRO EVALUATION

AUTHORS: **A. Ishikawa**, Y. Kobayashi, Y. Aoyama, M. Sekiguchi, S. Yajima, H. Sakurai;
AFFILIATION: National Tokyo Medical Center, Tokyo, Japan.

INTRODUCTION: Unintentional subarachnoid catheter migration or placement is a common complication. Catheter migration should be associated with mechanical aspects of epidural catheter (i.e., the catheter tip stiffness). This study was conducted to investigate the tip stiffness of different types of epidural catheters in a special apparatus designed to simulate subarachnoid catheter migration and quantitatively measure the penetration force of these catheters.
METHODS: We studied 3 types of epidural catheters. Three different manufacturers produced the catheters: (catheter A) 20 G Arrow FlexTip catheter (Arrow International, US), (catheter B) 18 G SoftTip catheter (B. Braun, US), and (catheter H) 18 G standard-tip catheter (Hakko, Japan). We obtained 5 samples of each type of catheter. Catheters were stored and studied under the same environmental conditions and were not exposed to extremes of temperature or humidity. In an experimental model, each catheter was placed through the epidural needle and the catheter tip was pulled out by 5 mm from the top of the needle and fixed. Subsequently, while each catheter was put perpendicularly towards a membrane filter (pore size = 0.45 micrometer, thickness = 150 micrometer) stretched over a horizontally placed drum, at a moving speed of 30 mm per minute, the maximum forces developed against the membrane were recorded with a calibrated force transducer. Thereafter, values for each of the three types of catheters were averaged (n = 5 per group). Analysis of variance and post hoc Tukey's t test were used for statistical analysis to identify differences in the maximum force between groups. Results were considered statistically significant at P less than 0.05.
RESULTS: The maximum forces for each of the three types of catheters (A, B, and H) were 56.94 +/- 8.71 gram force (mean +/- SD), 63.85 +/- 4.23, and 36.26 +/- 0.59, respectively. Catheter H showed a significant lower penetration force. Any sample of catheter A alone could not penetrate through a membrane filter, although there is not statistically significant difference between the mean forces for catheters catheter A and B.
CONCLUSIONS: Catheters in our study showed various range of the penetration force which should account for the catheter tip stiffness. Arrow FlexTip catheter should have less capability of subarachnoid migration comparing to the other manufactures. Our methods can be used to assess relative catheter tip stiffness, one important aspect of safety. However, clinical studies are needed to clarify the correlation between the incidence of unintentional subarachnoid catheter migration and the catheter tip stiffness.

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PHARMACODYNAMICS AND PHARMACOKINETICS OF ROPIVACAINE USED FOR UPPER THORACIC EPIDURAL ANESTHESIA

AUTHORS: M. Ma;
AFFILIATION: The 1st Affiliated Hospital, Zhengzhou University, Zhengzhou, China.

This study is to investigate the pharmacodynemics and pharmacokinetics of ropivacaine, to confirm the necessity of ropivacaine with adrenaline for upper thoracic epidural anesthesia (UTEA).

MATERIAL AND METHOD: This study included 20 female patients scheduled to undergo breast surgery under contious UTEA(ASAI~II, aged 20~47 years). They were randomly divided into Group RP (n=10)and Group RPAD (ropivacaine with adrenaline group, n=10). UTEA was performed at the T3~4 interspace by using epidural catherter. Patients of Group RP and RPAD received 5mg²L-1 RP 1.3mg²kg-1 and 5mg²L-1 RP 1.3mg·kg-1 plus adrenaline 5μg · kg-1 epidurally in 2 min, respectively. Sensory block was determined using a blunt point needle to test for loss and return of sensation to pin-prick. Motor block was assessed using a myodymamia scale (0~V). Blood samples were taken immediately prior to the start of epidural administration time 0, 10, 20, 30, 40, 50, 60, 90, 120, 150, 180, 240, 360 and 720 min after injection. The total plasma concentration of RP was determined by HPLC.The pharmacokinetic parameters were determined from plasma concentration-time data with 3P97 software package.

RESULTS: (1) The Group RP and RPAD were similar with respect to epidural block characteristics. No significant difference in onset time, time to maximum spread, segment of spinal nerve blocked and onset time of motor block were observed between groups (p>0.05). The number of patients with different degrees of motor block was similar in the two groups (p>0.05). Compared with Group RP, the duration of sensory and motor block prolonged slightly, and no significant difference observed. (2) The plasma concentration of RP in Group RP was higher than that in Group RPAD at 10~360min relation time-point and had significant difference (p<0.05 or p<0.01). The concentration-time curve in the Group RP and RPAD were adequately fitted to two-compartment open model.The pharmacokinetics parameters see table 1. The Cmax and AUC of Group RPAD were lower than that of Group RP and had significant difference (p<0.01).

CONCLUSION: (1)Ropivacaine 5mg²mL-1 used for UTEA of breast surgery patients, the onset time of sensory block was short, the extent of block was extensive, the duration was long and the analgesia effect was satisfactory. The onset time of motor block was slower than that sensory block. The degree of motor block was less and the duration of motor block was shorter than that of sensory block. The addition of adrenaline did not improve markedly the pharmacodynemic characteristics by ropivacaine 5mg²mL-1. (2)The addition of adrnaline significantly decreased the systemic plasma concentration, Cmax and AUC of ropivacaine 5mg²mL-1 after epidural injection in anesthetized patients. Therefore, the addition of adrenaline 5μg·mL-1 to ropivacaine may be a useful strategy to reduce the risk of systemic toxicity from systemic absorption of epidural ropivacaine.

Table1. The comparison of ADb on the pharmacokinetics parameters of RPa

Group	T1/2ka (h)	T1/2 (h)	Tmax (h)	Cmax (mg·L-1)	AUC (mg·h·L-1)	Cl/F (L·h-1)	V/F (L·kg-1)
RP Along	0.06±0.05	3.65±0.82	0.36±0.07	1.15±0.33	4.84±0.97	0.29±0.06	1.02±0.40
RP+AD	0.08±0.05	3.90±1.36	0.42±0.12	0.75±0.19	3.27±1.02	0.45±0.12	1.38±0.50
p	>0.05	>0.05	>0.05	<0.01	<0.01	>0.05	>0.05

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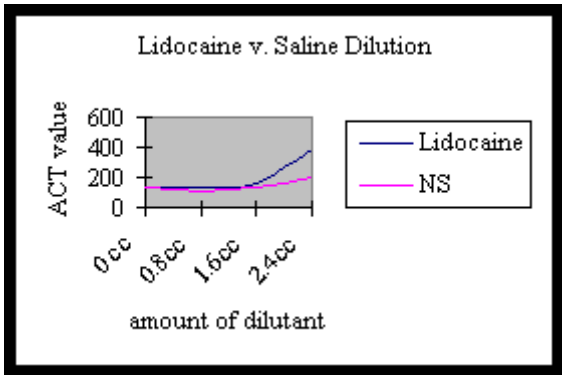
THE EFFECTS OF SALINE AND LIDOCAINE ON CLOTTING TIMES OF HEMODILUTED WHOLE BLOOD

AUTHORS: S. B. Groudine, K. El-Mohtar, F. Strickler, A. Plunkett;
AFFILIATION: Albany Medical Center, Albany, NY.

INTRODUCTION: Lidocaine can exert anticoagulation effects. Epidural hematoma is an important concern and the advisability of immediately dosing an epidural catheter after a traumatic insertion remains unknown. Immediate dosing will result in a high concentration of local anesthesia mixing with the fresh blood in the epidural space and around the traumatized blood vessel. Others have warned that this anticoagulant property of lidocaine can adversely effect the success of epidural blood patches[1]. The effects on the ACT (Activated Clotting Time) of various concentrations of lidocaine and saline mixed with fresh whole blood were compared to see if hemodilution with lidocaine impairs the coagulability of blood more than saline or the lack of hemodilution.

METHODS: After IRB approval 5 Medtronic Coagulation Time ACT machines were checked against controls for study use. An intravenous catheter was inserted in 3 of the authors and flushed with 2cc. of Normal Saline (NS). Before every blood draw 5cc of blood was withdrawn from the catheter and wasted. Blood was drawn from each volunteer 7 times. ACTs were obtained on the blood immediately. Blood was tested undiluted, and with 0.8 ,1.6, 2.4 cc's of 2% lidocaine and 0.8,1.6,2.4 cc's of NS to a total volume of 4ccs. These ACT machines use 0.4cc of blood for each test and can run two samples at the same time requiring 4ccs for ten tests. Results were pooled and compared using a Students T-Test with 95% confidence intervals and p< .05 for significance

RESULTS: Hemodilution with NS improved coagulation at .8cc/4cc dilution(mean ACT 109 v.128 ACT with undiluted blood). At all levels, lidocaine diluted blood had significantly greater ACTs than NS diluted blood. The difference increased with increasing concentrations of lidocaine.



DISCUSSION: Blood clotted fastest when it was diluted with .8cc/4cc of NS. This hypercoagulation effect has been previously described[2]. It was not seen when a similar dilution with lidocaine was undertaken. This study demonstrates that ACT is fastest with mild NS hemodilution and increased significantly with increasing hemodilution with lidocaine. In situations such as a traumatic epidural insertion immediate dosing of the catheter with lidocaine may impair the speed of coagulation. Coagulation of the epidural blood might be fastest if a small dose of NS is injected into the catheter. This in vitro study suggests that this is better than just capping the catheter. Additionally, mixing some NS with the blood before epidural injection during a blood patch may be beneficial. In vivo studies will be necessary to assess the effectiveness of these strategies in patients.

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S-279

SELECTIVE SPINAL ANESTHESIA TO EXPEDITE POSTOPERATIVE MOBILITY: HYPERBARIC SOLUTIONS OF BUPIVACAINE AND LEVOBUPIVACAINE COMPARED

AUTHORS: **R. K. Kan**, J. W. Chiu;
AFFILIATION: KK Women's & Children's Hospital, Singapore, Singapore.

INTRODUCTION: The use of low dose intrathecal agents has increased the selectivity and precision of spinal anesthesia while allowing the preservation of motor function (1). This study aims to compare subarachnoid administration of levobupivacaine (LB) with racemic bupivacaine (RB) in patients undergoing minor gynecological procedures.
METHODS: In this ongoing prospective, double-blind trial, 18 patients were randomized to receive either 5mg hyperbaric levobupivacaine + 25mcg fentanyl in 2.5ml normal saline (Group LB) or 5mg hyperbaric racemic bupivacaine + 25mcg fentanyl in 2.5ml normal saline (Group RB). Sensory block (loss of pinprick sensation), motor block (modified Bromage scale: 0= no motor block, 1= unable to perform straight leg raise, 2= unable to flex knee, 3= unable to move ankle joint), analgesic characteristics and post-block complications were evaluated. Statistical analysis comprised the Student's *t*-test and the Wilcoxon ranked sum test.
RESULTS: Patient characteristics in the 2 groups were not statistically different. 6 (75%) patients in the LB group did not experience any motor block while the remaining 2 patients (25%) had full recovery of muscle strength (Bromage scale 0) within 30minutes. In contrast, 8 (80%) patients in the RB group had a Bromage score of 2 or more. Only 2 (20%) patients in the RB group were able to perform a straight leg raise 60minutes after intrathecal drug administration. Others variables studied are depicted in Table 1.
DISCUSSION: The combination of hyperbaric 0.5% LB with 25mcg fentanyl conferred better patient satisfaction compared to RB with fentanyl. Motor block associated with LB was minimal and had a faster resolution. This may allow for PACU bypass, earlier postoperative ambulation and quicker hospital discharge.
REFERENCES: (1) Anesth Analg 2002; 94: 565-68

Table 1: Spinal block characteristics of the 2 study groups

	LB (*n*=8)	RB (*n*=10)
Median dermatome reached	T7	T6
Mean time (+/- standard deviation) to reach highest dermatome in minutes	4.0 +/- 1.1	5.4 +/- 3.0
Median motor block attained expressed using modified Bromage scale	0	2
Percentage of subjects able to perform straight leg raise after 60minutes	100*	20
Mean satisfaction score (+/- standard deviation) using VAS 0-100	95.6 +/- 7.3*	86.1 +/- 9.9

* $p<0.05$

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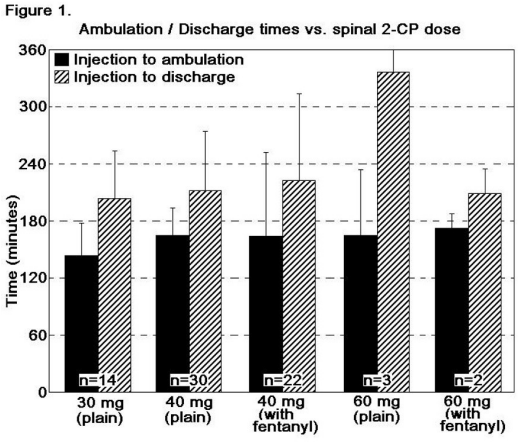
SPINAL 2-CHLOROPROCAINE FOR SURGERY: 10 MONTH EXPERIENCE

AUTHORS: **J. R. Yoos**, D. J. Kopacz;
AFFILIATION: Virginia Mason Medical Center, Seatte, WA.

INTRODUCTION: Spinal 2-Chloroprocaine (2-CP) is currently being investigated as a safe and effective short-acting alternative to lidocaine, which is known to frequently cause transient neurologic symptoms (TNS) in surgical patients (1). TNS has not been reported with 2-CP in human volunteers in doses ranging from 30-60 mg and appears to provide an excellent level of surgical anesthesia (2). The purpose of this retrospective study is to describe the experience with spinal 2-CP in surgical patients at our institution during its first ten months of clinical usage.
METHODS: Hospital records of all patients receiving 2-CP spinal anesthesia at Virginia Mason Medical Center from September, 2002 through June, 2003 were reviewed. Data collected include ASA class, surgical procedure, spinal 2-CP dose, adjuvant agents added, time of injection, block height, surgical start and end time, sedation and vasopressors given, time of first recorded ambulation, PACU side effects and discharge time.
RESULTS: During this 10 month period, 122 patients received spinal 2-CP (27 ASA class I, 73 ASA-II, 21 ASA-III, and 1 ASA-IV). The majority of patients had ambulatory procedures including 40 orthopoedic (knee arthroscopy), 30 general surgical (inguinal hernia repair, vericose vein stripping), 23 gynecologic (hysteroscopy), 29 genitourinary (cystoscopy, TURBT). Surgical time was longer than anticipated in four cases (98.7±11.8 minutes, mean±SD), requiring conversion to general anesthesia. These patients were therefore excluded from further analysis. Surgical procedure time in the remaining 118 patients was 32.3±18.4 minutes. Time from placement of block to end of surgical procedure was 53.1±20.7 minutes. None of these patients required any additional anesthesia. Times to ambulation and discharge were 155.1±34.7 and 207.9±69.4 minutes, respectively (Figure 1). Eleven patients complained of nausea in the PACU with symptom resolution before discharge (eight patients required treatment with ondansetron). Two patients complained of itching in the PACU, both of whom had fentanyl added to spinal 2-CP, with one requiring treatment with a single dose of benadryl 25 mg. Five patients were unable to void upon first attempt (four patients had TURBT). No patients reported symptoms of TRI. 2-CP is now the predominant short-acting spinal anesthetic used at VMMC.
DISCUSSION: 2-CP spinal anesthesia has proven to be a safe and effective alternative to lidocaine for ambulatory surgical procedures in the first 122 patients reviewed from our institution. All patients had adequate analgesia for surgery of an hour or less in duration, with a predictable regression of block height. No patients reported transient neurological symptoms after surgery.
REFERENCES: 1) Kouri M, Kopacz D. Spinal 2-chloroprocaine: A comparison to lidocaine in human volunteers. Anesth Analg 2003 (in press). 2) Smith KN, Kopacz D. Spinal 2-chloroprocaine: A dose ranging study and the effect of added epinephrine. Anesth Analg 2003; (96)2S: S-285.

Figure 1.



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THE INCIDENCE OF THE HEARING LOSS AFTER SPINAL ANESTHESIA IN YOUNG VERSUS ELDERLY PATIENTS

AUTHORS: **P. P. Nicolcescu**, F. O. Purcaru, I. P. Georgescu, A. I. Georgescu, I. N. Sosea, V. C. Calina;
AFFILIATION: University Hospital no1 Craiova, Craiova, Romania.

INTRODUCTIONS: We studied the incidence of hearing loss after spinal anesthesia in young versus elderly patients.
METHODS: After obtaining institutional approval and informed consent 120ASA physical status I or II male patients were included for this study. All patients were scheduled to undergo elective inghinal herniography. The patients were divided into two equal groups: group A: 60 patients aged 35 year or younger , and group B : 60 patients aged 35 year or older. The patients were evaluated by pure tone audiometry: low frequencies, speech frequencies and high frequencies on the day before and 2 day after spinal anesthesia. The audiologist was blinded to cases. Spinal anesthesia was performed into the L3-L4 interspace with a 22 gauge Quincke in the sitting position with a midline approach .3 ml isobaric Bupivacaine 0.5% was injected. Statistical analysis was performed by using Student t test for demographic data and the Mann Whitney tests for comparison of variation in hearing threshold with frequencies. The chi2 test was used for comparison of cases found to have hearing loss > 10 dB, $p<0.05$ was considered significant.
RESULTS: The low frequency hearing loss in elderly patients (group B) was significantly less than that found in young patients (group A) $p<0.01$.Hearing loss in high and speech frequencies was not significantly different. Mild hearing loss occurred more frequently in group A (young patients) (61% vs 19%, $p=0.021$)
CONCLUSION: The transient hearing loss was approximately 3 times more common in young patients. Although ,hearing loss is not an uncommon complication of spinal anesthesia ,the patient's age and the diameter of the needle may be an etiological factors.
REFERENCES: Anesth Analg 2002; 95:198-203
Reg Anesth 1997;22:539-42

S-282

POSTOPERATIVE PROTEIN SPARING WITH EPIDURAL ANALGESIA AND HYPOCALORIC DEXTROSE

AUTHORS: **T. P. Schricker**, F. Carli, L. Wykes, S. Meterissian;
AFFILIATION: McGill University, Montreal, PQ, Canada.

INTRODUCTION: Oxidative protein loss after surgery when coupled with prolonged inadequate oral intake may adversely affect the postoperative clinical course. Administration of dextrose spares protein but necessitates the infusion of large quantities. Epidural analgesia has been shown to facilitate glucose utilization (1) thereby presumably reducing the amount of dextrose required to attenuate protein loss.
To confirm this assumption, we investigated anticatabolic effects of epidural analgesia in patients receiving intravenous hypocaloric dextrose, the hypothesis being that epidural analgesia prevents the increase in amino acid oxidation after colorectal surgery.
METHODS: The study was conducted in accordance with the Declaration of Helsinki. We randomly allocated ten metabolically healthy patients scheduled for colorectal surgery to receive general anesthesia combined with intraoperative epidural anesthesia (bupivacaine) and postoperative epidural analgesia (bupivacaine/ fentanyl, n=10), and ten to receive general anesthesia followed by patient controlled analgesia with intravenous morphine. All patients received a peripheral 72-h infusion of hypocaloric dextrose 10% from the day before until the second day after surgery. Dextrose infusion was adjusted to provide 50% of the patient`s resting energy expenditure measured by indirect calorimetry. Whole body leucine kinetics (leucine oxidation, leucine rate of appearance, non-oxidative leucine disposal) were determined by L-[1-^{13}C]leucine on the day prior to sugery and on the second postoperative day. Results are expressed as mean± 1SD. Statistical analysis was by the Mann-Whitney U test.
RESULTS: In the intravenous analgesia group leucine oxidation increased from 19.3± 3.9 to 28.3± 6.4$\mu mol \cdot kg^{-1} \cdot h^{-1}$ ($p<0.01$ vs. epidural analgesia group) after surgery, whereas in the epidural analgesia group leucine oxidation did not change (preoperative 21.1± 5.8$\mu mol \cdot kg^{-1} \cdot h^{-1}$, postoperative 20.7± 5.2$\mu mol \cdot kg^{-1} \cdot h^{-1}$). The leucine appearance rate, an estimate of protein breakdown, and non-oxidative leucine disposal, an estimate of protein synthesis, increased to a similar extent in both groups.
DISCUSSION: Assuming that leucine represents 8% of body protein epidural analgesia and hypocaloric dextrose diminished the oxidative protein wastage after surgery by 22 g or more than 100 g of muscle mass per day. This extent of protein sparing is greater than that previously achieved with pharmacological or nutritional interventions in patients undergoing colorectal surgery (2).
REFERENCES
(1) Am J Physiol 2000; 279: 646-53, (2) Shock 1998; 10: 155-60, Supported by a grant from the International Anesthesia Research Society.

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