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
77th Clinical and Scientific Congress
New Orleans, LA
March 21-25, 2003

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IARS SCA SPA SAMBA ISAP STA

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Authors submitting abstracts have certified that if human research is reported, approval by an institutional human research committee has been obtained, or if animal research is reported, the usual standards and guidelines for animal care have been followed. Material published in this supplement has not undergone review by the Editorial Board of Anesthesia and Analgesia. Any of the abstracts in this supplement may have been transmitted by the author to IARS in various forms of electronic medium. IARS has used its best efforts to receive and format electronic submissions for publication in this supplement but has not reviewed each abstract for the purpose of textual error correction and is not liable in any way for any formatting, textual or grammatical error or inaccuracy.

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SOCIETY OF CARDIOVASCULAR ANESTHESIOLOGISTS (SCA) is a nonprofit, educational foundation and is a recognized sub-specialty organization of the American Society of Anesthesiologists. Membership dues for 2003 are $175 which include a reduced-rate subscription to ***ANESTHESIA & ANALGESIA***. *Residents*: see *Joint Resident Membership* information below. All SCA membership payments and correspondence should be sent to: SCA, 2209 Dickens Road, P.O. Box 11086, Richmond, Virginia 23230-1086. Telephone (804) 282-0084; Fax (804) 282-0090; e-mail: sca@societyhq.com; Web site: www.scahq.org

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SOCIETY FOR TECHNOLOGY IN ANESTHESIA (STA) The Society for Technology in Anesthesia is an international organization of physicians, engineers, students, and others with an interest in anesthesia-related technologies. Membership is open to all who are interested. The Society's mission is to improve the quality of patient care by improving technology and its application. The Society promotes education and research, collaborates with local, national, and international organizations, sponsors meetings and exhibitions, awards grants, and recognizes achievement. Membership dues for 2003, Regular Membership is $100 annually; Student/Resident membership is free. Add *Anesthesia and Analgesia* for only $85. All STA correspondence should be sent to: STA, Attn: Beverlee Anderson, PMB 300, 223 N. Guadalupe, Santa Fe, NM 87501. Telephone (505) 983-4923; Fax (505) 983-5109; e-mail: STA@AnesTech.org; Web site: www.AnesTech.org

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IARS 77th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Ambulatory Anesthesia

(S-1) Kranke, P., Saturday 8:00
(S-2) Ma, H., Saturday 8:00
(S-3) Van Den Kerkhof, E.G., Saturday 8:00
(S-4) Vila Jr., H., Saturday 8:00
(S-5) Tang, J., Saturday 8:00
(S-6) El-Hadidy, A., Saturday 8:00
(S-7) Kohjitani, A., Saturday 8:00
(S-8) Recart, A., Saturday 8:00
(S-9) Recart, A., Saturday 8:00
(S-10) Rafizadeh, M., Saturday 8:00
(S-11) Ates, Y., Saturday 8:00
(S-12) Fang, Z., Saturday 8:00
(S-13) Stice-Beredino, L.L., Saturday 8:00

Cardiovascular Anesthesia – Basic Science

(S-14) Kevin, L.G., Monday 8:00
(S-15) de Klaver, M.M., Monday 8:00
(S-16) Novalija, E., Monday 8:00
(S-17) Dworschak, M., Monday 8:00
(S-18) Kevin, L.G., Monday 8:00
(S-19) Mersmann, J., Monday 8:00
(S-20) Hara, T., Monday 8:00
(S-21) Hoffman, W.E., Monday 8:00
(S-22) Schwinn, D.A., Monday 8:00
(S-23) Westphal, M., Monday 8:00
(S-24) Fujisawa, T., Monday 8:00
(S-25) Sumita, S., Monday 8:00
(S-26) Hare, G.T., Monday 8:00
(S-28) Yoshimura, M., Monday 8:00
(S-29) Pandit, J.J., Monday 8:00
(S-30) Gust, A.M., Monday 8:00
(S-31) Urdaneta, F., Monday 8:00
(S-32) Hu, G., Monday 8:00
(S-33) Shiga, T., Monday 8:00
(S-34) Tse, J., Monday 8:00
(S-35) Yang, H., Monday 8:00
(S-36) Jahn, U.R., Monday 8:00

Cardiovascular Anesthesia - Clinical

(S-37) Girgenti, G.T., Sunday 8:00
(S-38) Park, K.W., Sunday 8:00
(S-39) Fukusaki, M., Sunday 8:00
(S-40) Aggarwal, S., Sunday 8:00
(S-41) Akhtar, S., Sunday 8:00
(S-42) Pandit, J.J., Sunday 8:00
(S-43) Pandit, J.J., Sunday 8:00
(S-44) Praetel, C., Sunday 8:00
(S-45) Bar-Yosef, S., Sunday 8:00
(S-46) Riedel, B.J., Sunday 8:00
(S-47) Fortier, J.D., Sunday 8:00
(S-48) Fortier, J.D., Sunday 8:00
(S-49) Isetta, C.J., Sunday 8:00
(S-50) Xia, Z., Sunday 8:00
(S-51) Xia, Z., Sunday 8:00
(S-52) Ansley, D.M., Sunday 8:00
(S-53) Gramlich, L., Tuesday 8:00
(S-54) Royston, D., Tuesday 8:00
(S-55) Takagi, E.N., Tuesday 8:00
(S-56) Ramachandran, S., Tuesday 8:00
(S-57) Welsby, I.J., Tuesday 8:00
(S-58) Donahue, B.S., Tuesday 8:00
(S-59) Yoshikawa, D., Tuesday 8:00
(S-60) Ishida, K., Tuesday 8:00
(S-61) Kawahara, F., Tuesday 8:00

Critical Care and Trauma

(S-62) Pandit, J.J., Monday 8:00
(S-63) Fan, Q., Monday 8:00
(S-64) Fan, Q., Monday 8:00
(S-65) Fan, Q., Monday 8:00
(S-66) Joshi, G.P., Monday 8:00
(S-67) Ogunnaike, B., Monday 8:00
(S-68) Toma, G., Monday 8:00
(S-69) Ghori, K., Monday 8:00
(S-70) Menzebach, A., Monday 8:00
(S-71) Yuan, S., Monday 8:00
(S-72) Johnson, C., Monday 8:00
(S-73) Bagchi, A., Monday 8:00
(S-74) Oku, S., Monday 8:00
(S-75) Urban, M.K., Monday 8:00
(S-76) Jahr, J.S., Monday 8:00
(S-77) Jahr, J.S., Monday 8:00
(S-78) Westphal, M., Monday 8:00
(S-79) McGlinch, B.P., Monday 8:00
(S-80) Scher, C.S., Monday 8:00
(S-81) Tungpalan, L., Monday 8:00
(S-82) Nakamura, T., Monday 8:00

Economics; Education and Patient Care

(S-83) Anderson, K.J., Saturday 8:00
(S-84) Kinsella, J., Saturday 8:00
(S-85) Maroof, M., Saturday 8:00
(S-86) Bilgin, H., Saturday 8:00
(S-87) Hilmi, I.A., Saturday 8:00
(S-88) Greenfield, M.V., Saturday 8:00
(S-89) Kovac, A., Saturday 8:00
(S-90) Minogue, S.C., Saturday 8:00
(S-91) Niemann, C.U., Saturday 8:00
(S-92) Lew, M.W., Saturday 8:00
(S-93) Cattano, D., Saturday 8:00
(S-94) Havidich, J.E., Saturday 8:00
(S-95) Turner, C.R., Saturday 8:00

IARS 77th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

(S-96) Cohen, I.T., Saturday 8:00
(S-97) Agarwala, A.V., Saturday 8:00
(S-98) Cook, R.I., Saturday 8:00
(S-99) Weinger, M.B., Saturday 8:00
(S-100) Sharma, R., Saturday 8:00
(S-101) Seiden, S., Saturday 8:00
(S-102) Ramachandran, S., Saturday 8:00
(S-103) Vohra, P., Saturday 8:00
(S-104) Souders, J.E., Saturday 8:00
(S-105) Weaver, J.M., Saturday 8:00
(S-106) Strum, D.P., Saturday 8:00
(S-107) Strum, D.P., Saturday 8:00
(S-108) Greenfield, M.V., Saturday 8:00
(S-109) Orkin, F.K., Saturday 8:00
(S-110) Singbartl, G., Saturday 8:00
(S-111) Singbartl, G., Saturday 8:00
(S-112) Singbartl, G., Saturday 8:00
(S-113) Singbartl, G., Saturday 8:00
(S-114) Knuepfer, P.E., Saturday 8:00
(S-115) Nakatsuka, M., Saturday 8:00

Equipment/Monitoring

(S-116) Sanderson, I.C., Sunday 8:00
(S-117) Sanderson, I.C., Sunday 8:00
(S-118) Brock-Utne, J.G., Sunday 8:00
(S-119) Rosenbaum, A., Sunday 8:00
(S-120) Rosenbaum, A., Sunday 8:00
(S-121) Hamza, M.A., Sunday 8:00
(S-122) Bryan, Y., Sunday 8:00
(S-123) Ryu, H., Sunday 8:00
(S-124) Robinson, M.B., Sunday 8:00
(S-125) El-Fandy, G., Sunday 8:00
(S-126) Nagata, O., Sunday 8:00
(S-127) Recart, A., Sunday 8:00
(S-128) Recart, A., Sunday 8:00
(S-129) Gasanova, I., Sunday 8:00
(S-130) Nishiyama, T., Sunday 8:00
(S-131) Nishihara, F., Sunday 8:00
(S-132) Manyam, S.C., Sunday 8:00
(S-133) Lennmarken, C., Sunday 8:00
(S-134) Deal, E.R., Sunday 8:00
(S-135) Viertiö-Oja, H., Sunday 8:00
(S-136) Hemmerling, T.M., Sunday 8:00
(S-137) Martin, G., Monday 8:00
(S-138) Roy, R.J., Monday 8:00
(S-139) Marcus, R.L., Monday 8:00
(S-140) Lichtenthal, P.R., Monday 8:00
(S-141) Yem, J.S., Monday 8:00
(S-142) Diemunsch, P., Monday 8:00
(S-143) Demirkiran, O., Monday 8:00
(S-144) Ito, S., Monday 8:00
(S-145) Aguilar, G., Monday 8:00
(S-146) Demirkiran, O., Monday 8:00
(S-147) Soto, R.G., Monday 8:00
(S-148) Lirk, P., Monday 8:00
(S-149) Tang, Y., Monday 8:00
(S-150) Schultz, J.R., Monday 8:00
(S-151) Uchida, I., Monday 8:00
(S-152) Verghese, S.T., Monday 8:00
(S-153) Horowitz, P.E., Monday 8:00
(S-154) Lewis, K., Monday 8:00
(S-155) Kawasaki, J., Monday 8:00
(S-156) Chen, F., Monday 8:00
(S-157) Hagberg, C.A., Monday 8:00
(S-158) Kumar, R., Monday 8:00
(S-159) Bolis, R.S., Monday 8:00
(S-160) Paulsen, A., Monday 8:00
(S-161) Chu, L.F., Monday 8:00
(S-162) Kling, J.C., Monday 8:00
(S-163) Yilmazlar, A., Monday 8:00
(S-164) Yilmazlar, A., Monday 8:00

Neuroanesthesia

(S-165) Kimotsuki, H., Saturday 8:00
(S-166) Bekker, A., Saturday 8:00
(S-167) Homi, H.M., Saturday 8:00
(S-168) Brock-Utne, J.G., Saturday 8:00
(S-169) Ghori, K., Saturday 8:00
(S-170) Paisansathan, C., Saturday 8:00
(S-171) Kitano, T., Saturday 8:00
(S-172) Verplancke, T., Saturday 8:00
(S-173) Pivalizza, E.G., Saturday 8:00
(S-174) Giffard, R.G., Sunday 3:00

Obstetric Anesthesia

(S-175) Chin, K., Sunday 8:00
(S-176) Uchida, J., Sunday 8:00
(S-177) Terui, K., Sunday 8:00
(S-178) Finegold, H., Sunday 8:00
(S-179) Denenberg, H., Sunday 8:00
(S-180) Megally, M., Sunday 8:00
(S-181) Bullough, A.S., Sunday 8:00
(S-182) Gonzalez, R., Sunday 8:00
(S-183) Cohen, S., Sunday 8:00
(S-184) Rinne, T., Sunday 8:00
(S-185) Chiu, J., Sunday 8:00
(S-186) Waibel, H.A., Sunday 8:00
(S-187) Ramanathan, S., Sunday 8:00

IARS 77th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Pain – Basic Sciences

(S-188) Lu, Y., Sunday 8:00
(S-189) Kroin, J.S., Sunday 8:00
(S-190) Kroin, J.S., Sunday 8:00
(S-191) Buvanendran, A., Sunday 8:00
(S-192) Nishiyama, T., Sunday 8:00
(S-193) Michael, R., Sunday 8:00
(S-194) Schumacher, M.A., Sunday 3:00

Pain - Clinical

(S-195) Recart, A., Saturday 8:00
(S-196) Munir, M.A., Saturday 8:00
(S-197) Aoki, T., Saturday 8:00
(S-198) Takada, M., Saturday 8:00
(S-199) Mamiya, K., Saturday 8:00
(S-200) Chaudhuri, K., Saturday 8:00
(S-201) Miguel, R.V., Saturday 8:00
(S-202) Kopf, A., Saturday 8:00
(S-203) Buvanendran, A., Saturday 8:00
(S-204) Blum, S.L., Saturday 8:00
(S-205) Coloma, M., Saturday 8:00
(S-206) Urban, M.K., Saturday 8:00
(S-207) Domsky, R., Saturday 8:00
(S-208) Khaleghi, B., Saturday 8:00
(S-209) Gratz, I., Saturday 8:00
(S-210) Ishikawa, A., Saturday 8:00
(S-211) She, S., Saturday 8:00
(S-212) Orkin, F.K., Saturday 8:00
(S-213) Panchal, S., Saturday 8:00
(S-214) Gonzalez, R., Saturday 8:00
(S-215) Yokoyama, M., Saturday 8:00
(S-216) Lierz, P., Saturday 8:00
(S-217) Hsu, E.S., Saturday 8:00
(S-218) Buvanendran, A., Saturday 8:00

Pediatric Anesthesia

(S-219) Verghese, S.T., Saturday 8:00
(S-220) Verghese, S.T., Saturday 8:00
(S-221) Mori, T., Saturday 8:00
(S-222) Kussman, B.D., Saturday 8:00
(S-223) Splinter, W., Saturday 8:00
(S-224) Bryan, Y., Saturday 8:00
(S-225) Orkin, F.K., Saturday 8:00
(S-226) Splinter, W.M., Saturday 8:00
(S-227) Okamura, H., Saturday 8:00

Pharmacology - Basic Science

(S-228) Fields, A.M., Sunday 8:00
(S-229) Fields, A.M., Sunday 8:00
(S-230) Fields, A.M., Sunday 8:00
(S-231) Fields, A.M., Sunday 8:00
(S-232) Yuan, C., Sunday 8:00
(S-233) Mitsuyo, T., Sunday 8:00
(S-234) Nakamura, S., Sunday 8:00
(S-235) Xia, Z., Sunday 8:00
(S-236) Lee, C., Sunday 8:00
(S-237) Gyermek, L., Sunday 8:00
(S-238) Lee, Y., Sunday 8:00
(S-239) Lirk, P., Sunday 8:00
(S-240) Shibata, O., Sunday 8:00
(S-241) Girard, T., Sunday 8:00
(S-242) Hahn, R.G., Sunday 8:00
(S-243) Michael, R., Sunday 8:00
(S-244) Uchida, I., Tuesday 8:00
(S-245) Veselis, R., Tuesday 8:00
(S-246) Pentyala, S., Tuesday 8:00
(S-247) Breukelmann, D., Tuesday 8:00
(S-248) Bar-Yosef, S., Tuesday 8:00
(S-249) Herroeder, S., Tuesday 8:00
(S-250) Herroeder, S., Tuesday 8:00
(S-251) Landrum, A.L., Tuesday 8:00
(S-252) Ueta, K., Tuesday 8:00
(S-253) Kariya, N., Tuesday 8:00
(S-254) Hollmann, M.W., Sunday 3:00

Pharmacology - Clincal

(S-255) Jorden, V., Saturday 8:00
(S-256) Stapelfeldt, C.K., Saturday 8:00
(S-257) Lewis, A., Saturday 8:00
(S-258) Fang, Z., Saturday 8:00
(S-259) Taboada, M., Saturday 8:00
(S-260) Akhtar, S., Saturday 8:00
(S-261) Sear, J.W., Saturday 8:00
(S-262) Feierman, D.E., Saturday 8:00
(S-263) Buvanendran, A., Saturday 8:00
(S-264) Sonoda, S., Saturday 8:00
(S-265) Ates, Y., Saturday 8:00
(S-266) Yazicioglu, H., Saturday 8:00
(S-267) Kodaka, M., Saturday 8:00
(S-268) El-Orbany, M.I., Saturday 8:00
(S-269) Hemmerling, T.M., Saturday 8:00
(S-270) Demirkiran, O., Saturday 8:00
(S-271) Lu, Z., Saturday 8:00
(S-272) Acalovschi, I., Saturday 8:00
(S-273) Kovac, A., Saturday 8:00
(S-274) Rhee, K., Saturday 8:00
(S-275) Norton, J., Sunday 3:00
(S-276) Muir, S., Sunday 3:00

IARS 77th Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Regional

(S-277) Mohajer, P., Monday 8:00
(S-278) Adsumelli, R., Monday 8:00
(S-279) Pandit, J.J., Monday 8:00
(S-280) Parnass, S.M., Monday 8:00
(S-281) Gonzalez, R., Monday 8:00
(S-282) Grant, S.A., Monday 8:00
(S-283) Rao, J.H., Monday 8:00
(S-284) Kurup, V.J., Monday 8:00
(S-285) Smith, K.N., Monday 8:00
(S-286) Tcherven, N., Monday 8:00
(S-287) Yilmazlar, A., Monday 8:00
(S-288) Yilmazlar, A., Monday 8:00
(S-289) Gonzalez, R., Monday 8:00
(S-290) Ozdilmac, I., Monday 8:00
(S-291) Nakatani, T., Monday 8:00
(S-292) Orkin, F.K., Monday 8:00
(S-293) Williams, B.A., Sunday 3:00

Ambulatory Anesthesia

S-1

EFFICACY AND SAFETY OF TROPISETRONS- FOR THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING: A QUANTITATIVE SYSTEMATIC REVIEW (METAANALYSIS)

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INTRODUCTION: To estimate the efficacy and harm produced by tropisetron in the prevention of postoperative nausea and vomiting (PONV) we performed a quantitative systematic review of randomised controlled trials that investigated tropisetron versus placebo to prevent postoperative nausea (PN) and vomiting (PV).
METHODS: Systematic search (MEDLINE, EMBASE, Cochrane-Library, hand-searching, bibliographies, all languages, up to December 2001) for randomised comparisons of tropisetron with placebo in surgical patients. Relevant outcomes were prevention of PN, PV, PONV, rescue treatment and adverse effects. Combined data were analysed using relative risk (RR) and number-needed-to-treat/harm (NNT/NNH).
RESULTS: In 19 trials and 22 comparisons 1,012 patients received a placebo and 1,267 patients tropisetron. In adults fixed intravenous doses between 0.5 and 7 mg were administered (14 trials). In children variable doses of 0.1 mg × kg^{-1} and 0.2 mg × kg^{-1} were used (4 trials). On trials tested oral tropisetron (5 mg) in adults. We were unable to demonstrate an apparent dose-response between fixed doses of 2 and 5 mg in adults, therefore, pooled analyses (2 – 5 mg iv) are presented. The RR for PN, PV and PONV with tropisetron was 0.72 (95%-CI: 0.62 – 0.83), 0.59 (95%-CI: 0.47 – 0.73) and 0.70 (95%-CI: 0.62 – 0.79), respectively. RR for rescue treatment was 0.63 (95%-CI: 0.54 – 0.74). RR in children for a variable dose between 0.1 and 0.2 mg × kg^{-1} was 0.49 (95%-CI: 0.38 – 0.63), 0.49 (95%-CI: 0.38 – 0.63) and 0.32 (95%-CI: 0.15 – 0.70), for PV, PONV and rescue treatment, respectively. Restricting the analysis to a predefined control event rate of 40-80% [1] revealed that about 6-7 patients need to be treated with tropisetron for one to prevent from PN who would have had PN had they all received a placebo (NNT=6.7; 95%-CI: 4.8 – 11.1). Corresponding NNT for preventing PV and PONV was 5.0 (95%-CI: 3.6 – 8.3) and 4.6 (95%-CI: 3.6 – 6.3), respectively. Reporting of adverse effects was variable to a large extend between the trials, as were the observed incidences of symptoms. For headache, for instance, analysis revealed that about 50 patients have to receive tropisetron for one additional patient to suffer from headache that would not occur had they all received a placebo. The use of tropisetron was not associated with serious adverse effects.
CONCLUSION: Tropisetron safely reduced the incidence of emetic symptoms. There is no clear evidence for a dose response between 2 and 5 mg iv. For children a dose of 0.1 mg × kg^{-1} of body weight is effective. Oral application cannot be recommended so far due to lacking data.
REFERENCE: [1] Anesth Analg 2002; 95: 133-143

S-2

ROFECOXIB PREMEDICATION IMPROVES OUTCOME AFTER OUTPATIENT INGUINAL HERNIORRHAPHY

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INTRODUCTION: As a result of concerns regarding side effects related to opioids, non-opioid analgesics are becoming increasingly popular as part of a multimodal regimen to control pain after ambulatory surgery. Rofecoxib, a COX-2 selective inhibitor, has been shown to produce comparable analgesic effects to conventional NSAIDs when administered for the treatment of acute pain. However, the analgesic effect of rofecoxib has not been extensively evaluated when administered for preemptive analgesia in the ambulatory setting. Therefore, we designed this randomized, double-blinded, placebo-controlled study to assess the analgesic efficacy of rofecoxib when administered for premedication prior to ambulatory surgery.
METHODS: 50 healthy outpatients undergoing inguinal hernia repair with local anesthetic-based anesthesia techniques were randomly assigned to one of two study groups (n=25/each): Control (Vitamin C), and Rofecoxib (rofecoxib 50 mg). The first oral dose of the study medication was administered 30 min before surgery and a second dose of the same medication was taken the first morning after surgery. Verbal pain scores were assessed at regular postoperative intervals, with 0=none, 1=mild, 2=moderate, and 3=severe. Recovery times, quality of recovery (0-18), the need for rescue analgesics, maximum pain score (0=none, 1=mild, 2=moderate, 3=severe), and postoperative side effects were also recorded. A follow-up evaluation was performed via telephone at 24 h after surgery to assess patient global evaluation of the study medication (0=poor, 1=fair, 2=good, 3=very good, 4=excellent), and the need for oral opioid-containing pain medication after discharge. A p-value <0.05 was considered statistically significant. (* p<0.05 vs Control).
RESULTS: The two study groups were comparable with respect to demographic characteristics, duration of surgery, and anesthetic drugs used during intraoperative period. The early recovery profiles with respect to the times to sitting up, tolerating oral fluids, standing up, ambulating, "fitness" for discharge, and actual discharge were significantly decreased in patients who received rofecoxib. Rofecoxib also significantly reduced the requirements for rescue pain medication during the 24 h study period, and was more effective in controlling postoperative pain without increasing side effects (e.g., bleeding, nausea, vomiting).
CONCLUSION: Rofecoxib, 50 mg oral, was highly effective in improving pain management and the quality of recovery after outpatient inguinal hernia repair surgery when administered preoperatively and on the first postoperative day without increasing intraoperative blood loss or producing wound complications.

	Age (yrs)	Weight (kg)	Surgery time (min)	Orientation (min)	Tolerating oral fluids (min)	Ambulating alone (min)	"Fit" for discharge (min)	Actual discharge (min)	Quality of recovery (n)	Hydromorphone used before discharge(mg)	Oral analgesic after discharge (n)	Maximum pain during the study period (n)	Global evaluation of the study medication (n)	Blood loss during surgery (ml)	Nausea and vomiting <24h(%)
Control	45 ± 12	73 ± 10	41 ± 15	10 ± 10	56 ± 28	99 ± 41	106 ± 41	127 ± 83	16.4 ± 1.3	0.13 ± 0.29	11 (1-33)	2 (1-3)	1 (0-3)	6.2 ± 2.3	21
Rofecoxib	46 ± 15	78 ± 14	43 ± 22	11 ± 11	43 ± 17*	82 ± 32*	84 ± 32*	88 ± 31*	17.5 ± 1.0*	0.04 ± 0.21	0 (0-20)*	1 (0-3)*	3 (1-4)*	5.7 ± 2.1	14

S-3

VALIDATION OF AN ELECTRONIC VS A PAPER VERSION OF THE SELF-COMPLETED PRE-ADMISSION ADULT ANESTHETIC QUESTIONNAIRE

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INTRODUCTION: Recent advances in hand held and wireless computing technology has provided an opportunity to improve access to patient information at the point-of-care[1]. Studies show that electronic, patient-completed questionnaires are effective in preoperative evaluation[2;3], however patient acceptance and questionnaire completion rates are highest when the computer used to administer the questionnaire does not resemble a traditional desktop computer[2;4]. The purpose of this study was to evaluate an electronic self-administered Pre-Admission Adult Anesthetic Questionnaire (PAAQ) with the existing paper questionnaire.
METHODS: This un-blinded randomized control trial was conducted in February/March 2002 and included patients seen in the Pre-admission Assessment Clinic who had completed a PAAQ in the surgeon's office. Patient consent and ethics approval were obtained. Patients were randomized to PAAQ completion using paper, handheld computer, touch screen desktop computer (Kiosk), or Tablet. Patients were then asked to complete a satisfaction survey. The main study hypothesis was that the electronic version of the PAAQ was equivalent to the paper version, with respect to comprehensiveness, accuracy and time-to-completion. The sample size of 360 provided the ability to detect a 20% difference in the completion rate and a difference in the mean completion times of 0.53 standard deviations between the electronic versus the paper arms, using a power of 90% and an alpha of 0.05.
RESULTS: Six patients refused to participate in the study. Of the patients who were recruited, all completed the study. Two-thirds of the patients were computer owners. Results are presented in the table.

Group	Paper	HH	Tablet	Kiosk
N	180	60	60	60
Mean age	54.5	55.5	52.9	52.2
Male:female ratio	38:62	37:63	35:65	45:55
Procedure (%)				
Ophthalmology	25	23	22	20
Orthopaedics	16	15	17	20
General surgery	17	10	23	12
Gynaecology	12	13	10	18
Ear/nose/throat/oral	13	15	10	10
Urology	4	8	3	5
Other	13	15	15	16
Mean % agreement**	94.0	94.0	94.5	94.5
Median time (sec)*	176	189	156	137
Patient survey:				
Use computer weekly	78	55	79	78
Easy to complete	95	98	100	93
Worry about computerized PAAQ loss	20	5	16	8
Worry about paper PAAQ loss	24	23	23	28
Comfortable completing	51	98	98	97
Prefer paper	36	3	7	0
Prefer computer	11	59	65	68
Prefer paper or computer	53	37	28	32

*Chi square = 14.5, P = 0.002; **$F_{3,120}$ = 0.108, P = 0.96
HH = handheld computer; Kiosk = desktop computer with touch screen; PAAQ = Pre Admission Anesthetic Questionnaire.

DISCUSSION: Touch screen computer technology is a valid, efficient platform for patient-administered PAAQ. Patients expressed comfort using the technology. The majority of patients indicated they would prefer the computer PAAQ over the paper PAAQ in future pre operative assessments. Further software development is required to integrate the patient questionnaire with an electronic perioperative patient record. Further research is needed to examine the impact of handheld computers on the doctor-patient encounter.
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S-4

FLORIDA OFFICE SURGERY AND AMBULATORY SURGERY CENTER OUTCOMES FOLLOWING IMPLEMENTATION OF OFFICE REGULATIONS

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INTRODUCTION: In Florida, there has been a literal explosion in the popularity of office surgery which, until recently, had little to no regulation or oversight.[1] In February 2000, the Florida Board of Medicine enacted regulations for office surgery that included requirements for limitations of the procedure, accreditation of the office facility, credentials of the surgeon, qualifications of anesthesia personnel, and mandatory reporting of adverse incidents.[2]
METHODS: This retrospective study reviews the first two years of mandatory reporting of adverse incident data from Florida offices and compares that to outcomes data from Florida ambulatory surgery centers (ASC) for a one-year period. All 182 adverse incident reports filed between April 2000 and April 2002 were reviewed. The reported volume of office surgery procedures was obtained from the Florida Board of Medicine and estimated for the study period. Ambulatory surgery center injury and death statistics and procedure volumes were obtained from the Florida Agency for Healthcare Administration and the website http://www.floridahealthstat.com.
RESULTS: There were 13 surgically related deaths and approximately 141,404 procedures performed in offices between April 2000 and April 2002. There were 18 reported deaths and 2,316,249 procedures in ambulatory surgery centers during 2000. Surgery related injury occurred at a rate of 66 and 5.3 per 100,000 procedures in offices and ambulatory surgery centers, respectively. The death rate was 9.2 and 0.78 deaths per 100,000 procedures performed in offices and ambulatory surgery centers, respectively. The relative risks for injuries and deaths for office procedures vs. ambulatory surgery centers were 12.4 (95% CI 9.5 to 16.2) and 11.8 (95% CI 5.8 to 24.1) respectively. These calculations suggest that if all of the procedures done in offices instead were done in ambulatory surgery centers, 43 injuries and 6 deaths per year could be prevented. In the office deaths, 84 percent of the physicians were board certified and held active hospital privileges, yet only 38 percent of the facilities were accredited and only 15 percent had a dedicated physician anesthesia provider.
DISCUSSION: The death rates for offices and ambulatory surgery centers found in this study are consistent with rates reported in previous studies which, in some cases, had depended upon voluntary reporting.[3,4,5] There is a more than ten-fold greater mortality in offices compared to ambulatory surgery centers despite Florida regulations.
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S-5

DOES CEREBRAL MONITORING IMPROVE RECOVERY AFTER AMBULATORY ANESTHESIA? A COMPARISON OF BIS AND AEP MONITORING DEVICES

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INTRODUCTION: The bispectral index (BIS) monitor has been reported to improve the titration of inhalational anesthetics during general anesthesia (1,2). The auditory evoked potential (AEP) has also been shown to be a quantifiable measure of the sedative and hypnotic effects of anesthetic drugs. This study was designed to assess the comparative effects of AEP and BIS monitoring on the utilization of desflurane and the recovery profiles after ambulatory surgery.
METHODS: 30 consenting women undergoing outpatient laparoscopic procedures were randomly assigned to one of three treatment groups. Anesthesia was induced with propofol, 2 mg/kg IV, and fentanyl, 1 µg/kg IV. Desflurane 2-4% in combination N_2O 60% in oxygen was administered for maintenance of anesthesia. In the Control group, the anesthesiologists were blinded to the AEP and BIS values, and desflurane was administered according to standard clinical practice. In the BIS group, desflurane was titrated to maintain a BIS value between 50-60. In the AEP group, desflurane was titrated to maintain an EEG-derived index (AAI) between 15-25. The AAI and BIS values, as well as the recovery times and side effects were recorded. Data were analyzed using one-way ANOVA for continuous variables, paired t-test for intragroup differences, and Chi-square test for categorical data. (* $p<0.05$ vs Control).
RESULTS: During the maintenance period, the BIS and AAI values were significantly lower in the Control group (mean BIS values of 42±12 and mean AAI values of 12±6) compared with the BIS-titrated group (mean BIS of 60±15), and AEP-titrated group (mean AAI of 21±10), respectively. Even though they failed to achieve statistical difference among the three groups, early recovery times to eyes opening, extubation, and orientation were consistently shorter in both the BIS and AEP groups (vs Control). However, the times to sitting up, the first time to take fluid, standing up, ambulating, "fitness" for discharge, and actual discharge were significantly decreased in both the AEP-titrated and BIS-titrated groups when compared to the Control group. There were no significant differences between the AEP and BIS groups.
CONCLUSIONS: Titration of desflurane using the AEP and BIS monitors contributed to a faster emergence and earlier discharge home following outpatient laparoscopic procedures. However, the AEP and BIS monitors were comparable in facilitating the recovery process.
REFERENCES:
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	Control	BIS	AEP
Age (yr)	45±8	40±7	39±14
Weight (kg)	60±5	65±13	66±13
Surgery time (min)	48±27	38±22	42±32
Eyes opening (min)	9±4	7±4	7±5
Orientation (min)	10±5	7±4	7±5
Taking fluid (min)	167±48	100±57*	109±52*
Ambulation (min)	196±59	126±54*	120±56*
Stay PACU time (min)	204±55	146±47*	149±44*
Actual discharge home (min)	216±58	144±43*	140±41*

S-6

BISPECTRAL INDEX MONITORING DURING SHORT SURGICAL PROCEDURES USING PROPOFOL ANESTHESIA

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INTRODUCTION: The present study aims to determine whether the electroencephalogram derived bispectral index monitoring during short term surgery using propofol infusion improves the accuracy of titration of the drug, monitoring awareness and leads to rapid recovery.
METHODS: A total of 60 patients scheduled for minor surgery (<45 minutes long) were subdivided into 2 equal groups: Group (I) [standard practice group], propofol adjustment was left to the discretion of the investigator based on clinical signs. Propofol infusion was started at 140 $g.kg^{-1}.min^{-1}$ and modified to maintain hemodynamic stability and avoid unwanted patient response. Group (II) [BIS group], propofol was adjusted according to BIS monitoring to achieve a BIS score of 45-60.
RESULTS: A statistically significant decrease in propofol consumption was found in the BIS group compared to the standard group. Also, a significantly lower infusion rate and a lower total amount of propofol were used. The heart rate and blood pressure did not significantly change throughout the study. End points of recovery (eye opening, response to simple commands) were reached at a faster level under BIS monitoring.
DISCUSSION: The bispectral index (BIS) is a processed EEG parameter incorporating coupling along with the frequency and amplitude of EEG waveforms.[1] It has been proposed as a measure of the pharmacodynamic anesthetic effect on the CNS. The level of 40-60 is the level of moderate hypnotic state or general anesthesia level with a low probability of consciousness or awareness.[2] Patients under BIS monitoring consume lower dosages of propofol, as measured by the mean infusion rate at different times during surgery. This matches the results of Gan et al.[3] However, special EEG electrodes are expensive for such short anesthesia.
CONCLUSION: Routine BIS monitoring in standard anesthetic practice can reduce propofol dosage and allow faster recovery with potential economic benefits.

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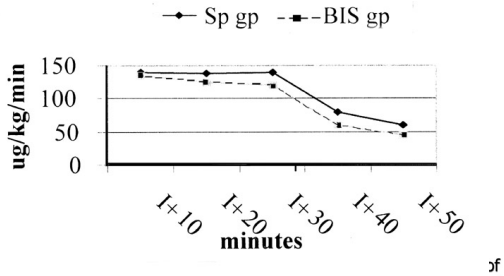

The BIS group shows a statistically significant lower level of infusion rates at different milestones during surgery.

S-7

OROPHARYNGEAL WATER ACCUMULATION INCREASES SUSCEPTIBILITY TO CHOKING DURING DENTAL TREATMENT OF INTELLECTUAL DISABILITY UNDER DEEP SEDATION

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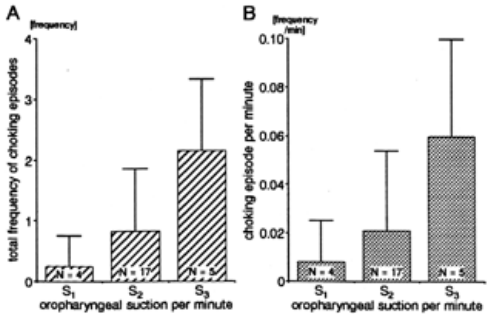
INTRODUCTION: In the dental treatment of intellectual disability under deep sedation, we should often cease dental procedure due to choking of patients, which is an airway protective reflex possibly induced by intraoral water use or by oral and/or pharyngeal secretion. We investigated the relationship between frequency of choking episodes and intraoral use of water, oropharyngeal water accumulation, and mean dose of propofol, during dental treatment of intellectual disability under deep sedation with midazolam and propofol, using a continuous oropharyngeal suction catheter.
METHODS: Twenty-one (12 males and 9 females) intellectual disability (mental retardation or autism) who scheduled for dental treatment under deep sedation were studied. After induction of sedation with midazolam (2 - 4 mg) and propofol (20 mg bolus and 4 - 9 mg/kg/hr), we inserted a 14 Fr. suction catheter about 10 - 15 cm nasally, and it was fixed at the nare where the pharyngeal suction could be done most effectively. Airway maintenance was performed by chin-lift, nasal airway insertion, or by both, to prevent subglottic airway obstruction. The volume of suctional water from the pharynx was measured using a graduated bottle situated in the suction circuit. As to counting intraoperative choking, a series of choking episodes which induced by an occasion was counted as 1 choking episode.
The patients were divided into 3 groups according to the intraoral water use (group W_1, treatments which scarcely require water; group W_2, treatments which require moderate amount of water; group W_3, treatments which require relatively large amount of water), to the amount of oropharyngeal suction per minute (group S_1, less than 0.2 ml/min; group S_2, 0.2 - 0.7 ml/min; group S_3, more than 0.7 ml/min), and to the mean dose of propofol (group P_1, less than 5 mg/kg/hr; group P_2, 5 - 7 mg/kg/hr; group P_3, more than 7 mg/kg/hr).
RESULTS: The amount of total oropharyngeal suction, and that of oropharyngeal suction per minute were significantly correlated with intraoral use of water. The frequency of total choking episodes and that of choking episode per minute were significantly correlated with the amount of oropharyngeal suction per minute. However, they did not correlate with the intraoral use of water and the mean dose of propofol.
DISCUSSION: These findings suggest that 1) the higher the use of water in the oral cavity, the higher the volume of water streaming down into pharyngeal space, even if we use intraoral vacuum during the dental procedures, 2) the higher the water accumulation in the oropharyngeal space, the higher the incidence of choking episodes.



S-8

EFFECT OF LABETALOL ON SEIZURE ACTIVITY AFTER ELECTROCONVULSIVE THERAPY

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INTRODUCTION: Labetalol is commonly administered to patients undergoing ECT to minimize the acute hemodynamic response following the electrical stimulus. However, the effect of labetalol on the duration of the ECT-induced seizure activity remains controversial[1,2]. Therefore, this randomized, double-blind, cross-over study was designed to assess the hemodynamic effect of labetalol during ECT, as well as its effect on the duration of motor and EEG seizure activity.
METHODS: 25 consenting ASA I-III depressed patients undergoing an acute series of ECT treatments under methohexital anesthesia were studied. After pre-treatment with glycopyrrolate 0.2 mg IV, patients were anesthetized with methohexital 0.75-1.25 mg/kg and remifentanil 0.75-1.25 g/kg. Following loss of consciousness, succinylcoline 1-1.25 mg/kg was administered. Approximately 1.5 min prior to administering the electrical stimulus, either labetalol 10 mg or saline (2 ml) was administered intravenously. The systolic (SBP) and diastolic blood pressure (DBP) values, as well as heart rate (HR) values were recorded at 1-2 min intervals. In addition, the duration of the motor and EEG seizure activity was recorded. Rescue boluses of labetalol, 5 mg IV were administered to treat persistently elevated SBP and DBP values after ECT.
RESULTS: Pre-ECT treatment with labetalol 10 mg IV, reduced the SBP immediate before and after the ECT stimulus. Labetalol had no effect on the duration of either the motor or EEG seizure activity. Finally, pretreatment with labetalol reduced the need for "rescue" doses of labetalol after the ECT stimulus.
CONCLUSIONS: Labetalol, 10 mg IV, improved hemodynamic stability during ECT without adversely affecting the duration of ECT-induced seizure activity.

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* P < 0.05 vs control group

	Control	Labetalol
Age (yr)	51±15	54±12
Weight (kg)	74±17	79±14
Motor seizure (sec)	42±14	40±13
EEG seizure (sec)	58±22	57±22
Baseline SBP	140±24	134±16
Pre ECT SBP	136±25	115±18*
Post ECT Peak SBP	173±32	155±21*
Max HR after ECT(bpm)	140±24	140±21
Rescue labetalol doses(n)	1(0-4)	0 (0-1)*

S-9

THE EFFECT OF REMIFENTANIL ON SEIZURE DURATION DURING ELECTROCONVULSIVE THERAPY (ECT)

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INTRODUCTION: Remifentanil (Ultiva®) is a short-acting opioid which is used for induction and maintenance of general anesthesia. Administration of remifentanil in combination with methohexital has been reported to be associated with increased seizure duration in patients undergoing ECT[1]. This prospective, randomized, double-blind, placebo-controlled crossover study was designed to compare different bolus dosages of remifentanil on the duration of ECT-induced motor and EEG seizure activity.
METHODS: 10 consenting patients with major depressive disorders receiving maintenance ECT participated in this study. A total of 40 ECT treatments were evaluated. All patients were premedicated with glycopyrrolate, 0.2 mg IV, and hypnosis was induced with a standarized IV bolus of methohexital 1 mg/kg and muscle paralysis was achieved with succinylcholine, 1.2 mg/kg IV. All patients received one of three different doses of remifentanil 25, 50 and 100 g or saline in a random sequence immediately after methohexital for four consecutive ECT treatments. A fixed "supra" threshold electrical stimuli was administered to elicit a seizure, and the times from the stimulus to the cessation of the motor and EEG seizure activity were noted. Standarized psychomotor recovery times were also assessed at specific intervals, statistical analysis consisted on ANOVA with p-values <0.05 considered statistical significance.
RESULTS: Three males and seven females with a mean (± SD) age of 54 ± 16 yr, and weight of 75 ± 18 kg participated in the study. All patients had similar baseline Hamilton depression scores. The duration of motor and EEG seizure activity were not significantly different among the four treatment groups. Furthermore,recovery times to eye opening, obeying commands, and the time to discharge did not differ among the four study groups.
CONCLUSIONS: Remifentanil in doses ranging from 25 to 100 g IV, had no effect on the duration of ECT-induced seizure activity. In addition, remifentanil did not prolong the recovery times or increased side effects.
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Remifentanil dose (mcg)	0	25	50	100
Depression Score (n)	15±9	13±7	15±8	12±8
Motor Seizure (min)	43±10	45±15	39±19	39±20
EEG Seizure (min)	56±16	60±22	57±12	58±34
Eye opening (min)	7±4	6±3	7±2	9±3
Obeys commands (min)	11±6	8±3	9±3	12±14
Discharge time (min)	25±4	22±3	24±6	26±3

S-10

THE EFFICACY OF REMIFENTANIL IN AMBULATORY PATIENTS

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INTRODUCTION: Remifentanil's short duration of action is due to its rapid hydrolysis by nonspecific esterases. Patients receiving remifentanil demonstrate rapid recovery. This feature of the drug makes it ideal in patients undergoing procedures that are relatively short in duration.
METHODS: This retrospective study investigates the use of remifentanil in female patients coming for ambulatory gynecological procedures at the Women's Center of this institution. The medical records of 189 patients for a 4 month period were analyzed and were divided into two groups: one group was administered remifentanil; the second group was administered sevoflurane. Patients in both groups received N_2O with O_2 and propofol as an induction agent. A bis monitor was used with all patients. Propofol was administered incrementally to maintain the bis at values between 40–60.
RESULTS: Remifentanil was administered to 116 patients: median age = 34 years, range 19 to 74 years. Seventy-three patients were administered sevoflurane: median age 34 years, range 18 to 59 years. Anesthesia times (means ± SEM) for the two groups were similar: remifentanil 30.7 ± 2.8 min and the control 28.5 ± 1.0 min, p = 0.54. There was no significant difference in the incidence of nausea and vomiting between the remifentanil patients (5 patients, 4.3%) and in the sevoflurane patients (6 patients, 8.2%). The time (means ± SEM) spent in PACU by the two groups was significantly different: remifentanil 40.4 ± 1.4 min and sevoflurane 49.8 ± 2.6 min, p = 0.002. The last Aldrete scoring taken to determine patients going to the step down PACU was significantly different: remifentanil 9.0 ± 0.1 and sevoflurane 8.1 ± 0.2, p = 0.001. The time spent in the step down PACU was not significantly different, but the remifentanil group's time was shorter: remifentanil 62.8 ±2.0 min, sevoflurane 66.7 ± 3.5 min, p = 0.33. The total time spent in both PACU's by the groups was significantly different: remifentanil 99.7 ± 2.9 min, sevoflurane 110.3 ± 4.2 min, p = 0.04. The patients' self scoring of pain showed significant differences in both PACU's, with remifentanil patients experiencing less pain in both units: p = 0.005 and p = 0.033 respectively.
DISCUSSION: Remifentanil shortens recovery time spent in the PACU and enables patients to experience less pain. Patients' recovery from pain is quicker, leading to a shorter stay in the PACU. This, in turn, may reduce patient costs in the PACU.

S-11

PATIENT-CONTROLLED SEDATION AND ANALGESIA WITH REMIFENTANIL-PROPOFOL FOR SHOCK WAVE LITHOTRIPSY; HAVE WE REACHED OUR ULTIMATE GOAL IN PATIENT COMFORT AND SAFETY?

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INTRODUCTION: Patient-controlled sedation and analgesia (PCSA) is a novel field of use for monitored anesthesia care (1, 2). Combination of propofol- remifentanil has been used for PCSA without a lockout interval in a recent study in patients undergoing extracorporeal shock wave lithotripsy (SWL)(1). Although promising in terms of patient comfort the high incidence of adverse effects have indicated a PCSA protocol incorporating a proper lockout interval should be investigated. In this study a low-dose continuous infusion of propofol-remifentanil combination was compared with a PCSA protocol including a presumably appropriate lockout interval.
METHODS: After IRB approval and patient consent was obtained; fifty ASA I-III adult patients undergoing SWL procedure were randomly allocated to two groups by sealed envelope technique. Patients with allergies to the study drugs, at risk for pulmonary aspiration, who could not understand the concept of PCSA before randomization were not included. Group I(n=25) solution containing remifentanil 2g/mL and propofol 1mg/mL was infused continuously at 3 mL/min following a loading dose of 10mL. Group II(n=25) PCSA solution containing remifentanil 4g/mL and propofol 2mg/mL was delivered using Abbott Pain Management Provider 13960-36 patient controlled analgesia pump (Abbott Laboratories, Chicago,IL) with a setting of 10mL loading dose, 5 minutes lockout interval and a bolus dose of 5mL on demand. Rescue medication in group I was 5mL of the study solution delivered by the one of the attending authors. Follow up parameters during SWL were; heart rate, noninvasive blood pressure, peripheral oxygen saturation (SpO_2), respiratory rate, sedation score and faces scale score. After the procedure; recovery time, patient's recall of procedure, pain score(VAS), satisfaction and drug usage were recorded. Data was analyzed by T-test for independent samples and ANOVA for repeated measures. P<0.05 was considered significant.
RESULTS: Patient characteristics, duration of the procedure, stone localization were similar between the two groups. There was no difference between the groups in terms of mean blood pressure and heart rate values. SpO_2 decreased significantly(<90%) at 10 min in group I (p<0.05).Sedation scores were higher in group I at 5, 10, 15 and 20 min compared to group II (p<0.05). Mean dose of propofol and remifentanil administered in group I was higher than the dose requested and delivered by PCSA pump in group II (p<0.01).Recovery time was longer in group I (p<0.05). Mean pain score regarding the procedure was <4 in both groups (10 pt scale). Patients in both groups were equally satisfied with the analgesic and sedative technique used.
DISCUSSION: In this study the PCSA protocol with propofol-remifentanil seems to provide adequate sedation and analgesia without significant side effects and with decreased drug consumption. Safer and effective protocols for PCSA may encourage its more extensive usage.
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S-12

A NOVEL MIXTURE OF PROPOFOL, ALFENTANIL AND LIDOCAINE FOR OPHTHALMIC SURGERY UNDER MAC

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INTRODUCTION: The combination of propofol, alfentanil and lidocaine is effective in providing sedation and analgesia for ophthalmic surgery with regional block under MAC. With IRB approval, we retrospectively analyzed 89 charts of patients sedated with this technique.
METHODS: 6 ml of propofol (10mg/ml), 2 ml of alfentanil (500g/ml) and 2 ml of 2% lidocaine (A6-2-2 mixture) were freshly mixed in a 10 ml syringe. The bolus dose was determined based on the patients' age: 5 g/kg of alfentanil (and 0.3 mg/kg of propofol) for patients > 75 years; the dose increased 1 g/kg per 10-year decrease in age, up to 9 g/kg of alfentanil (0.54mg/kg of propofol) for patients < 45years. The bolus was delivered by infusion pump and followed by a continuous infusion of the mixture with 0.75 g/kg/min alfentanil (and 45 mcg/kg/min of propofol) until block completion. Block was performed at 1 minute after bolus finished. oxygen was provided by nasal cannula and blow by. BP, SaO_2, ECG, capnography, clinical signs of sedation (spontaneous eye closure, sluggish speech, and decrease of respiratory rate), responses to block (head movement, eyebrow movement, complaints of pain), need for airway support, N&V, pain due to propofol infusion and recall were recorded. Patient and surgeon satisfaction was scored (1-10; 10 for complete satisfy) by standardized questioning. Chi-square test and T-test were used for statistical analysis. P< 0.05 was significant.
RESULTS: The average time for bolus was 0.29 $\pm$ 0.04 second per g alfentanil. 78% achieved analgesia and sedation without any adverse response to block. 12% achieved good analgesia and sedation with only eyebrow movement upon needle insertion. 27% had respiratory depression but were able to follow commands and maintained adequate ventilation. 2% had brief apnea alleviated by chin lift or jaw thrust. None had pain due to mixture infusion or N&V. Prior to sedation, average SBP was significantly increased (P<0.0001) compared to baseline. After sedation and block, SBP decreased 6% from baseline (P<0.005). Although 50% patients had recall, it was considered non stressful. Of the 39 patients undergoing < 30 minute procedures, only 7 (18%) required midazolam for anxiolysis during the procedure. Patients' and surgeons' satisfaction scores were 9.77 $\pm$0.58 and 9.60$\pm$0.78, respectively.

# pt	Had sec/ ss/drr	No Hm/ebm/cop	ebm Only	RD-FC	Apnea need airway support	SBP (pre –bl)	SBP (post – bl)	N/V	Non stressful recall
89	71 (80%)	69 (78%)	11 (12%)	24 (27%)	2 (2%)	13.7$\pm$22.97	-7.9$\pm$21.99	0	45 (50%)
						P<0.0001	P<0.005		

Sec =spontaneous eye closure; ss =sluggish speech; cop =complaint of pain; hm =head movement; ebm =eyebrow movement; RD-FC =respiratory depression but able to follow command; SBP(pre-bl) =difference of systolic blood pressure between that prior to sedation and pre-op baseline; SBP (post-bl)=Difference of SBP between that after sedation and pre-op baseline; N/V =nausea and vomiting.

CONCLUSIONS: With low incidence of need for airway support, no pain during the infusion and no N/V, the novel mixture of propofol, alfentanil, and lidocaine (A6-2-2 mixture) technique provided adquate analgesia and sedation in a predictable time manner (3-4 minutes) and hemodynamic stability for ophthalmic surgery under regional block. The sedation and comfort provided by the mixture typically lasts for approximately 30 minutes making the technique suitable for a variety of short procedures with blocks under MAC.

S-13

DEXMEDETOMIDINE SEDATION DURING REGIONAL ANESTHESIA: A PILOT STUDY

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INTRODUCTION: In this pilot study, dexmedetomidine (DMED) was compared to propofol for its ability to maintain a calm and cooperative patient during neck surgery under regional anesthesia.
METHODS: After IRB approval and informed consent, twelve patients presenting for partial/total thyroidectomy or parathyroidectomy, were randomly assigned to the DMED (n=6) or propofol (n= 6) group. There were no significant differences in the average age (52.2 yrs) or weight (66.6 kg) between the patients in each group. Thyroidectomy patients received bilateral superficial cervical plexus block placed by the anesthesiologist. Parathyroidectomy patients received local anesthesia administered by the surgeon. DMED infusion was started with a 1 g/kg bolus over 10 minutes and titrated from 0.2-0.7 g/kg/hr. Propofol infusion was started at 25 g/kg/min and titrated up to 100 g/kg/min. Heart rate, blood pressure, end-tidal carbon dioxide ($P_{et}CO_2$), respiratory rate, oxygen saturation (SpO_2), and Ramsay sedation scores were recorded throughout surgery by the anesthesiologist. If the patient had not reached a Ramsey sedation score of 4 despite a maximal infusion rate, midazolam and fentanyl were administered. A scale of 1-10 (1 = agitated, frequent movement; 10 = calm, cooperative) was used by the surgeon (blinded to the agent used) to evaluate the quality of sedation of each drug.
RESULTS: Significantly less DMED (39.3ml vs. 80.7 ml propofol, $p = 0.02$) and fewer adjustments in infusion rate (2 vs. 5, $p = 0.001$) were required to maintain the Ramsay score 4. The cost between the volumes infused was similar (DMED $30; propofol $29.86, US). No DMED patient required airway support, while two propofol patients did. Surgeons' satisfaction with DMED was greater than with propofol (7.5 vs. 5.7). There were no significant differences between groups with regard to SpO_2 (99.1% vs. 98.7%), $P_{et}CO_2$ (35.2 mmHg vs. 39.6 mmHg), respiratory rate (14.9 bpm vs. 14.0 bpm), or the percentage of time the Ramsay score was 4 (44.4% vs. 53.5%). The amount of midazolam (both DMED and propofol 0.04mg/kg) and fentanyl (DMED 2.6 mg/kg; propofol 3.6 mg/kg) supplemented as "rescue' medication was also not significantly different between the groups.
DISCUSSION: DMED is as effective as propofol in maintaining a stable level of sedation. However, sedation with DMED requires fewer dosage adjustments, and since DMED is more potent than propofol, it requires significantly less volume to maintain a constant level of sedation. The cost between the two drugs when used for sedation is comparable. Propofol requires more careful titration during deep sedation to avoid respiratory depression and the requirement for airway support, making it more labor intensive to use. DMED maintains deep levels of sedation without respiratory depression or any need for airway support.
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Cardiothoracic and Vascular – Basic Science

S-14

ANESTHETIC PRECONDITIONING: EFFECTS ON LATENCY TO ISCHEMIC INJURY IN ISOLATED HEARTS

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INTRODUCTION: Anaesthetic preconditioning (APC) is the phenomenon whereby brief exposure to a volatile anesthetic leads to a state of resistance to the effects of ischemia and reperfusion. APC has been shown to be protective with regard to several variables including left ventricular pressure (LVP), coronary flow (CF), free radical release at reperfusion, and infarct size. To our knowledge all previous investigations have used ischemic time as the independent variable and have quantified changes in dependent functional and structural variables. A more meaningful measure of the efficacy and potential clinical utility of APC may be the incremental time during ischemia that APC affords before irreversible ischemic damage occurs. The purpose of his study was to define the critical limits of efficacy of APC by varying the ischemic time.
METHODS: Isolated guinea pig hearts were perfused in crystalloid buffer at 55 mmHG; developed LVP, coronary flow (CF), superoxide ($O_2^{\bullet-}$) formation and infarct size were measured. Hearts underwent preconditioning (two pulses of sevoflurane 0.6 mm for 5 min) (APC), or no treatment (CON) prior to global ischemia and 120 min reperfusion. For both APC and CON hearts ischemia durations were 20, 25, 30, 35, 40 and 45 min (n=6/ischemia duration/treatment).
RESULTS: At 120 min reperfusion after ischemia, developed (systolic – diastolic) LVP was increased and $O_2^{\bullet-}$ formation and infarct size were decreased in APC compared to CON for ischemia durations 25 min-40 min; a bell-shaped distribution for APC-induced protection was apparent (Table). There were no differences in these variables when ischemia was 20 min or 45 min. CF and vasodilator response to bradykinin were similar between APC and CON when ischemia was 20 min, but were increased in the APC group for other ischemia durations. APC-induced preservation of CF and responsiveness to bradykinin were consistent for ischemia durations greater than 20 min (Table).

DISCUSSION: In this model of global ischemia, when ischemia duration is short (20 min) or long (45 min), APC failed to protect against decreases in contractile function or against increases in $O_2^{\bullet-}$ formation and infarction, thus a window-period exists wherein APC is effective. This suggests that although APC increases latency to ischemic injury, clinical application of APC may be limited to those patients who experience ischemia of relatively brief duration. APC-induced protection against vascular endothelial dysfunction is not limited by prolonged ischemia in this range however. This may reflect the lower metabolic rate of vascular endothelium compared to myocytes, leading to increased resistance to ischemia, or alternatively it may reflect protective effects of endothelial nitric oxide.

% Improvement in LVP and CF (APC vs CON) (*P < 0.05)

Duration of Ischemia	Developed LVP	Coronary Flow
20 min	8%	2%
25 min	24%*	32%*
30 min	37%*	34%*
35 min	28%*	28%*
40 min	14%	33%*
45 min	3%	27%*

S-15

DELAYED ANESTHETIC PRECONDITIONING OF THE ENDOTHELIUM AGAINST CYTOKINE-INDUCEDCELL DEATH

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INTRODUCTION: We recently showed that volatile anesthetic pretreatment has immediate protective effects against cytokine-induced cell death in endothelial and vascular smooth muscle cells. [1] A number of studies have described a second window for ischemic preconditioning (IPC), in which the myocardium is protected against an ischemia-reperfusion insult, 12-24 hrs after the IPC stimulus. [2-4] Likewise, Isoflurane (1 %) induces delayed (24 hrs) cardioprotective effects in rabbit hearts. [5] The objective of the present study was to investigate whether isoflurane also triggers delayed protection in endothelial cells from cytokines-induced cell death. We preformed a time course to compare the immediate protection with the delayed effects of isoflurane pretreatment.
METHODS: In our cellular model of inflammation human microvascular endothelial cells (HMECs), were exposed to cytokines (0.1 ng/ml TNF, 5.0 ng/ml IFN and 5.0 ng/ml IL1, dissolved in medium) for 72 hours, after pretreatment with isoflurane for 30 minutes in an airtight chamber by ventilating the chamber with 100% oxygen and 1.5% isoflurane. The exposure to cytokines was initiated directly after isoflurane pretreatment or with a period of delay, (1, 4, 12, 16, 20, 24 and 48 hrs). After cytokine exposure, the total number of cells and were counted and the surviving cells were identified using trypan blue exclusion.
RESULTS: Isoflurane pretreatment had immediate and delayed protective effects against cytokine-induced cell injury and death (figure). While the immediate effect of isoflurane pretreatment is lost if the time between isoflurane pretreatment and cytokine exposure is extended beyond 4 hrs, the protective effect is restored when the interval between isoflurane pretreatment and cytokine exposure is extended to 16 hrs or longer. Importantly, the delayed protective effect is equal to the immediate effect when the time between VA pretreatment and cytokine exposure is extended to 24-48 hrs in HMECs.
CONCLUSION: Isoflurane pretreatment has immediate and delayed protective effects against cytokine-induced injury. While other studies only investigated delayed preconditioning after 12 or 24 hours,[2-5] our results suggest that anesthetic preconditioning may be time-dependent. Protection is abolished after 4 hrs delay but regained after 16 hrs, and the delayed effects after 24 or 48 hrs are equal to the immediate effects. This study suggests that delayed anesthetic preconditioning has the potential to protect the endothelium from inflammation.

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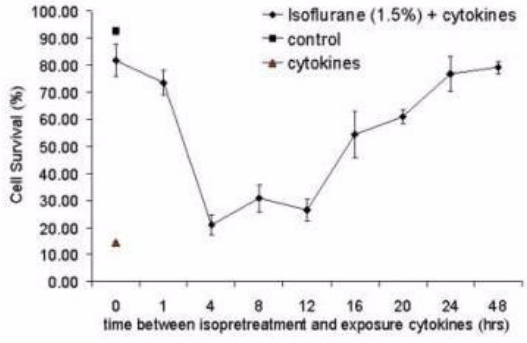

S-16

ANESTHETIC PRECONDITIONING TRIGGERED BY ROS IMPROVES MITOCHONDRIAL ATP SYNTHESIS AND DECREASES ROS FORMATION AFTER ISCHEMIA IN GUINEA PIG HEARTS

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INTRODUCTION: The anesthetic sevoflurane, if given transiently before ischemia (anesthetic preconditioning, APC), reduces infarct size and reactive oxygen species (ROS) formation on reperfusion (RP).[1] ROS scavenging during anesthetic exposure blocks protection and restores formation of ROS on RP.[1] In this study we tested if APC mediates protection in intact hearts and isolated mitochondria by preserving mitochondrial bioenergetics as shown by improved ATP synthesis and reduced ROS formation on reperfusion.
METHODS: Guinea pig hearts were isolated and perfused with crystalloid buffer at 55 mmHg and developed LVP was measured. 28 hearts were subject to 30 min global ischemia and infarct size was measured at 120 min RP. Groups were: untreated (ISC), sevoflurane (APC, 2.7 vol%), a ROS scavenger MnTBAP (TBAP, 40 M) and sevoflurane with the ROS scavenger (APC+TBAP). TBAP was infused 5 min before, during and 5 min after APC. All drugs were washed out 15 min before ischemia. An additional 20 hearts, subject to the same protocol, were removed at 1 min RP to measure ATP synthesis (luciferase luminometry) and ROS formation (DCHF fluorescence) in mitochondria isolated by differential centrifugation. A CON group was not subject to ischemia and RP. Data are means ±SEM ($p< 0.05$; * vs. ISC).
RESULTS: At 120 min RP, LVP (mmHg) was improved and infarct size (% heart weight) was reduced after APC (55±2*, 22±2*%) vs. ISC (22±2, 53±3%), TBAP (25±3, 57±2%), APC+TBAP (23±3, 56±4%). Mitochondrial ROS formation (units, 120 min incubation) and ATP synthesis rate (100% CON), respectively, were CON (405±22*, 100*%) vs. APC (387±59*, 92±2.6*%), ISC (601±92, 29±2.5%), TBAP (582±50, 28±2.0%), and APC+TBAP (591±52, 29±2.9%).
DISCUSSION: APC-induced protection is due, at least in part, to ROS formation triggered by sevoflurane. Moreover, mitochondrial oxidative phosphorylation is better preserved as shown by a higher rate of ATP synthesis after APC. This may be due to less damage to the electron transport chain as shown by reduced ROS formation during ischemia and initial RP.
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S-17

IMPACT OF ISOFLURANE DURING SIMULATED MYOCARDIAL ISCHEMIA/REPERFUSION ON INTRACELLULAR CALCIUM, ARRHYTHMIA AND CONTRACTILITY

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BACKGROUND: Administration of isoflurane is common before and during myocardial revascularisation. Isoflurane, however, interferes with the calcium handling capacity of cells, can inhibit the respiratory chain and produce oxygen radicals. We therefore investigated how isoflurane alters intracellular calcium and pH, and interferes with cellular contractility and stability of membrane potential when applied along with simulated ischemia and reperfusion.
METHODS: After institutional approval rats were anesthetized and their hearts rapidly excised. Single cardiomyocytes were obtained after enzymatic digestion. After staining with the ratiometric calcium fluorescent dye Fura-2 and the pH sensitive dye BCECF they were transferred into a flow-through chamber on the platform of an inverted microscope. Ischemia was simulated for 30 minutes by superfusing the cells with an acidic (pH: 6.3) substrate free modified Tyrode's solution containing 10 mM deoxy-glucose to inhibit glycolysis. It was vigorously bubbled with N2, which was also introduced underneath the hood that covered the superfusion chamber to prevent equilibration of pO2. These measures reduced pO2 to below 15 mmHg. Isoflurane treated cells (n = 30) were also exposed to 1MAC of isoflurane during ischemia (30 min) until the end of reperfusion (50 min) while control cells (n = 40) were exposed to air only. Fluorescence data were determined in five minute intervals as well as the occurrence of arrhythmic events and semiquantitative contractility. The cells were continuously stimulated at a frequency of 0.25 Hz. Multivariate tests with Bonferroni correction were employed for statistical analysis.
RESULTS: Intracellular calcium concentration is given as Fura-2 ratio. Ischemia caused a drop of pH from 7.3 to 6.4 in both groups without any difference between groups. After a brief recovery it remained depressed in both groups throughout reperfusion. Fura-2 ratio climbed in both groups over time. This increase was significantly more prominent in isoflurane treated cardiomyocytes where intracellular calcium more than tripled until the end of reperfusion ($p < 0.05$). In the control group the rise of calcium was not as steep. Calcium levels even dropped during early reperfusion but were overall about 50 % higher than baseline after reperfusion. Significantly more isoflurane treated cells became arrhythmic during ischemia and remained arrhythmic during reperfusion. Contractility declined in the course of ischemia independently of treatment. However, the recovery and the overshoot that control cells exhibited during early reperfusion was absent in isoflurane treated cardiomyocytes.
CONCLUSION: Isoflurane given during simulated ischemia and reperfusion leads to a marked rise of intracellular calcium as compared to control cells that is independent of pH changes. Additionally, isoflurane treated cells also exhibited a higher incidence of arrhythmic events and a depressed contractility that did not reach baseline values throughout reperfusion. These potentially harmful effects may be related to diminished calcium efflux and excessive oxygen radical generation.

S-18

HYPOTHERMIA INCREASES MITOCHONDRIAL CA^{2+} BUT ATTENUATES MITOCHONDRIAL CA^{2+} OVERLOAD DURING MYOCARDIAL ISCHEMIA AND REPERFUSION IN GUINEA PIG INTACT HEARTS

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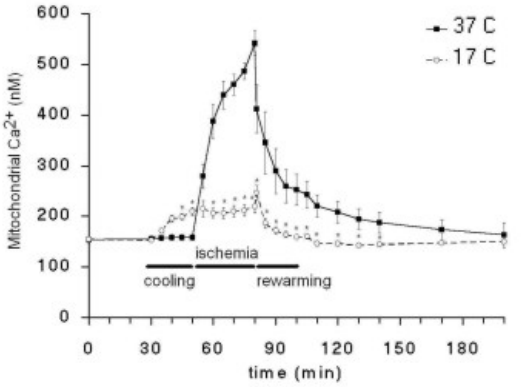
INTRODUCTION: Cardiac ischemia/reperfusion (IR) injury is associated with mitochondrial (m)[Ca^{2+}] overload. Hypothermia protects against IR injury. We hypothesized that hypothermia attenuates m[Ca^{2+}] overload during IR.
METHODS: Langendorff-prepared guinea pig hearts (n = 12) were loaded with the Ca^{2+}-specific fluorescent probe indo 1. After $MnCl_2$ perfusion to quench cytosolic Ca^{2+} fluorescence, mitochondrial Ca^{2+} fluorescence was excited at 350 nm and emissions were measured at 390 and 460 nm via a bifurcated fiberoptic cable placed against the left ventricular wall. To account for changes of the dissociation constant for indo 1 (K_d) with cooling and rewarming, the K_d was temperature-corrected at each individual time point. Left ventricular pressure (LVP) was measured isovolumetrically with a pressure transducer and a saline-filled latex balloon. After stabilization, hearts were either kept at 37ºC or cooled to 17ºC for 20 min before 30 min of global ischemia, followed by 120 min reperfusion at 37ºC. Infarct size was determined using TTC staining and cumulative planimetry. All values are mean±SEM. Statistics: Student's t-test (*P<0.05).
RESULTS: Baseline m[Ca^{2+}] was not different between groups and averaged 154±4 nM. Ischemia at 37ºC resulted in a continuous increase in m[Ca^{2+}] which peaked at 54±24* nM. Cooling to 17ºC significantly increased m[Ca^{2+}] to 210±8* nM before ischemia which did not further increase m[Ca^{2+}]. On reperfusion m[Ca^{2+}] fluorescence returned to pre-ischemic values faster in hypothermic than in normothermic hearts. At 120 min reperfusion, developed LVP (% of pre-ischemia) was 49±2 % for normothermic hearts, but 98±3* % for hypothermic hearts; infarct size was 56±2 vs 19±2* %, respectively.
CONCLUSION: m[Ca^{2+}] controls activation of Ca^{2+} sensitive dehydrogenases and oxidative phosphorylation in the mitochondria. A mild increase in m[Ca^{2+}] accelerates ATP synthesis during increased energy demand whereas excessive m[Ca^{2+}] overload has been causally implicated in IR injury and cell death. We show that hypothermia attenuates myocardial m[Ca^{2+}] overload during IR, as evidenced by on-line fluorescence measurements in intact hearts. Mitochondrial protection helps to explain preservation of cardiac function and tissue viability after hypothermic IR.



S-19

REDUCED LEUKOCYTE RECRUITMENT IN MICE DEFICIENT FOR THE UROKINASE RECEPTOR (U-PAR) IS ASSOCIATED WITH SMALLER INFARCTS AND IMPROVED REGIONAL FUNCTION AFTER TRANSIENT MYOCARDIAL ISCHEMIA

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INTRODUCTION: Myocardial ischemia and reperfusion (MI/R) poses a vital threat to over 5 million patients undergoing anesthesia each year. As leukocyte extravasation is a key event in MI its modulation may be a valid therapeutic strategy. Leukocyte adhesion to endothelial cells is regulated by integrins. The urokinase receptor (u-PAR) has been recognized to be critically involved in the regulation of -integrin activity(1). We therefore examined its role in MI/R using u-PAR deficient (u-$PAR^{-/-}$) or wild type mice (wt).
METHODS: 12-week-old gender-matched mice were barbiturate-anesthetized and ventilated with isoflurane in O_2. To induce MI/R the left anterior descending coronary artery (LAD) was ligated for 30 minutes. Reperfusion lasted 3 or 24 hours. Mice were saline-perfused and LV, area at risk (AAR) and infarct were planimetrically delineated using TTC/coomassie blue. Bone marrow-derived polymorphnuclear leukocytes (PMN) were fluophor-labeled and injected upon reperfusion. PMN were counted on 100m sections by epifluorescence microscopy. To detect inflammatory cells in the infarcted tissue sections of paraffin-embedded hearts were stained iummunohistochemically with monoclonal antibodies against CD45. Using 2D-guided M-mode echocardiography we examined regional ventricular function before and after myocardial ischemia using the wall thickening-fraction.
RESULTS: After 3h of reperfusion, u-$PAR^{-/-}$-infarcts were smaller than wt-infarcts (24±9 vs. 35±2.5 % infarct/AAR, u-$PAR^{-/-}$ vs. wt, n=7/5, p<0.05). Within 24h infarcts enlarged significantly less in u-$PAR^{-/-}$ compared to wt (32±2 vs. 49±2 % infarct/AAR, u-$PAR^{-/-}$ vs. wt, n=9/7, p<0.0001). To test to what extent reperfusion injury depended on u-PAR, we examined u-PAR- or wt-PMN homing to ischemic wt-myocardium (64±16 u-PAR-PMN vs. 228±115 wt-PMN, n=3). Only a trend for a reduction of PMN-homing was observed when wt-PMN were injected in u-$PAR^{-/-}$-mice (150±53 wt-PMN, n=3, ANOVA: p<0.05). 7 days after MI/R CD45-positive leukocytes are more abundant in wt-infarcts, whereas no leukocytes are detected in u-$PAR^{-/-}$-infarcts. 4 days post MI/R wt-wall-thickening fraction had significantly decreased by 26±7% (n=5, p<0.01) while regional function of u-$PAR^{-/-}$-mice remained largely unchanged (-5±5%, n=4).
DISCUSSION: u-PAR deficiency significantly reduces infarct size after transient myocardial ischemia by ameliorating reperfusion injury. This effect is associated with reduced leukocyte recruitment to post-ischemic tissue. Reduction of post-ischemic inflammation improves myocardial wound healing and thus mitigates the functional consequences of myocardial ischemia. We therefore predict u-PAR to be an attractive target for modulation of reperfusion injury.
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S-20

FENTANYL PROTECTS STUNNED MYOCARDIUM IN DOGS

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Although the activation of opioid receptors might be a mechanism in myocardial protection against the ischemia/reperfusion injury, cardioprotective effects of fentanyl are still controversial. In the Langendorff rat heart, fentanyl had no effects in recovery of contractility on stunned myocardium. Although fentanyl significantly improved contractility on stunned myocardium in the halothane anesthetized open chest dogs, volatile anesthetics has cardioprotective effects in stunned myocardium. We investigated the cardioprotective effects of fentanyl with no volatile anesthetics on stunned myocardium in dogs.
METHODS: After the approval of Animal Care Committee, 15 dogs were anesthetized with alpha-chloralose and acutely instrumented for measurements of systemic and coronary hemodynamics. The dogs were allocated to one of 3 groups (n=5 for each group) to receive each regimen; low-dose fentanyl (0.01 mg/kg + 0.01 mg/kg/h), high-dose fentanyl (0.1 mg/kg + 0.1 mg/kg/h) or drug vehicle (control). Stunned myocardium was produced by 15-min occlusion of left anterior descending coronary artery (LAD) and 90-min reperfusion in all dogs. Fentanyl was administered starting 15 min before LAD occlusion until the onset of the ischemia. Measurements were made before and during LAD occlusion and after LAD reperfusion. Statistical analysis was made by ANOVA followed by Scheffe's test. $P < 0.05$ was considered significant.
RESULTS: There were no significant differences in demographic data among groups. In the control group, %SS 90 min after reperfusion was 31.5 ± 5.1 % of baseline value. In the group of low-dose fentanyl, %SS showed no significant change compared to the control group. In the group of high-dose fentanyl, %SS showed improved recovery compared to the control group and the value 90 min after reperfusion was 69.3 ± 6.2 % of baseline value. There were no significant differences in coronary blood flow or coronary vascular resistance among groups.
CONCLUSIONS: Preischemic administration of fentanyl markedly improves myocardial contractile dysfunction dose-dependently after ischemia/reperfusion in dogs. Fentanyl protects myocardium against the ischemia/reperfusion injury in vivo.

S-21

THE EFFECT OF BUPIVACAINE ON MYOCARDIAL TISSUE HYPOXIA AND ACIDOSIS DURING VENTRICULAR FIBRILLATION

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INTRODUCTION: Ventricular fibrillation is associated with myocardial ischemia, tissue hypoxia and acidosis. It is likely that the rapid decrease in myocardial tissue pH during fibrillation can lead to irreversible tissue injury. Bupivacaine cardiac toxicity might also be exacerbated by worsening tissue acidosis during fibrillation. The purpose of this study was to measure the rate of decrease in myocardial tissue oxygen pressure (PmO2) and pH during fibrillation in dogs treated with 10 mg/kg bupivacaine intravenous or dogs treated with saline.
METHODS: These studies received animal care committee approval. Twelve dogs were anesthetized with propofol, their tracheas intubated and lungs ventilated with 1.5% end tidal isoflurane with an inspired oxygen content of 30%. The chest was opened and a paratrend fiber optic probe that contains sensors to measure PmO2, pH and temperature was inserted into myocardial tissue at a depth of 6 mm in the left ventricle within the distribution of the left anterior descending artery. The probe is 0.5 mm in diameter and was introduced into the tissue using a 21 gauge angiocatheter. Myocardial temperature was maintained at 38°C. After a 45 minute equilibration period, baseline measures of arterial blood pressure, heart rate, arterial blood gases and pH and myocardial tissue PmO2 and pH were measured. Each dog received either 10 mg/kg bupivacaine over 2 minutes (n = 7) or a sham saline treatment (n = 5). Three minutes later, ventricular fibrillation was initiated by touching a 9 volt battery to the heart. The rate of decrease in PmO2 and pH during ventricular fibrillation was measured in each dog.
RESULTS: Baseline blood pressure, heart rate, blood gas, myocardial PO2 and pH were similar in the two groups of dogs before ventricular fibrillation (table 1). There was a rapid decrease in PmO2 during fibrillation, and the rate of decrease was not different between sham and bupivacaine treated dogs. Tissue pH also decreased during fibrillation, and the rate of decrease was four times faster in sham compared to bupivacaine treated dogs.
DISCUSSION: These results show that in sham treated dogs, myocardial tissue oxygen and pH decreased rapidly during ventricular fibrillation. Bupivacaine significantly reduced the rate of decrease in pH during fibrillation by a factor of four. This may be related to the ability of bupivacaine to inhibit glycolysis or to inhibit myocardial contractility. At the same time, the rate of decrease in PmO2 was not changed by bupivacaine. This may be due to the uncoupling of oxygen utilization and adenosine triphosphate production produced by bupivacaine in the mitochondria.

Myocardial Tissue PO2 and pH during Fibrillation (* = $P < 0.05$ vs. sham)

	Basline PmO2 (mmHg)	PmO2 decrease (mmHg)	Time of PmO2 decrease (min)	Rate of PmO2 decrease (mmHg/min)	Baseline pH	pH decrease	Time of pH decrease (min)	Rate of pH decrease (units/min)
Sham (n = 5)	49±11	41±11	3.0±1.5	15±5	7.32±0.02	0.42±0.13	6.2±3.3	0.08±0.02
Bupivacaine (n = 7)	50±17	49±16	2.5±0.9	22±5	7.28±0.10	0.31±0.08	13.8±5.1*	0.02±0.01*

S-22

CLONING AND CHARACTERIZATION OF THE RAT ALPHA$_{1A}$-ADRENERGIC RECEPTOR GENE PROMOTER: DEMONSTRATION OF CELL-SPECIFICITY AND REGULATION BY HYPOXIA

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Recent studies revealed an important and distinct role for the cardiac $_{1a}$-adrenergic receptor. Surprisingly, given its importance in myocardial ischemia/reperfusion, hypoxia, hypertrophy, and frequent use of rat cardiomyocyte model systems, the rat $_{1a}$AR gene promoter has not been characterized. We isolated and characterized 4.1Kb of rat $_{1a}$AR 5'-regulatory sequence, identifying both a proximal and distal transcription initiation site located 131bp and 1.9Kb upstream from the initiation methionine, respectively. The proximal promoter, described here, lacks typical TATA or CCAAT boxes, but contains *cis*-elements for multiple myocardial-relevant nuclear regulators including Sp1, GATA, and CREB. Additionally, the proximal promoter appears to govern cell-specific basal expression as well as $_{1a}$AR transcription with hypoxic stress. Under normoxic conditions, deletion reporter constructs revealed the presence of several independent enhancer regions between -550/-48 important for basal transcription. Further analysis under hypoxic conditions reveals multiple, independent regions are important for hypoxia-specific transcriptional activity in myocardium, with the -819/-326 region conferring robust hypoxia responsiveness. Gel shift analysis across this region reveals a hypoxia-mediated shift located within -437/-389, which is independent of direct HIF binding. This binding activity was further defined to two 14bp stretches of sequence, previously undescribed for hypoxia responsiveness. These new findings for the $_{1a}$AR gene lay a critical foundation for future studies designed to elucidate specific $_{1}$AR-mediated pathways involved in distinct myocardial pathologies.

S-23

EMPLOYING DOPEXAMINE AS A USEFUL AGENT TO REVERSE THE ARGININE VASOPRESSIN-ASSOCIATED DECREASE IN OXYGEN DELIVERY DURING OVINE ENDOTOXEMIA

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INTRODUCTION: Arginine vasopressin (AVP) is increasingly used for hemodynamic support of septic patients (1). Via reflex mechanisms, AVP reduces cardiac index and in proportion oxygen delivery (2). This could be challenging during sepsis, where tissue oxygen requirements are increased. The purpose of this prospective, controlled study was to determine the efficacy of dopexamine (DPX) as an adjunct to AVP infusion.
METHODS: Healthy ewes instrumented for chronic study received a continuous AVP infusion (2.4 U·h^{-1}). One hour later, DPX was additionally administered at incrementing doses (1, 5, 10 g·kg^{-1}·min^{-1}; each dose for 30 minutes). Then, drug infusions were stopped. After a 24-hour period of recovery, endotoxin (salmonella typhosa, 10 ng·kg^{-1}·min^{-1}) was continuously infused to induce and maintain a hypotensive-hyperdynamic circulation. After 16 hours of endotoxemia, AVP and DPX were given as described previously. Since the same animals were studied in a healthy and a septic state, they served as their own controls (n=7 per group). For statistical analysis, a two-way analysis of variance with a Student-Newman-Keuls post hoc correction was used. Data are expressed as mean±SEM.
RESULTS: The AVP-associated increase in mean arterial pressure was associated with a reduction in cardiac index, thereby decreasing oxygen delivery in both health and endotoxemia. In addition, pulmonary vascular resistance index increased in endotoxemia (202±16 vs. 159±13; P < 0.05). Low doses DPX (1 and 5 g·kg^{-1}·min^{-1}) reversed the changes in cardiac index and pulmonary vascular resistance index and increased oxygen delivery. While high dose DPX (10 g·kg^{-1}·min^{-1}) reduced mean pulmonary arterial pressure in endotoxemic sheep (23±1 vs. 27±1.5; P < 0.05), mean arterial pressure decreased compared with baseline.
DISCUSSION: During ovine endotoxemia, concomitant infusion of AVP and low doses DPX reversed the hyperdynamic circulation and improved DO_2. Although high dose DPX also improved the pulmonary circulation, the aggravation of systemic hypotension might limit its therapeutic use.
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Effects of vasopressin and dopexamine on hemodynamics and oxygen delivery

parameter	state	baseline	sole AVP	AVP+DPX 1	AVP+DPX 5	AVP+DPX 10
MAP	health	101±2	112±3$^{\#}$	109±2$^{\#}$	99±4§	95±3$^{\#\S}$
	endotoxemia	86±2*	105±4$^{\#}$	103±4$^{\#}$	94±4$^{\#\S}$	80±3*§
CI	health	5.9±0.4	3.9±0.3$^{\#}$	5±0.3$^{\#\S}$	5.7±0.3§	7±0.4$^{\#\S}$
	endotoxemia	7.8±0.4*	4.6±0.4	5.1±0.3	6.6±0.5§	8±0.5§
DO_2	health	842±66	475±38$^{\#}$	607±46$^{\#\S}$	707±39§	851±61§
	endotoxemia	1073±49*	613±44*$^{\#}$	670±36$^{\#}$	863± 6§	1012±74*§

AVP=arginine vasopressin [2.4 U·h^{-1}]; DPX=dopexamine [µg·kg^{-1}·min^{-1}]; MAP=mean arterial pressure [mmHg]; CI=cardiac index [L·min^{-1}·m^{-2}]; DO_2=oxygen delivery [mL·min^{-1}·m^{-2}]

*P < 0.05 health vs. endotoxemia; $^{\#}$P < 0.05 vs. baseline; §P < 0.05 vs. sole AVP

S-24

THE EFFECT OF GP683, A NOVEL ADENOSINE KINASE INHIBITOR, ON HEMODYNAMIC AND SYMPATHETIC OUTFLOW IN NERVE-INTACT AND BARORECEPTOR-DENERVATED RABBITS

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INTRODUCTION: It has been reported that continuous i.v. infusion of GP683, one of the adenosine kinase inhibitors, decreased desflurane minimal alveolar concentrations in dogs(1). The purpose of the current study was to evaluate the effects of GP683(G) on mean arterial pressure(MAP), heart rate(HR), renal sympathetic nerve activity(RSNA) and baro-sensitivity, using nerve-intact and baroreceptor-denervated rabbits.
METHODS: New Zealand white rabbits were anesthetized with i.v. urethane, tracheotomized and ventilated. The left renal sympathetic nerves were isolated, and RSNA was recorded along with MAP and HR. In the baroreceptor-denervated group, all animals received a combined denervation of carotid sinus, aortic and vagal nerves. G was dissolved in solvent 5% dimethyl sulfoxide(DMSO). The animals were divided into 6groups (n=6 each): G0.5, 1.0 (0.5 and 1.0mg/kg) and SNP(40g/kg) for the intact group, and G1.0, 2.0 (1.0 and 2.0mg/kg) and 5%DMSO for the denervated group. Each agent was injected i.v. as a bolus and all variables were continuously recorded for the next 30 min. All data (mean±SD) were expressed as percent changes from control values, and ANOVA followed by Sceffe's procedure was used for statistical analysis. $^{*}P<0.05$ was considered statistically significant.
RESULTS: In the nerve-intact group, maximum reductions of MAP occurred within 1min (80.9±5.3%* with SNP, 84.5±6.1%* with G0.5 and 71.2±6.2%* with G1.0, respectively). MAP did not return to baseline values and remained slightly but significantly low with G0.5 and 1.0. After brief but significant baroreflex-mediated increases in RSNA and HR, they returned to baseline values in all groups. The ratios of maximum increase in HR and RSNA to maximum reduction of MAP were significantly reduced by G1.0 (HR/MAP 0.26±0.27, RSNA/MAP 1.64±0.69) in comparison with SNP (1.55±0.68, 6.22±2.97, respectively). There were dose-dependent and significant reductions of all variables in the baro-denervated group even at 30min with G (MAP 84.9±11.2%*, 59.7±12.7%*, HR 94.8±3.9%, 89.9±5.8%*, and RSNA 95.1±2.3%, 82.7±7.8%* for G1.0 and 2.0, respectively). The solvent produced no changes in MAP, HR or RSNA.
DISCUSSION: Since both arterial and cardiopulmonary baroreflexes were eliminated in the baroreceptor-denervated group, decreased RSNA indicates that GP683 directly depressed the central sympathetic nervous system. The significant reduction of the ratios of maximum increase in HR and RSNA to maximum reduction of MAP indicates that GP683 attenuates both cardiac and sympathetic baroreflex sensitivity. Therefore, reduction of sympathetic outflow and attenuated baroreflex sensitivity are contributing factors to GP683-induced arterial hypotention. These sustained effects of GP583 on the cardiovascular and sympathetic nervous systems suggest that GP683 administered by a bolus injection inhibits adenosine kinase continuously so that endogenous adenosine concentrations remain elevated.
Further study is necessary to elucidate whether a single administration of GP683 produces prolonged anesthesia sparing action in addition to hemodynamic and sympathetic depressant actions.
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S-25

DIRECT EFFECTS OF ROPIVACAINE AND BUPIVACAINE ON SYMPATHETIC NERVE ACTIVITY IN RABBITS

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INTRODUCTION: Ropivacaine (R) has been reported to cause less cardiovascular depression than equivalent concentrations of bupivacaine (B) (1,2). The reason may be, in part, related to their different degrees of depressive action to the central sympathetic nervous system. In the present study, we compared the direct effects of R and B on sympathetic nerve activity using baro-denervated rabbits.
METHODS: Twelve New Zealand white rabbits were anesthetized with 1 g/kg urethane iv, and anesthesia was maintained with continuous infusion of urethane (200 mg/kg/hr). All animals had a combined denervation of bilateral carotid sinus, aortic and vagal nerves to eliminate both arterial and cardiopulmonary baroreflexes. The animals were divided into two groups: R group and B group (n=6 for each group). In the R group, the rabbits received R infusion at a rate of 0.25mg/kg/min for 10 min. In the B group, they received B infusion at the same rate for 10 min. Heart rate (HR), mean arterial pressure (MAP) and renal sympathetic nerve activity (RSNA) were continuously recorded. All data (% change) were analyzed by ANOVA and Fisher's PLSD. *P<0.05 was considered significant.
RESULTS: Time course % changes of RSNA are shown in figure. In the B group, RSNA showed a bi-phasic pattern. RSNA initially increased significantly (the highest value; 167.7 ± 25.1%*, mean ± SD, at 4 min) and then, it started to decrease and remained significantly low (the lowest value; 70.1 ± 14.0%* at 15 min). In the R group, RSNA also showed the similar bi-phasic pattern, but there were no significant changes from the control value except at the 3 min measurement point (119.1 ± 15.0%*). Both MAP and HR decreased gradually and significantly during infusion in both groups.
DISCUSSION: Changes of RSNA were due to the direct effect of R and B on the central sympathetic nervous system since both arterial and cardiopulmonary baroreflexes were eliminated. The initial increase of RSNA with B may correspond to the seizure phase of B. Thereafter B significantly decreased RSNA even after its infusion was discontinued. On the other hand, RSNA did not change appreciably with R. Therefore, this may be one of the reasons why ropivacaine has less cardiotoxicity as compared with bupivacaine.
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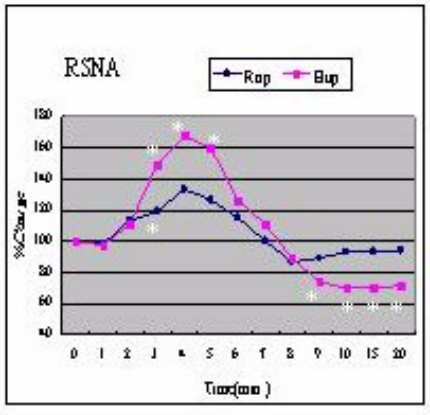

*: p<0.05 vs control

S-26

HEMODILUTIONAL ANEMIA CAUSES TRANSIENT CEREBRAL HYPOXIA AND INCREASED CORTICAL NNOS MRNA LEVELS.

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INTRODUCTION: Cerebral hypoxia may contribute to anemia induced impairment in cognitive function (1). The characteristic increase in cerebral blood flow (CBF) observed with anemia may represent a compensatory response directed toward augmenting cerebral oxygen delivery. Inhibition of neuronal nitric oxide synthase (nNOS) activity partially impairs this response, implicating nNOS as an important mediator of CBF during anemia. (2). Although increased cerebral nNOS mRNA has been demonstrated during hypoxia (3), such upregulation has not been demonstrated during anemia. This study tests the hypothesis that acute hemodilutional anemia causes cerebral hypoxia which triggers an increase in cerebral nNOS mRNA levels, supporting a role for an nNOS mediated increase in CBF.
METHODS: Anesthetized ventilated rats underwent tail artery and jugular vein cannulation. Mean arterial pressure (MAP) was continuously monitored. Blood gas analysis ensured maintenance of normocapnea and normoxia. Polarographic oxygen sensitive microelectrodes and laser doppler flow probes, placed using stereotaxic coordinates, measured cerebral tissue oxygenation ($P_{Br}O_2$) and CBF, respectively. Hemodilutional anemia (n=7) was achieved by exchanging 30 $ml \cdot kg^{-1}$ of blood with pentastarch over 10 minutes. Control animals did not undergo hemodilution (n=6). Cerebral cortical samples were harvested after 3 hours, snap frozen, total RNA extracted, and RT-PCR performed using primers for IL-1, eNOS and nNOS. Quantitation of RT-PCR product was performed using a digital imaging system. Statistical significance was assessed using Wilcoxon rank sum and signed rank tests (Mean ± SEM).
RESULTS: Hemodilution resulted in a final hemoglobin concentration of 51.0 ± 1.2 $g \cdot L^{-1}$ while MAP was maintained near baseline values (68.9 ± 2.8 mmHg). Blood gases did not change significantly (pH 7.40 ± 0.03, P_aCO_2 34.5 ± 1.8 and P_aO_2 125.5 ± 10.4 mmHg). $P_{Br}O_2$ decreased transiently, from 17.3 ± 4.1 to 14.4 ± 4.1 mmHg during hemodilution ($p< 0.01$), before returning to baseline after an additional 10 minutes. Normalization of $P_{Br}O_2$ occurred coincident with the maximal increase in CBF, 10 minutes after completion of hemodilution. After 3 hours, cerebral cortical nNOS mRNA levels were significantly higher in the anemic group relative to controls (2.6 ± 0.6 vs 1.2 ± 0.2 ng RT-PCR product per ng total RNA, respectively, $p<0.05$). No differences in IL-1 or eNOS, mRNA were detected.
DISCUSSION: These data support the hypothesis that acute hemodilutional anemia caused transient cerebral hypoxia which resolved once the maximal increase in CBF was achieved. The increase in cerebral cortical nNOS mRNA levels provide additional evidence that anemia resulted in cerebral hypoxia. Increased nNOS mRNA gene expression may be involved in the mechanism by which increased CBF is maintained during chronic anemia.
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S-27

EFFECTS OF SODIUM THIOPENTAL AND METHYL-PREDNISOLONE DURING OXIDATIVE STRESS IN HUMAN NEURONAL SH-SY5Y CELLS

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INTRODUCTION: Hypothermia is a major neuroprotectant during deep hypothermic circulatory arrest (DHCA). However, as brain cooling is an imperfect process, several pharmacologic adjuvants are also frequently used in an attempt to improve neuroprotection during DHCA (1).Oxidative stress occurring during brain reperfusion, plays a major role in ischemic brain injury. In this study we have compared the effects of sodium thiopental and the glucocorticoid methylprednisolone on hydrogen peroxide (H_2O_2)-induced cell death in cultured human neuronal SH-SY5Y cells.
METHODS: Necrotic cell death was assessed by measuring the enzyme activity of lactate dehydrogenase (LDH) released from the cytosol of cultured human neuronal SH-SY5Y cells into the supernatant. The release occurs upon damage of the plasma membrane. The maximum amount of releasable LDH enzyme activity was determined by the lysis of all cells with a detergent. Cell morphology was monitored using phase contrast microscopy and time lapse photography. The LDH enzyme activity was measured in the supernatants of cells incubated for 3 hours in the control medium with or without either 1 mM sodium thiopental (STP) or 0.3 mM methylprednisolone (MPS). During the last hour, oxidative cell injury was induced by exposure to 1 mM H_2O_2 and the LDH enzyme activity in the supernatants was then measured.
RESULTS: Incubation of neurons in the control medium for 3 hours induced only a minimal cell death (LDH activity 8.7 ± 1.1 % of maximum). Exposure to H_2O_2 produced a large increase in the LDH activity in the supernatants (53 ± 6.2 % of maximum, $n = 9$, $P < 0.05$) and a development of plasmalemmal blebs. The LDH release and the formation of blebs was significantly reduced by the treatment with STP (LDH activity 37 ± 5.1 % of maximum, $n = 9$, $P < 0.05$). However, H_2O_2-induced cell death was not reduced and was actually enhanced by the treatment with MPS, as the LDH activity reached 71 ± 9.6 % of maximum ($n = 9$, $P < 0.05$) and the formation of blebs was potentiated.
DISCUSSION: The neuroprotective effect of STP during H_2O_2 - induced oxidative stress is consistent with its ability to scavange free radicals (2). However, a potentiation of the oxidative injury by MPS is unexpected as glucocorticoids also have an antioxidant action (3). It is possible that this potentiation is caused either by MPS-induced inhibition of glucose uptake into neurons or by stimulation of glutamate-related Ca^{2+} signaling (4). The routine use of glucocorticoids during DHCA may be detrimental as their neurotoxic potential may outweigh their benefits.
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S-28

EFFECT OF SELEGILINE ON THE CONTRACTILE AND PHOSPHATIDYLINOSITOL RESPONSES OF RAT TRACHEA

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Selegiline, monoamine oxidase (MAO) -inhibitor, is widely used for Parkinson's disease and possibly for Alzheimer's disease. The patients treated with selegiline before surgery are increasing in number because the treatment of their diseases is increasing as the number of people with the diseases increases. On the other hand, bronchial hyper-responsiveness and asthma are prevalent among elderly population. Selegiline is reported to cause a transient intracellular influx of Ca^{++} in cultured neuronal cells [1]. Since intracellular Ca^{++} is partly regulated by phosphatidylinositol (PI) response and Ca^{++} is important for smooth muscle contractions, selegiline may affect the airway smooth muscle tension. However, the effects of selegiline on patients with asthma are not fully understood. Thus, we examined the effects of selegiline on acetylcholine (ACh)-induced contractile and PI responses of rat trachea.
METHODS: The studies were conducted under guidelines approved by the Animal Care Committee. Twenty male Wistar rats weighing 250-350g were used for the experiments. The rats were anesthetized with pentobarbital and their tracheas were rapidly isolated. The trachea was cut into 3-mm-wide ring segments or 1-mm-wide slices. Tracheal slices were incubated with [^{3}H]myo-inositol. ACh (3 M in a final concentration) or KCl (40 mM in a final concentration) was added to induce tracheal contraction, and ring relaxation was induced by additions of selegiline from 0 M to 1000 M in final concentrations. The [^{3}H] inositol monophosphate (IP_1), a degradation product of PI response, was measured with a liquid scintillation counter. Data were expressed as mean ± SE. Statistical significance ($P < 0.05$) was determined using ANOVA.
RESULTS: Selegiline attenuated ACh- and KCl-induced tracheal ring contraction dose-dependently. Fifty-percent inhibitory doses (ID_{50}) of selegiline against ACh- and KCl-induced contractions were 120 ± 30 M and 80 ± 20 M respectively. Basal and ACh-induced IP_1 accumulation were 2.51 ± 0.15 and 4.25 ± 0.13 Bq, respectively, and selegiline at a dose of 1000 M attenuated ACh-induced IP_1 accumulation (2.87 ± 0.13 Bq).
CONCLUSIONS: Selegiline inhibited ACh- and KCl-induced contractile responses and it attenuated ACh-induced IP_1 accumulation. These results suggest that selegiline inhibits contractile responses through the inhibition of voltage-operated Ca^{++} channels and the PI response. Thus selegiline would be safe for the patients with asthma.
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S-29

DOES READ'S REBREATHING TECHNIQUE OVER-ESTIMATE THE VENTILATORY RESPONSE TO CO_2?

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INTRODUCTION: Read (1967) described a rebreathing technique to measure the central chemosensory ventilatory response to CO_2 (1). Some studies since then have confirmed that the value obtained using this method is in agreement with the alternative, steady state method (2). However, other studies claim that the Read technique overestimates the response (3). Read's method is still widely used to assess the respiratory effects of many anesthetic drugs (4), so it is important to know whether it provides accurate results. In the absence of a single, very large study comparing steady state and rebreathing methods, one approach to resolving this issue is to conduct a quantitative review (meta-analysis) of published studies.
METHODS: A MEDLINE-assisted search was conducted, supplemented by use of reference lists, to obtain all papers which compared the ventilatory response to CO_2 in humans using rebreathing (Sr) with steady state (Ss) methods. All studies gave their results for Sr and Ss in l/min/mmHg. A value of Sr/Ss and confidence interval (95% CI) was calculated for each study. These values were combined by calculating the mean, weighted for study size (5). Confidence interval analysis was used to assess whether the final result was statistically significant.
RESULTS: A total of 11 relevant publications were found. The largest study used 12 subjects. Sr/Ss ranged from 0.86 to 2.82. The majority (9/11) studies yielded a mean Sr/Ss greater than 1, but in 8 of these, the 95% CI included an Sr/Ss value of 1, suggesting that these 8 studies could not individually detect with confidence any difference in the two methods. Combining the results showed a weighted mean Sr/Ss of 1.56 (95% CI 1.13 to 1.99), which was statistically significant ($P < 0.05$; Fig 1).
CONCLUSIONS: Read's method continues to be used in clinical, anesthetic and physiological studies (6). There are a number of theoretical arguments which question the validity of Read's technique (3), but its continued use appears to be based on misplaced confidence in a few, very small studies performed before 1991 (1,2). When results of all studies are taken into account, rebreathing overestimates the ventilatory CO_2 response by a mean of about 50%. This overestimate would have a profound effect on the interpretation of many clinical studies. Rebreathing techniques should be used with caution in drug or anesthetic studies which aim to assess ventilatory responses to CO_2.
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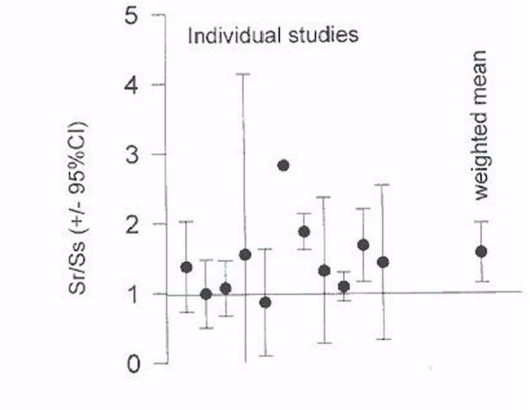

S-30

LEFT ATRIUM COMPUTER MODEL THAT ACCURATELY SIMULATES PRESSURE, FLOW, AND VOLUME,INCLUDING MASS EFFECT AND STARLING'S LAW.

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INTRODUCTION: The goal was the production of a circuit model of the left atrium that could be modeled in PSpice circuit simulation software. The ability of the circuit to accurately generate pressure, flow, and volume waveforms in physiologic units is the source of its flexibility and versatility. The presence of Frank-Starling behavior validated the ability of the model to compensate for varying volume loading conditions. This indicates its feasibility for incorporation into other circulatory and closed-system models. Many current models describe physiologic performance but a lack of flexibility detracts from their use as modular components exploring large-scale circulatory system behavior.
METHODS: The left atrium was modeled in OrCAD PSpice simulation software. The atrium was characterized by a time-varying elastance independent of loading conditions.[1] This is governed by E(t)=Pla(t)/[Vtot(t)-Vresid(t)], where E(t) is the time-varying elastance, and Pla(t), Vtot(t), and Vresid(t) are the time-varying left atrial pressure, total chamber volume, and residual volume, respectively. Values for these parameters were interpreted from Alexander's *in vivo* measurements of 12 anesthetized canines. The model describes the pulmonary veins and capillaries as a pressure source coupled to an R-L-C impedance network.[2] Included in the impedance network is an inductance, Lpv, simulating the mass effect of blood recoil upon contraction. The inflow is then related to the difference in pressures between the pulmonary veins and the left atrial pressure.[3] Volume of the chamber is determined by integration of the net flow as in LaMack et. al.[4] The outflow resulting from atrial systole contributes both to ventricular filling, represented by Qmv, and return flow to the pulmonary veins, Qpv.

RESULTS: The model produces, in physiologic units, pressure (including "v' and "a' waves), volume, and flow characteristic of in vivo data. Validation was performed by generating Frank-Starling curves of left atrial stroke volume as a function of preload. The relationship described by the model, under conditions of constant afterload, was SV=0.4185*Preload+0.0788mL. Yamaguchi et. al. measured 28 patients with ischemic heart disease and found SV=0.48*Preload-1.3mL.[5] The linear relationship between stroke volume and preload indicates the simulation of Frank-Starling behavior.
DISCUSSION: An interesting consequence of the time-varying elastance model in coupling pressure and volume is the dependence of atrial conduit, reservoir and pump function on loading conditions. Thus, the frequency-dependent impedance network plays a role in determining the optimal performance of the left atrium in filling the left ventricle. The model succeeds in providing accurate representation of physiologic behavior while maintaining flexibility for incorporating effects of pathologic conditions or pharmacologic interaction.[6]
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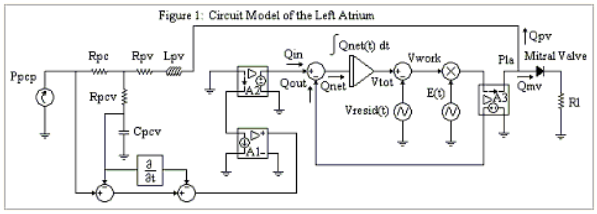
Figure 1: Circuit Model of the Left Atrium



S-31

EFFECTS OF A SILDENAFIL ANALOG; UK343-664, ON A PORCINE MODEL OF ACUTE PULMONARY HYPER-TENSION

AUTHORS: **F. Urdaneta**, N. Valdez, M. Bonnel, M. Palacios, D. Kirby, E. Lobato
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INTRODUCTION: Sildenafil has been associated with pulmonary vasorelaxation 1-3. A more potent sildenafil analog , UK343-664, has been developed but it effects in vivo have not been studied. This study evaluated the effects of UK 343-664 during acute pulmonary hypertension.
METHODS: 14 adult swine were anesthetized with 1 MAC isoflurane and mechanically ventilated with an Fi02 of 100%. End tidal C02 was maintained between 32- 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 . Animals were randomized to two groups. Group 1 (n=9) received 500 mcg of UK343-664 IV over 2 minutes. Group 2 (n=5) served as control. Data were recorded continuously for 60 minutes. Statistical analysis were performed with ANOVA and t tests. A $p < 0.05$ was considered significant
RESULTS: Pulmonary hypertension was achieved in all animals. The administration of UK343-664 was associated with a significant decrease in pulmonary artery pressure (30.3%; $p<0.05$), and pulmonary vascular resistance (42%;$p<0.05$), without systemic vasodilatation. This effects were partially maintained at 30 minutes (17.3% and 39% decrease respectively; $p<0.05$).
CONCLUSIONS: The administration of UK 343-664 was associated with significant vasodilatation without systemic effects. This may represent a significant advance in the treatment of acute pulmonary hypertension. It's potential clinical implications need to be explored

S-32

PRETREATMENT WITH VOLATILE ANESTHETICS PREVENTS NEUTROPHIL-INDUCED CONTRACTILE DYSFUNCTION IN ISOLATED RAT HEARTS: LACK OF ROLE FOR K_{ATP} CHANNELS

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INTRODUCTION: Volatile anesthetics have been shown to precondition the myocardium against functional depression and infarction following ischemia-reperfusion (1). Neutrophil (PMN) activation, adherence, and release of oxygen free radicals and proteolytic enzymes are known to play a major role in reperfusion injury. Our previous study suggested that an ability of volatile anesthetics to inhibit PMN-endothelium interactions may be involved in their cardioprotective effects (2). The present study was conducted in isolated crystalloid-perfused rat hearts to test the hypothesis that pretreatment with isoflurane (Iso) or sevoflurane (Sevo) can prevent the cardiac dysfunction caused by PMN activated with platelet activating factor (PAF). Because K_{ATP} channels have been implicated in the preconditioning effects of volatile anesthetics in vivo, we evaluated the role of these channels using the K_{ATP} channel antagonist glibenclamide (Glib).
METHODS: Studies were performed in 56 isolated, paced rat hearts. The hearts were perfused at constant flow with Kreb's buffer at a rate sufficient to achieve a perfusion pressure of 70 mmHg. Left ventricular developed pressure (LVDP) served as an index of myocardial contractility. The basic experimental protocol consisted of 10 min administration of PMN-PAF mixture followed by 30 min recovery. The intracoronary concentration for PMN and PAF were 3 x 10^5 PMN/ml and 1 nM, respectively. The main experimental groups were: 1) control group: no pretreatment; 2) pretreatment with Iso; 3) pretreatment with Sevo; 4) pretreatment with Iso during Glib (10 M); 5) pretreatment with Sevo during Glib. Pretreatment of the heart consisted of administration of 1 MAC Iso or Sevo for 15 min followed by 10 min washout prior to administration of PMN-PAF. Additional validation studies demonstrated: 1) that neither PMN alone nor PAF alone caused cardiac dysfunction, and 2) that, although Glib alone did not alter PMN-induced cardiac dysfunction, it prevented the protection conferred by the specific K_{ATP} channel opener pinacidil.
RESULTS: PAF-activated PMN caused marked, persistent reductions (>50%) in LVDP (Figure). Pretreatment with either Iso or Sevo abolished this effect. Glib did not alter this action of the anesthetics.
DISCUSSION: 1) The volatile anesthetics Iso and Sevo had a profound preconditioning effect on the heart; 1 MAC of each anesthetic was adequate to completely abolish the ability of activated PMN to cause cardiac dysfunction. 2) The inability of Glib to blunt this effect suggests that it was independent of the K_{ATP} channels in the myocytes and coronary vasculature.
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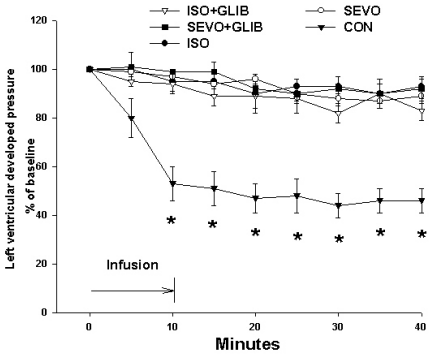

Values are Mean±SE. *, P<0.05 from treatment groups.

S-33

PROPOFOL INCREASES CONTRACTILITY DURING ENDOTHELIN-1 AND ANGIOTENSIN II RECEPTOR ACTIVATION IN RAT CARDIOMYOCYTES

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INTRODUCTION: Myocardial levels of endothelin (ET) and angiotensin (Ang) are elevated in patients with hypertension and congestive heart failure. Activation of ET-1 and Ang II receptors results in stimulation of parallel, yet divergent, signaling pathways. We previously demonstrated a propofol-induced potentiation of 1A-adrenoreceptor mediated increases in cardiomyocyte shortening via activation of a protein kinase C-dependent pathway (1). Our current objectives were to identify the extent to which propofol alters ET-1 and Ang II receptor-mediated cardiomyocyte inotropy.
METHODS: All procedures were approved by the Institutional Animal Care and Use Committee. Freshly isolated ventricular myocytes were obtained from 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 was 125 ± 5 m and baseline [Ca2+]i was 120 ± 13nM. Cell shortening induced by field-stimulation resulted in a twitch contraction that was 3.5 ± 0.4 m. Time to peak (Tp) [Ca2+]i and shortening were 107 ± 3 and 197 ± 26 msec, respectively. Time to 50% return (T50r) to baseline [Ca2+]i and shortening were 176 ± 12 and 177 ± 12 msec, respectively. Addition of ET-1 (10-7M) increased ($p < 0.05$) twitch contraction by 56 ± 17%, whereas peak [Ca2+]i only increased by 11 ± 6%. Tp and T50r for [Ca2+]i and shortening were unaltered by ET-1. In contrast, addition of Ang II (10-7M) increased ($p < 0.05$) both twitch contraction by 180 ± 16% and peak [Ca2+]i by 55 ± 14%. Tp for [Ca2+]i and shortening and T50r for [Ca2+]i were not altered by Ang II, but T50r for shortening decreased ($p < 0.05$) by 29 ± 7%. In the presence of ET-1 or Ang II-induced inotropy, addition of propofol (10-4 M) further increased ($p < 0.05$) twitch contraction by 38 ± 12% and 159 ± 24%, respectively, whereas peak [Ca2+]i only increased by 17 ± 8% and 14 ± 11%, respectively. Propofol did not alter Tp and T50r for [Ca2+]i or shortening.
DISCUSSION: These results demonstrate the predominance of a Ca2+ sensitizing action of ET-1 on cardiomyocyte function, whereas Ang II enhances both [Ca2+]i and myofilament Ca2+ sensitivity. These data suggest that distinct signaling pathways are involved in the ET-1- and Ang II-induced cardiomyocyte inotropy. Propofol further increased contractility during ET-1 and Ang II receptor activation, primarily via an increase in myofilament Ca2+ sensitivity.
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S-34

CYCLIC GMP PHOSPHODIESTERASE INHIBITION AND UNCOUPLING OF BETA-ADRENERGIC RESPONSES IN RENAL HYPERTENSION-INDUCED CARDIAC HYPERTROPHY

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INTRODUCTION: It has been shown that negative metabolic effects of cGMP were altered in renal hypertension-induced cardiac hypertrophy in rabbits (1,2). We tested the hypotheses that inhibition of cGMP degradation would decrease -adrenergic responses in cAMP production and contractile function in isolated cardiac myocytes and these effects would be altered in the hypertrophic myocytes.
METHODS: Freshly isolated ventricular myocytes were prepared from hearts of control (CON) and 1K1C (one-Kidney-one-Clip) renal hypertensive hypertrophic rabbits (35 days postoperatively). Percent cell shortening (PCS) was measured by a video edge detector. Myocyte levels of cGMP and cAMP were measured. Myocytes were treated with isoproterenol (ISO $10^{-8,-6}$ M) or selective cGMP phosphodiesterase (PDE) inhibitor zaprinast (ZAP 10^{-5}M) alone for 5 min or in combination. ANOVA was used for statistical analysis. A value of $p < 0.05$ was accepted as significant. Data were presented as Mean±S.E.M. (N=7)
RESULTS: Isoproterenol (10^{-6}M) increased cAMP level(+117%) (2.3±0.3 to 5.0±0.7 pmol /10^5 cells) and percent cell shortening (+33%) (4.8±0.2% to 6.4±0.3%) (see Figure: * significantly different from the Base value) in the control myocytes. In 1K1C myocytes, isoproterenol (10^{-6}M) increased cAMP (+55%) (4.9±0.8 to 7.6±1.4 pmol /10^5 cells) without changing percent cell shortening (5.3±0.4% to 4.9±0.3%) (see Figure: + significantly different from the CON-ISO-6 value). The basal level of cAMP was higher in 1K1C than the control myocytes. Zaprinast (10^{-5}M) increased cGMP (CON:150±20 to 209±14 fmol /10^5 cells; 1K1C: 182±23 to 233±24 fmol /10^5 cells) and decreased percent cell shortening (CON: 6.2±0.4% to 5.2±0.3%; 1K1C: 6.6±0.9% to 4.7±0.5%) in both groups. Furthermore, in the presence of zaprinast (10^{-5}M) , isoproterenol (10^{-6}M) increased cAMP (CON: 3.0±0.7 to 4.0±0.4 pmol /10^5 cells; 1K1C: 5.5±1.1 to 8.4±1.8 pmol /10^5 cells) without changing percent cell shortening (CON: 5.2±0.3% to 4.7±0.3%; 1K1C: 4.7±0.5% to 4.8±0.5%) in both groups.
DISCUSSION: The results show that the renal hypertension-induced cardiac hypertrophic rabbits had decreased cardiac contractile responses to -adrenergic stimulation. Furthermore, -adrenergic-induced contractile responses and cAMP production were uncoupled in the hypertrophic cardiac myocytes. Inhibition of cGMP degradation by zaprinast blunted the contractile functions without affecting cAMP production in control myocytes. This uncoupling effect of zaprinast seems similar to that of renal hypertension-induced cardiac hypertrophy.
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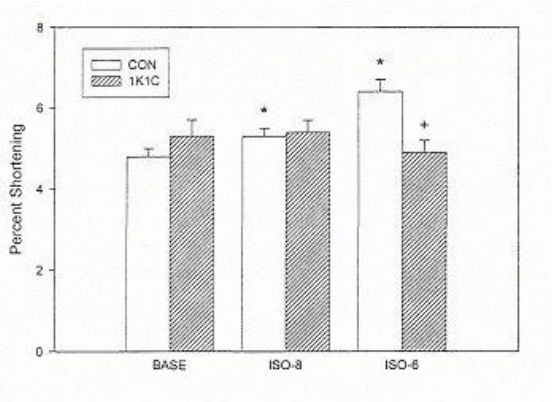

S-35

CARDIOPULMONARY BYPASS REDUCES THE MAC OF ISOFLURANE IN THE RAT

AUTHORS: **H. Yang**, H. M. Homi, B. E. Smith, H. P. Grocott
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INTRODUCTION: The influence of cardiopulmonary bypass (CPB) on anesthetic requirements has been the subject of past investigations, but definitive conclusions have been affected by methodologic limitations, lack of adequate controls, and other confounding physiologic variables (1,2). Recently, clinical data has also suggested a CPB-induced reduction in isoflurane requirements (3). The purpose of this investigation was to determine the influence of CPB on the minimum alveolar concentration (MAC) of isoflurane in a rat model of CPB.
METHODS: Male adolescent Sprague-Dawley rats (350-400 gm) were anesthetized with isoflurane, intubated, ventilated and surgically prepared for CPB following which they were randomized to either Sham-operated or CPB groups. The CPB group underwent 90 minutes of normothermic (37.5 ºC) non-pulsatile CPB (160-180ml/kg/min) utilizing a membrane oxygenator. The Sham group was cannulated but did not undergo CPB. Pre- and post-CPB MAC determinations, using a tail-clamp method (4), were compared within groups using an unpaired Student's T-test. Physiologic values were compared between groups using a paired Student's T-test with a Bonferonni correction to control for multiple comparisons. A $P < 0.05$ was considered significant.
RESULTS: Ten rats underwent CPB and 13 rats served as Sham-operated controls. The rats did not differ with respect to physiologic values with the exception of PaO_2 (445-462 mmHg, CPB vs 284-292 mmHg, Sham; $p = 0.005$) and pH (7.50-7.52, CPB vs 7.43-7.45, Sham; $p = 0.005$). The CPB group had a pre-CPB baseline isoflurane MAC of 1.09 ± 0.11 % vs. 1.09 ± 0.08 % in the Sham group ($p = 0.90$). Twenty minutes following CPB, the CPB group exhibited a 10% decrease in MAC to 0.98 ± 0.14 % ($p = 0.0026$, compared to baseline; Figure 1). The MAC in the Sham group was unchanged ($p = 0.585$, compared to baseline). Two hours after CPB, the CPB group MAC remained decreased compared to baseline at 0.99 ± 0.14 % ($p = 0.0032$).
DISCUSSION: CPB caused a small (10%) but significant reduction in the MAC of isoflurane. This finding may explain why the isoflurane requirements to maintain a constant bispectral index (BIS) in humans, when compared to pre-CPB, are decreased in the post-CPB period (3). The mechanism behind this reduction in MAC is not clear but may be related to cerebral injury (ischemia) or inflammation-associated cellular swelling (of brain and possibly spinal cord).
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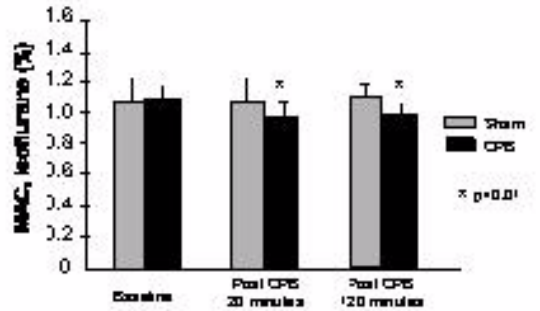

S-36

CIRCULATING PLATELET-LEUKOCYTE ASSOCIATES IN PATIENTS ON THE NOVACOR AND HEARTMATE VENTRICULAR ASSIST DEVICE

AUTHORS: **U. R. Jahn**, S. Christiansen, H. Van Aken, H. H. Scheld, D. Hammel, B. E. Kehrel
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INTRODUCTION: Platelet-leukocyte adhesion may occur as a consequence of both, platelet or leukocyte activation and result in the formation of platelet-leukocyte associates. They possibly play an important role in the deposition of activated platelets in a thrombus. Since hemostasis in patients with implanted left ventricular assist device (VAD) is still lacking knowledge, we were interested whether VAD´s differing in material and inner surface may differently activate the hemostatic system, which may lead to differences in platelet-leukocyte associates formation.
We therefore studied the *ex-vivo* platelet-leukocyte associates formation in patients on left ventricular assist devices with a pulsatile flow, with a smooth (Novacor) and rough (HeartMate) inner surface. We investigated the hypothesis, that a rough inner surface may have less platelet and leukocyte activating properties and may lead to less extended formation of platelet-leukocyte associates.
METHODS: Platelet-leukocyte associates were identified as platelet-granulocyte and platelet monocyte associates using flowcytometrical methods. They were quantified, measuring the percentage of leukocytes (granulocytes identified by FSC / SSC properties and monocytes marked with FITC-labeled anti-CD 14) positive for the platelet-specific marker CD42a.
The study was performed with whole blood samples of 5 patients on the Novacor VAD and 5 patients on the HeartMate VAD. All patients were anticoagulated with acetylsalicylic acid, dipyridamole and heparin. Assist device patients were only included in the study, when the last surgical intervention was at least 4 weeks ago, when they were on a normal ward expecting discharge and when they were without any infection problems.
RESULTS: In whole blood samples of Novacor VAD patients a significantly higher percentage of platelet-granulocyte associates and platelet-momocyte associates could be observed compared to the blood of patients on the HeartMate VAD. $P < 0.05$, ANOVA
DISCUSSION: Since the appearance of platelet-granulocyte and platelet-monocyte associates can be attributed to the activation of these different cells, our data indicate, that the degree of platelet and leukocyte activation might be significantly higher in the Novacor system, compared to the HeartMate system.

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S-37

CARDIAC ARRESTS DURING ANESTHESIA FOR NONCARDIAC SURGERY: REVIEW OF 518,249 ANESTHETICS BETWEEN 1990-2000 IN A TERTIARY REFERRAL CENTER

AUTHORS: J. Sprung, **G. T. Girgenti**, M. Warner, D. R. Schroeder, B. M. Christopher, D. O. Warner
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OBJECTIVE: To estimate the frequency of cardiac arrest during anesthesia and characteristics associated with immediate (1-hour) survival in patients who experience intraoperative cardiac arrest.
METHODS: We prospectively ascertained intraoperative cardiac arrests that occurred in patients undergoing noncardiac surgery between January 1, 1990 and December 31, 2000. Survival outcome and characteristics potentially associated with survival were abstracted from patient records. Logistic regression analysis was performed to assess characteristics associated with immediate survival. Type of surgery, ASA classification and urgency of procedure were included as adjuster variables in all models. Variables with some evidence (P<0.15) of an association with immediate survival from the adjusted univariate analyses were included in a multivariate analysis using backward elimination of non-significant variables. Two-tailed P-values <0.05 were considered statistically significant.
RESULTS: During the study period intraoperative cardiac arrest occurred in 233 of 518,294 anesthetics administered (4.3 per 10,000 anesthetics). One hundred and four (46.4%) patients survived at least 1 hour, and seventy-seven (34.5%) survived hospital discharge. Patients with increased ASA physical status (ASA 1-3 vs ASA 4-5) had lower likelihood of survival (P<0.001). Survival in patients who had emergency surgery was lower (30.6%) than in those undergoing elective surgery (59.2%)(P<0.001). From adjusted univariate analyses (adjusted for ASA status, and urgency of surgery), the likelihood of survival of at least one hour was increased with shorter duration of surgery prior to arrest (P=0.049), in patients not requiring continuous vasopressor infusions during surgery (P=0.004), in patients who did not have prolonged intraoperative hypotension before arrest (P<0.001). Also, patients who were not monitored before arrest with arterial line (P=0.004) and CVP (P<0.001) had better survival. Patients with hemorrhagic cardiac arrest arrested had the lowest likelihood of surviving (P<0.001). From multivariate analysis, after backward elimination of non-significant variables, the following characteristics were found to be independent predictors of immediate survival: non-diabetic patients (OR=3.3, P=0.009), patients who were not monitored with CVP (OR=2.5, P=0.018), those without intraoperative hypotension prior to arrest (OR=2.5, P=0.008), patients arresting during standard working hours [Monday to Friday 7:00 to 20:00] (OR=4.1, P=0.007), and cause of arrest (OR=1.0 for bleeding, OR=5.8 for cardiac and OR=13.5 for other, P<0.001).
CONCLUSION: Patients with cardiac arrest due to hemorrhage had worse immediate survival compared to those with other causes. Other predictors of poor outcome (diabetes, use of invasive monitoring, intraoperative hypotension) may be reflective of patients with preexisting co-morbidities. Those who arrested during regular working hours had better immediate outcome than patients that arrested during nights or weekends.

S-38

THE RISK OF PERIOPERATIVE CARDIAC COMPLICATIONS IS HIGH IN MAJOR VASCULAR SURGERY PERFORMED WITHIN A MONTH OF CORONARY ARTERY BYPASS GRAFT SURGERY (CABG): A CASE-CONTROL STUDY

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INTRODUCTION: Prophylactic coronary revascularization (PCR) may be considered before major noncardiac surgery, if the perioperative cardiac risk for the noncardiac surgery is significantly reduced by PCR. Although retrospective data suggest that prior CABG reduces the cardiac risk of subsequent noncardiac surgery, the interval between CABG and noncardiac surgery was not specified (1). We have previously showed that patients who had major vascular surgery performed within a month of CABG appeared to have very high cardiac complication rates (2). In this study, we extend our previous study to match the cases with controls and compare the cardiac complication rates.
METHODS: From our vascular surgical patient database from 1990-99, we identified 35 patients who had major vascular (16 aortic, 19 peripheral vascular) surgeries within a month of CABG. Three control patients were then identified per index case by matching age, gender, race, and type of surgery and by requiring maximum matching of the 5 intermediate clinical predictors of the American Heart Association (AHA) preoperative cardiac evaluation algorithm (3), which are insulin-dependent diabetes mellitus (IDDM), history of congestive heart failure (CHF), history of myocardial infarction (MI), stable angina, and serum creatinine > 2.0 mg/dl. Rates of cardiac complications (MI, CHF, death) were compared between the cases and controls by Monte Carlo randomization test of proportions, with $p < 0.05$ taken as significant.
RESULTS: Index cases and controls were exactly matched for age (68 ± 10), gender distribution (M:F=4:3), and type of surgery by design. Of the intermediate clinical predictors of AHA, history of CHF was more common among the index cases (20/35) than controls (33/105) ($P < 0.02$), while stable angina was less common among the index cases (0/35 vs. 20/105, $P < 0.02$). The frequency of the other 3 predictors was not significantly different: IDDM (11/35 vs. 44/105), history of MI (19/35 vs. 38/105), and serum creatinine > 2 g/dl (9/35 vs. 16/105). Compared to the control cases, the index cases had significantly greater rates of perioperative 30-day mortality (7/35 vs. 2/105, $P < 0.01$) and of death or nonfatal cardiac complications (12/35 vs. 8/105, $P < 0.01$).
DISCUSSION: When matched by demographic variables and by the intermediate clinical predictors of AHA, patients undergoing major vascular surgeries within a month of CABG had significantly higher cardiac complication rates than other patients having similar surgeries. The benefit of PCR by CABG may not be realized if the subsequent vascular surgery is performed within a month of CABG. Whenever possible, major vascular surgery should be delayed at least a month after CABG.
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S-39

A DOSE-RESPONSE STUDY OF PROSTAGLANDIN E1 ON RADICULAR BLOOD FLOW VELOCITY AFTER LUMBAR DISCECTOMY

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INTRODUCTION: Mechanisms of lumbosacral radiculopathy are hypothesized to be ischemic neuritis of the cauda equina or the nerve root. This study was designed to evaluate the dose-effect relationship of prostaglandin E1 (PGE1) on radicular blood flow velocity (RBFV) after lumbar discectomy.
METHODS: After institutional approval and informed consent, 48 patients undergoing lumbar discectomy were allocated to one of three groups. Anesthesia was maintained with N2O-O2-sevoflurane. After lumbar discectomy, a probe of laser doppler flowmetry was placed directly on L4 or L5 nerve root to measure RBFV. Group A (N=17) received intravenous infusion of normal saline for 10 minutes. Group B (N=18) received intravenous infusion of 20 mcg of PGE1, and group C (N=13) received intravenous infusion of 50 mcg of PGE1 for 10 minutes, respectively. The RBFV, mean arterial pressure (MAP), hematocrit (Hct), percutaneus oxygen saturation (SpO2), and end-tidal carbon dioxide tension (PETCO2) were measured before infusion (T1), 5 minutes after starting injection (T2), 10 minutes after starting infusion (T3), and 5 minutes after the end of infusion (T4). Statistical significance ($p<0.05$) were determined using ANOVA and Scheffe's test. Data were shown as mean ±SD.
RESULTS: The three groups were similar in Hct, SpO2, and PETCO2. In group A, MAP and RBFV showed no change throughout the time course. In group B, the MAP (86.5 ± 9.2 mmHg, at T1) showed a significant decrease at T2 (78.9 ± 9.1 mmHg, $p<0.001$ vs. T1), T3 (76.8 ± 6.8 mmHg, $p<0.001$ vs. T1), and T4 (77.7 ± 6.6 mmHg, $p<0.001$ vs. T1), while the RBFV (14.5 ± 6.6 ml/100g/min at T1) showed a significant increase at T2 (17.4 ± 6.8 ml/100g/min, $p<0.05$ vs. T1), T3 (17.8 ± 8.1 ml/100g/min, $p<0.05$ vs. T1), and T4 (19.2 ± 8.8 ml/100g/min, $p<0.05$ vs. T1). In group C, the MAP (86.2 ± 9.4 mmHg at T1) showed a significant decrease at T2 (77.3 ± 9.7 mmHg, $p<0.001$ vs. T1), T3 (70.2 ± 7.9 mmHg, $p<0.001$ vs. T1, $p<0.05$ vs. group B), and T4 (71.4 ± 9.6 mmHg, $p<0.001$ vs. T1, $p<0.05$ vs. group B), while the RBFV (14.8 ± 6.0 ml/100g/min at T1) showed a significant increase at T2 (17.7 ± 8.1 ml/100g/min, $p<0.05$ vs. T1), T3 (18.3 ± 10.8 ml/100g/min, $p<0.05$ vs. T1), and T4 (20.0 ± 10.2 ml/100g/min, $p<0.05$ vs. T1). There was no significant difference in the RBFV between group B and group C.
CONCLUSION: The results show that low- and moderate- doses of PGE1 increases radicular blood flow velocity after discectomy. A ceiling effect of PGE1 was observed at the dose of 20 mcg or more.

S-40

HTK VERSUS UW PRESERVATIVE SOLUTION: HEMODYNAMIC AND METABOLIC CHANGES DURING ORTHOTOPIC LIVER TRANSPLANTATION

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INTRODUCTION:
University of Wisconsin solution (UW) is at present the gold standard for liver preservation. However, UW solution is known to cause early failure of microcirculation in grafted liver from preservation/ reperfusion injury. In order to prevent this injury various other preservation solutions have been studied. Histadine-Tryptophan-Ketoglutarate preservative solution (HTK) has shown to improve the microcirculation of the grafted liver [1].
The purpose of this study is to underline the differences between the HTK and UW preservation solutions regarding the hemodynamic and metabolic effects and the incidence of postreperfusion syndrome (PRS) [2] (MAP < 30 % from baseline value within 5 minutes after reperfusion), during orthotopic liver transplantation (OLT).
METHODS: After IRB approval, 40 adult patients (55 ± 10 years), 23 males and 17 females undergoing first OLT were prospectively studied. They were divided into two groups of 20 patients each depending on preservation solutions used HTK versus UW. Before reperfusion grafted liver was flushed via the portal vein with cold lactated Ringer's solution in UW group while liver in HTK group was not flushed. Measured hemodynamic and metabolic variables included: heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), pulmonary artery pressure (PAP), cardiac output (CO), systemic vascular resistance (SVR) and serum potassium (K^+), ionized calcium (Ca++), base deficit (BE), serum lactate. Variables were measured at I +60 (60 minutes after skin incision), 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 is presented as mean value ± standard deviation.

RESULTS: Are shown in Table 1.

Table 1: Hemodynamic and metabolic changes during OLT in HTK and UW group

Variables	Groups	I + 60	III + 30 s	III +5	III + 30	III + end
HR beats/m	HTK	81±15	66±12[a,b]	80±8[b]	84±13[b]	84±14[b]
	UW	90±16	82±21	95±14	95±13	97±14
MAP mmHg	HTK	74±11	56±13[a]	68±11	74±10	71±8
	UW	77±9	60±13	67±11	71±11	69±9
K^+ mmol/l	HTK	4±0.5	4.8±1.2[a]	3.7±0.6	3.7±0.5	3.8±0.6
	UW	3.9±0.7	5.2±1.1[a]	3.9±0.9	3.8±0.7	3.8±0.6
BE mmol/l	HTK	-2.2±2.5	-3.2±3.4[b]	-2.6±2.9[b]	-2.7±3.3	-4±3.4
	UW	-4.1±3.3	-5.7±2.9	-5.1±3.3	-4±2.9	-3.4±3.6
Lactate mmol/l	HTK	2.4±2.3	6.1±1.9[a,b]	5.7±1.7[a,b]	5.6±2.3[a,b]	5.8±2.9[a,b]
	UW	3.8±2.6	9±3.7	8.7±3.5	8.3±3.8	8.1±3.6

[a] $p < 0.05$ from baseline, [b] $p < 0.05$ between the groups

Incidence of PRS was 40 % in HTK group and 25 % in UW group.
DISCUSSION: 1) In the HTK group the incidence of PRS is more frequent, however the recovery from hemodynamic instability is faster. 2) In HTK group, a lower serum lactate level indicates a better graft function.
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S-41

PREOPERATIVE BETA-BLOCKADE TO A DESIRED HEART RATE DOES NOT NECESSARILY ACHIEVE DESIRED INTRAOPERATIVE HEART RATE

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INTRODUCTION: b-blockers (BB) decrease postoperative cardiac morbidity and mortality1. Of the proposed mechanisms associated with their beneficial effects, a decrease in oxygen demand secondary to decreased chronotropy is hypothesized to play a major role. The 90% decrease in cardiac events reported by Poldermans et al1 was seen in a protocol where BB were titrated preoperatively to a heart rate (HR) =60 bpm (or to a max. of 10 mg bisoprolol, mean HR 66/min) and maintenance of stringent perioperative HR control. Recent ACC/AHA Guidelines recommend titrating preoperative BB to maintain resting HR between 50-60 bpm2. Recent recommendations by Auerbach and Goldman et al3 further define patients who may benefit from perioperative beta-blocker use. This study was conducted to determine: (1) the prevalence of BB use in high risk populations (as defined by Auerbach et al), and (2) to evaluate their baseline HR and peak intraoperative HR response as a measure of adequacy of perioperative b-blockade.
METHODS: A retrospective review of the pre-anesthetic assessment record was conducted on 188 consecutive patients who were scheduled to undergo major vascular surgery (CEA, supra and infrainguinal bypass, thoracic and aortic abdominal aneurysm) between Jan 2001 to March 2002 at Yale-New Haven Hospital. Demographic data, medications, pertinent review of systems and resting HR and BP, while in the Pre-Admission Center, were obtained from the electronic records. Peak intraoperative HR and BP were obtained from chart review. Patients were grouped as: i) vascular patients on BB (Vasc-BB), ii) vascular patients not on BB (Vasc-no BB). Data are presented as mean ±SD and analyzed by ANOVA and Fischer exact test. P 60 bpm for Vasc-BB vs. Vasc-noBB was significant (p<0.001, Fischer exact test). Surprisingly, the peak intraoperative HR response was not significantly blunted in Vasc-BB vs. Vasc-noBB (82.4/min ±13.0 vs. 85.2/min±15.8) (Table).
CONCLUSION: Our study suggests that a more aggressive approach is required to increase use of preoperative b-blocker therapy in suitable patients. Even though the average HR in patient on BB was similar to one achieved by Poldermans et al, intraoperative increase in HR was still significant. Anesthesiologist need to be vigilant, as routine preoperative BB use does not prevent intraoperative increase in HR and supplemental prophylactic BB may be required to control intraoperative HR effectively.
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Patients	Age (SD)	PAT HR (SD)	PAT SBP (SD)	PAT-DBP (SD)	PEAK Intraoperative HR/min (SD)	PEAK Intraoperative SBP (SD)	PEAK Intraoperative DBP (SD)
Vasc-BB	69.8 (9.6)	65.6 (10.8)	141.5 (23.6)	73.8 (11.2)	82.4 (13.1)	168.9 (20.1)	86.4 (14.3)
Vasc-no BB	70.1 (14.9)	71.5 (15.5)	139.2 (36.9)	71.5 (19.6)	85.8 (15.7)	167.2 (29.8)	85.2 (15.8)

S-42

TRACHEAL INTUBATION IN SIMULATED GRADE III DIFFICULT LARYNGOSCOPY: COMPARISON OF SINGLE-USE PLASTIC AND MULTIPLE-USE GUM ELASTIC BOUGIE

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INTRODUCTION: The gum elastic bougie is the most commonly used aid to facilitate intubation during grade III laryngoscopy (1). Traditionally in the United Kingdom, the multiple-use gum elastic bougie has been used (1), which is washed (but not sterilised) between uses. With increasing concern regarding multiple-use devices and cross-infection (2), a new single-use bougie has been introduced. Anecdotally, it appears that any bougie which lacks flexibility and curvature is more difficult to use (3,4). The purpose of this study was to compare success rates for tracheal intubation in simulated Cormack and Lehane Grade III laryngoscopy (3).
METHODS: We studied 32 ASA I and II adult patients (day-case dental procedures). Simulation of grade IIIa laryngeal view (epiglottis only just obscuring the view of the arytenoids) was achieved by lowering the Macintosh laryngoscope blade (5,6). One operator maintained the laryngoscope in position while another attempted intubation. Patients were randomised to either the new single-use plastic bougie (New) or multiple-use gum elastic bougie (Old). If the intubation failed with the first device (one attempt only), the alternative study device was used. Success rates and intubation times were recorded.
RESULTS: The Old bougie was successful in 15/16 cases; the New bougie in only 9/16 cases (^{2} test with Yates' correction, P<0.041). Of the 7 cases which failed with the New bougie, the Old was successful in 5. The New was successful in the single case in which the Old failed. Total intubating times were under 85 sec in all cases, and there were no significant differences between the groups.
CONCLUSIONS: The difference in success rates between the Old and New bougies is striking. Although minimising the risk of cross-infection is important, it is of concern that the newly-introduced device performs less well and introduces the more important risk of failed intubation. It is not possible to blind a study such as this, and it would be very important for others to repeat our findings, to minimise the risk of bias. A rational approach would be to suggest that: where a bougie is to be used routinely in all patients the single-use bougie should be used; in a lifesaving situation in occasional patients, the older, gum elastic type should be used. Alternatively, in the latter instance, a fibreoptic scope may also be used (7).
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S-43

TRACHEAL INTUBATION IN SIMULATED GRADE III DIFFICULT LARYNGOSCOPY: COMPARISON OF THE FIBREOPTIC SCOPE AND PLASTIC BOUGIE

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INTRODUCTION: The bougie is the most commonly used aid to facilitate intubation during grade III laryngoscopy (1). The technique is blind and multiple attempts may cause airway trauma. Flexible fibreoptic endoscopy offers a continuous view and may minimise trauma (2). We compared the fibreoptic scope and single use bougie for orotracheal intubation in two different simulated grade III laryngoscopic views.
METHODS: We studied 64 ASA I and II adult patients (day-case dental procedures). Simulation of laryngeal view was achieved by lowering the Macintosh laryngoscope blade (3). In 32 patients, a grade IIIa view was simulated (epiglottis only just obscuring the view of the arytenoids). In 32 patients a grade IIIb view was simulated (epiglottis touching the posterior pharyngeal wall). One operator maintained the laryngoscope in position while another attempted intubation. Patients were randomised to either fibreoptic scope or bougie. If the intubation failed with the first device (one attempt only), the alternative study device was used. Success rates and intubation times were recorded.
RESULTS: (A) Grade IIIa view: All 16 (100%) of the fibreoptic-guided intubations were successful compared with 8 (50%) where a bougie was used (^{2} test, $P<0.02$). The fibreoptic scope was successful in all 8 patients in whom the bougie had failed as the primary method. (B) Grade IIIb view: The fibreoptic scope was successful in 8 (50%) cases, compared with 1 (6%) case using the bougie (^{2} test, $P<0.02$). Where the bougie had failed as the original method, the fibreoptic scope was successful in 10 (67%) cases; where the fibreoptic scope was unsuccessful initially, the bougie succeeded in only 1 (13%) case (^{2} test, $P<0.04$). In all successful intubations using either technique, the total intubating times were within 120 sec and there were no significant differences between the times using the two devices.
CONCLUSIONS: In simulated grade IIIa laryngoscopy, the fibreoptic scope is very much more successful than the bougie as a device for intubation. The same dramatic degree of success could not be demonstrated in a grade IIIb laryngoscopy, although the fibreoptic scope was still statistically better than the bougie. The results have at least three important clinical implications: (a) previously suggested sub-divisions of the grade III view may be clinically important (4); (b) the bougie may not be the device of choice in an unexpected grade III laryngoscopy; (c) a patient with a known, previously recorded grade III laryngoscopy might reasonably be considered sufficiently "difficult' for an awake intubation technique.
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S-44

POSITIVE PRESSURE VENTILATION AND ISOFLURANE INCREASE PHYSIOLOGIC DEADSPACE VOLUME (VD_{PHYS}) IN PATIENTS RECEIVING GENERAL ANESTHESIA

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INTRODUCTION: Increased VDPHYS, including alveolar (VDALV) and anatomic deadspace volume (VDANA), predisposes to impaired arterial blood gas exchange. For patients receiving general anesthesia, the interaction effects of positive pressure ventilation (PPV) and inhaled isoflurane (Iso) on VDPHYS is not clear. We hypothesized both factors promote increases in VDPHYS and for different physiologic reasons.
METHODS: IRB consent was obtained on 18 adults scheduled to receive general anesthesia (age 50 ± 14 years, weight 79 ± 16 kg, 7 males, 11 females). A combined pressure/flow/carbon dioxide (CO2) sensor directed to a monitor (Novametrix-Respironics) was used to measure the various deasdspace volumes by the single breath CO2 elimination method.[1] The PaO2 / FIO2 ratio was calculated. Measurements were obtained preoperatively during spontaneous ventilation (SV) (sensor attached to mouthpiece) and intraoperatively (sensor attached to endotracheal tube), i. e., after induction during PPV and intravenous anesthesia and then 30 min later breathing 1 MAC Iso while maintaining minute ventilation, mean airway pressure, and mean arterial blood pressure constant. Data were analyzed using a repeated measures ANOVA; alpha was set at .05 for statistical significance.
RESULTS:

Condition	VD_{PHYS}	VD_{ALV}	VD_{ANA}	PaO_2/FIO_2
Pre-op SV	147 ± 51	42 ± 31	105 ± 28	395 ± 8
PPV	242 ± 67*	131 ± 46*	112 ± 34	383 ± 74
Iso plus PPV	289 ± 56$^+$	163 ± 40$^+$	126 ± 27$^+$	337 ± 86$^+$

$p < .05$, Pre-op SV vs PPV(*), PPV vs Iso plus PPV (+)

DISCUSSION: PPV increases VDPHYS; isoflurane significantly potentiates this increase. The significant increase in VDANA following isoflurane may be related to its bronchodilating effects. Compromised blood gas exchange, as reflected by a decreased PaO2/FIO2 ratio, most likely results from increased VDPHYS. During controlled mechanical ventilation with a paralyzed patient, as during general anesthesia, a disproportionate amount of the tidal volume is directed to the anterior nondependent lung regions predisposing to areas of increased ventilation-to-perfusion matching, i. e., increased VDPHYS.[2] A mechanism for how isoflurane increases VDPHYS is unclear, it may be the result of its vasodilating effects and possible redistribution of pulmonary blood flow.
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S-45

POSTOPERATIVE HYPERTHERMIA FOLLOWING OFF-PUMP VS. ON-PUMP CORONARY ARTERY BYPASS SURGERY

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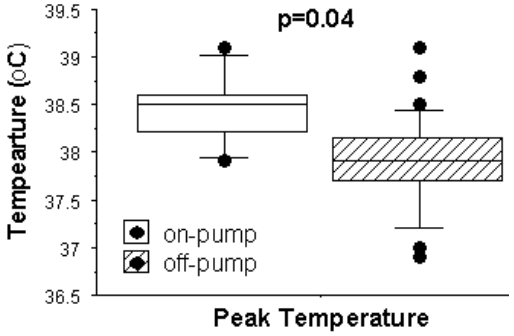
INTRODUCTION: Fever is common in the first 24 hours following coronary artery bypass graft surgery (CABG) utilizing cardiopulmonary bypass (CPB) [1]. The inflammatory response to CPB is often implicated in the etiology of this fever [2], which has recently been associated with an increase in post-cardiac surgery neurocognitive dysfunction [3]. The temperature pattern after off-pump cardiac surgery (OPCAB), where CPB is avoided, has not yet been described. The purpose of this study was to describe the post-operative temperature pattern following OPCAB and to compare it to that following on-pump cardiac surgery.
METHODS: Following IRB approval, patients undergoing either off-pump or on-pump CABG surgery were studied. The off-pump group was enrolled in an unrelated OPCAB study in which normothermia (nasopharyngeal temperature >36ºC) was maintained throughout the operation. The on-pump group was consented for the same OPCAB trial but subsequently converted to on-pump cardiac surgery using hypothermic (32-34ºC) CPB. All patients were managed identically after admission to the intensive care unit (ICU), including forced-air warming for those with a temperature <36ºC and acetaminophen for temperatures > 38ºC. Temperature measurements in the ICU were recorded hourly from the pulmonary artery catheter thermistor during the first 24 post-operative hours. To quantify temperature changes, the areas under the temperature-time curve (AUC) for temperatures >38ºC and <36ºC were calculated. Between group comparisons were made by Student's t-test or ^{2} test with P<0.05 considered significant.
RESULTS: Forty-one patients (age 61±10 years, 63% males) were enrolled, 32 in the off-pump group and 9 in the on-pump group. No differences were found between the off-pump and on-pump patients regarding ICU admission temperature, minimal temperature or AUC<36ºC. However, peak body temperature and AUC>38ºC were higher in the on-pump patients (38.5±0.4ºC, on-pump vs. 37.9±0.5ºC, off-pump, p=0.002; and 1.6±1.7ºCh, on pump vs. 0.4±1.2ºCh, off-pump, p=0.02). Of the on-pump patients, 89% had temperature elevations above 38ºC, vs. 44% of the off-pump patients (p = 0.04).



DISCUSSION: We have previously reported hyperthermia in the first 24 hours following conventional on-pump CABG [1]. In the current study, we found that off-pump surgery was accompanied by a lesser degree of early postoperative fever, although significant hyperthermia still occurred in both groups. This hyperthermia in OPCAB surgery may be related to a lesser, but still evident, inflammatory response [4]. However, the different fever patterns may also be related to differences in the extent of operative trauma, drug therapy, blood transfusion or pulmonary atelectasis [5].
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S-46

MEDIUM-TERM OUTCOME FOLLOWING CORONARY REVASCULARIZATION: CPB VERSUS OP-CAB

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INTRODUCTION: Ischemic myocardial injury (IMI) is abundant (up to 30%) following cardiac surgery,(1) with increasing evidence of associated adverse medium-term outcome.(2) Minimizing IMI is therefore an important goal. Studies have shown that off-pump coronary artery bypass surgery (OP-CAB) reduces IMI.(3) Similarly, we reported less IMI [troponin-I >15 g.L-1: 19.0% vs. 91.3%; p = 0.0001; troponin-I >30 g.L-1: 9.5% vs. 52.2%; p = 0.003] following OP-CAB compared to surgery using conventional cardiopulmonary bypass (CPB).(4) Here we report on the medium-term follow-up of this cohort of patients.
METHODS: Forty-four patients were followed-up at 6- and 12-months following elective multivessel coronary surgery using either OP-CAB (n = 23) or conventional CPB (n = 21) techniques. Medium-term outcome variables that were assessed by postal questionnaire and patient medical record review included indices of patient symptomatology, quality of life and the occurrence of cardiovascular events and death following hospital discharge. Data are presented as mean ± SD and as a percentage of the study group for continuous and categorical variables, respectively. Univariate analyses used Fisher's exact test for categorical variables and the Mann-Whitney U test for nonparametric variables. A p-value of <0.05 and <0.2 were regarded as statistically significant and as a trend towards difference between the two groups, respectively.
RESULTS: Preoperative and intraoperative data were similar between groups.(4) At medium-term follow-up significantly fewer patients required increased cardiovascular medication (5.6% v 47.1%; p = 0.007) in the OP-CAB group at 6-month follow-up. This advantage was no longer evident at 12-month follow-up (23.5% v 28.6%; p = 1.0). The OP-CAB group also demonstrated trends toward improved variables of symptomatology (shortness of breath indices at 6- and 12-months [New York Heart Association Classification 0.43 ± 1.17 v 1.00 ± 1.24; p = 0.06 and 0.38 ± 1.24 v 0.74 ± 0.96; p = 0.13]; postoperative angina score at 12-months [Canadian Cardiovascular Society Classification 0 v 0.33 ± 0.80; p = 0.05]) and quality of life at 6-months (Duke Activity Status Index 20.8 ± 5.6 v 19.0 ± 6.8; p = 0.13). No differences were observed in the incidence of cardiology-based intervention or death (3 v 4 patients and 2 v 1 patients, respectively) between groups.
DISCUSSION: The observed reduction in incidence of IMI associated with OP-CAB may contribute to the lower requirement for increased cardiovascular medication and observed trend in improved symptoms at medium term follow-up. Larger prospective, randomized studies are required to determine the impact of OP-CAB on medium- and long-term benefit in the cardiac surgical population.
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S-47

ULTRA-FAST-TRACK ANESTHESIA IN OFF-PUMP CARDIAC SURGERY: POSTOPERATIVE EPIDURAL ANALGESIA VERSUS PCA MORPHINE

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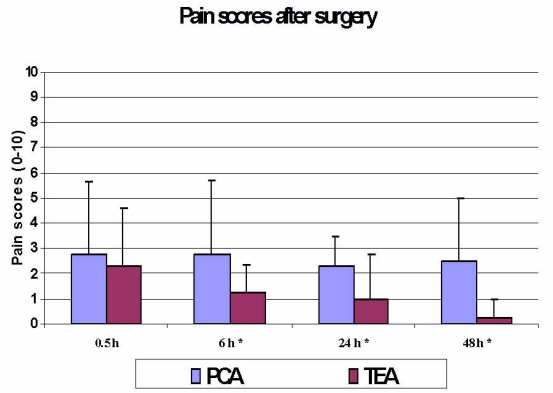
INTRODUCTION: This study investigated how operating room extubation can be achieved using either epidural based anesthesia or a modified balanced anesthesia during off-pump cardiac surgery (CABG).
METHODS: The study was designed as a prospective audit of 53 patients undergoing off-pump CABG. The goal was to maintain the patient's core temperature during surgery of more than 35.5 degrees C by active temperature control. Anesthesia was either an anesthesia using sevoflurane titrated by BIS and a continuous thoracic epidural analgesia (N=33, TEA group) or a modified balanced anesthesia using sevoflurane/fentanyl boli (<15 microg/kg total, PCA group) in patients on either low molecular heparine or intravenous heparine (N=20). If extubation could not be achieved within 30 min after surgery (or core temperature was below 35.5), the patient was transferred to the ICU intubated and ventilated. Postoperative analgesia during the first 48 hours was achieved by either thoracic epidural analgesia (TEA, bupivacaine 0.125 %) or patient controlled application of morphine (PCA, 1 mg, lockout period: 6 min). Anthropometric data, success of extubation, postoperative hemodynamic and respiratory parameters and pain scores are presented as means (SD) and compared between the two groups using t-test (P<0.05).
RESULTS: Fifty-three patients (10 women, 43 men) of mean age of 60 yrs (12), weight of 81 (15) kg and an ejection fraction of 55 (10) % undergoing off-pump CABG of 3 grafts (0.8) during surgery of 120 (28) min were included. The anthropometric data and surgery-related parameters (concomitant disease, ejection fraction, number of grafts, ischemic time) were not different between the two groups. Three patients were not extubated due to low core temperature. Time to extubation, first PO2 and PCO2 (FiO2 = 100 %) after extubation were 15 (4) and 14 (5) min, 158 (60) mmHg and 142 (44) mmHg, 47 (10) mmHg and 49 (8) mmHg in the TEA and PCA groups, respectively and not significantly different. Pain scores postoperatively were low in both groups, significantly lower in the TEA group than in the PCA group 6 - 48 h after surgery (Figure).



Six patients in the PCA group developed a confusional state necessitating abandoning the PCA. Six patients experienced paresthesia in both arms which stopped after diminishing the infusion rate of TEA without changing the quality of analgesia.
DISCUSSION: Our results indicate that Ultra Fast Track anaesthesia can be achieved with either TEA based or a conventional low dose fentanyl balanced anesthesia using sevoflurane. Maintenance of core body temperature is the most important task to allow operating room extubation. PCA morphine is an alternative for patients where TEA is contraindicated or impossible. Lower postoperative pain scores and better side effect profile, however, favor TEA as a technique when there are no contraindications for its use.

S-48

OPERATING ROOM EXTUBATION IN SIMPLE AND COMPLICATED AORTIC VALVE SURGERY: A FIRST EXPERIENCE

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INTRODUCTION: This study presents a first series of 10 patients where operating room extubation was achieved in simple (Aortic valve replacement only) and complicated (additional replacement of the ascending aorta or CABG) aortic valve surgery using either TEA based anesthesia or a modified balanced anesthesia.
METHODS: The study was designed as a prospective audit of 10 patients undergoing aortic valve surgery. The goal was to immediately extubate the patients. Anesthesia was either an anesthesia using sevoflurane titrated by BIS and a continuous thoracic epidural analgesia (N=8, installed at arrival in the OR) or a modified balanced anesthesia using sevoflurane/fentanyl boli (<10 microg/kg total, propofol/ remifentanil during bypass period, N=2). Postoperative analgesia during the first 48 hours was achieved by either thoracic epidural analgesia (TEA, bupivacaine 0.125 %) or patient controlled application of morphine (PCA, 1 mg, lockout period: 6 min). Anthropometric data, success of extubation, postoperative hemodynamic and respiratory parameters and pain scores are presented as means (SD).
RESULTS: All ten patients undergoing simple aortic valve surgery (N=6), aortic valve surgery and CABG (N=2) and Bentall procedure (N=2) could be extubated. Table 1 present anthropometric data and surgery-related parameters. Mean time to extubation was 14 (6) min, first PO2 and PCO2 (FiO2 = 100 %) after extubation were 144 (48) and 47 (2) mmHg, respectively. Pain scores postoperatively were low with 2.3 (2), 1.9 (1.8), 1.2 (0.8), 1 (0.9) immediately, 6 h, 24 h and 48 h after surgery, respectively. There were no complications. Two of the four patients where a mechanic valve was implanted had an epidural catheter inserted which was removed 52 h after surgery with INR lower than 1.4.
DISCUSSION: Our results indicate that Ultra Fast Track anaesthesia can be achieved in simple and complicated aortic valve surgery with either TEA based or a conventional balanced anesthesia using low dose fentanyl and sevoflurane.

TABLE N=10

Age (y)	61 (18)
Weight (kg)	71 (11)
Sex (m/f)	5/5
Valve (mech/bio)	4/6
Stenosis (Regurgitation)	7/3
Surgery (min)	123 (28)
Ejection fraction (%)	60 (8)
Systolic pressure immediately after surgery (mmHg)	123 (36)
Diastolic pressure immediately after surgery (mmHg)	59 (18)
Duration of TEA or PCA (d)	2.6 (0.7)

S-49

EARLY EXTUBATION IN 100 CONSECUTIVE PATIENTS AFTER CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS

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INTRODUCTION: Early extubation before the 6th postoperative hour (POH) after cardiac surgery with CP is a technique which may produce lower medical costs. Prospectively the practice of early extubation has been evaluated in 100 consecutive patients, including emergencies undergoing cardiac surgery with cardiopulmonary bypass (CPB)
METHOD: After approval by the local ethic comittee and informed written consent, data of the extubated patients up to (group A) and after (group B) the 6th POH werecompared. Anasthesia was inducted and mainained with thiopental (one single dose of 2 mg kg^{-1}), midazolam (M), sufentanil (S) and pancuronium (P). Enflurane was used to treat episodes of arterial hypertension. The extubation criteria were haemodynamic stability, no obvious neurological injury, arterial saturation>92% and PaCO2<86 kPa during spontaneous ventilation on a tube with 3 litres of oxygen min^{-1}. Statistical analysis was performed with analysis of variance, chi-squared or Pearson test as appropriate at P<0,05 (*). All results are expressed as mean +/- SD (table).
RESULTS: Of 100 patients, 62 were extubated up to the 6th POH (ventilation time: 4.5+/-1.1 h), 29 were extubated after the 6th POH (12.3+/-10.5 h). The operation for 9 patients was an emergency (4 patients died, 2 were extubated before the 6th POH and 3 after). One patient (group B) was re-intubated on the 9th POH (hypercapnia). One patient remained intubated (haemostatic surgery on the 7th POH). After the 2nd postoperative day, 4 patients were re-intubated because of a low cardias output (myocardial infarction) in one and infection pneumopathies in three, one in group A. Nine patients were never extubated (NE) and 12 patients died (3 in group B after re-intubation). In group B, 8 patients of 29 (28%) needed high dose inotropes, in contrast to none in group A. The preoperative left ventricle ejection fraction was not predictive of the length of the postoperative ventilation (A: 53+/-13, B: 57+/-15, NE: 66+/-22%). Age, surgery and CPB times were significant factors for early or late extubation.
CONCLUSION: In this study, failure of early extubation was related to the patient status (age, surgery, haemodynamic state) and not to the anaesthesia technique. Early extubation was achieved in 62% of the patients without complications.

	Group A	Group B	P (A/B)	NE
N*	62	29	<0.05	9
Age* (y)	33	16	<0.05	4
Weight (kg)	63+/-14	70+/-11	>0.05	74+/-7
A X-clamp (min)	71+/-29	78+/-25	>0.05	80+/-38
CPB time* (min)	104+/-40	129+/-40	<0.05	141+/-73
Surgery t* (h)	4.5+/-0.9	5.0+/-1.0	<0.05	5.4+/-1.3
S (mcg kg^{-1} h^{-1})	0.92+/-0.46	0.93+/-0.48	>0.05	0.88+/-0.29
M (mcg $kg^{-1}h^{-1}$	0.04+/-0.02	0.04+/-0.01	>0.05	0.03+/-0.02
P (mcg $kg^{-1}h^{-1}$	0.03+/-0.01	0.03+/-0.1	>0.05	0.03+/-0.01

S-50

INTRAOPERATIVE 15-F_{2t}-ISOPROSTANE (8-ISO-PGF_2) IS A PREDICTOR OF POST-OPERATIVE CARDIAC FUNCTION FOLLOWING WARM HEART SURGERY

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INTRODUCTION: Despite recent advances in surgical and anesthetic technique, postoperative low cardiac output syndrome still occurs in 10 to 20% patients (1,2). This reflects inadequate cardiac protection, which may attributable to oxygen free radical mediated ischemia-reperfusion injury. We postulated that intraoperative plasma 15-F_{2t}-isoprostane, a specific and bio-active (3) marker of oxidant stress, is a determinant of postoperative cardiac function.
METHODS: Following ethics committee approval, thirteen patients scheduled for coronary artery bypass grafting surgery (CABG) using CPB were enrolled. Patients were anesthetized with fentanyl 10-15 ug/kg and isoflurane 0.5-2% end tidal. Normothermic CPB and intermittent blood:crystalloid cardioplegia were utilized during surgery. Central venous blood samples were collected at baseline, 30 min global myocardial ischemia, 10 (Rep-10'), 30 (Rep-30'), 120 min (Rep-120') and 12 hours (Rep-12 hours) after aortic declamping (reperfusion). Plasma free 15-F_{2t}-isoprostane was measured by enzyme immunoassay. Inotropic support was defined as any use of dopamine > 4 g/kg/min, epinephrine > 0.04 g/kg/min, or milrinone 0.25 - 1.0 g/kg/min, alone or in combination, required for > 30 min during the first 6 hours postoperatively to achieve systolic BP > 90 mmHg and CI > 2.2 L/min/m^2. Patient data were analyzed as a whole and by group according to inotrope requirements for hemodynamic stabilization : Group I (n=7; no inotropes); Group II (n=6; two or more inotropes). Data were expressed as mean ± SEM.
RESULTS: There was no difference in age (age 69.0 ± 3.4 vs 60.3 ± 2.3 yr), gender (4/2 vs 5/2 male/female), preoperative LVEF (55.7± 6.3 vs 58.2 ± 3.0%), duration of ACC (108.5 ± 16.1 vs 112.7 ± 31.3 min), or CPB (150.8 ± 25.0 vs 141.0 ± 36.6 min) between groups. Plasma 15-F_{2t}-isoprostane increased significantly during ischemia in both groups (P < 0.01 vs baseline). 15-F_{2t}-isoprostane in group I decayed exponentially during reperfusion and returned to baseline at Rep-10' (P > 0.05 vs baseline). To the contrary, 15-F_{2t}-isoprostane in group II remained significantly higher than baseline at Rep-10' and Rep-30' (P < 0.001, vs baseline) until Rep-120' (P >0.05 vs baseline). The percentage change in F_{2t}-isoprostane from Rep-10' to Rep-30' was highly inversely correlated with postoperative cardiac index (CI) (n =13; r = -0.8361, 95%CI: -0.9496 to -0.5286, P = 0.0004).
CONCLUSION: The oxidative stress during myocardial reperfusion has significant impact on postoperative myocardial functional recovery. The percentage change in plasma 15-F_{2t}-isoprostane during the early phase of reperfusion may serve as a predictor of postoperative cardiac function following warm heart surgery.
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S-51

ANTIOXIDANT THERAPY DECREASES PLASMA ENDOTHELIN-1 AND THROMBOXANE B_2 AFTER CARDIOPULMONARY BYPASS IN PATIENTS WITH CONGENITAL HEART DISEASE

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INTRODUCTION: The endothelium-derived vasoconstrictor endothelin-1 (ET-1) is increased after cardiopulmonary bypass (CPB) surgery, which affects postoperative recovery (1). Oxidative stress has been reported to increase ET-1 synthesis in human coronary artery smooth muscle cells (2). The purpose of this study was to 1) determine if antioxidant therapy with salvia miltiorrhiza (SM) injection, an herb extract containing phenolic compounds with potent antioxidant properties (3), could prevent the postoperative increase of ET-1; 2) determine the relationship between ET-1 and the endothelium-derived vasodilator prostacyclin (PGI2) and vasoconstrictor thromboxane A2 (TXA2) postoperatively.
METHODS: Following ethics committee approval, 20 children with congenital heart defects (CHD) and moderate pulmonary hypertension (mean pulmonary pressure/mean systemic pressure 0.3 to 0.4) were enrolled. Prior to cardiac surgery, patients were randomly assigned to group A (placebo control; n=10) and B (200 mg/kg SM intravenously after anesthesia induction and at the time of rewarming; n =10). Central venous blood samples were taken: before operation (T_0), 10 (T_1) and 30 min (T_2) after starting CPB, 10 (T_3) and 30 min (T_4) after aortic declamping, 30 min (T_5) and 24 hours (T_6) after termination of CPB for determination of plasma malondialdehyde (MDA), creatine kinase MB (CK-MB), TXB2 and 6-Keto-PGF_1 (stable metabolites of TXA2 and PGI2). Postoperative inotropic support was defined as the use of dopamine 5 $g.kg^{-1}$ min^{-1} for a duration 30 min with or without concomitant application of epinephrine. Statistical analysis was performed using ANOVA. Data was expressed as mean± SEM.
RESULTS: ; There was no difference in age (8.6± 1.3 vs 8.1± 1.3 yr), body weight (22.9± 2.4 vs 21.9± 2.2 kg), aortic crossclamp (40.7± 3.7 vs 45.5± 3.9 min) and CPB times (75.7± 4.2 vs 77.6± 4.6 min) between groups. Baseline (T_0) values of MDA (3.07± 0.39 vs 2.85± 0.37 nmol/mL), CK-MB (21.7± 1.1 vs 22.3± 2.9 U/L), 6-Keto-PGF_1 , TXB2, 6-Keto-PGF_1 /TXB2 ratio and ET-1 did not differ between groups. MDA increased significantly at T_1 in group A and remained significantly higher than group B thereafter ($P<0.05$). MDA in group B did not significantly increase over time. At T_5, plasma CK-MB, TXB2 and ET-1 in group B were lower, and 6-Keto-PGF_1 /TXB2 ratio was higher than group A ($P<0.05$), MDA correlated significantly with CK-MB ($r=0.7074$, $P=0.0005$), and ET-1 ($r=0.5070$, $P=0.0225$). At T_6, ET-1 was negatively correlated with 6-Keto-PGF_1 /TXB2 ratio ($r= -0.6015$, $P=0.005$). Six patients in group A (6/10) and one in group B (1/10) needed postoperative inotropic support ($P<0.05$, Chi square test).
CONCLUSION: Antioxidant therapy with SM reduces postoperative myocardial damage and attenuates vascular endothelial dysfunction as expressed by ET-1 levels, resulting in reduced need for hemodynamic support following surgery for CHD.
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S-52

INVERSE CORRELATION BETWEEN OXIDATIVE STRESS AND INTERLEULIN-10/INTERLEULIN-6 RATIO IN PATIENTS UNDERGOING CARDIOPULMONARY BYPASS

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INTRODUCTION: Cardiopulmonary bypass (CPB) is associated with oxidative stress (1) and increased production of anti- and pro-inflammatory cytokines (2). The relationship between oxidant stress and postoperative cytokine balance is poorly understood. We postulated that postoperative interleukin (IL)-10/IL-6 ratio is influenced by the extent of oxidative stress evidenced by the production of 15-F_{2t}-isoprostane, a specific marker of *in vivo* lipid peroxidation.
METHODS: Following ethics committee approval, 10 patients scheduled for coronary artery bypass grafting (CABG) surgery using CPB were enrolled. Patients were anesthetized with fentanyl 10-15 ug/kg and isoflurane 0.5-2% end tidal. Normothermic CPB and intermittent blood:crystalloid cardioplegia were utilized during surgery. Central venous blood samples were collected at baseline, 30 min global myocardial ischemia, 10 (Rep-10'), 30 (Rep-30'), 120 min (Rep-120') and 12 hours (Rep-12 hours) after aortic declamping (reperfusion). Oxidant stress was determined by enzyme immunoassay of plasma free 15-F_{2t}-isoprostane. Molecules of equivalent soluble fluorochrome units (MESF) of IL-10 and IL-6 in monocytes were measured by flow cytometry of heparinized whole blood samples taken at baseline, Rep-120' and Rep-12 hours. Statistical analysis was performed using repeated measures of ANOVA. Data was expressed as mean ± SEM.
RESULTS: Seven males and 3 females (age 66.8 ± 2.9 yr) were studied. Mean pre-operative LVEF was 59.5 ± 3.9%. The aortic crossclamp (ACC) and CPB time were 118.3 ± 20.5 min, and 156.1 ± 23.2 min, respectively. Baseline plasma free 15-F_{2t}-isoprostane (103.4 ± 17.9 pg/mL) increased significantly during ischemia (255.8 ± 60.1 pg/mL, $P < 0.01$ vs baseline), and remained elevated at Rep-10' (133.9 ± 16.4 pg/mL) and Rep-30' (119.7 ± 19.3 pg/mL), until Rep-120' (83.6 ± 18.2 pg/mL). Monocyte production of IL-10 and IL-6 in MESF units are shown (Table 1). There was no correlation between oxidant stress or interleukin production with ACC or CPB. IL-10/IL-6 ratio at Rep-12 hours significantly correlated with postoperative cardiac index ($r=0.695$, $P=0.037$) and inversely correlated with logarithmic concentration of plasma 15-F_{2t}-isoprostane at Rep-10' ($r = -0.8849$, $P=0.0007$). The IL-10/IL-6 ratio was exceptionally low (0.26 and 0.27 at Rep-120' and Rep-12 hours) in one patient who needed prolonged postoperative inotropic support.
CONCLUSION: Oxidative stress occurs during myocardial ischemia and the early phase of myocardial reperfusion during CABG surgery. 15-F_{2t}-isoprostane production during early reperfusion is associated with postoperative interleukin-10 and interleukin-6 imbalance. This may be associated with complicated postoperative recovery secondary to low output syndrome.
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Table 1 (Mean ±SEM, *P < 0.05 vs baseline)

	Baseline	(N)	Rep-120 min	(N)	Rep-12 hours	(N)
IL-10 (MESF/cell)	153.2±45.6	8	69.5±16.8*	8	75.6± 24.1	10
IL-6 (MESF/cell)	3.0± 0.5	10	20.2±8.1*	8	13.8± 9.2	10
IL-10/IL-6 ratio	54.0± 15.8	8	18.0±9.6*	8	18.9± 6.3*	10

S-53

APROTININ PHARMACOKINETICS DURING CARDIO-PULMONARY BYPASS IN SMALL PEDIATRIC PATIENTS

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INTRODUCTION: Although the pharmacokinetics of aprotinin in adults has been well established (1), the optimal dosing to produce effective levels >200 KIU/ml (2) of this protease inhibitor has not been established in pediatric patients. The dosing variation utilized in various studies makes their comparison difficult. A limited amount of data has been reported on aprotinin blood levels in children (3). The goal of this study was to determine in pediatric patients less than 15 kilograms, if adequate aprotinin levels were achieved with a predetermined aprotinin bolus, maintained during initiation of bypass with a fixed amount of aprotinin added to the pump prime, and maintained with a constant infusion throughout the bypass period.
METHODS: Following IRB approval and informed consent, 11 cardiac surgery patients (ages 3mo-3 yr; weight 3.4-12.7 kg) were enrolled. Aprotinin was administered as a 35,000 KIU/kg load over 20 min before skin incision, an infusion of 25,000 KIU/kg/hr after the load and continued until skin closure, and an additional 35,000 KIU/kg was added to the pump prime immediately before initiating bypass. A baseline blood level was obtained before aprotinin administration. Subsequent levels were obtained 5 min after the aprotinin load, 5 min after initiating CPB, every 60 min during CPB, at skin closure, and at 6 and 12 hrs postoperatively. Aprotinin levels were determined using a functional chromogenic assay (4).
RESULTS: Ten of 11 patients achieved aprotinin blood levels >200 KIU/ml after the loading dose. Nine of 11 patients had levels >200 KIU/ml throughout the CPB period. The lowest level measured during CPB was 180 KIU/ml. Children whose pump prime volume (PPV): estimated blood volume (EBV) was > 2 trended toward lower aprotinin levels after initiating CPB, while those with PPV: EBV 2 trended toward increased aprotinin levels after the institution of CPB (p=0.08; Fishers exact test). No correlation was found between aprotinin levels and baseline hemoglobin levels, the amount of blood versus crystalloid added to the pump prime, weight, or age.
DISCUSSION: The optimal dosing for small pediatric patients has not been determined. It has been established that aprotinin dosing in pediatric patients is best calculated on a weight-adjusted basis. A 30,000 KIU/kg load plus 30,000 KIU/kg pump prime failed to achieve levels > 200 KIU/ml (3). Additional studies including aprotinin blood concentrations and standardization of dosing regimens will be required to define the minimal amount of aprotinin to maintain desired blood levels cost-effectively.
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(3) Ann Thorac Surg 1998;65:S45.
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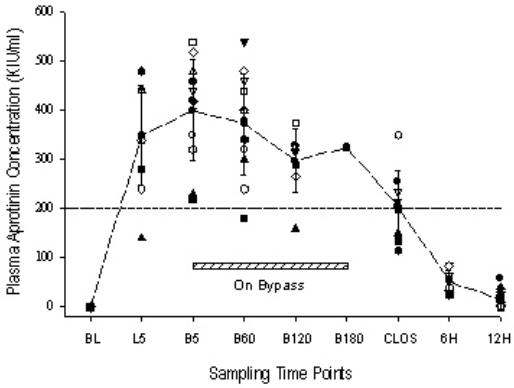

S-54

THE RAPIDPOINT HEPARIN MANAGEMENT TIME (HMT) IS NOT PROLONGED BY APROTININ FOLLOWING HEPARIN DOSES USED PRIOR TO CARDIOPULMONARY BYPASS BUT IS BY HEMODILUTION WITH COLLOID.

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INTRODUCTION: Aprotinin is an 'anticoagulant' protease inhibitor in vitro leading to the activated coagulation time (ACT) being prolonged above that produced by heparin alone. Although less likely to occur with kaolin it is still reported with concentrations of aprotinin (1) measured clinically (2). A point-of-care system (RapidPoint HMT) that uses a proprietary based activator incorporating Celite and a novel sensing system has been introduced to monitor moderate to high doses of heparin during surgical and non-surgical procedures. The aim of this study was to determine by in vivo and in vitro testing if there was an effect of high doses of aprotinin on this test system and if sample dilution to a hemoglobin observed clinically affected the assay.
METHODS: With IRB approval blood samples were taken from patients who had received either a large dose of aprotinin (Royston) or heparin to obtain a Celite ACT using the ITC Hemochron system and CA 505 tubes of at least 400 seconds.
When heparin had been administered first aprotinin was added to give a final concentration of 1, 3 and 10Mol (equivalent to 50,150 and 500 KIU/mL). In these samples also the hemoglobin was measured and sufficient colloid as a polygeline (Haemaccell) starch (HAES) or balanced starch (Hextend) solution were added to reduce the hemoglobin to a value of about 7 g/dL thus mimicking the effects of hemodilution with bypass. With prior aprotinin administration heparin 1, 2 and 5 IU / mL were added. Data are expressed as mean± SEM and analysis was with ANOVA followed by group comparison using Student-Newman-Keuls if appropriate
RESULTS: All data points represent the mean (SEM) of at least 6 individual results. Values in patient samples with heparin alone (406 (7.8) sec) did not increase significantly with addition of aprotinin using the RapidPoint system but there was a significant prolongation with the conventional Celite ACT (Figure). Aprotinin concentration is on logarithmic scale (I µMol is 50 KIU/mL). Baseline HMT of 550(7.1) second increased with all colloids. The prolonged duration with HAES and gelatin of 28.5(11.8) and 45(13.1) seconds were not statistically significant from zero (p=0.42 and 0.23 respectively). The rise in HMT with Hextend of 92(10.9) seconds was significant (p=0.003). These effects were not observed with crystalloid hemodilution
COMMENTS. These preliminary data suggest that the HMT is not affected by clinically achieved concentrations of aprotinin when the starting duration (>400- 480 seconds) is as anticipated following full-dose heparin administration to patients prior to surgery with cardiopulmonary bypass. The duration of the test is affected by hemodilution with colloids. These preliminary data suggest that administration of Hextend may have the most clinically relevant effect.
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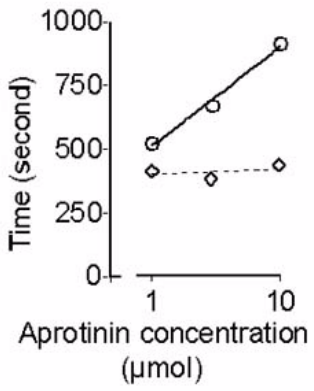

S-55

MONITORING PLATELET AGGREGATION DEFECT INDUCED BY CARDIOPULMONARY BYPASS: COMPARISON BETWEEN NOVEL WHOLE BLOOD AGGREGOMATER AND SONOCLOT ANALYZER

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INTRODUCTION: Platelet dysfunction has been postulated as a possible cause of postoperative bleeding after cardiopulmonary bypass (CPB) (1). However, conventional assay of platelet aggregation has several disadvantages. Recent investigations suggest promising application of intraoperative monitoring of platelet function by screen filtration platelet aggregometer (WBA analyzer, Mebanix, Japan) (2, 3). Another study reported significant correlation between platelet aggregation and a Sonoclot?- (Sienco, USA)-derived parameter; time to peak (TP) (4). In this prospective, observational study, we analyzed perioperative changes of platelet function with these two methods.
METHODS: With IRB approval, 26 adult patients who underwent cardiac surgery under cardiopulmonary bypass participated in this study. Arterial blood was drawn from arterial catheter at following time points: after anesthetic induction (Preop), at the sternal closure (Endop) and 1POD. Whole blood aggregation was initiated with 2 to 16 μM ADP and the filtration pressure caused by platelet aggregate was recorded. Simultaneously, the platelet aggregatory threshold index (PATI) was automatically calculated as the concentration of ADP inducing 50% of pressure rate. Sonoclot signature was also recorded with celite-activated cuvette and TP was recorded manually. Data were statistically analyzed with Friedman's non-parametric test and $P<0.05$ was considered significant.
RESULTS: Data of platelet function from 26 patients (age; 55±15 y/o, total CPB time: 190±49 min, postoperative chest tube drainage: 652±333ml/24hr) were summarized in the Table.
Platelet aggregation induced by ADP was significantly attenuated after CPB and returned to Preop level on 1POD, which was confirmed by increased PATI at Endop. On the contrary, TP did not show significant change after CPB and 1POD. There were no significant correlation between TP and aggregometer-derived parameters. Also, the amount of postoperative bleeding correlated with neither ADP-induced platelet aggregation nor TP.
CONCLUSION: This preliminary study suggests that whole blood aggregometer could be more sensitive indicator of platelet function rather than Sonoclot during in the perioperative period of cardiac surgery.
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(2) Thromb Res 2001;101:65
(3) Br J Phamacol 2001;133:1396
(4) Anesth Analg 1998;87:1228

Data were expressed as mean ± SD. *p<0.05 versus Preop

	Preop	Endop	1POD
Response to 2μM ADP (%)	31.1±37.7	0.6±2.9*	22.0±30.9
Response to 4μM ADP (%)	59.2±42.7	2.3±3.7*	50.8±42.8
Response to 8μM ADP (%)	78.5±26.8	13.6±22.2*	70.6±35.0
Response to 16μM ADP (%)	89.8±11.2	43.3±35.0*	82.1±21.1
PATI (μM)	4.6±3.4	14.1±3.1*	6.0±4.9
TP (min)	15.1±6.6	17.1±7.5	15.5±5.2

S-56

DIPHENHYDRAMINE ATTENUATES THE HEMODYNAMIC CHANGES ASSOCIATED WITH PROTAMINE ADMINISTRATION

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INTRODUCTION: Protamine is routinely administered to reverse the anticoagulant effects of heparin during cardiac sugery. Administration of protamine is associated with histamine release often resulting in tachycardia and/ or hypotension. Some surgeons and anesthesiologists routinely administer diphenhydramine (Benadryl) prior to protamine administration in the hope of mitigating any histamine related hemodynamic changes. This retrospective review was undertaken to determine the efficacy of this practice, following approval by institutional authorities.
METHODS: Intra-operative anesthesia records of 78 patients undergoing cardiac surgery with cardiopulmonary bypass and heparin anticoagulation managed by the same cardiac anesthesiologist between January, 2001 and December, 2001 were identified. Rate of protamine administration (dose completed over ten minutes) and method of administration (via peripheral IV) were thus standardized according to the anesthesia provider. 39 patients were pre-treated with 50 milligrams of diphenhydramine immediately prior to protamine administration. Patients were given diphenhydramine according to the standard preferences of the attending surgeons. No selection criteria were employed to determine which patients would receive diphenhydramine pretreatment. Likewise, 39 cases of surgeons who do not request the administration of diphenhydramine were examined. The mean arterial pressures and the mean pulmonary pressures immediately before and 15 minutes after the administration of protamine were noted for both groups of patients. The data was analysed using repeated measures ANOVA.
RESULTS: Administration of diphenhydramine pretreatment attenuates the decrease in mean arterial pressure associated with protamine administration.

The effects of diphenhydramine on mean arterial and pulmonary pressures

Diphen – hydramine	Time	Mean arterial pressures	Pulmonary pressures
No	Pre- protamine	78.4+/-1.3	23.8+/-0.9
No	Post-protamine	61.8+/-0.9	24.8+/-0.9
Yes	Pre-protamine	79.7 +/- 1.2	20.2 +/- 0.7
Yes	Post-protamine	78.8 +/- 1.3	20.2 +/ - 0.9

CONCLUSION: Although limited by its retrospective design, this analysis suggests that the routine administration of diphenhydramine immediately prior to protamine reversal of heparin anticoagulation attenuates histamine-mediated reductions in mean arterial pressures.
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S-57

SYSTEMIC HYPOTENSION AFTER PROTAMINE ADMINISTRATION IS ASSOCIATED WITH IN-HOSPITAL MORTALITY FOLLOWING PRIMARY CABG SURGERY

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INTRODUCTION: Protamine is universally accepted as essential for reversing heparin anticoagulation after coronary artery bypass grafting (CABG). Varying degrees of systemic hypotension are seen after protamine administration and are accepted by most clinicians as unavoidable. However, adverse events following protamine administration have been retrospectively linked to poor outcome (1), so we tested the hypothesis that systemic hypotension after protamine administration is associated with increased mortality following CABG after controlling for preoperative risk.
METHODS: We examined the computerized anesthesia records (Arkive, Arkive Inc.,CA), with 1 minute data recording intervals, for 6921 patients undergoing primary, elective CABG at Duke University Medical Center between 1993 and 2000. Porcine heparin was administered in a 300-400 units/kg bolus and the ACT maintained at >480 seconds. Protamine was administered until the ACT returned to baseline or the ratio of 1mg:100units heparin was reached. Systemic hypotension was defined as a 20% decrease in systemic mean arterial pressure (MAP) within 30 minutes after protamine administration compared to a baseline defined as the median MAP for the 5 minutes prior to protamine . A degree-duration integral of hypotension was also calculated from the area under the curve (AUC) of systolic blood pressure (sBP) <100mmHg over this 30 minute period (AUC<100) to associate the severity of hypotension with mortality. The AUC<100 was plotted against predicted probability of mortality, including 95% confidence intervals (Figure 1). For example, a sBP of 80 mmHg for 15 minutes would equal a AUC<100 of 300mmHg.min; an AUC of 1200 is equivalent to sBP = 60mmHg for 30 minutes. Contemporaneously calculated Hannan scores (2), were included to control for preoperative risk of death. In-hospital mortality was the primary outcome variable. Multivariate logistic regression models included the above variables as predictors to test for association with outcome (death); this association was expressed as an odds ratio with 95% confidence intervals.
RESULTS: Data were complete for 6846 patients. The mean (+/- standard deviation) protamine dose was 257mg (+/-95mg) and overall mortality was 2%. A 20% drop in MAP within 30 minutes after protamine administration occurred in 19% patients and was significantly associated with death, (odds ratio 1.85 [1.27-2.7], p< 0.001). Every 120mmHg.min increment in AUC<100 (=10mmHg decrease in sBP for 12 minutes) significantly increased mortality (p<0.001) by an odds ratio of 1.23 [1.16-1.36]. Figure 1 illustrates the increased probability of death [95% confidence intervals] with increasing AUC<100.
DISCUSSION: Systemic hypotension occurs commonly after protamine administration and is independently associated with mortality following primary CABG, after controlling for preoperative risk. Prospective studies are required to investigate potential mechanisms linking protamine administration with poor outcome.
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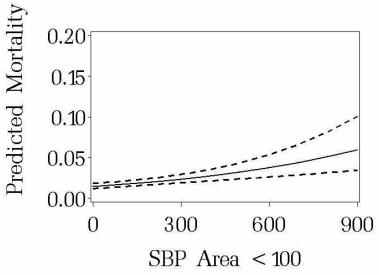

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FACTOR V LEIDEN PROTECTS AGAINST BLOOD LOSS AND TRANSFUSION FOLLOWING CARDIAC SURGERY

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INTRODUCTION: The impact of genetic variation on cardiac surgery outcome has not been systematically explored. Many have implied that factor V Leiden (FVL) may decrease hemorrhagic risk (1), or increase thrombotic risk (2-4), but clinical studies addressing this issue have frequently been underpowered. Here, we characterize the impact of FVL on blood loss and transfusion, using regression techniques in a population of cardiac surgery patients.
METHODS: We prospectively enrolled 517 cardiac surgery patients and evaluated the impact of FVL on blood loss and transfusion. Chest-tube output was measured at 6 and 24 hours after ICU arrival, and transfusion of blood components was recorded from time of operating room entry until discharge. Patient DNA was tested for FVL by *Mnl*I restriction fragment length (5). Univariate analysis of chest tube output employed t-test for independent samples. Multivariate analysis consisted of linear regression of known clinical variables, including FVL, on the dependent variables of blood loss and units of blood product transfusion. Logistic regression was performed using the same independent variables, and risk of receiving transfusion during hospitalization as the dependent variable (transfused vs not transfused).
RESULTS: For the 26 FVL carriers, mean blood loss at 6 and 24 hours was significantly less than that of noncarriers (see Figure; 238cc vs 358cc, and 522cc vs 730cc, respectively; p<0.001). Using linear regression, accounting for ethnicity and variables known to affect blood loss, FVL was a significant independent contributor at both time points (p=0.004 and 0.007, repectively). No effect of FVL was observed using similar linear regression approaches on units of blood components transfused. However, multivariate logistic regression of risk for receiving any transfusion, which controlled for confounding variables including ethnicity, demonstrated that FVL exerted a significant protective effect (p=0.010).
DISCUSSION: Current inferences regarding FVL in cardiac surgery are provocative, yet inconclusive, and do not characterize contributing factors. Our study is the first to report a significant, independent protective effect of FVL on postoperative blood loss and transfusion. Future investigations to evaluate FVL as a possible thrombotic risk factor in this population are warranted.
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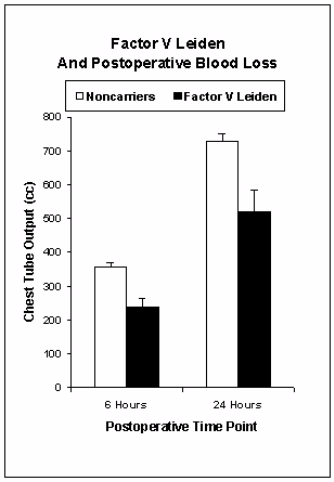

S-59

ELEVATED PLASMA CONCENTRATONS OF THE MATURE FORM OF ADRENOMEDULLIN DURING CARDIAC SURGERY AND HEPATOSPLANCHNIC HYPOPERFUSION

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INTRODUCTION: Adrenomedullin is a potent vasodilatory peptide. Plasma adrenomedullin (AM) concentrations increase during and after cardiopulmonary bypass (CPB). However, the cause of this elevation and its site of production have not been identified. We investigated the role of the hepatosplanchnic and cerebral circulations in the elevation of plasma AM, and whether tissue hypoxygenation is a cause of the AM elevation seen during CPB.
METHOD: We measured plasma total AM (AM-T) and the biologically active form of AM, AM-mature (AM-m), in 7 patients undergoing normothermic CPB. Anesthesia was induced with midazolam (0.2 mg/kg) and fentanyl (5 mcg/kg) and maintained with 15 mcg/kg fentanyl, 4 mg/kg/h propofol and 50% oxygen. Blood samples were obtained from the radial artery, the hepatic vein, and the jugular bulb simultaneously. Both AM-m and AM-T were measured by radioimmunoassay using commercially available kits (AM mature RIA Shionogi and AM RIA Shionogi; Shionogi Co., Osaka, Japan). Plasma concentrations of AMs were analyzed by two-way analysis of variance for repeated measures followed by Sheffe's test. Correlations between concentrations of AMs and oxygen tension or saturation were analyzed by calculating Pearson's correlation coefficients. A P value less than 0.05 was considered statistically significant.
RESULTS: Both plasma AM-T and AM-m concentrations increased significantly 60 min after weaning from CPB. The plasma AM-m concentration and the ratio of AM-m/AM-T in blood from the hepatic vein were significantly higher than those from the radial artery or jugular bulb. The AM-m/AM-T ratio decreased during CPB. Oxygen tension and saturation of hepatic venous blood were significantly decreased during CPB. Plasma AM-m concentrations sampled from the hepatic vein showed a significant negative correlation with oxygen tension and saturation at 10 min and 60 min after the onset of CPB.
DISCUSSION: AM is produced from its precursor by a two-step enzymatic reaction. First, the AM precursor is converted to glycine-extended AM-Gly. Subsequently, AM-Gly is converted to active, mature AM (AM-m), by enzymatic amidation. The AM-m/AM-T ratio decreased during CPB, suggesting that production of the intermediate form of AM, AM-Gly, is greater than AM-m. The plasma AM-m concentration and the ratio of AM-m/AM-T in blood from the hepatic vein were significantly higher than those from the radial artery or jugular bulb. Furthermore, oxygen tension of hepatic vein was selectively decreased during CPB and plasma AM-m concentrations sampled from the hepatic vein showed a significant negative correlation with oxygen tension. These data suggest that the hepatosplanchnic circulation is an important source of AM-m during CPB. Furthermore, hypoxygenation of the hepatosplanchnic region may be an important cause of this AM-m elevation.

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DISSOCIATION BETWEEN REGIONAL CEREBRAL AND JUGULAR VENOUS OXYGEN SATURATION IN CARDIOVASCULAR SURGERY WITH HYPOTHERMIC CARDIOPULMONARY BYPASS

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INTRODUCTION: Both regional cerebral (rSO_2) and jugular venous oxygen saturation (SjO_2) have been used to monitor cerebral oxygenation and to predict neurological complications during cardiovascular surgery. However, there have been few reports that examined the changes of both parameters simultaneously. The purpose of this study is to examine the concomitant changes of rSO_2 (measured at right and left forehead using INVOS 4100) and right SjO_2 (intermittent sampling), and to evaluate whether these parameters are useful to predict neurological complications.
METHODS: Eighteen patients were studied: 11 patients underwent coronary artery bypass graft surgery under conventional cardiopulmonary bypass (CPB group) and 7 patients underwent thoracic vascular surgery under CPB with selective cerebral perfusion (SCP group). Anesthesia was maintained with fentanyl (30ug/kg), midazolam (0.4mg/kg) and isoflurane (0.5-1%). CPB was established with a pump flow of 2.2-2.4 L/m^2/min at 32C(esophageal temperature). SCP was established with a pump flow of 10ml/kg/min at 21C. The values of rSO_2 and SjO_2 were measured simultaneously. All patients were neurologically assessed postoperatively.
RESULTS: In both groups, the mean values of rSO_2 (left/right=56±6/54±8%) were approximate to the values of SjO_2 (54±11%) after anesthetic induction. In CPB group, the mean values of rSO_2 decreased during aortic clamp (32.6±0.7C), returning to prebypass values after the termination of CPB. The mean values of SjO_2 were increased, the highest values being 71±8%. There were significant differences between rSO_2 and SjO_2 during hypothermic period. In SCP group, the decrease in rSO_2 (the lowest values of 39±7%) and the increase in SjO_2 (highest value of 81±9%) were similar to those in CPB group. rSO_2 decreased below 40% in six patients in CPB group and in three patients in SCP group. Neurological complication (cerebral infarction in right MCA region) was seen in one patient in SCP group, who showed decrease in rSO_2 (<40%) with side to side difference (left/ right=46/24%). The patient developed right hemiplegia postoperatively.
DISCUSSION: Dissociation between rSO_2 and SjO_2 occurred in the present study. The dissociation appeared to be mostly attributed to a temperature reduction. Reduction in rSO_2 is well compatible to the results of recent report that demonstrated the reduction of the brain tissue PO_2 during hypothermic therapy in head injured patients[1]. In the present study, only one of 9 patients who showed decreased rSO_2 (<40%) developed neurological complication, in whom SjO_2 (ipsilateral to infarct side) did not show a detectable decrease but showed side to side difference in rSO_2. Although the critical level of rSO_2 at which neurological complication occurs has not been established, meticulous care must be exercised when rSO_2 decreased below 40% with side to side difference greater than 10%.
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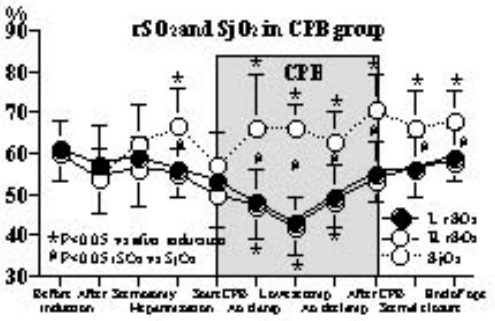

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SLOW REWARMING IMPROVES JUGULAR VENOUS OXYGEN SATURATION DURING REWARMING PERIOD

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BACKGROUND: There have been many studies regarding the etiology of postoperative cognitive dysfunction after CABG surgery. Although its etiology remains unresolved, one possible factor related to postoperative cognitive dysfunction is a reduced internal jugular venous oxygen hemoglobin saturation (SjvO2) during rewarming period. The purpose of this study was to examine the effect of rewarming rates on SjvO2 during rewarming period.
METHODS: One-hundred patients scheduled for elective coronary artery bypass graft (CABG) surgery were randomly divided into two groups; control group (0.48+/-0.09 degree) (n=50), slow rewarming group (0.24+/-0.09 degree)(n=50). After the induction of anesthesia, fiberoptic oximetry oxygen saturation catheter was inserted into the right jugular bulb to monitor SjvO2 continuously. Hemodynamic parameters, arterial and jugular venous blood gases were measured at nine time points.
RESULTS: Cerebral desaturation (defined as a SjvO2 value below 50 %) during rewarming period was more frequent in control group than in slow group. Cerebral desaturation time (duration when SjvO2 was less than 50 %) and the ratio of the cerebral desaturation time to the total CPB time in control group were significantly differed from those in slow group (control group: 17+/-11 min, 12+/-4 %, slow group: 10+/-8 min, 7+/-4 %, respectively, $p<0.05$). There was no significant difference in mini-mental state examination at the day before the operation and at one month after the surgery between four groups (At the day before the operation: control group;48+/-8, slow group;48+/-7, at one month after the surgery:control group;46+/-7, slow group;45+/-9).
CONCLUSIONS: Slow rewarming rate could prevent the frequency of the decrease in SjvO2 during rewarming period.

Critical Care and Trauma

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REDUCING BLOOD LOSS DURING BIMAXILLARY OSTEOTOMY: CASE SERIES OF HYPOTENSIVE ANESTHESIA

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INTRODUCTION: As many as one third of patients undergoing bimaxillary surgery will require blood transfusion (1). Numerous methods have been used to reduce perioperative bleeding, including the use of hypotensive anesthesia, auto-transfusion and hemo-dilution (1,2). Recently (2), aprotinin has been shown to reduce blood loss (from 986 ml in controls to 473 ml in 15 patients with aprotinin). However, in this study, 9 patients in the control group required blood transfusion. The levels of blood loss in "control' groups reported in the literature seemed to us to be high, and the purpose of this study was to assess the efficacy of simpler techniques to minimise transfusion requirements.
METHODS: We report a prospective study of 20 consecutive patients who underwent bimaxillary surgery under one surgical-anesthetic team. General blood saving techniques involved: 1. hypotensive anesthesia (using high dose isoflurane and where necessary, labetolol); 2. high head-up position during surgery; 3. application of local vasoconstrictors (bupivacaine/1:200,000 epinephrine); 4. meticulous surgical dissection according to the method of Obwegeser and Sailer (3).
RESULTS: The median blood loss was 373 ml (range 160-800 ml). There were no adverse events in the group. Only one patient needed blood transfusion, and this was because of severe epistaxis flowing nasotracheal extubation.
CONCLUSIONS: In the majority of cases, it appears possible to reduce blood loss and transfusion requirements to minimal levels using a simple combination of careful anesthetic and surgical techniques. Complex and expensive interventions might reasonably be reserved for those particular patients initially thought to be at greater risk of haemorrhage (eg, due to coagulopathy).

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S-63

COMPARISON OF THE EFFECTS OF PROPOFOL AND ENFLURANE IN THE CORRECTIVE SURGERY OF SCOLIOSIS WITH THE POSTERIOR INSTRUMENTATION

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INTRODUCTION: To study the propofol dose in anesthesia induction and maintenance infusion rate for the corrective surgery of scoliosis with the posterior instrumentation and to compare the effects of propofol in awaking test time and induced hypotension with enflurane.
METHODS: Forty-eight scoliosis patients undergoing general anesthesia were randomly divided into two groups (group A and group B). Group A and group B were re-divided into four sub-groups in accordance with age: group A_i (under 12 years) and group A_{ii} (above 12 years); group B_i (under 12 years) and group B_{ii} (above 12 years). All groups were induced with fentanyl, propofol and atracurium. The anesthesia was maintained with an infusion of either propofol and 50% N_2O-O_2 in group A_i and group A_{ii} or enflurane and 50% N_2O-O_2 in group B_i and group B_{ii}. The HR, MAP, SpO_2, BIS and SEF were monitored intraoperatively(1).
RESULTS: The induction dose of propofol was 2.88±0.25 $mg \cdot kg^{-1}$ in children and 1.56±0.38 $mg \cdot kg^{-1}$ in adult. The maintenance infusion rate of propofol was 10.35±1.65 $mg \cdot kg^{-1} \cdot h^{-1}$ in children and 8.40±2.25 $mg \cdot kg^{-1} \cdot h^{-1}$ in adult. The maintenance of enflurane level was 2.10±0.34 MAC in children and 1.22±0.32MAC in adult. Awaking test time, postoperative awaking time, orientation recovery time(2) and the vomiting incidence in group A_i and group A_{ii} were much lower than those in group B_i and group B_{ii} (Table). The induced hypotension of the group A_i and group A_{ii} was also better than that of group B_i and group B_{ii}.
SUMMARY: Propofol is a proper anaesthetic for the corrective surgery of scoliosis with the posterior instrumentation.

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Table Comparison of the time of peri-operative in four groups (`m±SD)

	Awaking test time (min)	Postoperative awaking time (min)	Orientation recovery time (min)	Nausea and vomiting incidence(%)
Group A_i	9.60±3.40	15.25±5.75	18.60±5.55	5.88±1.26
Group A_{ii}	9.82±2.90	16.40±4.90	19.60±6.50	5.45±1.35
Group B_i	20.80±3.60**	24.10±8.60*	27.50±4.20*	37.86±4.50**
Group B_{ii}	22.90±4.05**	25.25±7.50*	26.45±5.75*	35.20±4.30**

* P value < 0.05 , Group B_i *vs* Group A_i; Group B_{ii} *vs* Group A_{ii}, ** P value < 0.01, Group B_i *vs* Group A_i; Group B_{ii} *vs* Group A_{ii}

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A COMPARISON OF EFFECTS OF PERIOPERATIVE PULMONARY FUNCTION IN LAPAROSCOPIC AND LAPAROTOMIC CHOLECYSTECTOMY IN ELDERLY PATIENTS

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INTRODUCTION: To compare the effects of perioperative pulmonary function in laparoscopic and laparotomic cholecystectomy in elderly patients.
METHODS: One hundred and twenty patients suffering from cholecystitis and undergoing laparoscopic or laparotomic cholecystectomy were divided into two groups on the basis of the normal or abnormal pulmonary function. A standardized general anesthetic technique was used for all patients. All pulmonary function parameters were monitored during the operation to compare the effects of pulmonary function in either laparoscopicor or laparotomic cholecystectomy (1,2).
RESULTS: (1) In laparoscopic groups with normal and abnormal pulmonary function, the end tidal carbon dioxide pressure (PetCO2), airway peak pressure (Ppeak), airway plat pressure (Pplat), and arterial carbon dioxide pressure (PaCO2) were increased (14.5%, 45.1%, 60.0% and 18.5% respectively) during the peritoneal insufflation, whereas, both respiratory compliance (C) and pH value (pH) were decreased significantly (42.0% and 2.7%) as compared with the pre-insufflation value ($p<0.01$). After deflation of peritoneal cavity, the PetCO2, Ppeak, Pplat, C, pH, and PaCO2 recovered to pre-insufflation level. (2) In laparotomic groups with normal or abnormal pulmonary function, no striking difference could be found during and after laparotomy in PetCO2, Ppeak, Pplat, C, pH, and PaCO2. (3) Between laparoscopic groups and laparotomic groups, striking difference was found during the operation, but not after the operation. (4) The postoperative pulmonary complications were much more and hospitalization was much longer in laparotomic groups than that of in laparoscopic groups.
CONCLUSION: Laparoscopic cholecystectomy is better than that of the same procedure performed via laparotomy in elderly patients with mild or moderate pulmonary dysfunction.

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S-65

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

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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. Fresh gas flow was delivered at a rate of 1000ml per minute in Group A and 500ml per minute in groups B and C. 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)(1).
RESULTS: 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. Consumption of sevoflurane in groups A, B and C was 13.3 ± 1.6 ml per hour, 9.6 ± 1.5 ml 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 ± 3.3 minutes, 10.5 ± 2.8 minutes and 7.5 ± 2.6 minutes respectively. The times to full orientation in Groups A, B and C were 24.5 ± 6.1 minutes, 17.4 ± 5.5 minutes and 12.7 ± 4.8 minutes 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 $14.5\% \pm 2.6\%$, $10.1\% \pm 2.3\%$ and $7.5\% \pm 2.1\%$ 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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BISPECTRAL INDEX MONITORING IN MECHANICALLY VENTILATED CRITICALLY ILL PATIENTS

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INTRODUCTION: Critically ill patients in the intensive care unit (ICU) requiring mechanical ventilation experience anxiety and discomfort which may have detrimental physiological consequences, and can cause agitation and psychosis. Therefore, these patients receive sedative-hypnotics to improve patient comfort. Clinical scores used to assess the depth of sedation in this patient population are subjective and inadequate. The bispectral index (BIS) derived from the electroencephalograph (EEG) has been shown to be a quantifiable measure of the depth of sedation (1). This study examined the depth of sedation, as determined by BIS monitoring, maintained in mechanically ventilated ICU patients at our institution.
METHODS: Thirty-five mechanically ventilated ICU patients without any central neurological injury were included in this study. The sedation regimen was similar in all patients. The hypnotic-sedatives drugs (i.e., lorazepam and midazolam) were titrated to maintain a modified Ramsay score of 4-5. The modified sedation score was as follows: 1=anxious, agitated, restless; 2=cooperative, oriented, tranquil; 3=drowsy, responds to commands only; 4= brisk response to shaking or loud sound; 5= sluggish response to shaking or loud sound; and 6=no response. In addition, BIS values were recorded hourly for 8 h but the nurse caring for the patient was blinded to the BIS values. The BIS values between 65 and 85 were considered to be appropriate for sedation (1). Data were analyzed using Students' t-test or Chi-square test with Yates' correction, with $p < 0.05$ considered significant.
RESULTS: The BIS values were recorded at 204 time points and ranged between 30 and 95. Of these time points, BIS was maintained between 65 and 85 in 28% (57/204) instances. In 12% (25/204) observations, the BIS values were greater than 85 while in 60% (122/204) of the times the BIS values were lower than 65.
DISCUSSION: This study suggests that the depth of sedation maintained in our patients was greater than that necessary to provide adequate hypnosis. The use of objective measure (e.g., BIS monitoring) to assess the depth of sedation should avoid excessive sedation, which may facilitate ventilatory weaning, and reduce the ICU stay and costs.
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S-67

SEDATION IN MECHANICALLY VENTILATED CRITICALLY ILL PATIENTS: USE OF BISPECTRAL INDEX MONITORING

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INTRODUCTION: Critically ill patients in the ICU requiring mechanical ventilation experience anxiety and discomfort that may have detrimental physiological consequences, and can cause agitation and psychosis. Therefore, these patients receive sedative-hypnotic medications administered according to clinical sedation scores. However, the sedation scores used to assess the depth of sedation are subjective and inadequate. The bispectral index (BIS) derived from the electroencephalograph (EEG) has been shown to be an objective measure of the depth of sedation (1). This study examined the value of BIS monitoring in assessing the depth of sedation in mechanically ventilated ICU patients, compared with clinical sedation scores.
METHODS: Thirty-five mechanically ventilated ICU patients without any central neurological injury were included in this study. The sedation regimen was similar in all patients. The hypnotic-sedatives drugs (i.e., lorazepam and midazolam) were titrated to maintain a modified Ramsay sedation score of 4-5. The modified sedation score was as follows: 1=anxious, agitated, restless; 2=cooperative, oriented, tranquil; 3=drowsy, responds to commands only; 4= brisk response to shaking or loud sound; 5= sluggish response to shaking or loud sound; and 6=no response. In addition to sedation scores, BIS values were recorded hourly for 8 h but the nurse caring for the patient was blinded to the BIS values. The BIS values between 65 and 85 were considered to be appropriate for sedation (1). Data were analyzed using Students' t-test or Chi-square test with Yates' correction, with $p < 0.05$ considered significant.
RESULTS: The sedation scores and BIS values were recorded at 204 time points and ranged between 30 and 95. The sedation scores were 1-3 at 38/204 (19%) of the instances. Of these the BIS values were greater than 85 at 24% of the times. The sedation scores were 4-5 at 92/204 (45%) of the times with BIS values of 65-85 at 27% instances while 61% had BIS of less than 65 and 12% had BIS of greater than 85. The sedation score of 6 was noted at 74/204 (36%) time points with BIS less than 65 at 73% of time points.
DISCUSSION: These data suggests that significant number of patients were maintained at deeper than necessary depth of sedation. There was no correlation between sedation scores of 4-5 and the BIS values 65-85 which were considered as adequate sedation. Our results are similar to Frenzel et al (2) who reported a mean BIS value of 57 for a modified Ramsay score of 4-5 while a mean BIS of 44 had a score of 6. Use of objective measure to assess the depth of sedation should avoid excessive sedation, which may facilitate ventilatory weaning, and reduce the ICU stay and costs.
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S-68

CEREBRAL OXYGEN METABOLISM AND TRANSCRANIAL DOPPLER ULTRASONOGRAPHY MONITORING IN NEUROSURGICAL COMATOSE PATIENTS WITH UNFAVORABLE OUTCOME

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INTRODUCTION: Despite the implementation of aggressive strategies of diagnosis and treatment based on the control of ICP, the incidence of mortality and severe disability in neurosurgical comatose patients remains frustratingly high.[1] Cerebral oxygen metabolism monitoring and TCD ultrasonography have become the most useful bed-sited methods for diagnosis, evaluation and prognosis of patients with cerebral hypoxia/ischemia and relative cerebral hyperperfusion.[2] We examined the incidence of oligemic cerebral hypoxia (SjO_2 <55%) and cerebral hyperperfusion (SjO_2 >75%) in neurosurgical comatose patients with poor outcome.
METHODS: Jugular bulb oxyhemoglobin saturation (SjO_2), cerebral extraction of oxygen (CEO_2), arteriojugular oxygen content difference ($AVDO_2$) and middle cerebral artery (MCA) systolic flow velocity (FV) using TCD were monitored in 56 patients with unfavorable outcome in our NICU. All patients were ventilated, positioned in bed with approximately 30-degree head tild, sedated and treated aggressively to keep ICP < 20 mm Hg and CPP >60-70 mm Hg (with vasopressors if needed). Patients were divided in two groups: group I- severe disability/vegetative state (GOS 3-2, 16M/5F, 37.6yo) and group II-dead (24M/11F, 39.2yo). 37.5% of patients were operated because of aneurysmal SAH, 28.7% had severe TBI, 12.5% had intracerebral hemorrhage, 14.2% had complicated tumor surgery and 7.1% of patients had global cerebral hypoxia during episodes of massive cerebral air embolism.
RESULTS: Multiple jugular venous desaturations were found in 66.7% and 36.4% of patients of group I and II respectively. Episodes of relative cerebral hyperemia were found in 44.4% and 59.1% of patients with GOS 3-2 and GOS 1 respectively. Daily physiological patterns are shown in Table 1.

Daily Physiological Patterns for Patients with Unfavorable Outcomes.

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Group I								
GCS		6.1± 0.6	5.8± 0.5	6.0± 0.6	6.4± 0.7*	6.4± 0.7*	6.1± 0.7	6.8± 0.8*
SjO_2 (%)	54.0±6.9	59.2± 3.5*	63.6± 4.5	63.5± 3.6	67.7± 3.6	67.4± 3.3	67.9± 3.3	66.2± 4.5
CEO_2 (%)	41.9± 5.7	39.4± 3.5*	32.7± 4.7	35.1± 3.5	30.3± 3.9	30.5± 3.4	31.3± 4.6	32.8± 4.9
$AVDO_2$ (ml/dl)	8.4± 1.5*	5.6± 0.8	5.0± 0.7	5.3± 0.6*	4.9± 0.8*	4.7± 0.6	4.2± 0.5	5.5± 0.8*
FV (cm/sec)	195± 43	165± 28	203± 17	149± 19	172± 16	182± 25	213± 33	171± 17
Group II								
GCS		6.6± 0.5	6.0± 0.5	5.2± 0.4#	4.8± 0.4*#	4.8± 0.5*#	4.9± 0.5#	4.9± 0.6*#
SjO_2 (%)	60.2± 5.4	67.9± 2.8*	67.7± 4.2	71.3± 4.9	72.8± 5.3	64.1± 5.0	69.3± 7.3	69.0± 5.8
CEO_2 (%)	38.5± 6.1	29.7± 2.8*	30.0± 4.1	27.7± 4.8	25.6± 5.1	34.7± 4.9	29.7± 7.1	29.9± 5.6
$AVDO_2$ (ml/dl)	6.8± 1.2*	5.4± 0.5	4.8± 0.6	4.0± 0.7*	3.6± 0.8*	5.0± 1.0	4.0± 1.0	4.3± 0.7*
FV (cm/sec)	206± 22	218± 22*	224± 19	222± 22*	241± 20*	246± 20*	213± 17	216± 20*

All dates are mean± SEM, *p<0.05 between groups; #p<0.05 in the same group
DISCUSSION: These results demonstrate that cerebral oligemic hypoxia and relative cerebral hyperemia are very common events in neurosurgical comatose patients with unfavorable outcome. Concomitant decreases in CEO_2 and increases in cerebral FV, indicating hyperoxic uncoupling between global cerebral consumption of oxygen and CBF, are very poor prognostic events and are significantly more pronounced in the nonsurvival group.
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S-69

EFFECT OF MIDAZOLAM ON EXPRESSION OF NEUTROPHIL ADHESION MOLECULES CD11B & CD18 IN VITRO

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INTRODUCTION: The benzodiazapenies are commonly used in clinical practice, with established anxiolytic effects. The presence of benzodiazepine receptors has been observed on many immune cells (1) including neutrophils and the binding of benzodiazepine drugs has been shown to play an important role in decreasing the release of cytotoxic reactive oxygen species (2). Neutrophil adhesion molecules play an important role in the neutrophil-endothelial interaction (3). The objective of this study was to examine the effect of midazolam on the expression of neutrophil adhesion molecules (CD11b & CD18).
METHODS: The expression of neutrophil CD11 & CD18 molecules after exposure to different concentrations midazolam (0, 0.5,1,10 times of therapeutic plasma concentrations (300 ng/ml) for 30 min at 37ºC was compared with that of time-matched controls. Aliquots of each group were stimulated with N-formyl-methionyl-leucyl-phenylalanine (fMLP) (10 nM) for 15 min at 37ºC to assess differences in the upregulation of CD11b & CD18. The expression of adhesion molecules was measured by flow-cytometry. Data is given as mean channel flurescence (MCF).
RESULTS: The expression of neutrophil CD11b & CD18 was decreased by pretreatment with midazolam when compared to control {(92 vs 162)(P=0.03) and (43 vs 53)(p=0.01)} respectively at therapeutic plasma concentration. There was no further decreased expression of these molecules at higher drug concentrations.
DISCUSSION: This study demonstrates the inhibitory effect of midazolam on neutrophil CD11b & CD 18 expression at clinically used dose. This effect may have important clinical implications.

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S-70

A MURINE MODEL FOR POST-ISCHEMIC INFLAMMATORY ORGAN DAMAGE AND FUNCTIONAL RECOVERY AFTER CARDIOPULMONARY RESUSCITATION (CPR)

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INTRODUCTION: Annually up to 750.000 Americans require cardiopulmonary resuscitation (CPR) after cardiac arrest (CA). About 30% reach the hospital, while only 14% are ultimately discharged. Post-CPR, patients suffer from a syndrome resembling systemic inflammatory response syndrome (SIRS) (2). Here, we use a murine model of global ischemia, to elucidate molecular mechanisms causing post-resuscitation inflammation and organ failure.
METHODS: Arterial and venous femoral access was established for pressure recordings, blood draws, and drug administration in swiss mice. Cardiac arrest (CA) was electrically induced (50 Hz, 10 V) and maintained for 5 minutes. Mechanical chest compression commenced and epinephrine and bicarbonate were administered. Ventricular fibrillation was terminated by defibrillation (1 J). Return of spontaneous circulation (ROSC) was documented based on blood pressure. After weaning and extubation, mice were followed for up to 48h. At sacrifice, blood from CPR and sham mice was drawn for liver and renal chemistry. Liver, kidney and brain were harvested for ICAM-1/VCAM-1 Western blots and leukocyte stainings. Data are presented as mean±sem. Statistical significance was accepted when non-parametric testing revealed $p<0.05$.
RESULTS: CA resulted in loss of perfusion pressure (MAP 65±13 vs 9±1, mmHg, baseline (bsl) vs CA, n=6, p<0,05). Blood gas analyses drawn with commencing CPR indicated prior hypoxia during CA (pO_2 363±143mmHg vs 100±51mmHg, bsl vs CA, n=5/5, p<0,05), acidosis (pH 7.44±0,07 vs 7.08±0,22, bsl vs CA, n=5/5, p<0,05) and lactate levels of up to 10 mmol/l. CA had a mortality of 42%. Mice with ROSC were still acidotic (pH 7,12±0,27, n=3) but not hypoxic (pO_2 338±93mmHg, n=3) or hypotensive (MAP: 58±10 mmHg, n=11). CPR-mice displayed significantly increased plasma ALT-levels (17±2 vs 140±64 U/L, bsl vs CA, n=6, p<0.001), whereas sham-operated mice showed no increase in transaminases (17±1vs 17±2 U/L, bsl vs 2 days, n=7). Creatinine after CPR was doubled compared to bsl (0.2±0.03 vs 0.5±0.08, n=6, p<0,01), while sham-mice remained stable (0.2±0.1 vs 0.3±0.05 mg/dl, n=7). Sensorimotoric performance scoring (0-8 points) revealed 7.3±1 points for sham-mice while CPR-animals only reached 5.4±1 points (n=9/10, p<0,001). By Western blotting, only in CPR-mice upregulation of VCAM-1 and ICAM-1 in heart, liver and kidney was detected. Neurophils judged by immunohistochemistry were more abundant in CPR than in sham liver and hearts.
DISCUSSION: Global ischemia causes an early systemic inflammatory response syndrome with augmented adhesion molecule expression and consequent neutrophil recruitment, ultimately leading to impaired sensomotoric performance but also renal and liver damage. Taken together we here present evidence for multi-organ failure (MOF) due to SIRS after resuscitation in mice. This murine model for post resuscitation MOF will be very useful to study the role of individual proteins in this setting by utilizing gene-deficient mice.
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S-71

EFFECTS OF HYPERTONIC-HYPERONCOTIC SOLUTION ON THE CELL VOLUME AND VIABILITY OF HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS TO HYPOXIA AND REOXYGENATION

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INTRODUCTION: The beneficial cardiovascular effects of hypertonic-hyperoncotic solution (HHS) resuscitation in the treatment of hemorrhagic shock are well known. Recent experimental and clinical investigations have suggested that HHS prevents the occurrence of complications (for example: ARDS, Sepsis, MOF) after shock. However, the mechanism is poorly defined. The function of the vascular endothelial cell is a key element in the pathogenesis of organ dysfunction after shock. We hypothesized that HHS resuscitation, in addition to enhancing hemodynamic recovery, protects vascular endothelial cell. The effects of hypertonic-hyperoncotic on the volume and viability of human umbilical vein endothelial cells to hypoxia and reoxygenation were investigated in this article.
METHODS: To model a clinically relevant hypertonic-hyperoncotic environment, human umbilical vein endothelial cells (HUVECs) in experimental group were preincubated in hypertonic saline and hydroxyethyl starch (HES) added to medium for 15 minutes (final osmolarity: 350mOsm/ml, 2.5mg/ml HES in medium). HUVECs in control group were preincubated in normal medium for 15 minutes. All HUVECs in both groups were exposed for 8 hours to hypoxic medium (95%N_2, 5%CO_2) and then for 16 hours to normoxic medium (95% air, 5%CO_2). HUVECs volume was evaluated by [14C]urea determination of intracellular water space. Cell viability was analyzed by vital dye staining.
RESULTS: Cell volume in control group was significantly increased after hypoxia/reoxygenation, and cell viability was significantly decreased (P<0.05 or 0.01). Cell in experimental group shrunk after treatment with HHS for 15 minutes (P<0.05) and then swelled again to baseline value (P>0.05). Cell viability remained unchanged (P>0.05).

Tab 1: Relative cell volume and cell viability in response to hypoxia/ reoxygenation and pretreatment with HHS.

	control group		experimental group	
	relative cell volume(%)	viability(%)	relative cell volume(%)	viability(%)
baseline	100±14.33	99.7±0.45	100±13.72	99.5±0.73
15min	101.3±14.65	99.3±0.36	76.2±9.32$^{*\#}$	99.2±4.89
8hrs	126.4±16.97**	82.7±6.32*	93.6±10.64$^{\#\#}$	95.3±5.83$^{\#}$
24hrs	147.8±24.57**	72.2±5.39**	97.3±16.38$^{\#\#}$	92.7±5.62$^{\#\#}$

vs baseline value, *P<0.05, **P<0.01. vs control group, #P<0.05, ##P<0.01. n=12
DISCUSSION: These results indicate that hypoxia/reoxygenation result in significantly endothelial cell swelling and decreased viability. Pretreatment with hypertonic-hyperoncotic solution should be established to prevent hypoxia/reoxygenation-induced cell swelling and cell death.
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S-72

TRAUMA DEMOGRAPHICS FOR LA COUNTY AND PRIVATE HOSPITALS: TRENDS IN TRAUMA ADMISSIONS

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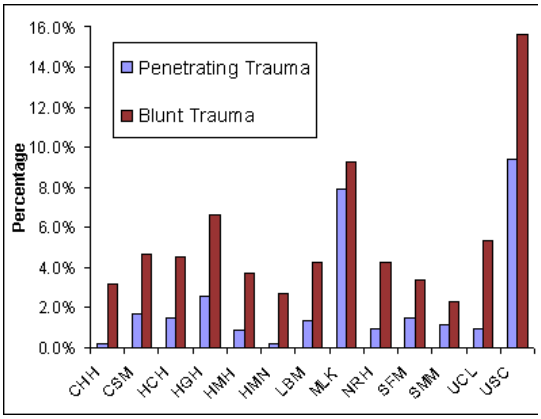
INTRODUCTION: Los Angeles County provides trauma services both through public and private hospitals. Disparities in types of trauma and demographics between institutions exist. This study describes demographics for the 13 accredited level I trauma centers in Los Angeles County based on trauma admission data over a 10-year period (1992-2001).
METHODS: Trauma data in Los Angeles County from 1992 to 2001 were separated by hospital, age, gender and type of trauma (penetrating vs. blunt). Data from the following public hospitals: Harbor/UCLA (HGH), MLK/Drew (MLK), LAC+USC (USC) were compared with the following private hospitals: Children's Hospital (CHH), Cedars-Sinai (CSM), Providence Holy Cross (HCH), Huntington Memorial Hospital (HMH), Henry Mayo Newhall Memorial Hospital (HMN), Long Beach Memorial (LBM), Northridge Hospital (NRH), St. Francis (SFM), St. Mary (SMM), UCLA (UCL). We analyzed the disparities in trauma admissions for each hospital based on the type of trauma.
RESULTS: In 124,342 trauma admissions over the 10 year period in LA County, 64.573 or 51.9%, were to the 3 county Trauma Hospitals (HGH, MLK, and USC). There were 59.769 (48.1%) admitted to the 10 Private Trauma Hospitals (CHH, CSM, HCH, HMH, HMN, LBM, NRH, SFM, SMM and UCL). There was a significant difference between hospitals in the number of patients with penetrating and blunt trauma admitted. Public hospitals admitted a higher percentage of penetrating injuries as compared to blunt injuries. Penetrating injuries were 66% of the total injuries reported by public hospitals, whereas they were 38% for private hospitals. USC and MLK admitted the highest percentage of blunt and penetrating trauma cases, comprising 25% and 17.2% of the total trauma respectively. One hospital (CHH) had the smallest penetrating caseload (0.2%). SMM admitted the lowest (2.3%) percentage of blunt trauma compared to all hospitals. USC admits the highest percentage of blunt trauma as compared to all hospitals. The 3 county hospitals (HGH, MLK, USC) admit the highest percentage of penetrating trauma overall (Figure 1).
DISCUSSION: Trends in particular injuries may represent areas in which prevention efforts and specialized services may be concentrated. The differences between hospitals are of significant epidemiological concern. The utilization of trauma centers is dependent on many factors, and accurately predicting the future need of trauma centers is an important financial goal. The significantly different rates of blunt and penetrating trauma between both private and public hospitals in Los Angeles County demonstrate areas in which efforts could be targeted to certain types of trauma and design of further studies is warranted.

Figure 1: Percentage of Penetrating and Blunt Trauma for each hospital based on the total trauma from 1992-2001



S-73

COMPARISON OF APACHE II AND LODS (LOGISTIC ORGAN DYSFUNCTION SYSTEM) IN AN INDIAN MULTIDISCIPLINARY ICU

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INTRODUCTION: APACHE II and LODS have been used to predict outcomes in intensive care units (ICUs) in many international studies. However, such studies from developing countries like India remain scanty. The aim of this study was to compare these two models in an Indian ICU.
METHODS: After institutional review board approval, this prospective cohort study was done in our 10-bedded multidisciplinary ICU of a 1000-bedded tertiary care center. During the study period (January to December 2001), 295 patients were admitted to the ICU. Patients with age less than 17 years, ICU stay shorter than 24 hours and those requiring readmission were excluded from analysis. APACHE II and LODS scores were calculated for the remaining 203 patients. Discrimination was assessed by comparing the area under the receiver operating characteristic (ROC) curves, constructing classification tables and calculating the correct classification rates (CCR). Calibration was tested using calibration curves and Hosmer-Lemeshow "C' and "H' statistics. Discrepancies in the predictions of the two models were analyzed by cross-tabulating their predictions at a decision criterion of 50% using McNemar's chi-square statistic.
RESULTS: The mean observed in-hospital mortality was 28.1% (n=57; ICU deaths=55, ward deaths=2). We observed an inverse relationship between length of stay in ICU (LOS) and mortality. The mean predicted mortality was 19.7% for APACHE II (Standardized mortality ratio 1.43) and 28.9% for LODS (standardized mortality ratio 0.97). The mean APACHE II score for survivors was 11.85 $\pm$ 5.64 and for non-survivors was 19.93 $\pm$ 6.94 ($p<0.005$), while the mean LODS score for survivors was 4.32 $\pm$ 2.63 and for non-survivors was 8.13 $\pm$ 3.58 ($p<0.005$). Both models showed similar discrimination (CCRs of the two models at decision criteria of 20, 50 and 80% were 78.33, 77.83 and 78.38% for APACHE II and 60.59, 80.79 and 77.34% for LODS. The areas under the ROC curve were 0.819 and 0.794 for APACHE II and LODS, respectively). However, LODS proved to be significantly better calibrated than APACHE II ($C=14.70$; $H=5.16$, $p>0.10$ for LODS and $C=20.94$; $H=21.24$, $p<0.01$ for APACHE II). The calibration curves for the two models are shown in Fig. 1. LODS predicted death more accurately than APACHE II (Mc Nemar's $^2=6.67$, $p<0.01$).
DISCUSSION: The inverse relation of LOS to mortality and our low post ICU discharge mortality (2 out of 57 deaths) are at variance with previous reports[1, 2]. LODS is simpler and more user friendly than APACHE II, and avoids some of problems associated with the use of APACHE II[3]. We conclude that of the two models, LODS is better suited to our patient population.
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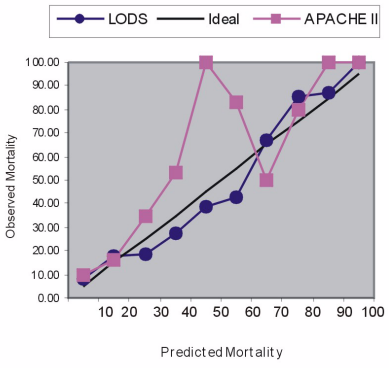
Fig. 1
Calibration Curves-APACHE II and LODS



S-74

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS IN A GENERAL ICU IN JAPAN: FIVE YEAR SURVEY

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INTRODUCTION: Methicillin-resistant Staphylococcus aureus (MRSA) infection has been spreading among medical facilities, and has been a serious medical and social problem in Japan. We retrospectively investigated MRSA infection and colonization in a general intensive care unit (ICU) in teaching hospital over the five year period.
METHODS: 2516 patients who admitted to general ICU at university hospital from 1997 to 2001 were examined. To detect MRSA organisms, specimens from sputa, pharynx or possible infected sites were obtained from all the patients three times per week, and were sent to the Central Laboratory. We calculated APACHE II scores of the patients who admitted in the year of 2001 and compared the scores between MRSA positive and negative patients. Non paired t-test and ANOVA with Duncan's test were used for statistical analysis, and p less than 0.05 was considered to be statistically significant.
RESULTS: 283 patients (11.2%) were positive for MRSA. Positive rate gradually decreased year by year (13.6% in 1997, 9.8% in 2001). Positive rate in emergency-admitted patients (25.5%) was significantly greater than that in planned-admitted patients (4.9%). Although positive rates did not change in planned-admitted patients, significant consecutive reduction of the rates in emergency-admitted patients was observed (32.6% in 1997, 20.6% in 2001). The majority of MRSA positive patients were admitted to the ICU either identified as MRSA positive or cultures taken on admission were positive. Mean of APACHE II score in MRSA positive patients (17.4 ± 6.2) was significantly higher than that in MRSA negative patients (12.9 ± 7.9).
DISCUSSION: Recent awareness and measures against MRSA may affect the consecutive improvement of MRSA infection and colonization. Significant reduction of positive rate in emergency-admitted patients would be responsible for this improvement. In most cases, MRSA was thought to be brought into ICU from the wards or other hospitals. Therefore, in order to reduce MRSA infection and colonization further in ICU, it would be essential to intensify the infection control in entire hospital or community. Since the patients who have MRSA were demonstrated to be sicker, we should care these patients cautiously even if the positive culture is considered to be only colonization.

S-75

PULMONARY INJURY IN PATIENTS UNDERGOING COMPLEX SPINE SURGERY

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INTRODUCTION: After sequential anterior-posterior spinal fusions (AP) for spinal deformities a significant number of patients demonstrate pulmonary injury in the form of elevated pulmonary vascular resistance and hypoxemia. We reported that the bronchoalveolar lavages (BAL) of these patients revealed increases in neutrophils and lipid laden macrophages (LLM). This report includes the analysis of the BAL for cytokine levels: TNF- and IL-6.
METHODS: With IRB approval, 15 adult patients for elective AP fusions underwent BAL. Following induction of general anesthesia, BAL was performed prior to surgery (baseline), after insertion of the posterior spinal instrumentation (PSF), and the morning after surgery prior to extubation (POD1). The BAL was 3-washes of 60cc of 0.9% saline from a fiberoptic bronchoscope wedged in the right middle lobe and lingual. BAL fluid was concentrated via centrifugation and assayed for IL-6 and TNF- using commercially available ELISA kits.
RESULTS: As a group, patients exhibited increases in BAL cytokine levels with surgery. Increases in TNF- correlated with increases in IL-6. There was also a strong correlation with the concentration of IL-6 and the number of LLM. Patient 8, who had the highest levels of BAL lipid laden macrophages and acute lung injury, also had high levels of IL-6 and TNF- on POD1. Six patients exhibited significantly elevated TNF- and IL-6 levels and 3 of the 6 had evidence for acute lung injury.
CONCLUSION: Acute lung injury is a diffuse pulmonary response to direct injury to lung tissue. There are multiple possibilities for the cause of direct lung injury during AP spine fusions including the embolization of fat and bone marrow debris. This probably triggers the release of acute phase reactants including cytokines. Cytokines are known to amplify inflammatory responses in the lungs, and an elevated IL-6 level has been found in the BAL of patients at risk for adult respiratory distress syndrome. We have demonstrated that the BAL fluid of patients undergoing AP fusions has elevated cytokine levels and in some of the patients this may be the cause of acute lung injury.
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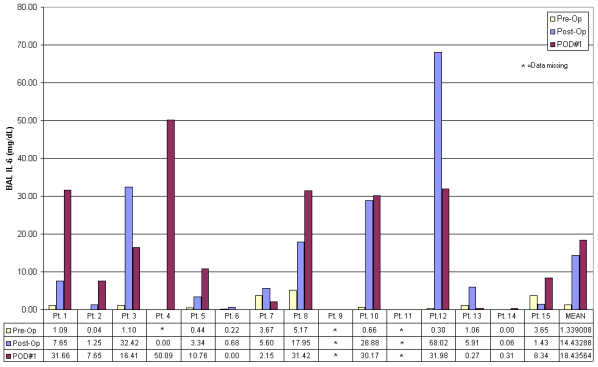

	Pt. 1	Pt. 2	Pt. 3	Pt. 4	Pt. 5	Pt. 6	Pt. 7	Pt. 8	Pt. 9	Pt. 10	Pt. 11	Pt.12	Pt. 13	Pt. 14	Pt. 15	MEAN
Pre-Op	1.09	0.04	1.10	*	0.44	0.22	3.87	5.17	*	0.66	*	0.30	1.06	0.00	3.65	1.339008
Post-Op	7.65	1.25	32.42	0.00	3.34	0.68	5.60	17.95	*	28.88	*	68.02	5.91	0.06	1.43	14.43288
POD#1	31.66	7.65	16.41	50.09	10.76	0.00	2.15	31.42	*	30.17	*	31.98	0.27	0.31	8.34	16.43564

S-76

ACCURACY OF LACTATE MEASUREMENT IN BOVINE BLOOD SAMPLES CONTAINING VARYING CONCENTRATIONS OF HEMOGLOBIN-BASED OXYGEN CARRIER (HBOC): A TEST OF TWO LACTATE ANALYZERS

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INTRODUCTION: Lactate level is critical for understanding oxygen delivery to peripheral tissues, especially in hemorrhagic shock and during resuscitation with HBOCs. In our previous studies in a canine hypovolemia model, administration of HBOC lead to improvement of hemodynamic parameters and decrease in lactate levels. It is not clear if the HBOC preparation itself could interfere with the measurement of lactate concentration in the circulation and if variation exists between different lactate analyzers used in clinical practice when HBOC is present. We evaluated two lactate analyzers for their detecting accuracy by determining recovery rate of lactate in mixed HBOC/ bovine blood samples that contained various concentrations of lactate.
METHODS: Samples containing l-lactic acid (5-50 mmol/L, Sigma, St. Louis, MO) and HBOC (0.65-13g/dL, Hemoglobin gluatamer-200, Biopure Corp., Cambridge, MA) in Plasmalyte A (pH=7.4, Baxter, Deerfield, IL) were prepared. 25-mL of bovine blood was collected in tubes containing sodium fluoride and potassium oxalate (Becton Dickinson, Franklin Lakes, NJ) as anticoagulants. 42 samples containing different final concentrations of HBOC (0.13-5.0g/dL) and lactic acid (0.62-8.56mmol/L) were generated by mixing bovine blood with lactic acid and HBOC stock solutions. All samples were measured in Model 2300 and 1500 (YSI Inc., Yellowsprings, OH) lactic acid analyzers simultaneously.
"True" lactic acid concentrations were calculated based on the amount of lactate added to each test sample combined with the background lactate concentration measured in each native HBOC or blood sample. "True" or calculated values were then compared to lactate concentrations measured by Model 2300 and 1500 YSI instruments to determine recovery rate. An agreement in method Bland-Altman analysis compared the calculated with the measured values for each instrument. Repeatability analysis was not performed.
RESULTS: Lactate recovery rate of the YSI 1500 instrument was 100 % when compared to calculated lactate values, whereas the YSI 2300 significantly under measured the calculated values ($p<0.05$), especially at higher lactate concentrations (see Figures). Adding HBOC in variable concentrations, ranging from 0.13-5.0g/dL, did not interfere with the linearization coefficients of results measured by the two instruments ($r=0.97$-0.99).
DISCUSSION: This investigation is a pilot of a larger interference study to determine the effect of varying concentrations of HBOC and blood in enzymatic-based lactate measurement systems. With only single measurement at each data point, we could not perform the traditional second stage of the Bland-Altman analysis, assessing repeatability.
In summary, the YSI 2300 significantly under measured the calculated values the true (i.e. calculated) values especially at higher calculated lactate concentrations, whereas the YSI 1500, while showing a similar tendency to underestimate lactate concentrations, showed consistently less measurement bias than the YSI 2300.
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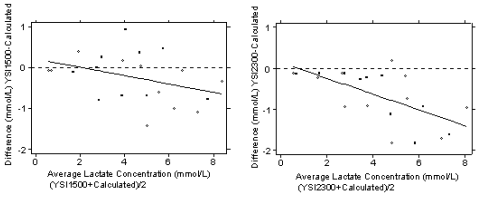

S-77

LEAD EFFECTS: OXYGEN HEMOGLOBIN DISSOCIATION IN BOVINE BLOOD USING OXYGEN CONTENT FROM TONOMETRY AND A LEXO2CON OXYGEN ANALYZER

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INTRODUCTION: Two in a thousand bags of packed red cells contain toxic lead levels (1). High lead levels interfere with oxygen loading in blood of fresh water field crab (2). This study evaluated the effects of varying lead levels on oxy-hemoglobin dissociation using bovine blood.
METHODS: Remainder sample single healthy donor bovine blood was obtained and baseline lead level measured. The samples were blended using two IL tonometers at six oxygen concentrations (2.5, 5, 8, 10, 21, and 95%) with 5 % CO2 in nitrogen for five minutes after a fifteen minute wash-in period with each level of oxygen. Three sets of samples were performed at each oxygen level: 2ml bovine blood with 100 µL normal saline (control), 2mL bovine blood with toxic lead levels (70µg/ dL) added, 2mL bovine blood with low lead levels (22µg/dL) added. Samples were anaerobically removed from the tonometer and immediately evaluated in the LEXO2CON oxygen analyzer for oxygen content. Oxygen saturations were calculated from the O2 content with the following formulas: O2 SAT = O2 content - (PaO2 x 0.003)/1.32 x Hb, where PaO2 = (O2 concentration in supplied tanks) x (PBAR - PH20), (Hufner factor of bovine blood is 1.32). Oxygen saturation was plotted against PO2 fitting a fourth order polynominal non-linear regression to the data, using Kelman's model (3).
RESULTS: Baseline lead level in bovine blood was 1.9 µg/dL. No clinically significant differences were noted as a function of lead concentration. See Figure 1.
CONCLUSION: No in vitro effects of low or high levels of lead on the hemoglobin dissociation curves were observed using bovine blood. In vivo long-term lead exposure resulting in high levels should be evaluated for changes in oxy-hemoglobin dissociation.

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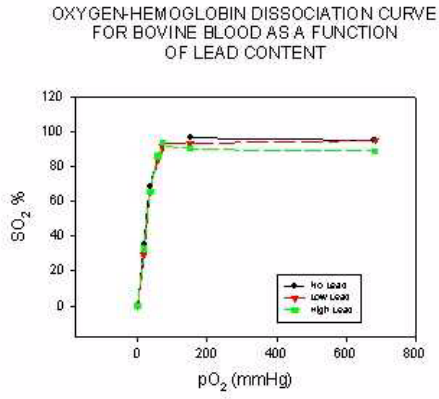

S-78

ARTERIOVENOUS CARBOXYHEMOGLOBIN DIFFERENCE IN CRITICAL ILLNESS: FICTION OR FACT?

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INTRODUCTION: It is still debated whether the paradox arteriovenous carboxihemoglobin (COHb) difference found in critical illness is a) due to increased COHb production by the pulmonary enzyme heme oxygenase (HO-1), b) dependent on oxygen tension, or c) caused by technical artifacts using spectrophotometry (1, 2). This study was designed as a prospective, controlled laboratory experiment to determine if arteriovenous COHb difference occurs only in critical illness, e.g. endotoxemia, or whether this gradient is also existent in health.
METHODS: Six adult ewes, weighing 38 ± 3 kg were instrumented for chronic study. At baseline in the healthy state, cardiopulmonary data were obtained and blood gases were analyzed for arterial and mixed venous COHb concentrations. Subsequently, the sheep were subjected to a continuous infusion of Samonella typhosa endotoxin (10 $ng \cdot kg^{-1} \cdot min^{-1}$) for 24 hours. Then, measurements were repeated. COHb concentrations were analyzed with both, a standard ABL 625 and an updated ABL 725. The latter one was accurately calibrated for COHb wavelengths (SAT 100) to eliminate the FCOHb dependency on oxygen tension, thereby excluding technical artifacts (1). Using Student's t-test, differences in and between groups were calculated. Data are presented as mean ± SEM.
RESULTS: All endotoxemic sheep exhibited a hypotensive-hyperdynamic circulation with a decreased systemic vascular resistance index (767 ± 39 vs. 1277 ± 78 $dyne \cdot cm^{-5} \cdot m^2$; $P < 0.001$) and an increased cardiac index (8.4 ± 0.3 vs. 5.8 ± 0.3 $L \cdot min^{-1} \cdot m^{-2}$; $P < 0.001$). In addition, endotoxin infusion was accompanied by pulmonary hypertension. Arteriovenous COHb difference occurred in both health and endotoxemia. Interestingly, arterial and mixed venous COHb concentrations determined with the ABL 625 were significantly lower than those measured with the ABL 725.
DISCUSSION: Since arteriovenous COHb difference occurred in health and endotoxemia, this gradient appears not to reflect critical illness. In addition it is noteworthy that measurements performed with an ABL 625 obviously underestimate COHb concentrations, most likely due to technical artifacts (1).
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	COHb concentration [%]			
	ABL 625		ABL 725	
blood gases	health	endotoxemia	health	endotoxemia
arterial	1.42 ± 0.19	1.46 ± 0.13	3.2 ± 0.09#	3.1 ± 0.14#
mixed venous	0.15 ± 0.01*	0.07 ± 0.01*	1.5 ± 0.08*#	1.48 ± 0.25*#

*P < 0.001 arterial vs. mixed venous; #P < 0.001 ABL 625 vs. ABL 725

S-79

THE USE OF PREHOSPITAL RAPID SEQUENCE INTUBATION BY PARAMEDICS FOR AIRWAY MANAGEMENT IN MEDICAL EMERGENCIES

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INTRODUCTION: Rapid Sequence Intubation (RSI) is a therapeutic intervention utilized by paramedics in many Advanced Life Support (ALS) Emergency Medical Services (EMS) systems for trauma airway management but its use in medical emergencies is not widely reported. We report our experience with this intervention in patients with medical emergencies.
Objective: To assess utilization of, indications for and frequency of use of RSI by paramedics in medical emergencies.
METHODS: Retrospective, observational review of an RSI database for utilization of prehospital RSI for medical emergencies. Indications for RSI: Glasgow Coma Score (GCS) <8, rapidly declining hemodynamic or respiratory stability, and/or mechanism of injury warranting prompt airway management (e.g. burns). Patients postictal from seizures were excluded from the RSI database. Two paramedics were required on-scene for RSI interventions. Patients were classified as RSI Indicated-Performed or RSI Indicated Not Performed.
RESULTS: In a 25 month period, 41 trauma and 81 medical patients met RSI criteria. Etomidate-succinylcholine facilitated RSI was performed in 37/81 (46%) of the medical patients. Neurological conditions (excluding seizures) were present in 16/37 (42%), respiratory distress in 12/37 (32%), and drug overdoses in 6/37 (16%). In 34/37 (92%) patients endotracheal intubation was achieved during the first or second attempt. In 2/37 (5%) patients cricothyroidotomy was indicated due to unsuccessful intubations and failed Combi-tube placement in the presence of oxygen desaturation. One patient was transported with bag-valve-mask ventilation (oxygen saturations >93% en route) after three unsuccessful intubation attempts. No undetected/unrecognized esophageal intubations occurred. Proximity to hospital and crew configuration (presence of only one RSI-trained paramedic on-scene) were frequent reasons for not performing RSI when clinically indicated.
DISCUSSION: Our data demonstrates that prehospital RSI is utilized twice as frequently for medical emergencies when compared with trauma. Neurological emergencies were the most frequent indication for RSI followed by respiratory distress then drug overdoses. Endotracheal intubation is accomplished by the second attempt in most patients. Failed intubations indicate the need for paramedic training in alternative airway devices as well as cricothyroidotomy. RSI by paramedics can be an effective intervention for airway management in medical emergencies in the prehospital environment. Studies are needed evaluating patient outcome after the prehospital RSI intervention to determine its clinical value.

S-80

CONTINOUS OXYGEN INSUFFLATION (SWINE): AN ADDITIONAL TOOL FOR FAILED INTUBATION

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INTRODUCTION: While Transtracheal Jet Ventilation(TTJV) is an accepted therapy on the ASA Difficult Airway Algorithim, the technique requires equipment that is not widely available in clinical settings. Transtracheal Continuous Oxygen Insufflation (TT-COI) can performed with any oxygen source, oxygen tubing, one stop cock and one large bore intravenous needle. We tested the efficacy of TT-COI vs. TTJV in maintaining adequate oxygen tension and hemodynamic stability.
METHODS: With Institutional Animal Care and Use Committee approval, 5 swine weighing 20-30 kg were anesthetized and intubated. Pancuronium was administered to prevent spontaneous respiration. Femoral PA and arterial catheters were surgically placed. To facilitate tracheal cannulation with a 14gauge needle a limited neck dissection was necessary in this species. Each animal received fifteen minutes intervals of TTJV and TT-COI. ETCO2, SP02, arterial blood gases, heart rate, PA and arterial blood pressure was measured.
RESULTS: Both TTJV and TT-COI maintained oxygen tension above 200 mmHg for each 15-minute interval. Significant hypercarbia occurred with TT-COI but not with TTJV. In TT-COI, elevations of PA pressure, heart rate and arterial pressure reflected increasing CO2 tension. ETCO2 could not be measured during TT-COI.
TABLE:

TTJV 15 min				TT-COI 15 min			
Pig	pH	pCO_2	pO_2	Pig	pH	pCO_2	pO_2
1	7.58	31	232	1	7.04	100	221
2	7.38	52	273	2	7.09	169	245
3	7.42	41	486	3	7.05	106	265
4	7.48	41	479	4	7.05	118	315
5	7.43	58	330	5	7.09	96	274

CONCLUSION: TT-COI is as efficacious as TTJV in maintaining oxygen tension for at least fifteen minutes, allowing the clinician time to secure a more definitive airway.

S-81

EFFECTS OF WEIGHT AND MODE OF VENTILATION ON RESPIRATORY SYSTEM MECHANICS AND OXYGENATION DURING LAPAROSCOPY

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OBJECTIVE: To test the hypothesis that the increases in either tidal volume (TV) or respiratory rate (RR) can improve lung mechanics (static compliance,Cst,rs, and inspiratory resistance,RI,rs) and oxygenation in MO patients during laparoscopy.
METHODS: We studied the effects of body weight, position (supine, head-up and head-down), and pneumoperitoneum on Cst,rs, RI,rs and arterial oxygenation (PaO2) in 6 NW (BMI=21 ±3 kg/m2) and 6 healthy MO (BMI=48 ±5 kg/m2) patients during laparoscopy. All measurements were performed at: 1) TV 800 mL and 10 breaths/min ("baseline"); 2) TV 1600 mL ("double TV") and 10 breaths/min; and 3) TV 800 mL and 20 ("double rate") breaths/min. A Servo Screen 390 V2.0 pulmonary monitor was used to calculate the Cst,rs and RI,rs. End-tidal CO2 was measured with a mass spectrometer and PaO2 and PaCO2 with continuous blood gas monitor (Paratrend 7). Using the alveolar oxygen equation and arterial oxygen tension, the alveolar-arterial oxygen gradients (A-aDO2) were calculated. Data were analyzed using repeated measures ANOVA. Statistical significance was set at $P<0.05$.
RESULTS: Supine anesthetized MO patients had on average 29% lower Cst,rs compared to the NW patients (44 vs 62 mL/cmH2O) ($P<0.001$). Positioning the patients into the head-up or head-down before pneumoperitoneum did not affect significantly Cst,rs in neither MO nor NW groups ($P = 0.8$). Doubling the TV, but not RR, had trend to increase Cst,rs in both groups (to 69 and 57 mL/cmH2O in NW and MO, respectively). Pneumoperitoneum induced large decrease in Cst,rs: in NW to 34 mL/cmH2 O and in MO to 25 mL/cmH2O, (both $P=0.7$). Before pneumoperitoneum RI,rs was higher in the supine MO patients compared to the NW patients regardless of body position (19 vs. 10 cmH2O/L/sec, $P=0.001$). Doubling the RR or TV before abdominal insufflation did not have significant impact on RI,rs in either group. After pneumoperitoneum RI,rs increased in MO patients with "baseline" ventilation in head-down position to 26 cmH2O/L/sec ($P<0.01$) and in NW patients "double TV" head-up and head down groups to 19 cmH2O/L/sec ($P<0.05$). Regardlesof experimental condition A-aDO2 was always higher in MO patients (139±41 vs. 54±20 mmHg in MO and NW group, respectively, $P<0.001$). The A-aDO2 was not affected by either the body position, pneumoperitoneum or the mode of ventilation.
DISCUSSION: During laparoscopy MO patients have lower static respiratory system compliance and higher inspiratory resistance compared to the normal weight patients. Arterial oxygenation during laparoscopy was affected only by body weight and not by intraoperative body positioning, pneumoperitoneum, or the mode of ventilation.

S-82

CONTINUOUS RESPIRATORY MANAGEMENT WITH A TRANSPORT VENTILATOR FOR THE PATIENTS AFTER CARDIAC SURGERY

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INTRODUCTION: Transport ventilators with a patient-triggered function have become commercially available. Previous studies have suggested that transport ventilators have performance indexes comparable to the ventilator currently used in ICUs1. The advantages they offer compared with manual ventilation in terms of continuous use of them from transportation until the weaning from them in ICU have not been fully investigated. The present study was carried out to compare the two types of respiratory management, i.e., the management with a transport ventilator and that with manual ventilation followed by a conventional respirator, during the period from transportation until the weaning from them.
METHODS: With their informed consents, adult patients after cardiac surgery requiring intrahospital transport postoperatively from operation room to ICU were randomly assigned to two groups. Group M (n=11) was managed with manual ventilation during transport followed by a conventional respirator in ICU. Group V (n=10) was managed with transport ventilator (LTV 1000: Pulmonetic systems) throughout the time course. Patients in both groups received 100% oxygen during transport. Manual ventilation was provided by attending anesthesiologists via a self-inflating bag at a flow rate of 10 L/min. Arterial blood gas analysis (pH, $PaCO_2$, PaO_2), respiratory rate (RR), PEEP and tidal volume (VT) were measured at baseline, i.e., 15 min before transport (TB), on arrival to ICU (T0) and immediately before extubation (TE). The data were expressed as mean±SD. Statistical significance ($p<0.05$) was determined using ANOVA and t-test.
RESULTS: $PaCO_2$ (32±7mmHg) at T0 in group M was significantly lower than that at TB (41±3, $p<0.01$) and than that in group V at T0 (41±3, $p<0.01$). RR and VT (13±4/min and 635±123mL) at T0 in group M tended to be higher than those at TB (9±1, $p=0.056$, and 529±110, $p=0.062$). PEEP (0.6±0.5cmH_2O) at T0 in group M was significantly lower than that at TB (2.9±1.0, $p<0.01$) and than that in group V at T0 (4.6±0.7, $p<0.01$). There was no deterioration of oxygenation and hemodynamics in either group throughout the time course. Patients in either group had no trouble in the weaning from mechanical ventilation. The durations of mechanical ventilation and the lengths of stay in ICU were similar between group M and V (340±51 min vs 329±34, and 4.2±0.3 days vs 4.5±0.3).
DISCUSSION: Transport ventilator provides more stable respiratory support than manual ventilation during transportation, and they could be used safely until the weaning in ICU thanks to the patient-triggered function.
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Economics; Education & Patient Safety

S-83

A SYSTEMATIC REVIEW OF THYROMENTAL DISTANCE AS A PREDICTOR OF DIFFICULT LARYNGOSCOPY

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INTRODUCTION: Thyromental distance (TMD) is one of numerous predictive tests suggested to screen for difficult laryngoscopy or intubation. Its predictive utility been measured in a variety of studies. Systematic review with meta-analysis has been used to combine studies increasing their overall precision and reliability. This may allow anesthesiologists to quickly assimilate large amounts of information to apply to their patient population. The limitations are publication bias can limit search for appropriate studies, and heterogeneity of study groups can make meta-analysis misleading if not adjusted for. The object of this systematic review was to attempt to combine the results of all English language studies that measured TMD and prospectively related this to laryngoscopy grading during general anesthesia.
METHODS: A systematic search was performed of Pubmed, Embase and the Cochrane Controlled Trials Register. All prospective English language studies that measured of TMD and Cormack and Lehane grading (CLG) at laryngoscopy were included. Southeast Asian studies were excluded because sub-analysis revealed that their TMD was significantly different to other populations. Studies that included known cases of difficult intubation, or groups known to be at increased risk of difficult intubation were excluded. All studies were examined in detail for acceptable design, and presentation of results. If TMD was presented in such a way that we could not extract TMD related to CLG, we contacted the authors for the original data. Difficult laryngoscopy was defined as CLG 3 and 4. Studies commonly used different cut-off values (e.g. <7cm) for abnormal TMD, so results were combined for each cut-off. Data was extracted into a standard 2x2 table with abnormal/normal TMD on one axis and easy/difficult laryngoscopy on the other. From this we calculated the performance (sensitivity, specificity, positive predictive value (PPV) and likelihood ratio (LR)) of TMD at each cut off for each study. Meta-analysis combined the performance of each study at each cut-off by weighting each parameter (multiplying the log by the inverse of the variance)[1].
RESULTS: 8 studies with a total of 15168 patients were included [2-9]. The combined performance (95% Confidence Interval) of TMD at each cut of value is summarized below.

TMD cut-off (cm)	Sensitivity	Specificity	PPV	LR
6.0	0.07 (0.07-0.08)	0.99 (0.99-0.99)	0.30 (0.29-0.30)	9.0 (0.08-964.9)
6.5	0.04 (0.03-0.05)	0.98 (0.98-0.99)	0.15 (0.13-0.17)	3.1 (0.00-1476.8)
7.0	0.47 (0.45-0.49)	0.89 (0.88-0.90)	0.03 (0.02-0.04)	3.7 (1.4-10.4)
7.5	1.0 (0.99-1.0)	0.64 (0.61-0.66)	0.01 (0.00-0.02)	2.5 (1.4-4.2)

DISCUSSION: The sensitivity can be improved by using a greater TMD as the cut-off for the test. This reduces the specificity and increases the false positive rate (1-PPV). Likelihood ratios were low except at 6cm cut-off where the confidence intervals were very wide. The low PPV and LR suggest that TMD alone is a poor predictor of difficult laryngoscopy.

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S-84

POPULATION THYROMENTAL DISTANCE CHANGES WITH ETHNICITY

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INTRODUCTION: Many tests including the thyromental distance (TMD) have been suggested to screen for difficult laryngoscopy or intubation. Their predictive utilities have been subsequently tested in different populations. For a measurement like TMD there is a range within any population, this could conceivably vary in ethnic groups with different body morphology. To use it as a screening test a cut-off for an "abnormal" value must be arbitrarily decided. A low value for one ethnic group may be a normal value for another. Hence, a major problem in applying the results to ones practice is to decide if the sample population is representative of your patients. If TMD differs with ethnic origin, this would cast doubt on the ability of a clinician in one country to apply the results of a study from a group of patients of different ethnicity to his patients. The objective of this study was to determine if TMD changes with ethnicity.
METHODS: studies were identified by a literature search of Pubmed, Embase and the Cochrane Controlled Trials Register. Authors were contacted for original TMD measurements. Most only recorded whether the each patient had TMD less or greater than their cut-off. From 2 papers we could extract data from published histograms[1-2]. These used ranges of TMD (e.g. 7-7.5cm), for these we used the mid point of the data range (i.e. 7.25cm). One author[3] sent us original TMD measurements to the nearest 0.1 cm. Only study 3 was normally distributed. Groups were compared by Kruskal-Wallis H test (KWH). Post hoc comparisons between each pair of groups were performed by Mann-Whitney U-test (MWU). Results were analysed using Minitab 12.2 for windows.
RESULTS: the descriptive statistics for identified studies are summarised below.

Ethnicity	Data Extracted	n	Median TMD (cm)	Interquartile Range (cm)
Singaporean	Histogram Data range 0.5cm intervals	211	6.5	5.5 to 7.0
Saudi Arabian	Histogram Data range 0.5cm intervals	350	7.25	7.25 to 8.25
UK	TMD to nearest 0.1 cm	244	8.0	7.1 to 8.9

All groups had a significantly different TMD (KWH, $p<0.001$). Post hoc tests confirmed that UK, Saudi and Singaporean patients all had different TMD (MWU, $p<0.001$ for each comparison).
DISCUSSION: There is a range of TMD within each population. The reference TMD changes with the ethnicity of the reference population. The median TMD was greatest for the UK population and smallest for the Singaporean population. Anesthesiologists should take care when applying the performance of TMD in predicting difficult laryngoscopy in populations different to their patients. There may be difficulties in combining the results by meta-analysis of studies on different populations. In particular South-East Asian populations have a statistically and clinically significantly different TMD from Middle-eastern or European populations.

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S-85

A COMPARISON OF LARYNGEAL MASK AIRWAY AND PA XPRESS

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INTRODUCTION: PAX_{PRESS} by VITAL SIGNS Inc [1] is a supraglottic airway device with presence of gills at the tip and an inflatable pharyngeal cuff proximal to the distal opening of the airway. They are convex posteriorly and tapered distally, so as to be accommodated in the hypopharynx. The current 'gold standard' of a supraglottic airway device is the Laryngeal mask airway, which forms a seal with the peri-glottic tissues. The aim of the present study was to determine the ease and speed of placement and post-operative laryngo-pharyngeal morbidity of the PAX compared to the Laryngeal mask airway.
METHODS: 60 adult (ASA I & II) patients of either sex were studied to compare the ease and speed of placement and post-operative laryngo-pharyngeal morbidity between the Laryngeal Mask Airway and PAX in patients undergoing minor peripheral surgery under general anesthesia. The patients were randomly divided into 2 groups of 30 each (Laryngeal mask airway, n=30; PAX, n=30). Both the airway devices were inserted by a single operator who had an experience of more than 50 insertions of each. Laryngeal mask airway sizes 4 & 5 were inserted in female and male patients respectively. The same size of PAX was used in both female and male patients because no other size was available by the manufacturer.
RESULTS: In 90% patients the Laryngeal mask airway was correctly placed in the first attempt as compared to 66.6% first attempt placements with PAX ($p<0.01$). 13.3% patients required 3 attempts and there were 2(6.7%) failures in the PAX group as compared to none requiring 3 attempts and no failure in the Laryngeal mask airway group. The mean total placement time was significantly more in PAX group (35.4 ± 2.5 seconds) than in Laryngeal mask airway group (24.6 ± 3.1 seconds). The commonest complication was sore throat, which was significantly more with PAX (53.5%) than with Laryngeal mask airway (26.4%).
CONCLUSION: Our data has shown that correct Laryngeal mask airway placement not only required significantly fewer attempts and less overall time, but also demonstrated fewer incidences of trauma and post-operative complications as compared to PAX placement. The marked difference in efficiency between them could probably be due to the one size limit of the PAX, or the actual difference in design of the PAX. However, further studies should be undertaken to compare the safety and cost-effectiveness of Laryngeal mask airway and PAX once different sizes of the PA_{XPRESS} are introduced into the market.

Comparison attemts tro place and time taken in seconds

	1st attempt	2nd attempt	3rd attempt	TotalTime
LMA N=30	27, 90% p<0.01*	3, 10% p>0.05	0 p<0.01*	24.6 SD=3 p<0.01*
Pax N=30	20, 67%	4 , 13%	4, 13%	35.4 SD=2.5

S-86

COMPARISON OF THE SUCCESS RATES USING THE INTUBATING LARYNGEAL MASK WITH AND WITHOUT FIBEROPTIC GUIDANCE.

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INTRODUCTION: The intubating laryngeal mask (ILMA) allows blind intubation of the trachea in patients with/without difficult airways, which has a success rate of 82-99.3% (1, 2). The aim of this prospective randomized study was to compare of the success rates for intubation using the ILMA blind or fiberoptic guidance.
METHODS: After Ethic Committee approval, 80 patients scheduled for servical spine pathologies, aged 18-78 years, and ASA I-II were included. After preoxygenation and induction of anesthesia with propofol 2.5$mgkg^{-1}$ and fentanyl 1 gkg^{-1}, the ILMA was inserted. Following successful ILMA insertion, vecuronium 0.1 $mgkg^{-1}$ was given. After 2 minutes, patients were intubated using ILMA with either fiberoptic guidance (ILMA-FOB, n=40) or blindly (ILMA-Blind, n=40). The ILMA insertion time was defined as the time from removal of the face mask to the time ventilation was established through the airway with CO_2 confirmation. Tracheal intubation time was defined as the time from loss of CO_2 due to disconnection of the circuit for tracheal intubation to the time of reapperance of the CO_2 from the tracheal tube with no evidence of cuff leak with positive pressure ventilation. Times for successful airway insertion and tracheal intubation, the number of attempts for successful airway insertion and tracheal intubation, the incidence of sore throat in both groups were recorded. Statistical analysis was performed using Fisher's exact test. $p<0.05$ was considered statistically significant.
RESULTS: Success rates of the first attempt and overall for the ILMA insertion were 90%-95% for the ILMA-Blind group, and also 90%-100% for the ILMA-FOB group. First attempt and overall success rates for tracheal intubation were 80%-95% for the ILMA-Blind group, and also 100%-100% for the ILMA-FOB group. In four patients of the ILMA-Blind group, successful ventilation were performed at the third attempt. In two of these patients, tracheal intubation had failed. In four patients of the ILMA-FOB group, the ILMA was inserted successfully at the second attempt. The time for tracheal intubation was longer for the ILMA FOB group ($p<0.001$). The incidence of sore throat was 11% for the ILMA-Blind group, but 0% for the ILMA-FOB group ($p<0.001$).
DISCUSSION: As a conclusion, the time for intubation using the ILMA with fiberoptic guidance was longer. However, using fiberoptic guidance during intubation with ILMA has advantages of increasing success rates and performing intubation without sore throat.
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S-87

THE INCIDENCE & ETIOLOGY OF REINTUBATION DURING THE FIRST 24 HOURS FOLLOWING SURGERY AND ANESTHESIA: A TWO YEAR RETROSPECTIVE ANALYSIS

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INTRODUCTION: Laryngoscopy and endotracheal intubation causes a marked sympathetic response with the potential to elicit deleterious side effects in some patients (1). In addition to undesired sympathetic stimulation, premature extubation lead to other serious complications (2). Urgent reintubation during the first 24 hours following anesthesia not only predisposes patients to all of the serious complications associated with airway management, but may increase hospital cost due to prolonged PACU stay and possible ICU admission.
METHODS: A retrospective 2-year case analysis was performed on patients who received an anesthetic and were reintubated during the first 24 hours postoperatively. For our control group we randomly selected 400 patients who were successfully extubated. The following data were collected and analyzed: age, weight, ASA physical status, type of surgery, type of anesthesia, intraoperative medications, transfusion therapy, location and timing of re-intubation. We reviewed the documented reason for reintubation, duration of PACU stay, ICU admission, and the seniority of the anesthesiologists. Data was analyzed using the Chi-Square and Kruskal-Wallis tests. P value of 0.05 was significant.
RESULTS: Our hospital performs more than 25, 000 surgical procedures/year. During 2 years, 93 patients (0.2 %) were urgently reintubated 24 hours postoperatively. There were equal numbers of males and females in both groups. The median age in the study and control groups was 68 years and 58 years respectively ($p < 0.001$). In the study group the procedures were abdominal 39 (42 %), thoracic 21 (22 %), neurosurgical 15 (16 %), vascular 9 (10 %), orthopedic 9 (10 %) and other 9 (10 %) (Table 1). In the control group 22% were abdominal cases and 12% thoracic ($p < 0.001$); 42 junior and 52 senior anesthesiologists participated in their care; ASA physical status 1 & 2 was 40%; ASA 3 & 4 was 60%. The total ICU admission in the control group was 10%.

Table 1: Study Group Data

Category		Count	
ASA	1 and 2	22	
	3 and 4	71	76 %
Surgery	Elective	86	
	Emergency	7	8 %
Age	< 60 years	29	
	> 61 years	64	69 %
MD	Senior	68	
	Junior	25	27 %
Reintubation	Floor	9	
Location of	OR	45	49 %
Patient	PACU	38	41 %
ICU	Admission	38	
Reason for Reintubation	Respiratory	74	
	Cardiac	10	11 %
	Miscellaneous	9	10 %

DISCUSSION: The reported incidence of reintubation in ICU patients is 20 % (3). There is no published data for the incidence of reintubation immediately following surgery and anesthesia. In our study, the incidence of urgent reintubation following anesthesia is 0.2 %. The characteristics of the study group are advanced age, weight > 101 kg, ASA physical status > 2, and elective abdominal and thoracic surgery. The average PACU stay for the study group was 5 hours, almost twice the average PACU stay for the control group. The study group also had a much higher incidence of ICU admission. It is surprising that most of the patients who required reintubation had a senior anesthesiologist (> 5 years experience) involved in their care.
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S-88

QUALITY OF STUDY PROTOCOLS AND DATA ANALYSES IN RANDOMIZED CONTROLLED TRIALS AMONG GENERAL ANESTHESIOLOGY JOURNALS

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INTRODUCTION: Medical treatments and procedures require validation before they are determined to be of benefit to patients. Recent emphasis (1,2) on the quality of clinical trials in the medical literature reflects the ongoing concern among clinicians. We studied all randomized clinical trials in four general anesthesiology journals in the year 2000 to identify specific areas for improvement in the conduct, implementation, analysis, and reporting of clinical trials.
METHODS: All Randomized Clinical Trials (RCTs) published between January 2000 and December 2000 in four anesthesiology journals (*Anesthesiology, Anesthesia & Analgesia, Anaesthesia, Canadian Journal of Anaesthesia*) were retrieved with a MEDLINE search. Articles were limited to (1) publication date between January and December 2000, (2) human trial, and (3) a publication type of randomized controlled trial. Three hundred thirty-nine articles met our study search criteria. We excluded 59 papers that were studies of pharmacokinetics, cadavers, or healthy volunteers. The study articles were photocopied with all identifiers removed; the reviewers (MG and AR) were blinded to the journal and authors. We used the modified Chalmers quality assessment tool to determine a quality score for each article (3,4). Assessment included rating the appearance of control treatment, blinding of randomization process, blinding of patients and observers, sample size estimation and power analysis, compliance measures, results of randomization on pretreatment variables, major end points, post-beta estimates, confidence intervals, statistical analyses, withdrawals, and side effects discussions. Points were assigned by consensus. Scores were weighted using the following formula: points achieved/total possible points) times 100.
RESULTS: Data are presented for Journal 1, Journal 2, Journal 3, and Journal 4, respectively. The journals are listed in a blinded, random order. The mean quality scores were 47%, 38%, 46%, and 43% (Table). Among the four journals higher scores were assigned for control appearance (80%, 69%, 85%, and 73%) and discussions of side effects (74%, 61% 68%, 65%). However, scores were very low for randomization blinding (6%, 7%, 3%, and 4%), blinding observers to results (2%, 0%, 2%, 0%), post-beta estimates (12% 33%, 16%, 3%), and discussion of withdrawals (4%, 0%, 9%, 6%).
DISCUSSION: Among four major general anesthesiology journals in the year 2000, on average, none achieved even a 50% quality score for their randomized clinical trials. Our results suggest that investigators need to improve the rigor of study protocols and data analysis. Moreover, peer reviewers can advance the quality of randomized clinical trials by more critically appraising the process of randomization, power analysis and sample size estimation, and how observers are blinded to results of ongoing studies.
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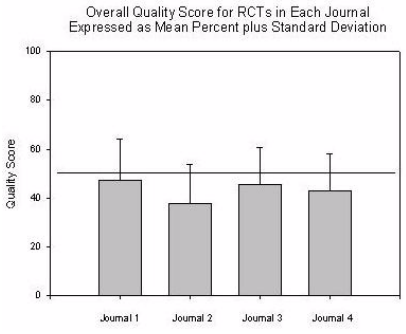

S-89

VARIABILITY OF EXCLUSION CRITERIA USED IN MUSCLE RELAXANT RANDOMIZED CONTROLLED TRIALS

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BACKGROUND: A goal of anesthesia research is to validate or refute existing knowledge or generate new information regarding drugs or techniques to improve patient outcomes. Many randomized controlled trials (RCT) may restrict their sampling population excluding certain types of subjects (1). Literature review has found variability in the exclusion criteria identified in similar RCTs (2-4). Furthermore, the exclusion criteria may not be well defined or justified. The purpose of this study was to compare exclusion criteria cited in anesthesia masters theses involving muscle relaxant RCTs conducted at our hospital.
METHODS: This retrospective study was IRB exempt and reviewed exclusion criteria of 16 masters theses which involved muscle relaxant RCTs conducted from 1987 to 2000.
RESULTS: In 16 RCTs, a total of 21 unique exclusion criteria were used. The mean (+/-SD) number of exclusion criteria used for each study was 6.0 +/-1.63 (range 4-6). The most frequently cited exclusion criteria was neuromuscular or nervous system disease (15/16,94%), followed by drug interactions (75%), ASA class (75%), pregancy (68%), liver/renal disease (56%), obesity (37%), type of intubation (37%), drug allergy (25%), age limits (19%), and length/type of surgery (6%). Ten exclusion criteria were each used in only one (6.25%) of the 16 studies. These included increased intraocular pressure, surgery time less than 90 min, age>65 years, age>75 years, drug abuse, facial surgery, hiatal hernia, premedication, protruding incisors, and tobacco use.
DISCUSSION: All but one study used the presence of neuromuscular disease or nervous system disorder as an exclusion criteria as these disorders can affect the duration of neuromuscular block which would alter results. Of the 21 listed unique exclusion criteria, 13 were cited in 25% or fewer studies and 10 were used in only one study. This reveals that there is a great amount of variability between the exclusion criteria used in similar study types. This may be explained by the fact that certain studies may have actually used some of the exclusion criteria without listing them as criteria for their study.
None of the studies reported the proportion of patients excluded from their studies, making it impossible to determine actual exclusion numbers.
Conclusions There was significant variability among the use of exclusion criteria for similar types of muscle relaxant RCTs which could lead to different study populations and ultimately produce different results. Use of standard methodology and set of exclusion criteria is necessary in similar studies to eliminate this variability.
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S-90

THE EFFECTS OF RANITIDINE, OMEPRAZOLE AND PLACEBO ON INTRA OPERATIVE GASTRO-OESOPHAGEAL REFLUX IN PATIENTS WITH SYMPTOMS OF REFLUX

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INTRODUCTION: Pulmonary aspiration is a rare but devestating complication of general anaesthesia.The mortality associated with this event has been reported as being over 60% for severe cases[1]. Due to an awareness of the problem and changes in clinical practice intended to prevent it, the incidence has decreased dramatically.One factor likely to contribute to the incidence of aspiration is the presence of Gastro-esophageal reflux disorder.Five to ten percent of the adult population suffer from GERD[2].The presence of "heartburn" and acid regurgitation is predictive of GERD and thus puts the patient at increased risk for perioperative reflux of gastric content[3].Agents which alter the volume and acidity of gastric contents may decrease the likelihood of adverse outcome associated with this condition.The aim of this study is to compare the effects of ranitidine and omeprazole on intra-operative reflux in patients symptomatic for GERD undergoing elective surgery.
METHODS: With IRB approval and informed patient consent,thirty ASA I and II adult patients describing specific symptoms of GERD and undergoing elective surgery were enrolled and then randomly allocated to recieve placebo, ranitidine or omeprazole as a premedicant. Following administration of a standard general anaesthetic, a pH probe was introduced into the esophagus, esophageal pH monitored and episodes of reflux (defined by an abrupt decrease in the pH to a value of <4) measured and recorded using a Synectics digitrapper.Statistical analysis was performed using unpaired one tail t- tests and Chi squared tests as appropriate.P< 0.05 was taken to indicate significance.
RESULTS: The groups were simliar in terms of age, weight, height and Body Mass Index.as was the symptom score between the two groups. The number of acid refluxes / hour in the placebo group was significantly greater then in the ranitidine group and just outside the level of significance when compared to omeprazole.There was no difference in the number of acid refluxes / hr. between ranitidine and and omeprazole. The "mean pH < 4" was significantly different when comparing placebo to omeprazole and just outside the level of significance comparing placebo to ranitidine. Again there was no significant difference between "mean pH <4" for omeprazole compared to ranitidine.
CONCLUSIONS: The most important finding of our study is that the preoperative administration of ranitidine and omeprazole decreases the incidence and duration of acid regurgitation in patients undergoing general anaesthetics and that there is no difference in the incidence of regurgitation in the group recieving omeprazole as a premedication compared to the group receiving ranitidine.These data support the routine preoperative administration of these agents to patients with symptoms suggestive of GERD.
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S-91

EVOLUTION OF ANESTHESIA MANAGEMENT FOR BARIATRIC SURGERY

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INTRODUCTION: Morbid obesity has become a significant public health problem in the USA. Patients do not frequently respond to diet and exercise as a means of weight loss. Surgical treatment by gastric bypass surgery is increasingly used as an alternative. We report the result of a study examining the evolution of the surgical and anesthetic approach in this patient population.
METHODS: We reviewed the charts of 32 patients undergoing gastric bypass at our institution. Group A (n=16) represents patients (BMI 49±10) who had open gastric bypass surgery in 1998 (when the program was initiated at our institution) until early 2000, while Group B (n=16) consists of patients (BMI 50±9) who had the same procedure more than one year later.
RESULTS: We noticed significant changes in the length of anesthesia time, intraoperative crystalloid administration, and a decrease in blood loss with increased experience (table1). In addition, we examined the use of intraoperative opioid use in all patients receiving general anesthesia *versus* combined general-epidural anesthesia (thoracic). Perhaps the most important observation was a significant decrease in intravenous intraoperative opioid usage, in patients receiving a combined epidural and general anesthetic.
Table1:

	GROUP A Mean± SEM	GROUP B Mean± SEM	DIFFERENCE Mean± SEM
ANESTHESIA TIME	343 min ±17.11 N=16	277 min ±11.09 N=16	66 ± 21 p= 0.0032
CRYSTALLOIDS	4.8 L ±3.87 N=16	3.5 L ±1.6 N=16	1.3 ± 4 p=0.0045
EBL	416 ml ±58 N=16	256 ml ±39 N=16	160 ± 70 p=0.029
	GENERAL ANESTHESIA	GENERAL-EPIDURAL ANESTHESIA	DIFFERENCE Mean± SEM
INTRAOPERATIVE OPIOIDS	598 µg ± 103 N=13	294 µg ± 35 N=19	304 ± 95 p= 0.0033

DISCUSSION: We conclude that with experience in this procedure, operative time, blood loss and fluid resuscitation are decreased. More important, we strongly advocate a combined general -epidural anesthesia which results in significant reduction of intraoperative opioid use and may facilitate extubation and reduce the risk of respiratory depression and sleep apnea.

S-92

THE PULMONARY CHANGES IN LAPAROSCOPIC RADICAL PROSTATECTOMY USING INTRAOPERATIVE SPIROMETRY

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INTRODUCTION: Complex procedures, such as radical prostatectomies are being done laparoscopically. There has been no data regarding the effects of this surgical procedure on a patient's pulmonary physiology. The closest data has been on patient's undergoing laparoscopic cholecystectomies.[1] Because of the unique considerations in a laparoscopic prostatectomy, we seek to determine the statistical significance of positioning and pneumoperitoneum on the pulmonary function.
METHODS: After the approval of the City of Hope National Medical Center IRB, thirty consecutive laparoscopic prostatectomy charts were retrospectively reviewed. The D-lite flow sensor (Datex-Ohmeda) was applied in all of our cases. The mean age of the patients was 65.5 years of age with an average ASA Class of III and a mean body mass index (BMI) of 27.4. After induction of general anesthesia, the ventilator was set to a tidal volume of 10 ml/kg, a rate of 8, and an I:E of 1:2.5. The peak pressure, plateau pressure, tidal volume, dynamic compliance, and airway resistance were measured in the supine position, the Trendelenburg position (35 degrees), and the Trendelenburg/ pneumoperitoneum position (intraabdominal position of 15mmHg). The differences in the pulmonary values were compared among the supine position, the Trendelenburg position and the Trendelenburg/ pneumoperitoneum position. Means were compared using paired t-test. The influence of BMI on the change in pulmonary values were assessed by Pearson correlation analysis.
RESULTS: The Trendelenburg position caused a significant increase in the peak pressure, plateau pressure, and airway resistance ($p<0.0001$); a significant decrease in the compliance and tidal volume ($p<0.002$) compared to supine position. The initiation of the pneumoperitoneum significantly exacerbated the change in all of the pulmonary variables ($p0.38$, $p<0.04$ for all pairwise differences). Reduction of tidal volume did not correlate with BMI.

Mean (SD) of the pulmonary values at three different statuses

Variable	Supine	Trendelenburg	Trendelenburg/ Pneumopitoneum
Peak Pressure (mmHg)	20.6(4.2)	24.4(4.7)	33.8(5.8)
Plateau Pressure (mmHg)	17.2(4.2)	20.8(5.2)	32.1(5.9)
Tidal Volume (ml)	942.7(129.9)	866.3(124.7)	773.0(129.4)
Compliance (cm H2O)	68.8(14.1)	49.7(11.9)	26.2(5.8)
Resistance (cm H20/1/s)	12.2(2.8)	15.2(5.0)	19.2(9.0)

DISCUSSION: The steep Trendelenburg position and the pneumoperitoneum produce significant decreases in dynamic pulmonary compliance and tidal volume while increasing both peak and plateau pressure and airway resistance. BMI appears to have a role on the changes in pressures and resistance. Though we have not seen a change in morbidity or mortality, this procedure places compromised patients at an increase anesthetic risk, especially for obese patients.
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S-93

POSTOPERATIVE COGNITIVE DYSFUNCTION (POCD) AND DELIRIUM IN A SHORT TIME SURVEY

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INTRODUCTION: **P**ostoperative cognitive dysfunction POCD is recognized occurring after general anaesthesia and mostly in elderly patients [1]. Usually it is a benign and transient condition but long-term effects could arise [2]. Delirium could present as a postoperative cognitive impairment, especially in elderly patients, and it is associated with a substantial morbidity and mortality rate ranging 20-50% [3]. Delirium is characterized by acute and fluctuating impairment of cognition i.e. altered consciousness and attention as memory, language, perception and thinking, associated commonly to agitated behaviour, disturbed psychomotor activity and sleep-wake cycle [4]. Delirium often occurs in hospitalized patients (10-20%), particularly in postsurgical (10-15%) and in ICU (30%) admitted patients [4,5,6].Within a broader project of research on aging process and vulnerability of the old patient, the aim of the present study was to evaluate during a short period of observation of 60 postsurgical hours the incidence rate of postoperative cognitive dysfunction (POCD) and of Delirium, and to assess possible risk factors in a surgical adult population.
METHODS: Retrospective study on 2547 (1231 M, 1316 F) ASA I-III of 6600 consecutive patients undergoing abdominal, vascular, urologic and trauma surgery in general anaesthesia with no dementia or psychosis history. Each patient was evaluated every 6 hours with a specific registration form. The model analysed four parameters to recognize every impairment of cognition (confusion, disturbed psychomotor activity, altered mood, sedation), every alteration of sleep-wake cycle and well-being factors as pain relief (good pain control). All these parameters were clinically assessed by a physician. Statistical analysis was performed using Chi-Squared test.
RESULTS: A total of 286 pts (48.5 F; 51.5 M; median age 58 yrs old) had at least a single episode of POCD. Delirium presented in 46 pts (1.8%) no sex differences; 8 pts received general anaesthesia for more than 3 hrs and 35 underwent inhalational anaesthesia (P< 0.002); 83.2% were premedicated and 62.2% used to be antagonized for muscle relaxants. Differences were significative at awakeness for length group (P< 0.001) and at 36-48 hrs interval for age group (P= 0.006). No complications were reported.
DISCUSSION: Postoperative cognitive dysfunction occurred at awakeness from general anaesthesia with an incidence higher in at risk group patients (surgery length 180 minutes). Delirium seems to appear later and related to age factors. General anaesthesia seems to predispose to develop POCD and Delirium. Postoperative cognitive deficit is frequent, it is usually benign and transient, but a clear definition and a time limit diagnosis has not yet been defined.
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S-94

THE EFFECT OF THE ADDITIONAL (PGY-4) YEAR ON SUBSPECIALTY EDUCATION: A TEN YEAR REVIEW

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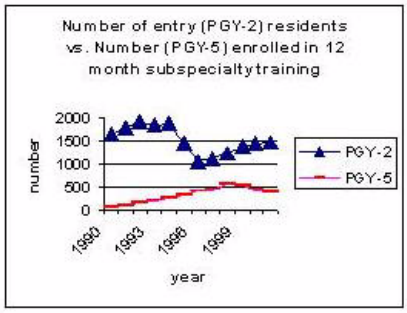
The purpose of this study is to determine the long-term effect of requiring an additional year of anesthesia residency (PGY-4) instituted in 1989 by the American Board of Anesthesiology (ABA) on the number of individuals who pursued twelve-month subspecialty anesthesia training. We tested the hypothesis that extending education by a year would decrease the number of trainees.
METHODS: Surveys were collected from approved Anesthesia Residency Training programs in the United States from 1989-2001. The questionnaires were designed to determine the number of individuals pursuing subspecialty training during the PGY-4 and PGY-5 years. The time periods were divided into three categories: 6 months, 6 to 12 months, and 12 months of subspecialty training. The subspecialties are cardiac anesthesia, pediatric anesthesia, pain management, obstetrical anesthesia, outpatient anesthesia, intensive care medicine, and research. We report only twelve-month data.
RESULTS: The number of anesthesia residents (PGY-5) pursuing 12 month subspecialty training has increased over the last decade despite a noted decrease in residents (PGY-2). (See graph). However, the specific subspecialty distribution of fellows has changed. Pain Management increased the most from 11% during 1989-90 to 45% in 2001. The greatest decline in the number of fellows has occurred in Critical Care medicine. In addition, the number of individuals pursuing specialty training during the PGY-4 year has declined



.**DISCUSSION:** In 1988-89, the ABA required a PGY-4 year for entry into the examination and certification process. Prior to this time, the PGY-4 year was an elective year in which individuals could pursue subspecialty training. At the time this policy was instituted, there was concern this mandate would result in a decrease in the number of anesthesia subspecialists[1]. Our data illustrates an increase in the number of individuals pursuing twelve month subspecialty training. The increase of residents in fellowship training occurred at a time when the total number of anesthesia residents in training decreased. Our data also indicates major changes in the subspecialty pursued during the last decade. Pain management comprises nearly one half of all individuals pursuing 12 month subspecialty training during the PGY-4 and PGY-5 years. We conclude that factors other than the duration of training influence the selection of subspecialty education.
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S-95

A SIMPLE METHOD FOR ASSESSING KNOWLEDGE GROWTH DURING SUBSPECIALTY ANESTHESIA TRAINING

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INTRODUCTION: Residency training often lacks objective evaluation of learning within the educational program. Accurate outcome measurements are needed so that changes to the educational process can be evaluated and followed over time. Furthermore, the ACGME has recently introduced a requirement for an objective assessment of learning during anesthesia subspecialty rotations without specifying how that should occur (1). Our objective was to demonstrate an outcome assessment tool using written pre- and post-rotation examinations to judge the acquisition of knowledge by anesthesia residents during a neuroanesthesia rotation.

METHODS: Questions were chosen specifically based on the published objectives of the rotation and were written by our neuroanesthesia faculty or obtained from outside sources. Questions were often rewritten extensively to clarify, update, or target the questions to specific areas and were paired, e.g., a question on brain death on the pretest would be matched to a question of similar complexity regarding brain death on the posttest. Questions were administered on a web-based testing system (UM Lessons©). Test integrity was assured by allowing only defined residents access to the tests and verifying their identities using high-level (Kerberos) passwords. Residents took the tests within a few days of beginning or ending their neuroanesthesia rotation. Residents also completed subjective questionnaires evaluating the experiences.

RESULTS: Pretest and posttest scores for each resident as a function of the month of their Neuroanesthesia rotation (Academic Year 2001-2002) are shown in the figure. Mean pretest score was 48% and mean posttest score was 71% for the group. The mean difference in pretest and posttest scores was significantly different (Student's T-test, T-statistic = 12.44, df 20, $p<0.0001$). There was a statistically significant increase in pre-rotation neuroanesthesia knowledge as the academic year progressed (F Statistic = 7.25, df = 19, $p = 0.014$) but this effect was minor compared to the neuroanesthesia learning that occurred during each rotation. Residents felt more positively about the testing after the rotation: 67% (pretest) vs 88% (posttest) felt that the tests would help their Anesthesiology In-training Examination scores. 94% of the residents felt they tested better after the rotation. Most residents liked testing online (78% pre, 88% post).

DISCUSSION: We have presented an evaluation of a simple tool for assessing the acquisition of factual knowledge during an anesthesia subspecialty rotation. This tool will allow us to modify subspecialty teaching to investigate the effects of altered educational techniques on the learning of didactic knowledge within these rotations. Most of the anesthesia residents using this tool felt that the testing was a useful experience.

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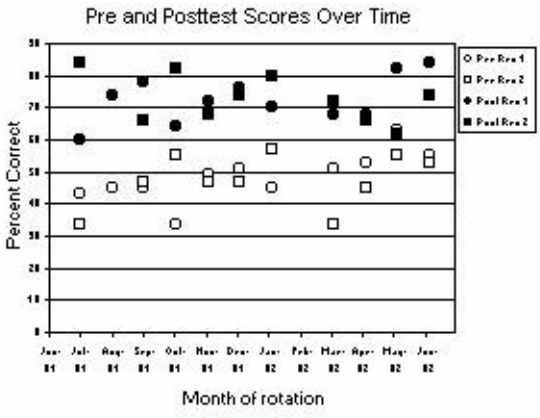

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THE LEARNING STYLES OF ANESTHESIOLOGISTS

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INTRODUCTION: Do anesthesiologists, as a group, have a learning style profile? Learning styles and strategies are the strengths and preferences that form our educational experience. Numerous investigators including Myers-Briggs, Koch, Strenberg and Felder have examined these characteristics. Myers and Briggs observed that their indicators often correlated with academic and professional pursuits. In this study, the learning styles and strategies of anesthesiologists were assessed to determine if any trends exist in our medical specialty.

Method: At the 2002 Spring Meeting of the Society for Education in Anesthesia, attendees were surveyed using the Index of Learning Style Questionnaire[1]. The questionnaire, initially designed to assess engineering students, consists of forty-four questions and scores the respondent in four dichotomous areas: Active vs. Reflective, Sensory vs. Intuitive, Visual vs. Verbal, and Sequential vs. Global. Individual scores range along a continuum (0 to 11) for each area. A score of 4-7 signifies an essentially balanced condition, 2-3 and 8-9 reflects a moderate preference towards one pole, 0-1 and 10-11 reflects a strong preference towards one pole. The results were assessed using descriptive statistics and chi square analysis.

RESULTS: Of the 139 registered attendees, 59 (42.4%) returned the questionnaire. Three questionnaires were incomplete and were not included in the group data. A review of the scores showed a strong polarization towards Reflective and Visual learning styles and a more balanced result in the Sensory-Intuitive and Sequential-Global areas. Table 1 contains the group's results presented as percentages and compared with the results of other studies.

Table 1. SEA Learning Style Group Results

Group (n)	Responder Type	Active	Reflect	Sensory	Intuit.	Visual	Verbal	Sequen.	Global
SEA (56)	Anesthesia Educators	41%	59%[a]	64%	36%	79%	21%	48%	52%[b]
UMI[2] (858)	Engineering Students	67%	33%	57%	43%	69%	31%	71%	29%
UMD[3] (369)	Adult Ed. Tech mangs.	50%	50%	60%	40%	73%	27%	51%	49%

[a] - SEA vs. UMI: $p < 0.0001$ [b] - SEA vs. UMI: $p = 0.0003$

DISCUSSION: The anesthesiologist's percentages are similar to those obtained at University of Michigan, School of Engineering, for Sensory vs. Intuitive and Visual vs. Verbal. This is consistent with previous studies of math-science students.[4] In contrast to the engineering students, our results show a significant greater percentage scored as "Reflective" learners and an split evenly in the Sequential - Global category. Reflective learners prefer individualized learning environments. This is consistent with the anesthesiology experience and its focus on one-on-one patient care and teaching, as opposed to clinics and serial group rounds. The more balanced picture in the last category may be the norm, with high Sequence scores being particular to engineers.

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S-97

SURVEY OF PERSONAL DIGITAL ASSISTANT USE IN ANESTHESIOLOGY RESIDENCY PROGRAMS IN THE UNITED STATES

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INTRODUCTION: In recent years, medical information has rapidly expanded and technology has advanced to allow portable electronic devices to contain vast stores of information. Medical personnel are now beginning to take advantage of this capacity to optimize patient care and facilitate administrative functions. At the current time, the pervasiveness of personal digital assistants (PDAs) in academic anesthesia is not known, and information about useful software programs is communicated by "word of mouth.' This study aims to systematically collect information on the use of PDAs in academic anesthesia settings. The purpose of collecting this information is the following: 1) to determine how widespread the use of PDAs is in academic anesthesia, 2) to determine which operating system platform is preferred, 3) to determine which medical and administrative functionalities have been facilitated by the use of PDAs.
METHODS: After Institutional Review Board approval, participation in the study was solicited via email messages sent to representatives from each of the 132 Anesthesiology residency programs in the US. Participants completed an email or online survey about PDA use within anesthesiology residency programs and departments, including types of hardware and software required or commonly utilized. Participation was voluntary. Respondents included residents, fellows, faculty, and program coordinators. Survey data were aggregated and analyzed.
RESULTS: 73 responses from 37 residency programs were obtained. 90% (n=66) reported using a personal digital assistant, with 80% (n=53) of these using a Palm OS device, 14% (n=9) using a Pocket PC device, and 6% (n=4) using both types. 32% (n=12) of programs were reported to require use of a PDA by residents. The average percentage of residents reported as using a PDA was 72%. The average percentage of faculty reported as using a PDA was 41%. Of those that use a PDA, the most common use reported was for drug reference (71%, n=47), followed by case log software (62%, n=41), medical calculations (39%, n=26), departmental directory (29%, n=19), general medical reference (29%, n=19), anesthesiology reference (21%, n=14), scheduling (9%, n=6), and quality improvement (2%, n=1). Development of proprietary software was limited and was reported primarily for case log (16% of programs, n=6) and scheduling (13% of programs, n=5).
DISCUSSION: Though penetration of PDAs as a required tool for academic anesthesiologists is low, 90% of respondents reported voluntarily using such a device. The results suggest that PDAs are useful in the academic anesthesiology setting, especially as a drug reference tool and for case log purposes. Thus far, few departments have developed proprietary software, but this may be expected to grow in the future as the full potential of personal digital assistants is realized.

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***BEING BUMPABLE*: CONSEQUENCES OFRESOURCE SATURATION AND NEAR-SATURATION FOR COGNITIVE DEMANDS ON ICU PRACTITIONERS**

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We report a set of projects that characterize technical work in the setting of resource saturation and near saturation (e.g. 100% bed occupancy or a full operating room schedule). Cost and resource limitations drive ICUs and OR utilization towards saturation.
Near-saturation conditions place a premium on practitioner cognition, especially on the ability to anticipate and prepare to cope with shifting clinical demands using available resources.[1] The conditions are regarded as normal and practitioners become adept at coping with them. One coping strategy, *bumping*, is remarkable because it is ubiquitous and reflects the contingent and conflicted nature of technical work.[2]
In bumping, a new, high priority demand is accommodated by diverting resources already in use. In the setting of an ICU, bumping involves moving one patient out of the ICU in order to allow another one in. In the operating room, bumping occurs when a scheduled case is held so that another, more urgent case can go forward. The need for bumping arises, from the indivisible nature of resources (patients, beds, and rooms are quanta that cannot be further divided); from the irreducible uncertainty that pervades healthcare settings; and from the high consequence and time pressure that characterize acute care settings.
The results from our operating room and the intensive care unit studies suggest that bumping reflects normal functioning. It is a means for meeting near-saturation resource demand. Although each location has formal mechanisms for bumping, these are used to justify rather than guide practitioner decisions. The requirement for practitioners to meet the needs of patients plays out as a complicated naturalistic decision making activity [3] during which practitioners assess conditions, identify and acknowledge conflicts, forecast future developments and events, make hedges against uncertainty, and tradeoff goals in order to fashion solutions that can withstand both operational pressure and the threat of future *ex post facto* evaluations by outsiders. Bumping is neither purely medical nor purely managerial but rather reflects the synthesis of clinical factors and operational requirements. Successful bumping reflects refined practitioner skill and requires substantial effort in assessment, planning, and coordination (often across service and professional boundaries). Unsuccessful bumping creates discontinuity of care. [4] This research describes bumping and the associated cognitive activities and their impact on patient safety.
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S-99

THE EFFECT OF READING ON THE VIGILANCE, CLINICAL WORKLOAD, AND TASK DISTRIBUTION OF ANESTHESIA PROVIDERS

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INTRODUCTION: During routine cases, anesthesia providers may read materials that are directly related (e.g., medical records) or unrelated to patient care. While some feel this is poor patient care, others have argued that reading may obviate boredom that could otherwise decrease vigilance. To study this issue, behavioral task analysis and workload assessment were conducted to measure the effects of reading on vigilance, workload, and task distribution.
METHODS: After IRB approval and informed consent, 172 general routine surgical cases involving general anesthesia were studied. A trained observer sat in the OR and categorized the clinician's activities into 37 possible tasks [1]. Only data from maintenance, the phase in which all reading occurred, was included in the analysis. The spare capacity of the anesthesia provider was measured by the time it took for them to respond to a random "vigilance light". At 7-15 min. random intervals, psychological workload was measured using a Borg Workload (6 to 20) scale [2], first by the observer and then by the subject. The workload density was calculated by multiplying the duration of each task actually performed during the maintenance phase of the case by that task's workload factor score.[3] Task data were analyzed using two-way mixed ANOVA while workload was analyzed using Mann-Whitney U test and vigilance using one-way ANOVA.
RESULTS: In 60 of the 172 cases (35%), some intraoperative reading occurred. In these 60 cases, anesthesia providers read 25±3% of the maintenance period. When reading, the clinicians spent 44±3% of the time reading while time-sharing with other tasks. The observer-rated workload, subject-reported workload and workload density values were significantly *lower* during reading (R) than non-reading (NR) periods (Table). There was no significant difference in vigilance between the two groups. The distribution of non-reading tasks differed significantly between R and NR periods in the same case. During NR periods, the anesthesia providers spent significantly more time on record keeping (NR 15.7±1.0% vs. R 5.1±0.9%; p<0.001) and on "Other Care Tasks" (i.e., patient care-related manual tasks that did not fall into more specific categories) (NR 10.8±1.0% vs. R 2.9±0.5%; p<0.001). During R periods, subjects spent significantly less time performing manual (R 7.2±1.3% vs. NR 19.7±0.9%; p<0.001) and conversational tasks (R 9.7±2.0% vs. NR 16.8±1.6%; p<0.05).
DISCUSSION: These results demonstrated that subjects read selectively during low workload periods and when they did read, their vigilance was not significantly impaired. This preliminary study suggests that reading may have limited effects on vigilance and therefore may not *a priori* put patient's safety at risk. *(Supported by AHRQ & VA HSRD).*
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Table 1. Workload Ratings and Vigilance - Maintenance

Task	Reading	Non-Reading
Observer Workload*	7.6 ± 0.1 (7-11)	8.6 ± 0.1 (7-14)
Subject's Workload*	7.9 ± 0.1 (7-12)	8.9 ± 0.1 (7-15)
Workload Density*	0.7 ± 0.04 (0.0-1.9)	1.2 ± 0.02 (0.8-1.4)
Vigilance Latency	27.9 ± 3.3 (1-207)	29.4 ± 2.3 (1-506)

Data are presented as mean ± SEM (Min-Max).
* = p<0.001, Reading vs. Non-Reading

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INFORMATION OVERLOAD: DO ANESTHESIOLOGISTS EXCEED PATIENTS' CAPACITY TO LEARN?

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INTRODUCTION: Patient education is a critical part of preparation for surgery. Communication research pertaining to provider-to-patient teaching, though consistently showing deficits, has not been conducted with a systematic focus on the limits of human learning and memory. Our goal was to quantify the information load given by healthcare providers (HPs) to patients in a clinical setting, the Pre-admissions Testing Area (PATA) at Massachusetts General Hospital. Pre-anesthetic consultations in the MGH-PATA are conducted by both nurse practitioners (NP) and physicians. We predicted that there would be a difference in the information load presented by NPs and physicians.
Method: We compared quantitative and qualitative aspects of NPs' and physicians' communicative content through the analysis of transcribed audiotapes of 26 pre-anesthetic consultations. The transcripts were analyzed according to a novel coding system developed to examine the HP's communication patterns with the following categories: quantity of information, frequency of explained and unexplained medical terms, the number of patient questions, and the number of reinforcements during the consultation. Two raters independently coded 100% of the transcripts.
RESULTS: Comparisons of the physician and NP's communicative content with an independent samples t-test indicated that NPs gave more pieces of information (M = 111.86, SD = 37.16) than physicians (M = 48.50, SD = 24. 59), t(24) = -5.03, p < .0001. The number of patient questions did not influence the amount of information given, t(24) = -.47, p = .64. No significant differences between NPs and physicians were found in the remaining categories (frequency of reinforcements, medical terms). Additionally, no significant differences were detected among any of the provider-patient gender combinations.
DISCUSSION: We observed an extreme tendency toward information overload by healthcare-providers, as well as a failure to utilize memory-enhancing techniques. Traditionally, greater information-giving has been favorably viewed in studies of the provider-patient relationship. When patients are presented with a large quantity of material about the anesthetic and operative processes, the question arises of how crucial is it to learn and recall such extensive, specific information? At baseline, an average individual can recall approximately seven chunks of new information (Miller, 1956). Even considering the memory enhancing factors built into the context, such as personal relevance and scripted sequencing, how can an individual possibly be expected to encode 50 to more than 100 medical descriptions and instructions, or to filter and recall the most relevant ones? Our application of basic behavioral science elements to the field of HP-to-patient teaching suggests that reducing information overload should be a goal when conducting the pre-anesthetic consultation. A structured educational content, reinforced by concise written material could bring the necessary information load within the limits of patient's ability to learn.
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S-101

WRONG SIDED ANESTHETIC AND SURGICAL PROCEDURES: ARE THEY PREVENTABLE?

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INTRODUCTION: Performing a wrong-sided procedure is a tragic event for the patient and the surgical team. However, bilateral symmetry of organs creates the potential for wrong- sided anesthesia and surgery, especially for percutaneous blind procedures such as nerve blocks. Research has documented the prevalence of wrong-sided surgeries but investigation of wrong-sided anesthesia is lacking. To prevent adverse events we must first understand how and where the systems and predictable cognitive failures occurred. This requires a comprehensive understanding of the environments and behavioral circumstances surrounding adverse events, the epidemiology of such events, and the development of systemic, environmental and behavioral mechanisms to prevent the recurrence. From 1995-2002 the JCAHO identified 197 wrong-site procedures accounting for 11.3% of reported adverse events,[1] and the Physician's Insurance Association of America includes 1000 closed claims involving wrong-sided procedures.[2] Database analayses identified as risk factors: multiple procedures and surgeons during one operating room trip, unusual anatomy, and time constraints.[2] Estimates suggest that voluntary reporting underestimates the incidence of wrong-sided events by a factor of 20 or more.[2]
METHODS: Descriptive epidemiologic series of seven cases from hospitals in Denmark, United States, and Australia comparing wrong-sided procedures according to factors associated with the event.
RESULTS: Preliminary results (see table 1) suggest that the risk factors for performing a wrong-sided procedure include: ambulatory surgery setting (n=5); older age (n=6); female gender (n=5); left-sided procedure (n=6); regional anesthesia (n=6); and morning surgery during high clinic workload (n=6). The involvement of multiple team members including residents, attendings and nurses (n=7) did not prevent laterality errors, nor did existing "paper-checks" such as peri-operative checklists (n=3); laterality specified on consent form (n=6), or institutional laterality policy (n=5). Patient harm occurred in all cases, and ranged from inconvenience to respiratory arrest, yet an incident report was filed in three cases, and full patient disclosure occurred in only four cases.

						Risk factors for laterality errors						
ID	Age	Sex	Laterality Error	Inpatient/ Outpatient	Workload	Use of checklists	Consent form indicates laterality	Patient Educ. Level	Incident report filed	Review of laterality error	Patient Harm	Full disclosure of laterality error
1	65	M	Right femoral nerve block instead of left	Outpatient	High	Yes	No	MD	No	Yes. Root cause analysis	24 hr. hospital stay	Yes
2	68	F	Right scalene block instead of left	Outpatient	High	Yes	Yes	High school	Yes	Yes. Root cause analysis	Increased hospital stay	Yes
3	61	F	Right axillary block instead of left	Outpatient	High	Yes	Yes	N/A	No	Yes. Root cause analysis	No	Yes
4	25	M	Right leg 3-1 block instead of left	Outpatient	High	N/A	Yes	N/A	No	Yes. Root cause analysis	No	Yes. Mother informed
5	70	F	Left Carotid/neck blocked instead of right	Inpatient	Normal	No	Yes	< High School	Yes	N/A	Resp. arrest and use of ventilator	No. Internist told pt, surgical team did not.
6	50s	F	Right lower quadrant incision instead of left	Inpatient	High	No	Yes	High school	Yes	N/A	Yes. Unnecessary incision.	No
7	81	F	Right breast localization needle inserted instead of left breast	Outpatient	High	N/A	Yes, but maybe incorrect	N/A	No	Yes. Root cause analysis	Yes. Unnecessary right breast needle insertion	Unknown, but pt concious throughout procedures.

DISCUSSION: While only seven cases are presented, the lack of other studies on the risk factors and epidemiology of wrong-side procedures make these cases significant. Trends worthy of further investigation include the apparent ineffectiveness of "paper" based protections against laterality errors. In addition, the preponderance of older aged patients, regional anesthesia, and outpatient, high-workload environments, all warrant further study. These data demonstrate that latent errors lie dormant and are realized when conditions become rifht for thier expression. Educational and preventive strategies that focus on cognitive and systems issue may have great potential in enhancing the safety of anesthetic care. Systems practices to successfully reduce wrong-sided procedures will likely combine a standard method of sidedness marking supported by a collaborative team and systems effort.
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FACTORS CONTRIBUTING TO HUMAN ERRORS BY ANESTHESIA PROVIDERS

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INTRODUCTION: Approximately 10 % of adverse perioperative outcomes are due to human errors by anesthesia providers(1). The authors investigate the effects of anesthesia provider training and concurrent patient disease on human error rates.
METHODS: Adverse perioperative outcomes at two university- based hospitals between Jan 1st 1998 and July 31st 2002 underwent a previously described peer review process to determine the human error contribution(1).All anesthetics involved direct patient care and / or supervision by an attending anesthesiologist. Human error rates, stratified by anesthesia provider training and ASA physical status (ASA PS), were examined using contingency tables and statistical significance was determined using Pearson chi square test.
RESULTS: Human errors by anesthesia providers increases logarithmically with increasing ASA PS. CAY 1 anesthesia providers have higher human error rates than other anesthesia providers at all levels of ASA PS.

ASA1	CAY	NON ERRORS	SYSTEM ERRORS	SYSTEM ERROR INCIDENCE%	HUMAN ERRORS	HUMAN ERRORS INCIDENCE%
	1	8319	77	0.916	6	0.071 *
	2	10506	63	0.596	1	0.009
	3	6811	62	0.901	2	0.029
	ATT	27056	174	0.639	3	0.011
ASA 2	1	7189	175	2.372	14	0.189 *
	2	15172	131	0.856	7	0.045
	3	14432	132	0.906	5	0.034
	ATT	53789	559	1.028	20	0.036
ASA 3	1	7645	191	2.431	20	0.254 *
	2	7381	126	1.676	10	0.133
	3	7288	129	1.737	9	0.121
	ATT	27920	524	1.840	24	0.084
ASA 4	1	637	39	5.718	6	0.879 *
	2	2131	68	3.088	3	0.136
	3	2621	68	2.526	3	0.111
	ATT	5708	231	3.882	11	0.184
ASA 5	1	33	14	29.166	1	2.083 *
	2	87	19	17.924	0	0.000
	3	139	15	9.740	0	0.000
	ATT	282	57	16.666	1	0.294

DISCUSSION: Level of training and ASA PS affect human error rates of anesthesia providers, despite supervision by attending anesthesiologists.
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S-103

EVALUATION OF HOUSESTAFF AND MEDICAL STUDENT ATTITUDES TOWARDS ADVERSE MEDICAL EVENTS

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INTRODUCTION: There has been a renewed interest in reducing medical errors and improving patient safety[i]. One mission of academic hospitals is to reach exceptional levels of patient care education for medical students and housestaff. There has been little previous research on housestaff and medical errors[ii]. This study examines the process by which physicians-in-training (PITs-medical students and housestaff) respond to adverse events in patient care and incorporate lessons into their practice at a city teaching hospital.
METHODS: We recruited 700 PITs to complete an anonymous electronic questionnaire on a secure website. Questions assessed knowledge of methods to improve patient safety, beliefs in their ability to reduce medical errors, and their experiences with adverse events. Questions were categorized using an affinity sort into five scales: *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. Multivariate regression analyses were performed to examine the influences of independent variables such as department, level and length of post-graduate training, and previous adverse event exposure on the PSS. Pairwise Pearson correlation coefficients were obtained for the scales. Two sample t test was conducted to compare those exposed to adverse events with their counterparts.
RESULTS: Preliminary analysis of this ongoing survey of respondents to date (response rate of 4.7% (n=33)) demonstrates that 45.5% had been exposed to an adverse event (n=15) and 21.2% (n=7) had attended a Adverse Event meeting. Mean PSS score was 303 (SD=52). Demographic data or training program did not influence PSS score. The self-efficacy scales were positively correlated with knowledge (r=0.41, p=0.017), safety culture (r=0.56, p<0.001), barriers (r=0.73, p<0.001), and the safety culture and barriers scales (r=0.52, p=0.002). Those exposed to adverse events reported a lower overall awareness of safety culture (p=0.039).

Internal Consistency Reliability Coefficients, Means, and SDs

Scale	No. of Items	Cronbach's alpha	Mean (SD)
Knowledge	7	0.73	66 (14.3)
Self-Efficacy	5	0.80	66 (21.3)
Safety Culture	10	0.82	78 (15.5)
Barriers/Facilitators	6	0.75	47 (18.2)
Human Factors	6	0.57	49 (8.1)

DISCUSSION: Preliminary results suggest that the exposure of PITs to medical errors affects their attitudes and behavior toward patients. Exposure of respondents to events may decrease error reporting and willingness to adopt safety practices. 25% of respondents were unaware of error reporting systems. The low means on human factors and safety barriers scales suggest the need for a formal safety curriculum. PITs with confidence in their ability to improve patient safety may have a more accurate view of the barriers and facilitators to error reduction and display more patient safety-promoting behaviors than PITs with less confidence. The learning experience of housestaff exposed to errors has not been positive and the lessons have not been incorporated formally into their training. A patient safety curriculum that helps PITs learn from adverse events is needed.
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ROLE OF ANESTHETIC CARE IN UNEXPECTED PERIOPERATIVE DEATHS IN VETERANS AFFAIRS HOSPITALS

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INTRODUCTION: Death within 24 hours of elective surgery is an uncommon event for ASA Class 1-3 patients. We hypothesized that anesthesia-related problems would constitute a significant proportion of such deaths. The National VA Surgical Quality Improvement Program (NSQIP) is a prospective, multicenter, observational study of risk-adjusted surgical outcomes in 123 hospitals. Our goal was to use this database to ascertain whether identifiable patterns of operative deaths emerge that could improve anesthetic care.
METHODS: Elective operations performed on ASA 1-3 patients under general, spinal, and epidural anesthesia from 1995-99 were eligible for inclusion. There were 147 deaths within 24 hours of surgery. Fifty-two charts for ASA 2 and 3 patients were obtained and reviewed by two anesthesiologists experienced in quality assurance reviews. The role of the anesthetic care in the death was judged as follows: strongly contributory, possibly contributory, non-contributory, or impossible to judge.
RESULTS: ASA physical classification was a strong predictor of the risk of death within 24 hours of surgery. There were no ASA 1 patients among the 147 deaths recorded in the 5-year period studied.

ASA Classification	Number of cases	Number of deaths	Frequency (%)
1	23,333	0	0%
2	165,955	12	0.007%
3	240,448	135	0.056%

Of the 52 charts reviewed, anesthetic care was possibly contributory in 18 deaths. Anesthetic care was strongly contributory in 8 deaths, and all were ASA 3. ASA 3 patients were seven times more likely than ASA class 2 patients to die within 24 hours of elective surgery (p<0.01, chi-square). It is notable that in 5 of these 8 patients (62.5%), the adverse event occurred during patient transfer from the operating room.
DISCUSSION: ASA classification remains important in determining the relative risk of elective surgery. This study found that deaths in the intra-operative and immediate post-operative period have a relatively small likelihood of being related to anesthesia care. There were no intraoperative deaths attributable to unexplained hypoxemia, hypotension, or arrhythmia. This contrasts with older data from the American Society of Anesthesiologists Closed Claims Project. Of interest is the number of adverse events that occurred during the transfer of the patient in the immediate postoperative period. The end of the case may be a critical period for improvement in the quality of anesthetic care during major surgical procedures. Supported by a grant from the VA Epidemiology Research Information Center.

S-105

THE GAS USAGE MONITOR OF THE DATEX-OHMEDA S/5 ADU DIGITAL ANESTHESIA MACHINE FACILITATES TEACHING OF CLOSED CIRCUIT ANESTHESIA

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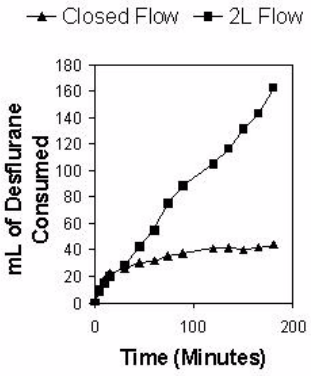
INTRODUCTION: The Datex-Ohmeda S/5™ Anesthesia Delivery Unit is a newly available digital anesthesia machine capable of real-time measurement in 5-milliliter increments of liquid volatile agent consumed. We propose this machine is well suited to use as an educational tool for teaching the concept of closed circuit anesthesia. The benefits of closed circuit anesthesia are well described in several review articles (1) (2). However, 90% of anesthesia practitioners use fresh gas flow rates between 2 to 5 L/min (1). Combining these high flow rates with volatile agents such as desflurane may needlessly increase costs. Therefore, based on the new ACGME core competency of systems-based practice, residency programs should increase efforts to teach the technique of closed circuit anesthesia.
METHODS: After IRB approval, a team consisting of experienced and inexperienced closed circuit anesthesia providers completed ten anesthetics. All patients received a general endotracheal tube anesthetic with IV induction of the practitioner's choice and then maintenance with desflurane. The initial wash-in phase employed high gas flows of 6 L/min until the end-tidal desflurane concentration reached the practitioner's choice of 0.8 to 1.3 MAC. The remainder of the anesthetic was maintained at 0.8 to 1.3 MAC with either a 2 L/min (medium flow) or a 0.25 L/min (closed circuit) fresh gas flow of O_2. The data was monitored by the practitioner using the ADU's gas usage monitor at 5, 10, 15 minutes and for 15 minute intervals thereafter.
RESULTS: All practitioners easily collected the data on the first attempt and reported similar results. The data were averaged to produce the graph. The average ml of desflurane used in the first thirty minutes for both techniques was similar. When compared to the closed circuit, the medium flow technique used 72% more desflurane by the 60-minute mark and 180% more by the 120-minute mark.



DISCUSSION: The volatile agent usage feature of the Datex-Ohmeda S/5™ ADU offers a new and easy to use educational tool for teaching closed circuit anesthesia concepts. The integrated gas analyzers and digital fresh gas flow settings allowed all five practitioners to participate in this study on their first attempt. The experienced anesthesia providers found the real-time gas usage data invaluable in teaching the inexperienced providers closed circuit anesthesia. The gas usage monitor allowed for direct comparison of the two anesthetic techniques, and all practitioners revealed that the amount of volatile agent saved with a closed circuit was much greater then they would have predicted. Because of the learning experience provided by this study, the inexperienced practitioners are now using closed circuit anesthesia with selected patients.
REFERENCES:
1). Canadian Journal of Anaesthesia, 44:6, pp.643-53, 1997.
2). Anaesthesia, 50, pp.37-44,1995.

S-106

CODING PERMUTATIONS MAY BE REDUCED PRIOR TO MODELING OF DUAL PROCEDURE SURGERIES

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INTRODUCTION: Better time estimates are important to improve surgical scheduling and reduce operational costs. Multiple procedure surgeries are difficult to model because experience with them is sparse and because coding permutations (order dependent combinations of similar CPT codes) exist that further reduce the case numbers available to model. To determine if permutations should be modeled separately or reduced, we tested if coding permutations represent statistically different surgeries with respect to total surgical time (TT).
METHODS: With institutional approval, we studied 10,740 dual procedure surgeries each with 2 different component CPT codes performed at a large teaching hospital (1). Each dual procedure surgery (CPT1-2) was provider designated by combinations of 2 procedures (CPT1-2). Permutations were observed in which the order of the same 2 component codes was reversed (i.e. CPT1-2 coexisted with similar surgeries CPT2-1). To explore differences in TT, we reordered provider assigned codes (CPT1-2) arbitrarily to eliminate permutations. The new order of CPTs (CPTA-B) was determined by ordering the CPT with the greatest numeric value of the CPT as CPTA and that with the lessor numeric value as CPTB. Because the numeric values for CPT codes are assigned on anatomic and pathologic grounds, we considered the values of the codes are arbitrary with respect to TT. Permutations were identified by comparison of the provider ordered and numeric value ordered codes. To investigate systematic differences among permutations with respect to TT, we fit an aggregate linear model of the form:
lnTT = CPTAB + Anes + Perm + Error
where lnTT = natural log of TT (2), Perm = 0 if CPTA > CPT1 and Perm = 1 if CPTA < CPT1 numerically, and Anes = categorical variable for type of anesthesia. Only 336 CPTA-B combinations had coding permutations.
RESULTS: Independent factors CPTAB and Anes explained 89% of the variability in lnTT. The interaction CPTAB * Anes was not tested because many surgeries were associated with a single type of anesthesia, i.e. general. All other first order interactions were not significant. Permutations of dual procedure surgeries did not differ with respect to lnTT.
CONCLUSIONS: Permutations do not appear to represent statistically distinct procedures (in any systematic way) with respect to TT. This result implies that sample sizes may be increased and scheduling estimates improved if coding permutations are reduced prior to modeling of dual procedure surgeries.
REFERENCES:
1. Bashein et al: Anesthesia Analgesia 1985; 64:425-431.
2. Strum et al: Anesthesiology 2000; 92:1160-67.

ANOVA Table (r2 = 89%, n = 1,862 surgeries, 336 CPTAB combinations)

Factor	Sum Squares	DF	MSE	F-Ratio	P value
CPT-AB	443.671	59	7.520	112.242	0.0000
Anes	17.657	3	5.882	87.798	0.0000
Perm	0.036	1	0.036	0.537	0.4637
Perm * Anes	0.073	3	0.024	0.362	0.7806
Perm * CPT-AB	3.670	59	0.062	0.929	0.6304
Error	111.307	1736	0.067		

S-107

FACTORS AFFECTING THE VARIABILITY OF TIME ESTIMATES FOR DUAL PROCEDURE SURGERIES

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INTRODUCTION: Better estimates of surgical times are needed to improve scheduling and reduce costs. Surgeries comprised of exactly one surgical procedure (CPT) have been modeled using the lognormal model (1). Modeling of dual procedure surgeries (CPT1-2) is more difficult because these surgeries are less common and conventions do not exist to model them. It is logical to assume that times estimates for CPT1-2 surgeries may be constructed using estimates derived from component CPTs. We studied CPT1-2 surgeries and their component CPTs to identify factors associated with variability in dual procedure surgery times.
METHODS: With institutional approval, we studied, retrospectively, 10,737 CPT1-2 surgeries and 46,322 single CPT surgeries performed at a large teaching hospital (2). CPT1-2 surgeries were named jointly for both procedures, one designated 1st (CPT1) and the other 2nd (CPT2). We used multivariate linear models to study some factors that affect variability in total time (TT) and surgical time (ST) for CPT1-2 surgeries. To do this, we fitted a 7-factor main effects model of the general form:
lnTT = MTE1+MTE2+Anes+Emerg+Age+SPEC1+SPEC2+error
where MTE1 = median time estimate for CPT1, MTE2 = median time estimate for CPT2, Anes = type of anesthesia, SPEC1 = surgical specialty of CPT1, SPEC2 = surgical specialty of CPT2, 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 provide MTEs, single CPT surgeries were summarized by their medians and matched to CPT1-2 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 ($p < 0.05$) and together explained 69% of the variability in lnTT. Independent factors ordered by decreasing importance (by factor F-ratio) were MTE1, MTE1, Anes, Emerg, Age, SPEC1, and SPEC2. Results were similar for ST.
CONCLUSIONS: This research identifies factors associated with variability in dual procedure surgeries. Knowledge of the sources of variability is needed to improve modeling of multiple procedure surgeries and to improve surgical schedules.
REFERENCES:
1. Strum et al: Anesthesiology 2000; 92:1160-67.
2. Bashein et al: Anesthesia Analgesia 1985; 64:425-431.

ANOVA Table for lnTT (r2 = 68.7%, n = 9,876 CPT-12 surgeries)

Factor	Sum Squares	DF	Mean Square	F-Ratio	P value
MTE1	780.90	1	780.90	6064.18	0.0000
MTE2	110.60	1	110.60	858.88	0.000
Anes	61.42	3	20.47	160.00	0.0000
Emerg	2.34	1	2.34	18.18	0.0000
Age	1.47	1	1.47	11.46	0.0007
SPEC1	15.36	17	0.90	7.01	0.0000
SPEC2	11.54	18	0.64	4.98	0.0000
Error	1266.22	9833	0.13		

S-108

THE RELATIONSHIP BETWEEN SELECTED RISK FACTORS AND ADVERSE OUTCOMES IN PATIENTS UNDERGOING THORACIC, OTOLARYNGOLOGIC, ORTHOPAEDIC, UROLOGIC, AND GENERAL SURGERIES

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INTRODUCTION: The goal of this study was to create models to predict post-operative complications in surgeries generally considered to have very low complication rates.
METHODS: This study examined 48,550 patients aged 13 to 101 years (mean age 49.7) at the University of Michigan Health System who underwent thoracic, otolaryngologic, orthopaedic, urologic, or general surgery from 1995 to 2000. A logistic regression model was used to examine predictors including age, gender, tobacco use, sleep apnea, risk of aspiration, arrhythmia, asthma, diabetes, heart failure, hypertension, recent myocardial infarction, obesity, central nervous system disorders, congenital heart disease, chronic obstructive pulmonary disease, and diseases of the coronary arteries, liver, or kidneys. Also considered were surgery duration and type of anesthesia administered. Outcomes studied were unanticipated difficult airway, reintubation, cardiac arrest, death, myocardial infarction, significant dysrhythmia, central nervous system injury, aspiration, and respiratory arrest. All analyses controlled for year of surgery and surgical service. One model studied all complications; a second model was limited to cardiovascular complications. To study individual risk factors, we excluded ASA status. Emergency surgeries or ASA status >=5 were excluded.
RESULTS: There were 252 (252/49,550 or 0.5%) surgeries with a least one complication, and of these 125 (125/49,550 or 0.25%) had cardiovascular complications (myocardial infarction, cardiac arrest, significant dysrhythmia, or death). The logistic regression model for all complications was significant (likelihood chi-square ratio = 179.72, df = 47, $p < 0.0001$, Nagelkerke r-square = 0.06). Taking all predictors of complications together and controlling for year of surgery and service, this model revealed the following significant predictors: increased length of surgery ($p = 0.003$) advancing age ($p = 0.002$), female gender ($p = 0.0096$), history of arrhythmia ($p = 0.0006$), myocardial infarction in the past six months ($p = 0.0304$), and type of anesthesia ($p = 0.0023$). The logistic regression model for cardiovascular complications was also significant (likelihood chi-square ratio = 170.19, df = 46, $p < 0.0001$, Nagelkerke r-square = 0.10); significant predictors of cardiovascular complications were increased length of surgery ($p = 0.0003$), advancing age ($p < 0.0001$), history of arrhythmia ($p < 0.0001$), myocardial infarction in the past six months ($p = 0.037$), and coronary artery disease ($p = 0.0084$).
DISCUSSION: Both models revealed unexpected associations: In the all complications model, women were 1.5 times more likely to have complications compared with men; odds of complications were greater with general anesthesia than with central neurologic blockade (1.9), and general anesthesia combined with peripheral (3.5) or combined with central blockade (2.7). In both models, patients having a surgery length between 5-6 hours had the greatest odds of having complications even when compared with surgeries lasting much longer. Lack of significance (in either model) for diabetes, hypertension, or obesity was noteworthy.

S-109

THE CHARLSON COMORBIDITY SCORE AS AN ALTERNATIVE TO THE ASA PHYSICAL STATUS CLASSIFICATION

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INTRODUCTION: ASA Physical Status Classification (ASAPS) enjoys widespread use as a convenient and valid way to characterize patient health status and risk for mortality and morbidity in relation to anesthesia and surgery. Yet, classifying patients' health status may be somewhat subjective, and ASAPS is generally not recorded in observational databases increasingly used for outcomes research. A potential alternative is the Charlson Comorbidity Score (CCS) whose additive 'points' reflect the presence of specific, clinically important medical diagnoses commonly present in observational databases. CCS is predictive of death within one year[1] and has been used and validated in outcomes research in general medicine. This study evaluates usefulness of CCS as an alternative to ASAPS in outcome comparisons among surgical patients.
METHODS: A quality-improvement project team created an observational database of 832 consecutive major joint arthroplasty procedures performed in the mid-1990s. Among data were postoperative length of stay (LOS), adjusted hospital charges (Charges, from institutional financial system), ASAPS (from anesthetic record), presence of the 18 medical diagnoses (e.g., myocardial infarction, congestive heart failure, chronic pulmonary disease, diabetes mellitus with complications) used for computing CCS,[1] and CCS. Summary statistics, Spearman rank-order correlation analysis, parametric (t-test) and nonparametric (Mann-Whitney U test) comparison of means, and linear discriminant analysis were used to compare ASAPS and CCS values and two outcomes in this dataset.
RESULTS: CCS correlated modestly (r 0.45) with ASAPS, reflecting differences in patient distributions: 4.4%, 59.3%, 33.5%, and 2.8% of patients were distributed among ASAPS Classes 1 to 4, respectively; whereas 66.7%, 20.8%, 7.8%, and 4.7% were spread among CCS 0, 1, 2, and >2 points. Distinguishing ASA>2, CCS>0, and CCS>1 (each as evaluated as an individual cohort) from all other patients were presence of clinically important medical diagnoses. These three comorbidity cohorts individually were also associated with increased LOS of 14-19% and increased Charges, 22-43% (all, P <0.001).
DISCUSSION: CCS has face validity resembling ASAPS as a descriptor of important comorbidity and as a predictor for adverse outcomes. CCS should be evaluated further along with ASAPS as a stratification variable in outcomes comparisons using observational data sets.

[1] Charlson ME, et al. J Chron Dis 1987;40:373-83.

S-110

RATIONAL MEDICAL DECISION MAKING IN AUTOLOGOUS TRANSFUSION IMPROVES EFFICACY AND COST-EFFICIENCY.

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INTRODUCTION: Limitation of resources of the public health system urge clinicians to reconsider their clinical practice. This study analyses its impact on cost-efficiency (CE) of peri-operative blood-salvage with mechanical processing (BS), pre-operative autologous blood donation (PABD), and autologous plasmapheresis (APPH) before (ATC I) and after (ATC II) changing the autologous transfusion concept (ATC).
METHODS: Contrary to ATC I with deliberate indication for BS, PABD, and APPH, in ATC II BS and PABD were applied only, if an increase in RBC mass (+RBC) of at least 1 RBC-U (190 ml) was expected; APPH was cancelled. Calculations concerning APPH considered it with 20 % on coagulation reasons and 80 % a intravascular volume substitute; it was replaced by an artificial colloid. Since basics for fixed cost did not change, in order to avoid disturbances due to changes in charges to be paid by the hospital, and to make comparisons easier, CE exclusively considered direct / variable cost (d/vC) inclusive disposables, consumables, volume substitutes, type, screen, infectious / serological testing. Thus, identical measures caused identical d/vC in ATC I and II (BS: € 188.10. PABD: € 36.05 p. 1 PABD, €60.10 p. 2 PABDs: APPH: €89.10); 1 = 1$.
RESULTS: Comparing BS in ATC II vs. I, number of BS-sets consumed decreased by 30.6% (from 2,690 to 1,866) resulting in a decline in d/vC by € 154,994 (from € 505,989 to € 350,994). Number of processing-cycles p. pat. increased from 1.98 to 2.54, increasing +RBC by 63 ml p. pat. (from 223 to 286 ml). Reduction in BS-sets consumed and increase in efficacy improved CE of BS by € 207,420. Concerning PABD in ATC II vs. I, number of PABDs increased by 62.9% (from 3,110 to 5,065); i. e. from 1 to 1.95 PABDs p. pat., thereby causing an increase in d/vC by € 40,087 (36%) (from € 112,116 to 152,203). Increase in number of PABDs p. pat. together with increase in time-interval between first PABD and surgery from 14 to 36 days resulted in an increase in +RBC by 208% (from 81 ml in ATC I to 250 ml p. pat. in ATC II). This increase in +RBC equalled to gaining of additional 2,006 RBC-U, and net-improvement in cost-efficiency of € 89,468. Cancellation of APPH in ATC II reduced d/vC by € 468,289. Considering APPH on coagulation reasons with 20% and the remaining units a volume substitute (80%), and replacing them by an artificial colloid, reductions in d/vC still amounted to € € 237,469. Total savings by ATC II amounted to € 534,357.
DISCUSSION: Rational medical decision making concerning autologous transfusion measures was associated with an increase in efficacy and considerable improvement of cost-efficiency.

S-111

ONLY TWO CLINICAL PARAMETERS ARE OF DECISIVE IMPACT ON INCREASE IN TOTAL RBC-MASS BY PRE-OPERATIVE AUTOLOGOUS BLOOD DONATION – A PROSPECTIVE STATISTICAL ANALYSIS IN 704 PATIENTS

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INTRODUCTION: Pre-operative autologous blood donation (PABD) is an established measure to reduce the need for allogeneic blood. However, to make it an efficacious, effective and cost-efficient alternative to allogeneic blood transfusion, it is important to know those clinical parameters that are of impact on increase in RBC mass (+RBC).
METHODS: Prospective data analysis with IRB-approval concerning +RBC by PABD in 704 pats. (with either one or two PABDs) scheduled for major orthopaedic surgery. +RBC was analysed with respect to age, gender, patient's estimated blood vol. (EBV), blood vol. collected (BV coll) on each PABD-session, ASA-score, time-interval between PABD and surgery (T – S [days]), and hct on PABD-session. EBV was calculated according to Nadler. Pat.'s RBC-mass resulted from EBV*systemic hct. +RBC by PABD1 (+RBC1) was obtained from RBC-mass on visit2 (RBC2) minus RBC-mass on visit 1 (RBC1) plus RBC-mass harvested on PABD-session1. +RBC2 was calculated from RBC-mass preop. minus RBC-mass on visit2 plus RBC-mass collected on PABD-session2. Statistical analysis was performed by univariate multiple analysis of variances, correlation analysis (correlation coefficient – CC, and partial correlation coefficient – PCC), ANOVA with Scheffe´-test; statistical significance was considered with $p < 0.01$** with Bonferroni correction.
RESULTS: Only two parameters were demonstrated of consistent (i.e. in patients with either one or two PABDs) and decisive impact on +RBC: T – S which correlated positively with +RBC, and hct on PABD which correlated negatively with +RBC. Gender correlated only inconsistently with +RBC (i.e. in pats. with 1 PABD only). Age, EBV, and ASA-score did not correlate with +RBC. Corresponding data (F-values) of multiple, univariate analysis concerning +RBC in 1 PABD (I) and 2 PABDs (II) were as follows: Hct: 228.0**(I); 42.3**(II). T – S: 69.6**(I); 27.8**(II). BV coll: 1.6(I); 0.7(II). Gender: 7.3**(I); 0.04(II). Age: 0.2(I); 5.6(II). EBV: 0.9(I); 2.4(II). ASA-Score: 1.7(I); 0.2(II). Corresponding results concerning CC and PCC were found: +RBC vs. T – S: I: CC r = 0.353**; PCC r' = 0.323**. II: CC r = 0.342**; PCC r' = 0.303**. +RBC vs. Hct: I: CC r = -0.487; PCC r' = -0.581**. II: CC r = -0.380**; PCC r' = -0.467**.
DISCUSSION: These data reflect the importance of adopting the PABD-program to the physiologic basics if erythropoiesis: 1st a long time interval between last PABD and surgery in order to enable an appropriate RBC-regeneration. 2nd to collect a larger volume of RBC-mass (than the so far routinely collected equivalent of only 1 RBC-unit per PABD-session) on less PABD-sessions in order to lower more effectively the pat.'s hct to an individually adopted anaemic hct level, and, thereby, stimulate erythropoiesis as strong as possible.

S-112

ADOPTING PREOPERATIVE AUTOLOGOUS BLOOD DONATION TO THE PHYSIOLOGIC BASICS OF ERYTHROPOIESIS IMPROVES INCREASE IN TOTAL RBC MASS

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INTRODUCTION: Only two clinical parameters were demonstrated of impact on RBC-regeneration (+RBC) due to preoperative autologous blood donation (PABD): 1st time-interval between blood donation and surgery (T – S), that correlated positively with +RBC; 2nd hct-level on PABD, that correlated negatively with +RBC. Thus, collecting the equivalent of two PABDs on one session (double deposit - DD) should optimise efficacy of PABD when compared with that of two separately collected units (2 SCU) on two separate PABD-sessions.
METHODS: Prospective preference study with IRB-approval in pats. scheduled for major orthopaedic surgery (DD: n=100. 2 SCU: n=60). Blood volume collected was 860 ml in DD, and 2*430 ml in 2 SCU. Pat.'s blood volume (EBV) was calculated according to Nadler. RBC-mass was calculated with EBV*systemic hct. In DD, +RBC resulted from RBC-mass pre-op. minus initial RBC-mass plus RBC mass collected by DD. In 2 SCU, +RBC1 by PABD1 was calculated from RBC-mass on PABD2 minus RBC-mass on PABD1 plus RBC collected on PABD1; +RBC2 resulted from RBC-mass pre-op minus RBC-mass on PABD2 plus RBC-mass collected on PABD2. Statistical analysis was performed by t- / U- / H-test, ANOVA with Scheffe's test; statistical significance was considered with $p<0.05$ with Bonferroni's correction.
RESULTS: No differences were demonstrated between patients with 2 SCU vs. DD concerning base parameters (gender, age, height, weight, EBV, hct init, RBC-mass init). Referring to 'blood data', no differences were demonstrated concerning total RBC-mass collected (2 SCU vs. DD: 347 ± 30 vs. 343 ± 36 ml) and total time-interval between (first) PABD and surgery (T1 – S in 2 SCU vs. DD: 26.9 ± 2.5 vs. 25.9 ± 2.5 days). In the subgroups of 2 SCU, time-interval between PABD1 and PABD2 (T1 – 2) was 14 ± 1 days, and between PABD2 and surgery (T2 – S) 13 ± 2.4 days. However, total +RBC was greater ($p<0.000$) in DD than in 2 SCU (261 ± 114 vs. 168 ± 133 ml). In 2 SCU, +RBC and +RBC2 were not different (89 ± 119 and 79 ± 119 ml).
DISCUSSION: Though no differences were demonstrated concerning base data and total time-intervals in 2 SCU vs. DD, total +RBC was higher ($p<0.000$) in DD than in 2 SCU. Both the longer time-interval for T – S in DD compared to those of the two separate time-intervals T1 – 2, and T2 – S in 2 SCU, and the stronger decline of hct in DD due to collecting a greater RBC-mass on only one PABD-session are considered the underlying mechanisms of these results. Thus, adopting the PABD-concept to the physiologic basics of erythropoiesis improves efficacy of PABD. (This analysis was supported in part by a grant from Haemonetics GmbH, Munich, Germany).

S-113

PERI-OPERATIVE BLOOD SALVAGE: THE QUALITY-PROBLEM OF THE LAST, INCOMPLETELY-FILLED LATHAM BOWL - ANALYSIS OF ELIMINATION OF BY-PRODUCTS BY THE COMPLETELY AND INCOMPLETELY-FILLED DISCONTINUOUSLY-PROCESSING LATHAM-BOWL-SYSTEM AND THE CONTINUOUSLY-PROCESSING CHAMBER-SYSTEM

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INTRODUCTION: Due to physical basics of mechanical processing of salvaged blood, only completely-filled Latham-bowls should be processed with discontinuously-processing systems (DPS). No data have been published comparing product quality of incompletely and completely-filled and processed DPS (Dideco Inc., Italy) with that of continuously- processing system (CPS) (Fresenius Transfusion GmbH, Germany).
METHODS: Prospective lab-study of blood salvaged during infective surgery. In DPS (n = 10), filling, washing and emptying speed was 300 ml p. minute each, 5,600 RPM, 1,000ml of saline as washing solution, and administering the routinely used 'better-wash-quality' program (BWQ). In CPS (n = 10), the routinely used 'quality-wash' program (QW) was applied; it chooses automatically the appropriate processing parameters according to hct of salvaged blood. Following parameters were determined before and after processing of incompletely (I) and completely-filled (II) DPS-bowls, and corresponding RBC-equivalent (III, IV) of CPS: Hct, WBC, platelets, total protein content, plasma-hb, heparin, D-Dimers, F1+2, PMN-Elastase, IL-6. Elimination-rate (ER - %) and transfusion-rate (TR - cells / substrate p. litre RBC-mass transfused) were calculated. Statistical analysis mean(±SD) by t-/U-/H-Test, ANOVA with Scheffe´-test; statistical significance with $p<0.01$ (^{a,b,c,d,e}) with Bonferroni correction.
RESULTS: Hct of processed blood in I [0.3 (0.04) ^{a,b,c}], II [0.54 (0.03) ^{a,d,e}], III [0.63 (0.06) ^{b,d}] and IV [0.68 (0.04) ^{c,e}] differed ($p<0.01$) from each other. Mechanical processing was effective ($p <0.01$) in eliminating by-products in either group. However, no differences were demonstrated concerning ER and TR both within DPS (I vs. II) and CPS (III vs. IV), and between DPS and CPS (I vs. II vs. III vs. IV). ER and TR in I, II, III, and IV of the above named parameters were as follows: WBC: ER: 62(12); 64(16); 74(11); 66(14). TR: 11(4); 10(4); 8(5); 8(5). Platelets: ER: 91(10); 92(7); 88(10); 84(10). TR: 54 (69); 51(59); 76 (85); 84 (74). Total Protein Content: ER: 93(9); 96(5); 98(1); 98(1). TR: 1 (2); 1(0.3); 0.4(0.2); 0.4(0.1). Plasma-Hb: ER: 93(4); 96(3); 96(2); 95(2). TR: 315(200); 218(165); 143(63); 144(45). Heparin: ER: 99(2); 99(1); 99(0.3); 99(0.5). TR: 0.3(0.2); 0.1(0.1); 0.3(0.1); 0.3(0.2). D-Dimers: ER: 94(10); 98(2); 95(3); 93(7). TR: 1104(574); 435(207); 1948(1676); 1480(1185). F1+2: ER: 98(3); 99(1); 99(1); 99(1). TR: 28(27); 10(12); 22(12); 21(10). Elastase: ER: 95(2); 97(2); 95(7); 97(2): TR: 348(167); 280(224); 235(192); 203(197). IL-6: ER: 99(1); 99(0.2); 99(1); 99(1). TR: 78(114); 33(66); 66(64); 59(42).
DISCUSSION: Normal QW in CPS is as efficacious as BWQ in DPS concerning ER. The reason for these unexpected results concerning incompletely-filled DPS-bowls might be as follows: 1st administering BWQ in DPS abolished the disadvantages of incompletely-filled DPS-bowls; 2nd filling DPS-bowls with salvaged RBC-mass equalling to half the volume of completely-filled DPS-bowls might have been too much to demonstrate differences concerning ER and TR of these systems.

S-114

MODERN ANAESTHETIC AGENTS FOR GENERAL ANAESTHESIA IN THIRD WORLD COUNTRIES

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INTRODUCTION: The vast majority of people in the Third World are excluded from medical treatment. One severe problem is adequate general anaesthesia for surgical procedures. Anaesthetic methods are often dangererous (diethylether)[1] . Perioperative mortality is 100 to 200 times higher compared with western countries[2]. The use of remifentanil[3] in combination with methohexithal or ketamine is a possibility to perform safe anesthesia[4].
METHODS: In 1998 and 2001 we performed operations on 228 patients in rural Guinea, West Africa. In 45 patients (ASA 1-3, 42,6 ± years, 53,1 ± 15 kg, 158,4±14,8 cm) we administered general anaesthesia for surgical procedures. Atropine 0,5 mg, 0,05 mg/kg midazolam and 0,5 mg/kg ketamine were given as premedication. For induction 1 mg/ kg methohexital, 1 mg/kg succinycholine and 0,08 mg/ kg vecuronium or 1mg/kg cisatracurium were administered. 27 of the patients received fentanyl (20-40 µg/kg), alfentanil (100-200µg/kg) or sufentanil (0,5-1µg/kg) to support induction. As maintenance infusions 21 patients received a combination of remifentanil (0,2-1,2 µg/kg/min, 20µg/ml) and methohexital (1-3/kg/h, 1mg/ml). Both anaesthetics were also applied together in one infusion of sodium chloride. 15 patients were anaesthetized with ketamine (2-3 mg/kg/h, 1mg/ml) and remifentanil. 7 patients received alfentanil (30-60 µg/kg/h,10µg/ml).
Postoperative analgesia was provided with either tramadol (1-2mg/kg) and metamizol (10-20 mg/kg).
DISCUSSION: Remifentanil is appropriate to administer general anaesthesia, even in technical limited settings. Additionionally remifentanil was given with opioids like fentanyl, alfentanil or sufentanil as induction supplements, which did not prolong recovery-time. The alfentanil-drip had to be reversed in 3 cases with naloxone. Ketamine for maintaining anaesthesia produced more secretion. Remifentanil did not induce bradycardia. Hemodynamic stability was best with remifentanil and methohexital.Costs for 1 hour anaethesia with both agents is about 20 dollars.

Data are expressed as mean ± SD		
Procedure duration (min)		138,2 ± 104,9
Remifentanil (g/kg/min)		0,82 ± 0,47
Methohexital (mg/kg/h)		3,75 ± 2,13
Ketamine (mg/kg/h)		5,82 ± 3,11
Alfentanil (mg/kg/h)		2,23 ± 1,32
	Before induction	During anaesthesia
Blood pressure		
Systolic (mmHg)	129,8 ± 105,8	103,2 ± 25,4
Diastolic (mmHg)	76,3 ± 32,5	69,6 ± 15,1
Heart rate	99,4 ± 40	89,5 ± 32,5
Surgical Procedures Performed under General Anaesthesia		
Diagnosis		No. of anaesthesias
Goitre		31
Hernia		4
Utero-vaginal prolapse		5
Cesarean section		1
Rupture of the bladder		1
Hemotoma of the neck		1
Tumor of the mandible		1
Analprolapse		1

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S-115

DOES PRIOR PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY AND/OR STENT INSERTION CHANGE CARDIAC MORTALITY OF SURGERY ON FEMORAL PSEUDOANEURYSM, COMPLICATED FROM CARDIAC CATHETERIZATION

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INTRODUCTION: Perioperative myocardial infarction is a major cause of morbidity and mortality after non-cardiac surgery in-patients with coronary artery disease (CAD).
Recently it was reported that patients with CAD who underwent non-cardiac surgery within 90 days of PTCA had an increased adverse cardiac outcome compared with non-revascularized patients (1). Current ACC/AHA guideline for perioperative cardiac evaluation for non-cardiac surgery recommends that delaying surgery at least 1 week after PTCA and if a coronary stent is used, delaying surgery of at least 2 weeks and ideally 4 to 6 weeks before non-cardiac surgery.
However, some patients with CAD returned to operating room due to complication of cardiac catheterization with complication of femoral pseudoaneurysm within several days.
We reviewed the incidence of cardiac death following anesthesia and surgery for femoral pseudoaneurysm after cardiac catheterization with PTCA and / or stent within 1 week at the same admission.
METHODS: We reviewed entire cardiac catheterization data at our university hospital from 1992 to 2002.
Patients were categorized into two groups. (1) primary cardiac catheterization group whose primary reason of admission was to have cardiac catheterization and (2) secondary cardiac catheterization group who required cardiac consultation after admission and subsequently underwent cardiac catheterization.
Surgery for pseudoaneurysm of femoral artery following cardiac catheterization within 1 week at the same admission were divided into 2 groups
(A) Cardiac catheterization without PTCA and Stent
(B) Cardiac catheterization with PTCA and Stent.
Data on death rate among each category were evaluated following cardiac catheterization at the initial same admission. Data were analyzed by chi-square probability and person's coefficient.
RESULTS: There were significantly increased rates of death following PTCA among secondary catheterization group compared with among primary catheterization group ($P < 0.0001$)
There were more death among patients with cardiac catheterization without PTCA than with PTCA ($P < 0.0001$). Patients who had stent insertion had significantly less death rate compared with patients without stent ($P < 0.01$).
In patients who underwent repair of femoral pseudoaneurysm within 1 week and the same admission, after cardiac catheterization, there were no significant difference in death rate between patients with PTCA and stent and patients without PTCT and stent.
DISCUSSION: Patients who had cardiac catheterization with PTCA and / or stent had better outcome of cardiac death compared with patients who simply had cardiac catheterization without PTCA and stent. No significant differences in death rate with repair of femoral pseudoaneurysm done within 1 week after cardiac catheterization between in-patients without PTCA and stent and in-patients with PTCA and stent.
It seems reasonable not to delay repair of femoral pseudoaneurysm which develop as a complication of cardiac catheterization whether PTCA with stent or without PTCA since expanding nature of pseudoaneurysm.
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Cardiac Catheterization	Number	Number of Deaths	P-Value
1(A) PTCA among primary cath	5726	39	<0.0001
(B) PTCA among secondary cath	853	61	
2(A) with PTCA	6579	92	<0.001
(B) without PTCA	14790	327	
3(A) with Stent	3043	43	<0.01
(B) without Stent	17826	376	
4 Surgery on Femoral Pseudoaneurysm			
(A) Cardiac Cath without PTCA and Stent	133	5	0.59
(B)Cardiac Cath with PTCA and Stent	46	1	

Equipment/Monitoring

S-116

SECURE ACCESS TO ANESTHESIA RECORDS AND OPERATING ROOM SCHEDULES USING AN INTERNET BROWSER

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INTRODUCTION: Duke University Hospital has used Anesthesia Information Management Systems (AIMS) to document over 300,000 anesthesia records. However, until now the only means of accessing past patient records has required accessing a custom point-of-care workstation, which is not optimal for planning clinical care, QA or administrative use in highly distributed hospital systems. Providers often had no knowledge of a patient's past anesthesia history even though it had been recorded using the AIMS. Clinical staff often plan patient care with other anesthesia providers outside the operating room suite, sites for which an AIMS client installation would be expensive and difficult to maintain.
METHODS: We have implemented an extension to our AIMS which enables secure access to patient anesthesia records and other derived information in near-real time over the Internet. Our system consists of web-applications that access the database of our AIMS. The client application is any web-browser and the response is a dynamic HTML page showing the anesthesia record over the Internet. The system addresses security concerns using 128 bit Secure Socket encryption, user authentication and audit to prevent inappropriate access. It also fully supports an Application Service Provider model where one central server can provide the anesthesia records for multiple hospitals.
RESULTS: In 10 months the system has generated a user base of over 200 and an average of 750 requests/day. It is used extensively for looking up personal anesthesia schedules, past anesthesia histories and current cases. A typical usage pattern is for providers to review their schedule of cases from home and examine past anesthesia histories and cases. A derivative of the system provides a Big Board view of the whole operating room suite displayed on 5 flat-panels. As data updates, the display refreshes automatically every minute to provide a near-real time status monitor of operative stage and patient location. Staff in the waiting area use the system to keep patients and relatives informed. It is used extensively in the billing and denials offices and it forms the basis of a QA cycle that enables the review of QA events recorded in the AIMS, feeding-back recommendations by email to the providers involved. A popular feature of the system is a page of secure personalized views of data, including a summary of all cases, QI incidents and schedules. The system has the potential for use in remote, real-time consultation of ongoing anesthetics from any location using a web-browser.
DISCUSSION: The secure availability of anesthesia records and derivatives of AIMS data over the Internet has led to a surge of use of this information in our institution. This type of access has already impacted positively upon patient care and on our hospital's operational efficiency.

S-117

THE USE OF AN INTERNET-BASED PHARMACY BILLING SYSTEM WITH AN AUTOMATED ANESTHESIA RECORD

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INTRODUCTION: Charging for anesthesia drugs is a complex process involving manual data entry before the patient or insurance company is properly billed. Anesthesia Information Management Systems (AIMS) have claimed the automation of pharmacy billing as a benefit. In theory the best solution is direct data transfer from a point-of-care recording device to a pharmacy billing system using an HL7 interface, but in practice this has rarely been achieved. Numerous obstacles lie in the way, the most significant being data entry artifact and the custom of anesthesia providers to document administered drugs without regard for vial size and wastage.
At Duke University Hospital we have a large AIMS installation (Draeger Inc, Telford, PA) with over 150 workstations and 200 users in 3 hospitals covering the perioperative process. Our original drug billing procedure was heavily manual, with pharmacy staff documenting drug usage from cassettes issued to providers for each case. An audit of 15 cases revealed inaccuracies in patient charges compared to the drugs documented in the AIMS, with underbilling of over $100 in 20% cases. Our new Internet-based system uses AIMS data to summarize pharmacy charges, allowing non-controlled drugs to be dispensed from open carts in the operating rooms and stocked by pharmacy.
METHODS: Our solution relies on the premise that pharmacy charges should originate from AIMS documentation at the point-of care. Billing codes have been determined statistically and financially to incorporate wastage. The tool is a dynamic, Internet-based pharmacy report called Saturn Agent Summary (SAS). The SAS is generated using a middle-tier Java web-application accessing the AIMS database. Pharmacy staff at a remote location can review the SAS for each case using an Internet Browser. Privacy concerns are addressed by the use of data encryption, user authentication and user audit.
RESULTS: SAS has allowed the abolition of the cassette system for dispensing drugs and fluids, except controlled substances, which are still centrally managed using a much simplified system. The pharmacy maintains stocked carts in the operating rooms, and anesthesia staff have convenient access to a wider range of drugs.
DISCUSSION: The use of a thin Internet client with an underlying web-application architecture for the SAS has advantages in a complex and geographically distributed billing environment. The remote billing office only has to open up an Internet Browser to process anesthesia pharmacy charges. A second phase is planned in which the web-application will generate XML as well as HTML output. This will enable a completely automated charging solution with no intervening manual steps except audit and review. With automated and more accurate pharmacy billing, we will continue to reengineer drug distribution systems to minimize waste, focus on medication safety and realize significant cost savings.

S-118

HUMIDITY IN ANESTHESIA BREATHING SYSTEMS

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INTRODUCTION: A preliminary study done in 1981 suggests that the Mapelson D (Bain system) offers higher humidity in the system compared to most other systems, even the semi-closed circle absorber system. [1] This has not, as far as we are aware, been substantiated. The object of this study was to compare the absorber system to the Bain system using the Narcomed2B (North American Draeger, Telford., PA 18969) anesthesia machine for both systems.
METHODS: Twenty-four patients ASA 1 and 2, between the ages of 36 and 55, scheduled for non-thoracic surgical procedures under general anesthesia were enrolled after written informed consent had been obtained. The study was approved by the University Panel on Human Subjects in Medical Research. General anesthesia was induced and the trachea intubated in routine fashion. Anesthesia was maintained with N2O and oxygen 30% with isoflurane 05-1%. Fresh gas flow was kept at 2L/min with the absorber system (A) and 70ml/kg with the Bain (B). Relative humidity and absolute humidity of the airway gases were measured with a humidity sensor (Gibeck, Indianapolis, IN 46236). Fifteen minutes of baseline measurements were done prior to randomly studying each breathing system in the same patient. Results were expressed as mean (SD) or median (interquartile range), and analyzed by a paired T-test or Wilcoxon Signed Rank test. $P<0.05$ was considered significant.
RESULTS: The results for relative humidity (median and interquartile range) were A=96.3 (6.3) and B=96.1 (7.9). The results for absolute humidity (mean and interquartile range) were A=34.1 (2.3) and B=34.6 (2.6).
SUMMARY: In this clinical study we did not find any difference in relative or absolute humidity between the absorber system and the Bain system. The importance of these results is the subject of further studies.
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S-119

NOVEL BENCH VALIDATION OF A NEW, FAST-RESPONSE AIRWAY SENSOR OF HUMIDITY AND TEMPERATURE

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INTRODUCTION: Measurement of pulmonary O_2 uptake (VO_2) should help detect metabolic derangement during anesthesia and non-steady state critical events. Due to non-steady state conditions, use of N_2O, presence of high inspired O_2, and difficulty to measure mixed expired oxygen fractions during anesthesia, VO_2 must be measured by $V_I \cdot F_IO_2 - V_E \cdot F_EO_2$, where V and FO_2 are gas volumes and oxygen fractions in inspiration and expiration (1). The higher temperature (T) and humidity of expired gas (relative to inspired gas) must be measured or the error in VO_2 can reach 50% during O_2 breathing (1)! Accordingly, we have developed a fast response airway opening humidity sensor (HS) (2), which incorporates dry and wet tiny thermocouples. Humidity is measured by psychrometry, where dry gas causes evaporative cooling to decrease wet T below dry T. Psychrometric principles require a threshold gas velocity to measure humidity (5 L/min for the dimensions of our HS). Accordingly, we designed a special dynamic bench set-up to test and validate the HS over a wide range of gas T and humidity.
METHODS: In a circular circuit (Figure), a coil of copper tubing (1.1 mm ID) was placed in a T-controlled water bath and connected through vinyl tubing (1.7 cm ID) to the HS, the thermohygrometer, to a parallel circuit that allowed controlled gas flow through a water desiccant (8 mesh $CaSO_4$) chamber, and to an occlusive roller pump (5 L/min). The copper tubing allowed rapid heat transfer from the water bath to control T of gas delivered to the humidity sensor. Metered volumes of water were injected into the copper tubing to increase gas humidity, while the water desiccating circuit was adjusted to remove humidity. The psychrometry equation was solved for the psychrometry coefficient, A, knowing relative humidity (RH) measured by the thermohygrometer and the measured wet and dry T from the humidity sensor.
RESULTS: Over the clinical range of delivered T (20-40ºC) and RH (0-100%) in 6 different experiments (20 measurements/experiment), correlation of measured RH by the humidity sensor versus the value from the thermohygrometer were excellent (R^2=0.972±0.023, slope=0.975±0.061 and Y-intercept=0.435±1.005).
DISCUSSION: The HS provides highly accurate airway measurements over a wide range of gas T and humidity. The accuracy of the HS, together with its fast response, will support the ability to measure VO_2 (and VCO2) during anesthesia, and help introduce non-invasive detection of metabolic derangement during anesthesia and non-steady state critical events (1).
REFERENCES:
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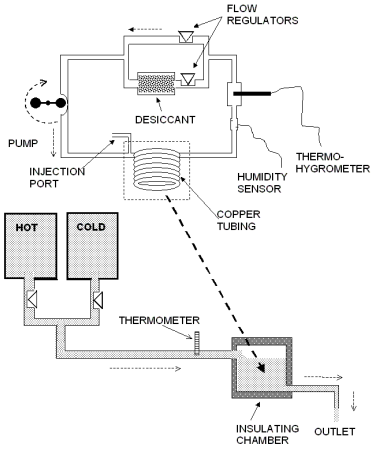

S-120

CAN AIRWAY HUMIDITY SENSOR THERMOCOUPLES BE CALIBRATED IN TEMPERATURE-CONTROLLED WATER BATHS?

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INTRODUCTION: Pulmonary O_2 uptake (VO_2) is given by $V_I \cdot F_IO_2 - V_E \cdot F_EO_2$, where V and FO_2 are gas flows and oxygen fractions in inspiration and expiration. The higher temperature (T) and humidity of expired gas (relative to inspired gas) must be measured or the error in VO_2 can reach 50% during O_2 breathing (1)! Accordingly, we have developed a fast response airway opening humidity sensor (HS) (2), which incorporates dry and wet tiny thermocouples. Humidity is measured by psychrometry, where dry gas causes evaporative cooling to decrease wet T below dry T. Calibration of thermocouples in gas is problematic because constant and adjustable gas T is difficult, thermal conductivity of air is 23 times less than that of water (3), and gas must be saturated to avoid evaporative cooling. In this study, we develop an apparatus and hypothesize that thermocouple calibration in hot and cold water baths is identical to the measurements in the gas phase.
METHODS: We constructed a double-walled chamber by gluing a small beaker (1.2 L) onto the inner bottom of a larger beaker (8 L). From an elevated supply reservoir (20 L), water flowed (730 ml/min) and circulated through the outer chamber to provide a water jacket around the inner closed gas chamber (Figure). Baseline supply reservoir water temperature was about 40ºC. Then, ice was added to the supply reservoir to generate 8 water T levels down to 5ºC, measured by precision mercury bulb thermometer. A small amount of water (< 1 ml) was placed in the inner gas chamber in order to maintain 100% RH. The HS and a precision thermohygrometer (Oakton WD-35612-00, Vernon Hills, IL), were placed inside the inner chamber. Prior to a trial, a two-point calibration of the HS, spanning the measurement range, was performed in a precision T-controlled water bath.
RESULTS: Over the T range of 0 to 40 ºC, linear regression of thermocouple T versus air chamber T was excellent (R^2=0.9998, slope=1.05, y-intercept=-0.82). Because measured inner gas chamber RH was always 100%, measured wet and dry T were equal (no evaporation from wet thermocouple to decrease its T).
DISCUSSION: We conclude that calibration of thermocouples in T-controlled water baths is identical to, and much easier than, calibration in the gas phase. Accordingly, HS measurements of airway gas T and humidity are reliable. Airway humidity and T measurement allows accurate determination of VO_2 (and VCO_2) during anesthesia, and helps support, we believe, future non-invasive detection of changes in metabolism and critical events during surgery (1).
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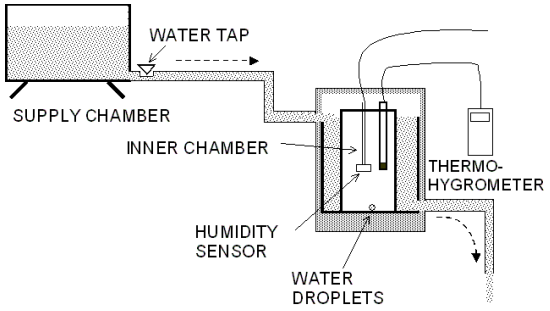
Support by NIH R01 HL-42637.



S-121

ROLE OF HEATED AND HUMIDIFIED INTRAPERITONEAL GASES DURING LAPAROSCOPIC ROUX-EN-Y SURGERY - EFFECT ON CORE TEMPERATURE AND POSTOPERATIVE PAIN

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INTRODUCTION: Intraoperative hypothermia occurs commonly during major laparoscopic procedures.[1] Controversy exists regarding the efficacy of heated and humidified intraperitoneal gases in maintaining core body temperature.[2,3] Therefore, we designed a sham-controlled study to evaluate the effect of the Insuflow® device on perioperative body temperatures and postoperative analgesic requirements.
METHODS: 18 morbid obese patients undergoing laparoscopic Roux-en-Y procedures under a standardized general anesthetic technique were randomly assigned to either a control (Sham) group receiving an 'inactive' Insuflow device, or an active treatment (Insuflow) group receiving warmed and humidified intraperitoneal gases. Esophageal (core) temperature was measured intraoperatively and tympanic membrane temperature was measured postoperatively. No other active warming devices were used during surgery. Verbal pain scores (0=none to 10=maximal) were recorded in the postoperative period. In addition, the postoperative opioid analgesic requirement and quality of recovery (0-18) were recorded on the day of surgery, as well as postoperative days 1(POD 1), 2 (POD 2) and 3 (POD 3).
RESULTS: Use of the active Insuflow device was associated with higher intraoperative temperatures. Although pain scores were lower in the early postoperative period (i.e. PACU), there were no significant differences in the opioid analgesic requirements after surgery. The lengths of PACU and hospital stays were shorter in the Insuflow group (98±31 vs 134±92 min and 56±6 vs 66±9 h, respectively). No patients developed severe intraoperative hypothermia in either group. Furthermore, no differences were observed on the quality of recovery throughout the postoperative period.
CONCLUSIONS: The Insuflow device may be a useful alternative to other active warming devices (e.g., forced air warming) for maintaining temperature during laparoscopic surgery. These preliminary findings suggest that the device may also be associated with lower pain scores in the early postoperative period and shorter recovery times. However, further studies are needed comparing this device to other active warming devices.
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	SHAM (n=10)	INSU-FLOW(n=8)		SHAM (n=10)	INSU-FLOW(n=8)
Age (yr)	**42±16**	**48±7**	First pain rescue (min)	**49±25**	**53±35**
Weight (kg)	**124±18**	**114±16**	PACU stay (min)	**134±92**	**98±31**
Gender (M/F)	**1/9**	**0/8**	Pain score PACU (0-10)	**5 (0-8)**	**2.5 (0-8)**
Surgery time (min)	**100±27**	**109±24**	Morphine in PACU (mg)	**14±8**	**11±11**
Insuflation volume (L)	**222±77**	**200±96**	Pain score at 24 hr (0-10)	**5 (1-10)**	**4 (0-6)**
Temperature @ start of surgery (C)	**36.2±0.4**	**36.1±0.5**	PCA morphine < 24 hr (mg)	**33±11**	**22±15**
Temperature @ 90 min (C)	**35.3±0.1**	**35.7±0.7**	Quality of recovery score at 24h (n)	**12±3**	**12±3**
Temperature @ end of surgery (C)	**35±0.2**	**35.4±0.2**	Total hospital stay (hr)	**66±9**	**56±6**

S-122

DIFFERENCES IN TYMPANIC AND RECTAL TEMPERATURE CHANGES AFTER MRI OF THE BRAIN IN CHILDREN AFTER GENERAL ANESTHESIA

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INTRODUCTION: Using clinical temperature monitoring equipment is incompatible in the MRI due to the strong magnetic field and therefore specialized fluoroptic systems are required. (1) The introduction of radiofrequency radiation is known to be thermogenic and causes tissue heating. (2) Adults undergoing MRI of the head experienced increases in their forehead skin temperatures. (3) We thought to determine if there was a difference in the core body temperature changes between the rectum and tympanic membrane in children that underwent MRI of the brain.
METHODS: With IRB approval, we prospectively studied 17 children who underwent MRI of the brain without contrast under general anesthesia. The ages ranged from 19 months to 13 years and weights from 10.8 to 77 kg. The induction and emergence occurred in a room adjacent to the MRI were the ambient temperature ranged from 22-24 C. 16 were induced with sevoflurane with LMA placement. One patient received propofol and mivacurium for induction and was intubated. Maintenance was with sevoflurane with patients breathing spontaneously.The children were covered with a hospital gown and cotton blanket; no other heating device was used. Rectal and tympanic temperatures were measured immediately after induction prior to MRI and after MRI prior to emergence from general anesthesia.
RESULTS: The mean difference in pre and post-scan rectal temperature was -1.1 +/- 0.3 C while the mean difference in pre and post-scan tympanic temperature was - 0.52 +/- 0.5 C. The mean rectal temperature was 37.2 +/- 0.3 C before MRI and 36.0 +/- 0.3 C after the MRI. The mean tympanic temperature was 36.7 +/- 0.4 before the MRI and 36.2 +/- 0.3 C after the MRI. The mean times between pre to post-scan rectal and tympanic temperature measurements were similar.
DISCUSSION: Our study indicates that there was a difference in the mean core body temperature change measured at two different sites. A greater mean temperature drop was seen in the rectum over the tympanic membrane. Potential reasons may have been due to uneven absorption of radiofrequency radiation within the body resulting in local heating of the head or a lag in the temperature measured in the rectum. Further studies of temperature monitoring during MRI scanning are needed in order to understand the changes in temperature occurring at different body sites.
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S-123

CARBON DIOXIDE LEVELS IN THE OPERATING ROOM DURING GYNECOLOGICAL LAPAROSCOPIC SURGERY

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INTRODUCTION: Carbon dioxide (CO_2) is used in laparoscopic surgery to insufflate the abdominal cavity for a better view and access of the operating field. There seems to be a tendency for anesthesiologists to be somewhat more drowsy and less focused during laparoscopic surgery. Factors that may contribute to this tendency include relatively dark operating room, relatively stable patient's conditions associated with surgery and the possibility of high CO_2 levels. This study evaluated the CO_2 level in two operating rooms during gynecological laparoscopic surgery.
METHODS: CO_2 level was checked using a portable gas detector, Q check (TSI Inc., USA), during 15 and 17 cases of laparoscopic surgery in two different operating rooms, A and P. The detecting bar was placed between two IV poles used for tenting aseptic drapes. Mean, high, and low levels of CO_2, and the number of persons in the operating room were checked during the first 15 minutes of anesthesia, each 15minutes after CO_2 insufflation until CO_2 insufflation was stopped, the first 15minutes immediately after the cessation of CO_2, and the 15 minutes after the end of surgery. Air change rates and room dimension of both operating rooms were also measured.
RESULTS: There was a significant increase in mean CO_2 level in room P compared to room A ($p = 0.0002$), but the average difference was 137 ppm. Mean CO_2 levels in room P was under 1000 ppm except in one case in which it rose up to 2200 ppm, whereas in room A, all mean CO_2 levels were less than 800 ppm. Air exchange rate and room dimension for room A were 16.4 / hr and 113.2 m^3, while for room P, they were 19 / hr and 63.5 m^3 respectively.
DISCUSSION: Moderately elevated levels of CO_2 are well tolerated. CO_2 levels increased during laparoscopic surgery, but the mean concentration was below 1000 ppm for both operating rooms. But in many cases, the high levels of CO_2 were above 1000 ppm. The American Society of Heating, Refrigerating and Air-Conditioning Engineers, Inc. (ASHRAE) guideline for indoor air CO_2 is less than 650 ppm above outdoors, about 950 - 1000 ppm, and the US Building Owners and Managers Association (BOMA) recommends indoor CO_2 levels less than 800 ppm. One more thing of note is that the volume of the operating room seems to be more important than the air exchange rate. We suggest that laparoscopic surgeries using CO_2 should be performed in large well-ventilated rooms and guidelines for CO_2 levels in operating rooms should be proposed. The effect of moderately elevated CO_2 on the ability of the surgeon and the anesthesiologist to focus on their jobs requires further evaluation.

S-124

UNPREDICTABLE POTASSIUM CHANGES IN DONATED BLOOD FOLLOWING WARMING

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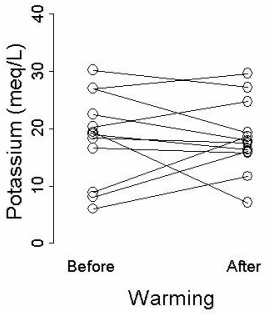
INTRODUCTION: Common clinical practice for administering donated packed red blood cells uses countercurrent warming to prevent hypothermia. The maximum temperature for warming is currently 42 degrees since blood will hemolyze at a rate of 2.26 mg Hgb/ 100cc/min when heated to 50 degrees, but blood warmed in a water bath does not have significant hemolysis below 40 degrees (1). No published data demonstrate if there is clinically significant hemolysis using current standard practices with countercurrent warming devices set to 42 degrees. Since a rise in potassium has been shown to be a sensitive indicator of as little as 1% of hemolysis (2), we measured the potassium of donated blood before and after warming through a countercurrent device. Since hyperkalemia could also be of concern, recipient potassium levels were also studied.
METHODS: Potassium levels from 12 donated packed red blood cell units were measured both before and after warming using Hotline countercurrent heat exchange (SIMS Level 1, Rockland, MA) at modest flow rates. Units were handled in the usual clinical practice, each kept in a cooler bucket until use, then allowed to drain by gravity through a Hotline device, with average flow rates of 80 ml/min and outlet temperature of 34.8 degrees Celsius. Simultaneous samples were drawn immediately before and after the large bore warmer tubing for analysis. Recipient arterial blood gases were measured immediately before and again 3-5 minutes after transfusion of the heated red blood cells. Medications known to alter potassium were avoided. All data are expressed as a mean +/- standard deviation. A paired t test was used for group comparisons, and relationships between potassium levels and blood unit storage duration were examined using regression analysis.
RESULTS: Average potassium values measured in the packed red blood cell units before warming (18.6 +/- 7.8 meq/l) were not different from the values after warming (18.5 +/- 6.3 meq/l); both potassium levels demonstrated wide variability (see figure). The serum potassium levels of the recipients before blood administration (3.7 +/- 0.7 meq/l) were similar to levels after transfusion (3.8 +/- 0.7 meq/l), with much smaller variability. Interestingly, there was no significant relationship between any of the measured potassium levels and storage duration of the blood.



DISCUSSION: The results above indicate that potassium levels on average are unchanged after heating though a Hotline. However, in individual units an unpredictable increase or decrease may be observed. It is not clear if these changes are a result of warming or simply reflect a very heterogeneous potassium distribution in a unit of packed red blood cells.
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S-125

EFFECT OF INCREASED INTRA-ABDOMINAL PRESSURE ON LIVER FUNCTIONS DURING LAPAROSCOPIC CHOLECYSTECTOMY IN PATIENTS ANESTHETIZED WITH HALOTHANE VERSUS ISOFLURANE

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INTRODUCTION: The present study aims to evaluate the effects of increased intra-abdominal pressure on liver functions during laparoscopic cholecystectomy compared to open cholecystectomy under halothane and isoflurane anesthesia.
METHODS: A total of 60 patients scheduled for cholecystectomy in 2 groups of 30 patients each, further subdivided into equal subgroups: Subgroup [A] receiving halothane (0.2-0.4%) and subgroup [B] receiving isoflurane (0.2-0.3%): Group (I) patients underwent conventional open surgical cholecystectomy. Group (II) patients were submitted to laparoscopic excision of the gall bladder. Anesthesia was maintained throughout with nitrous oxide in oxygen (1:1) and incremental doses of fentanyl and vecuronium. Peripheral venous blood samples were obtained preoperatively, immediately postoperatively and at 24 hours, then at 5 and 7 days postoperatively. Liver functions (total bilirubin, serum albumin, AST, ALT, -GT and ALP) were assessed.
RESULTS: A statistically significant increase in liver enzymes was reported in Group (I) only after halothane anesthesia and returned to normal within 7 days postoperatively. A similar increase was detected in both subgroups of Group (II) which lasted for 5 postoperative days with isoflurane and 7 days with halothane.
DISCUSSION: Laparoscopic cholecystectomy is a widely accepted alternative to laparotomy because of its limited surgical invasiveness and shorter hospital stay.[1] However, high intra-abdominal pressure over an extended period of time may be associated with detrimental impairment of liver functions. This may be due to disturbances in hepatic perfusion but may also be due to manipulations of the liver and neurohumoral mediated response to surgical stress. Another possible factor may be the ischemic reperfusion injury after deflation. Halothane produces a more sustained increase in liver enzymes because of the larger production of toxic metabolites compared to isoflurane. Persistence in elevated -GT to the 7th postoperative day with halothane may be due to the generalized microsomal enzyme induction. On the other hand, isoflurane facilitates oxygen delivery to the liver by preserving hepatic arterial blood flow.[2]
CONCLUSION:
Laparoscopic cholecystectomy had better be avoided in compromised liver functions and, if necessary, halothane should be substituted by isoflurane.
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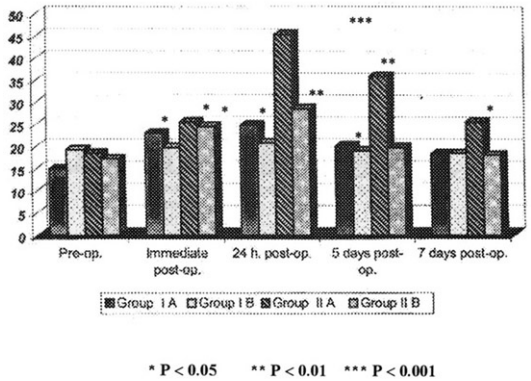

Serum AST levels at different time intervals before and after operations in different groups

S-126

PHARMACOKINETIC SIMULATION EXPLAINS THE MEASURED PROPOFOL CONCENTRATION RISING HIGHER THAN THE PREDICTED VALUE

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INTRODUCTION: It is said that the target-controlled infusion (TCI) pump has not been approved for clinical use in the USA as the FDA has a concern about accuracy of the TCI system because there was a case where the measured blood propofol concentration was about 4-fold higher than the predicted concentration in a patient with deteriorated cardiac function. It is widely known that errors are caused in pharmacokinetic approach such as pharmacokinetic model because of inter-individual variability and intra-individual variability. However, there have been few investigations conducted on the conditions that fit well to pharmacokinetic model, which is based on an assumption that drug is diffused uniformly in compartments. Thus, we conducted an analysis by simulating propofol circulation in the body, and uniform diffusion in the blood (compartment) after administration into the blood vessel, with an aim to examine differences between the measured concentration and blood concentration predicted by the compartment model.
METHODS: Since pharmacokinetics of propofol follow 3-compartment model, change in blood propofol concentration p(t) after a single dose can be expressed by sum of 3 exponential functions. We defined the dose m(t) of propofol at each time point during TCI administration at interval of 1 second through simulation, assuming that the target propofol concentration was 3 g/mL. Because the parameters in dye-dilution technique (DDT) have correlation with a cardiac index, we defined three dye-concentration functions f1(t), f2(t), and f3(t) for three cardiac conditions. With these functions, we analyzed the predicted propofol concentration C_{predit} (t), and propofol concentration in the peripheral tissue $C_{transit}$ (t) by simulation.
RESULTS: In models with normal cardiac output, low cardiac output, and extremely small cardiac output, the maximal blood concentrations appeared around 19 seconds, 23 seconds, and 33 seconds with concentration level 3.6-fold, 4.4-fold, and 5.1-fold as high as the target concentration, respectively. Under all conditions blood propofol concentration showed a sharp decline near to the target concentration after reaching the maximal level, and reached to a plateau at a level higher than the target concentration.
DISCUSSION: The analysis by simulation using findings from the DDT gave us explanation for a large difference between the target blood concentration and measured blood concentration with a basic mechanism that decreased cardiac function leads to prolonged circulation time. In our simulation, the concentration profile of intravenously administered drug was analyzed using dye-dilution curves available from dye dilution method on the basis of several assumptions. Accordingly, there is a possibility that the concentration ratio between the maximal level and concentration after uniform diffusion of the drug is different between dye and propofol, suggesting likely differences between the simulation results and the measured concentration of propofol.

S-127

EFFECT OF AEP MONITORING ON INTRAOPERATIVE DRUG USAGE AND RECOVERY AFTER INPATIENT SURGICAL PROCEDURES: A CLINICAL UTILITY STUDY

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INTRODUCTION: The auditory evoked potential (AEP) monitor has been recently introduced as a more “physiologic” approach to monitoring the central nervous system effects of anesthetic drugs. The AEP monitor provides an EEG-derived index (AAI) in response to an auditory stimulus. This study was designed to determine if the availability of information on the AAI value during surgery would influence the administration of anesthetic and analgesic drugs, and improve the recovery profile after inpatient surgical procedures.
METHODS: 60 consenting inpatients undergoing elective general surgery procedures were randomly assigned to one of two study groups: (1) Standard Practice or (2) AEP Monitored. Although the AEP monitor was connected to all patients, the information on the AAI was only made available during the procedure to anesthesiologists assigned to the AEP Monitored group. All patients received midazolam, 1-2 mg IV, for premedication. Anesthesia was induced with propofol, 1.5-2 mg/kg, and fentanyl, 50-100 µg, followed by variable concentrations of desflurane, 3-6% ET, and intermittent boluses of fentanyl, 50g IV, for maintenance of anesthesia. In the AEP Monitored group, the inspired desflurane concentration was titrated to maintain an AAI value of 15-25. In the Standard Practice group, the inspired desflurane concentration was varied based on standard clinical signs. The recovery times to achieve a fast-track (FT) score >12 and an Aldrete score of 10, as well as PACU stay, were recorded. Data was analized using ANOVA and x^2 with $p<0.05$ considered statistically significant. Patient satisfaction was recorded on a 100-point verbal analog score.
RESULTS: Use of the AEP monitor reduced desflurane consumption by 25% compared to the Standard Practice group ($P<0.01$). In addition, the AEP Monitored group received less intraoperative fentanyl and more rapidly achieved FT eligibility after anesthesia ($P<0.05$). Finally, the time required to achieve an Aldrete PACU discharge score of 10 and the length of recovery room stay were both significantly reduced in the AEP monitored group ($P<0.05$). There was no difference between the two groups in postoperative side effects or complications.
CONCLUSIONS: Use of the AEP monitor during general anesthesia reduced the anesthetic and analgesic requirements, as well as the length of the PACU stay. This clinical utility study suggests that AEP monitoring may be useful in facilitating the recovery process after inpatient surgical procedures.

	STANDARD PRACTICE (n=29)	AEP MONITORED (n=31)
Age (yr)	43±14	44±15
Weight (kg)	110±47	94±50
Surgery time(min)	113±47	103±41
Fentanyl (mcg)	400±158	270±120*
Desflurane (ET%)	4.9±0.8	3.7±0.6*
Extubation (min)	10±6	7±5
FT score>12 (min)	54±32	29±19*
Aldrete score>10 (min)	100±52	60±31*
PACU stay (min)	106±49	78±31*

*P < 0.05 vs Standard Practice group

S-128

IS THE BISPECTRAL INDEX USEFUL IN PREDICTING SEIZURE TIME AND AWAKENING AFTER ELECTROCONVULSIVE THERAPY?

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INTRODUCTION: The EEG bispectral index (BIS) measures the hypnotic component of the anesthetic state and is alleged to be useful in predicting awakening from general anesthesia. This study was designed to evaluate the changes in BIS values during and after electroconvulsive therapy (ECT) under methohexital anesthesia. We hypothesized that the BIS would be useful in predicting ECT-induced seizure times and awakening after ECT.
METHODS: 25 consenting patients with major depressive disorders receiving a total of 100 maintenance ECT treatments participated in this prospective study. Al patients were premedicated with glycopyrrolate, 0.2 mg IV, and anesthesia was induced with methohexital, 0.75-1.25 mg kg^{-1} IV. The EEG-BIS was monitored continuously throughout the ECT procedure and BIS values recorded at specific endpoints including pre-anesthetic (baseline), after induction of anesthesia (pre-ECT), end-ECT (peak), post-ECT (minimum), and upon awakening (eye opening). The durations of motor and EEG seizure activity were correlated with the seizure duration and the maximal increase in the BIS during the ECT procedure.
RESULTS: The baseline BIS was 95±4 in this severely depressed patient population. The pre-ECT BIS value (39±9) correlated with the duration of both motor (r=0.34) and EEG (r=0.38) seizure activity. The peak post-ECT value (63±15), correlated with the duration of the EEG seizure activity (r = 0.39). A positive correlation was also found between the EEG seizure duration and the time to eye opening (r = 0.29). However, the BIS values upon awakening from methohexital anesthesia varied from 29 to 97, and was <60 in 75% of the cases.
CONCLUSIONS: Although the peak increase in the BIS value after ECT correlated with the duration of EEG activity, the BIS values at awakening varied widely among patients. These data suggests that BIS values on awakening following ECT reflects the residual effects of methohexital, as well as post-ictal depression.

	Factors studied	Correlation coefficient	P-value
Baseline BIS	**Age**	-0.25	0.1
Baseline BIS	**Depression Score**	-0.1	0.3
Pre ECT BIS	**Peak Post ECT BIS**	0.4	<0.01
Pre ECT BIS	**Awakening time**	0.5	0.01
Pre ECT BIS	**EEG Seizure**	0.38	<0.01
Pre ECT BIS	**Motor Seizure**	0.34	<0.01
EEG Seizure	**Post ECT peak**	0.39	0.01
EEG Seizure	**Post ECT supres-sion**	-0.05	0.1
EEG Seizure	**Eye opening time**	0.29	<0.01

S-129

DOES CEREBRAL MONITORING FACILITATES RECOVERY AFTER GENERAL ANESTHESIA? A COMPARISON OF AEP AND BIS MONITORING

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INTRODUCTION: The availability of cerebral monitoring has improved the ability of practitioners to titrate anesthetic drugs[1,2]. However, controversy exists regarding the impact of these monitors in facilitating the early recovery process after surgery. This prospective study was designed to evaluate the impact of intraoperative cerebral monitoring using either a bispectral index (BIS™) or auditory evoked potential (AEP) monitor on the time to discharge from the recovery room.
METHODS: 61 inpatients undergoing general surgery procedures using a standardized general anesthetic technique were randomly assigned to one of three monitoring groups: (1) Standard Practices (Control), (2) BIS-guided or (3)AEP-guided. Prior to induction of general anesthesia, both the BIS and AEP monitors were connected to each patient's head. In the standard practices group, the anesthesiologists were not permitted to view the BIS or AAI values during anesthesia. In the BIS-guided group, the volatile anesthetic was titrated to maintain a BIS value in the range of 45-55. In the-AEP guided group, target range was 15-25. The end-tidal desflurane concentration was recorded at 5 min intervals. Recovery times to awakening, extubation and PACU discharge were recorded. In addition, patient satisfaction with anesthesia (0-100) was evaluated at 24 hrs after surgery.
RESULTS: The AEP and BIS guided groups received lower average end-tidal concentrations of desflurane than the Standard Practice group.However there were no significant difference between these two monitoring groups. Although the emergence and extubation times were consistently shorter in the AEP and BIS groups, this difference was not significantly different from the Control group. However, the length of stay in the PACU was significantly shorter in both the AEP and BIS-groups.
CONCLUSIONS: Cerebral monitoring led to a reduced maintenance anesthetic (desflurane) requirement, and a shorter length of stay in the PACU after general surgery.
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	CONTROL (n= 21)	AEP MONITORED (n=20)	BIS MONITORED (n=20)
Age (yr)	49±14	44±14	46±17
Weight (kg)	93±27	91±30	90±21
Fentanyl (g)	378±178	325±133	283±118
Desflurane (ET%)	4.7±0.8	3.5±0.7*	3.7±0.4*
Surgery time (min)	112±47	105±33	107±49
Eye opening(min)	9±6	7±4	6±5
Extubation (min)	13±4	9±5	8±5
PACU stay (min)	113±51	56±20*	63±19*
Patient satisfaction (%)	85	95	96

· * P < 0.05 vs control group

S-130

COMPARISON BETWEEN A-LINE ARX INDEX AND BISPECTRAL INDEX DURING PROPOFOL-FENTANYL-NITROUS OXIDE ANESTHESIA

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INTRODUCTION: Autoregressive model (ARX) with exogenous input of middle-latency auditory evoked potentials (AEP) has been proposed to monitor the depth of hypnosis using an A-line autoregressive index (AAI).[1] The purpose of this study was to compare the changes of AAI and bispectral index (BIS) during propofol-fentanyl-nitrous oxide anesthesia.
METHODS: After informed consent, 40 female, aged 40 to 60, without any complications scheduled for partial mastectomy were divided into AAI and BIS groups of each 20 patients at random. Midazolam 5 mg and atropine 0.5 mg were administered intramuscularly 30 minutes before start of anesthesia. Anesthesia was induced with propofol 2 mg/kg and fentanyl 3 g/kg. After loss of consciousness, laryngeal mask (LMA) #3 was inserted. Anesthesia was maintained with propofol 4 mg/kg/h, fentanyl 1 g/kg (total 4 g/kg), and nitrous oxide 4 L/min in oxygen 2 L/min. Blood pressure, heart rate, and AAI or BIS were monitored before, during and after surgery. AAI was measured by A-line™ AEP monitor (Danmeter A/S, Odense, Denmark) and BIS was measured by A-2000 BIS™ monitor (Aspect Medical Systems, Newtown, USA).
RESULTS: Blood pressure and heart rate decreased significantly by anesthesia induction and returned to the baseline at the end of surgery in both groups without any differences between the two groups. The numbers of AAI and BIS are shown in the table as mean values.

	1	2	3	4	5	6	7	8	9
AAI	72	26	12	18*	14	19*	20	47	78
BIS	89	40	40	39	47	50	57	69	85

1, before anesthesia; 2, loss of consciousness; 3, before LMA insertion; 4, just after LMA insertion; 5, 3 minutes after LMA insertion; 6, start of surgery, incision; 7, end of propofol infusion; 8, respond to verbal contact; 9, extubation. *: $P < 0.05$ vs. the value before LMA insertion (4) or incision (6). The BIS number became > 60 in four cases but no patients showed AAI number > 30 during anesthesia.
DISCUSSION: BIS numbers between 40 and 60 and AAI numbers < 30 are thought to be adequate during general anesthesia. Both AAI and BIS numbers decreased during propofol-fentanyl-nitrous oxide anesthesia. However, four patients showed BIS number > 60 while no patients had AAI number > 30. In addition, AAI number increased in response to LMA insertion and incision, but BIS number did not respond to them. Therefore, AAI number might be more precise than BIS number in propofol-fentanyl-nitrous oxide anesthesia.
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S-131

ADJUSTMENT OF ANESTHESIA DEPTH BY BISPECTRAL INDEX ELONGATED SEIZURE DURATION IN ELECTROCONVULSIVE THERAPY

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INTRODUCTION: In the clinical practice of electroconvulsive therapy (ECT), extremely short seizure and abortive one are considered to be ineffective (1). Since significant correlation between seizure duration and bispectral index (BIS) value immediately before electrical stimulus has been reported (2), adjustment of anesthesia depth by BIS may be effective to obtain a desired seizure length. In the present study, we examined the hypothesis in the subjects who had short seizure length in an ECT trial.
METHODS: ECT was prescribed to 15 patients suffering from endogenous depression. Atropine (0.01 mg/kg) *im* was given as premedication. The BIS electrode was attached to forehead of the patients as instructed by the manufacturer. Single lead electroencephalography (EEG) was recorded on the same monitor. General anesthesia was induced with propofol (1-2 mg/kg). After loss of consciousness, succinylcholine chloride (1 mg/kg) was administered and ventilation was assisted using a face mask and 100% oxygen. The electroshock stimulus was delivered by a trained psychologist using ECT-stimulator. The efficacy of electrical stimulation was determined by tourniquet technique, electromyogram and electroencephalography. Consciousness was assessed by calling patient's name every 30 seconds after the start of spontaneous respiration. When a patient had a short seizure, in the next ECT trial, the patient received electrical stimulus after waiting an elevation in BIS value (+10-20). Intensity of electrical stimulus and anesthesia condition were identical in the two trials.
RESULTS: The patients ranged from 22 to 80 years of age. Intensity of stimulus was 36±15%. No patient could recall ECT procedures, and no complaint was reported after ECT regardless the BIS score prior to electrical shock. All patients had longer seizures when stimulus was delivered after BIS elevation. Seizure duration measured by muscle movement was 36±10 s when stimulus was delivered without waiting and 49±15 s when delivered after waiting . There was significant difference in seizure duration between the two values ($p<0.01$).
DISCUSSION: Although the view that seizure duration is a primary determinant of treatment efficacy is changing, extremely short seizure is still believed to be ineffective. In conclusion, seizure duration has a positive correlation with BIS value immediately before electrical shock. Anesthesists can adjust anesthesia depth by BIS value to obtain a longer seizure.
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S-132

THE AUDITORY EVOKED POTENTIAL AND THE BISPECTRAL INDEX: A COMPARISON STUDY EXAMINING SIGNAL RESPONSES TO INADEQUATE ANESTHESIA

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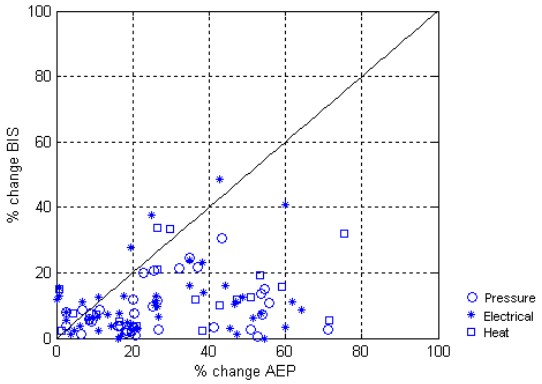
INTRODUCTION: The processed auditory evoked potential (AEP) and the bispectral index scale (BIS) of the electroencephalogram are two mechanistically different technologies used to assess the effect of anesthetics on the central nervous system. The aim of this study was to examine how the AEP and BIS change in response to noxious stimulation when anesthesia is inadequate.
METHODS: After obtaining institutional approval and informed consent, 8 healthy adult male and female volunteers were enrolled. Volunteers received remifentanil (REMI) and sevoflurane (SEVO) at various target concentration pairs (TCPs) spanning the entire clinical spectrum (i.e., REMI from 0-80 ng/ml by computer controlled infusion and SEVO from 0-7%). AEP, BIS and heart rate (HR) were digitally acquired for later analysis. Baseline AEP and BIS values were recorded at each steady state TCP after which a series of experimental pain measures were randomly applied (pressure algometry on the leg to 50 psi, electrical tetany on the leg to 50 milliamps and thermal stimuli to the forearm to 50 C). Inadequate anesthesia was defined as subject movement or a HR increase of 20%. The magnitude of AEP or BIS change in the first minute after inadequate anesthesia was observed was considered the outcome of interest; these maximal AEP and BIS values were extracted from 10 second time averaged AEP and BIS signal from the digital data files. AEP or BIS signal with artifactual corruption (e.g., movement, etc.) was not analyzed. The magnitude of the changes normalized to the maximal AEP and BIS values (in the first minute after stimulation) were plotted for each painful stimulus at all TCPs.
RESULTS: All 8 subjects completed the experiment. Percentage increase in AEP and BIS for each painful stimulus type are shown in the figure for all TCPs. A greater percentage increase in AEP than BIS is seen in most observations.



* The study was supported in Part by Alaris medical systems
* Dr. Talmage Egan is a consultant to Alaris medical Systems

S-133

INCIDENCE OF AWARENESS USING BIS-MONITORING

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INTRODUCTION: Explict recall (ER) of events during relaxant anesthesia is evident in approximately 0.2% of cases when no neurophysiological monitoring is used to guide the conduction of anesthesia (1). The likelihood of severe neurotic sequelae among patients experiencing intraoperative wakefulness with ER is substantial (2). No previous study has assessed if incidence of ER can be reduced by neurophysiological methods. We assessed the incidence of ER when BIS monitoring was used.
METHODS: BIS monitoring was used in 5057 consecutive patients older than 16 years undergoing relaxant anesthesia. The patients were interviewed for ER on three occasions within the first 14 days after anesthesia. The result was compared with historical data on the incidence of ER when no neurophysilological monitoring was used from the same two institutions (1).
RESULTS: 2 cases with ER were identified among 5057patients (0.04%); $p<0.039$ as compared with our historical material. Both identified cases were aware during intubation and were associated with significantly higher BIS values than the patients with no ER. The BIS values in these 2 patients were also higher than the highest value recommended by the manufacturer.
DISCUSSION: The use of BIS in relaxant anesthesia was associated with a significantly reduced incidence of ER as compared with a historical material from the same 2 hospitals. The incidence found is the lowest ever reported in a reasonably large study. The interpretation of this should take the Hawthorne effect and other possible factors due to the non-randomized design into consideration.
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S-134

EVALUATION OF BISPECTRAL INDEX (BIS) IN TRAUMATIZED PATIENTS PRESENTING ACUTELY TO THE OPERATING ROOM

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INTRODUCTION: Trauma is one of the leading causes of morbidity and mortality in young and middle age Americans. Many present to Trauma Centers in need of emergent or urgent surgical intervention. Frequently these patients are told they are going to be "put to sleep" to help control their pain and anxiety. The Bispectral Index is frequently used as an adjunct in the monitoring of patients receiving anesthetic care. The BIS is a dimensionless scale based on EEG, Beta activity and burst suppression. The purpose of this investigation was to evaluate the level of sedation by utilizing the BIS monitor in traumatized patients who presented to the operating room after being anesthetized and intubated in the trauma area.
METHODS: Thirty-two trauma patients who presented to the OR in this IRB exempt study for orthopedic, intra-abdominal, intra-thoracic or vascular procedures, were evaluated using a (BIS) monitor prior to receiving anesthetic agents in the operative suite. Patients who had known neurologic injuries were excluded from the investigation.
RESULTS: The range of the collected data was 51-94. The mean was 74.1 and the median was 76.5. There were 11/32 - 34.4% patients with BIS readings greater than 80. 16/32 - 50% had a reading between 60 and 80 and 5/32 had a reading less than 60.
DISCUSSION: Trauma continues to play a pivotal role in healthcare today. Many are faced with the challenges of adequately managing a patient who has recently been involved in a major trauma. Frequently these traumatized patients are brought to the operating room for emergency operative procedures. These may be orthopedic, vascular or exploratory in nature. Many of these patients are anesthetized in the trauma area for pain management and anxiolysis. In our investigation 11/32 or 34.4% of the patients had a BIS reading greater than 80, indicating that perhaps up to the 1/3 of the patients may not be adequately sedated, and be cognizant of their surroundings. Care must be taken to assure an adequate anesthetic depth prior to a surgical stimulus or be aware of the fact that the patient may have awareness of ongoing events.
We must attempt to identify those subclasses of patients who are at risk of recall of surgical stimulus and treat appropriately. Further investigations are needed to determine if in these particular patient populations higher BIS readings lead to an increase in postoperative recall of preoperative events. The use of suitable protocols for the proper titration of sedation of mechanically ventilated patients and the monitoring of the level of sedation appears indicated. None of the patients in this small study reported recall of preoperative events.

S-135

MONITORING ENTROPY OF THE COMPOSITE EEG AND FEMG SIGNAL DURING GENERAL ANESTHESIA

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INTRODUCTION: In information theory and signal analysis, entropy addresses the irregularity, complexity, or unpredictability characteristics of a signal [1]. With respect to anesthesia, there is ample evidence that electroencephalographic (EEG) signal data contains more "order", i.e. less "irregularity", and lower entropy at higher concentrations of an anesthetic agent, than at lower concentrations [1-3]. Entropy is a scale-invariant measure that is independent of the frequency and amplitude scales of the signal. This suggests that it may better accomodate to the interindividual variability of the EEG rhythms than the conventional techniques.
METHODS: Clinical application of the concept of spectral entropy, to quantify the irregularity of a biopotential signal including EEG and facial electromyographic (FEMG) signals, is investigated. The contribution to spectral entropy from any particular frequency range can be explicitely separated. It is informative to define two entropy indicators: 1) State Entropy is computed over the EEG dominant frequency range alone whereas 2) Response Entropy includes both EEG and FEMG components. Sudden appearance of FEMG activity often indicates that the patient is responding to an external stimulus, such as a intubation. Such a response may result if the level of analgesia is insufficient. FEMG can also provide a rapid indication of impending arousal. As the FEMG signal consists of higher frequencies than the EEG signal, the response time of Response Entropy may be significantly faster (2 s) than the response time of State Entropy (15 s). These entropy parameters were measured for 69 patients undergoing general anesthesia. Anesthetics included propofol, thiopental, sevoflurane, and a combination of midazolam and alfentanil. Patients were considered unconscious when they no longer responded to verbal commands.
RESULTS: Figure 1 shows the probability of consciousness as a function of Response/State Entropy values for 18 patients with sevoflurane induction. The probability curves were calculated using logistic regression analysis. On average, these patients lost consciousness at SE/RE values of 81/86. For the other drug combinations, the corresponding values were 76/81 (propofol), 82/87 (thiopental) and 78/81 (alfentanil + midazolam).
DISCUSSION: The steep probability curve for State Entropy in Fig. 1 indicates that all the patients induced with sevoflurane in this study lost consciousness at approximately the same State Entropy value. This suggests that this parameter well accommodates to interindividual variations. Response Entropy was found informative in providing rapid indication of FEMG reaction to nociceptive stimulation and during emergence from anesthesia.
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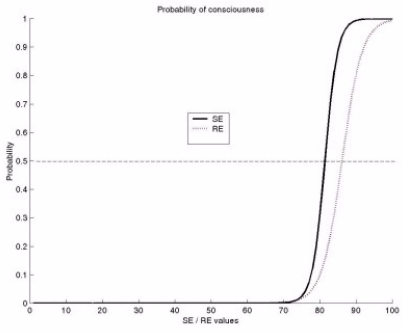

S-136

A PROTOTYPE NEUROMUSCULAR MONITOR USING PHONOMYOGRAPHY

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INTRODUCTION: Recently, phonomyography using small condenser microphones has proven to be a reliable monitor of neuromuscular blockade, applicable at different muscles, such as the larynx (1), corrugator supercilii muscle (2) or adductor pollicis muscle (3). This project was aimed to develop a prototype neuromuscular monitor using phonomyography to simultaneously monitor the evoked response of the corrugator supercilii muscle and the adductor pollicis muscle.
METHODS: The prototype neuromuscular monitor consists of a portable, equipped with a Labview software and data acquisition card. The data acquisition card receives signals from two amplifiers, amplifying the phonomyographic signals of two small condenser microphones placed over the corrugator supercilii muscle and adductor pollicis muscle as described before (2,3). Stimulation of the ulnar and facial nerve is performed using routine nerve stimulators. The project consisted of using Labview software to design a neuromuscular monitor surface displaying evoked signals from the two muscles in real time (after either single-twitch or train-of-four stimulation), digitising the evoked signals in reference to control amplitude defined with supramaximal stimulation for both muscles during induction period before applying the muscle relaxant. Thus a graphical trend of the neuromuscular blockade during surgery should be displayed in percentage of the control signal. A significant part of the project consisted of analysing and diminishing artifact influences due to electric appliances in the OR.
RESULTS: Figure 1 shows the display screen of the prototype. It shows the signals of the two muscles in real time (here TOF stimulation, corrugator supercilii muscle left) and allows the objective determination of signal shape, possible artefacts, signal quality and fade. Train-of-four ratio is automatically detected and digitally displayed. The wide, two bottom screens show T1 signal height in percentage of the control signal height during surgery, signals measured, recorded and displayed according to the stimulation frequency (here every 12 s). The lower graphic shows the typical early onset and recovery of the corrugator supercilii muscle. This two graphical displays of neuromuscular blockade of the two muscles during surgery can be separately printed either for research purposes or clinical documentation. The program is designed in such a way that any signal with an amplitude greater than 150 % of the reference amplitude is automatically erased. Using this design, we could erase electrocautery artefacts in the trend graphics.
CONCLUSION: This prototype allows the simultaneous measurement, recording and display of two phonomyographic signals. It is a first step towards a more detailed and sophisticated neuromuscular monitor for daily practice using phonomyography

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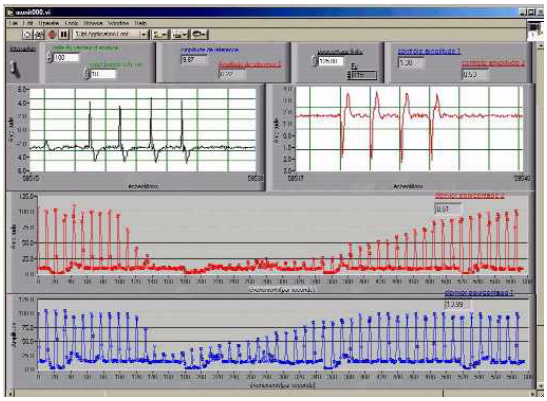

S-137

CORRELATION BETWEEN STROKE VOLUME AND LEFT VENTRICULAR EJECTION TIME IN THE PRONE POSITION USING TRANSESOPHAGEAL ECHO-DOPPLER MONITORING.

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INTRODUCTION: The relationship between stroke volume (SV) and left ventricular ejection time (LVETi) in the prone position has not been examined. In the supine position there appears to be a strong positive clinical correlation between LVETi and SV. [1] LVETi is the time from opening to closure of the aortic valve indexed to the heart rate, and is an indicator of preload. We examined the relationship between SV and LVETi in the prone position after rapid colloid administration using a Transesophageal echo-doppler monitoring device (Hemosonic ®, Arrow International, Reading, PA). [2] This is a non-invasive, real-time monitor of cardiac function allowing the measurement of aortic blood flow, cardiac output, SV, total systemic vascular resistance, and LVETi.
METHOD: Institutional review board approval for this study was obtained. Seven patients undergoing lumbar spinal instrumentation in the prone position were included in this study. Anesthetic management was standardized for all patients. An esophageal echo-doppler was placed in all patients after induction of anesthesia and baseline hemodynamic variables were monitored once the patient was in the prone position. Patients were challenged with repeated 250 ml boluses of colloid over 2.5 min in an effort to increase their SV by 5 - 10% from baseline. Data was recorded from the transesophageal echo-doppler monitor at baseline, prior to each fluid bolus, and at the end of each fluid bolus. Spearman rank correlation coefficients were used to assess the association between SV and LVETi. A $p < 0.05$ was considered significant.
RESULTS: The mean (SD) SV change from before to after the third fluid bolus was -9.5 mL (16.4) with p=0.2. The corresponding mean (SD) LVETi change was -24.7 ms (31.5) with p=0.08. The correlation coefficients between SV and LVETi for all seven patients was s=0.71 (p=0.07). Individual patients showed a strong clinical correlation between SV and LVETi for multiple time points throughout the study (s > 0.5).
DISCUSSION: There was a strong positive clinically significant correlation between SV and LVETi in the prone position for all seven patients. Approximately 50% of change in SV variance was explainable by changes in LVETi. LVETi, an indicator of preload may be a useful parameter in maximizing SV of patients undergoing surgery in the prone position. It is likely that the inability to obtain the conventional threshold of statistical significance even though the magnitude of the correlation was clinically significant is related to the small sample size.
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S-138

EVALUATION OF A CARDIAC OUTPUT MONITOR (NICO) DURING AORTIC ANEURYSM REPAIR

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INTRODUCTION: Following introduction[1] of a CO2 based differential Fick method to measure cardiac output, the non invasive cardiac output (NICO)[2] device (Novametrix Corp.) was introduced and has received clinical acceptance[3] in a range of situations.This study looked at patients undergoing aortic aneurysm repair using the retroperitoneal approach, requiring positioning in the right lateral position. This combination often has significant fluid shifts combined with ventilation-perfusion abnormalities which may present a difficult challenge for this technique.
METHODS: Following induction, an A-line and a S-G catheter were placed. Arterial blood gas values initialized the NICO and updated the NICO every hour. Every 15 min. a thermodilution (TD) cardiac output (CO) was obtained and recorded along with the CO reading of the NICO. For each of the 25 patients a plot of the simultaneous values of the TD and NICO was made. The statistical studies made on this data were correlation, Bland Altman, percentile closeness of fit, and a judgment made for each patient by a group of anesthesiologists as to whether the fit by the NICO compared to the TD was either Excellent, Good, Fair, or Poor.
RESULTS: A total of 323 paired values were obtained. The correlation coefficient between these paired values was 0.61. The Bland -Altman study shows a bias of -0.70 with 95% limits of agreement (-3.1,1.7). The S.D. of the difference was 1.21. The percentage of NICO points lying within 10% of the TD values was 33.7%, and within 20% was 54%. The consensus opinion of the anesthesiologists as to the fit of the NICO compared to the TD on each of the 25 patients was E: 4, G: 7, F: 5, P: 9. Thus, in only 11 of the 25 cases was the NICO considered to be a good to excellent substitute for the TD, and in 14 of 25 cases it was considered to be a poor to fair substitute.
CONCLUSIONS:. The NICO device employs a differential form of the Fick equation, thus making it unique among the methods used to measure CO. There are problems in measuring differential CO2 production, as well as problems in using differential end tidal CO2 as a measure of differential arterial CO2. The cases examined show a remarkable disparity in results. Over half the results were not acceptable for clinical use, while almost half were considered to be good to excellent. The reasons for this disparity are not clear, but it appears that patient habitus and position may cause ventilation-perfusion ratios that are difficult to handle with the present software.
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S-139

NONINVASIVE CARDIAC OUTPUT MONITORING FACILITATES INTRAOPERATIVE FLUID MANAGEMENT FOR MAJOR GYNECOLOGIC ONCOLOGY PROCEDURES

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INTRODUCTION: Perioperative hemodynamic monitoring and fluid management is often challenging in the ovarian cancer patient undergoing hysterectomy and staging laparotomy. The noninvasive transesophageal echo-Doppler device (*HemoSonic™ 100* Arrow International, Reading, PA) allows for easy, real time assessment of cardiac output, stroke volume, left ventricular ejection time$_{corrected}$ ($LVET_c$) and calculated total systemic vascular resistance. This study evaluated the effectiveness of the *HemoSonic*™ as an aid to intraoperative fluid management in this patient population.
METHODS: Following IRB approval 22 patients diagnosed with ovarian cancer and scheduled for hysterectomy and staging laparotomy were randomized to two groups: Group A: (protocol) subjects received 100 cc boluses of hetastarch (*Hextend*™Abbott Laboratories, North Chicago, IL) to maintain stroke volume 10-15% above the baseline obtained 15 minutes after induction of anesthesia. If stroke volume was within normal range but the patient's MAP was below 30% of baseline, obtained in our preoperative clinic, fluid therapy was instituted as in the control group.
Group B: (control) subjects received 100cc boluses of hetastarch when MAP decreased below 30% . Each group received 100 cc boluses of hetastarch for urine output <0.5ml/kg/hr. Blood loss was replaced 1:1 with hetastarch. For Hgb< 7.0 g/dl or < 8.0 g/dl in patients with significant cardiac disease, PRBCs were transfused. Preoperative fluid management, anesthetic technique and postoperative epidural analgesia were standardized in both groups.
RESULTS: Seventeen patients completed the study. Patient demographics, surgical time, fluid intake (crystalloid + colloid), blood loss, episodes of nausea, vomiting, ascites, gas pain, reaccumulation of ascites, abdominal distention or diarrhea were not significantly different between groups. Urine output was significantly greater in Group A: 80cc/hr surgery (24-138)(median, range) vs. Group B: 37 (27-60) cc/hr surgery (P=0.05). Group A: 126 min $LVET_c$> 350ms (78-268) (median, range). Group B: 53 min $LVET_c$ > 350 ms (13-195) (P<0.05)
Patients postoperative length of stay for Group A: 2.91 (1.25-7.06) days (median, range)vs. Group B: 3.98 (2.29-8.98) days (P=0.21).
DISCUSSION: This study has demonstrated that intraoperative fluid management and optimization of left ventricular performance in major gynecologic oncology surgery is facilitated by use of the *HemoSonic*™. LVETc, a quantitative assessment of left ventricular performance, was above 350ms (reference range: 330-360ms)[1] more often in Group A. This may explain the greater intraoperative urine output in Group A despite having similar fluid intake and blood loss as in Group B. After accounting for initiation of chemotherapy, Group A's duration postoperative stay was one day shorter than Group B. This is clinically significant and may impact on cost of care. Another study involving intraoperative fluid expansion guided by esophageal Doppler reported a mean reduction in hospital stay by 2 days.[2]
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S-140

TRUCCOMS--AN ACCURATE SYSTEM FOR CARDIAC OUTPUT MEASUREMENT?

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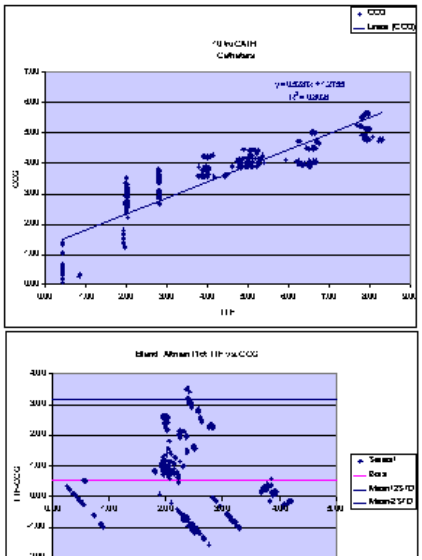
A new method for continuous cardiac output (CCO) determination based upon heat transfer technology was recently introduced (truCCOMS, AorTech International, Plc, Scotland). The method utilizes a heated coil placed on a pulmonary artery catheter. The heat transfer method relies on maintaining a constant temperature difference between the heated coil and the blood. The power necessary to maintain this temperature difference is proportional to the blood flow.
METHODS: We investigated the accuracy of the truCCOMS using a Donovan Mock Circulation Tank with a CardioWest Artificial Heart providing pulsatile flow. A glycerol solution at 37 C with heat capacity and viscosity similar to blood was used in the tank. The flow in the pulmonary artery of the mock circulation was measured with a transit time ultrasonic flow probe (TTF) (Transonic) and compared to flow measurements obtained by truCCOMS. Fluid flows from 1 - 8 L/min were utilized to test 10 heat transfer pulmonary artery catheters.
RESULTS: Thr relationship between CCO and TTF was examined using bias and precision, linear regression and Pearson correlation coefficient. The correlation was r^2= .803 (Fig 1 top) and bias = 0.53 L/ min with a precision of +- 1.33 L/min (Fig 1 bottom).
DISCUSSION: The lack of precision or high degree of scatter in Figure 1 can be explained by the dependence of heat transfer technology on predictable turbulent flow for accuarate measurement. Furthermore, heat transfer technology is in general best applied to constant flow. The flow pattern of the pulsatile flow in the pulmonary artery is dependent on geometry of the vessel as well as speed of contraction and geometry of the pulmonic valve. Despite the constant geometry and diameter of the pulmonary artery and pulmonic valve in the model, large variations were found in the truCCOMS CCO determinations.

CONCLUSION: In the clinical situation there will be wide variation in the conditions encountered by the heat transfer device (heated coil) in the pulmonary artery. The change in the artificial heart stroke volume, especially at low stroke volumes with short systolic time, models well the clinical response to hypovolemia. The resultant turbulent conditions may lead to overestimation of flow by the heat transfer technology. Hence, clinically unacceptable values may result in patients with hypovolemia and tachycardia. Further refinements of this technology is needed prior to its use in clinical care.



S-141

SOURCES OF ERROR IN NON-INVASIVE PULMONARY BLOOD FLOW MEASUREMENTS BY PARTIAL RE-BREATHING: A COMPUTER MODEL STUDY

AUTHORS: **J. S. Yem**, Y. Tang, M. J. Turner, B. A. Baker
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INTRODUCTION: Partial re-breathing is a non-invasive method for measuring pulmonary blood flow (PBF). The technique requires the subject to breathe through an altered dead-space and uses a differential form of the Fick mass balance equation to calculate PBF from end-tidal airway CO_2 partial pressures ($P_{et}CO_2$) and airway CO_2 flux. [1] This study examines the systematic errors produced by the partial re-breathing technique utilising a comprehensive mathematical model of the cardio-respiratory system of a healthy 70 kg adult male.
METHODS: The model simulates tidal breathing through a branched respiratory tree [2] and incorporates the effects on CO_2 dynamics of lung tissue mass [3], vascular transport delays [4], multiple body compartments [5] and realistic blood-gas dissociation curves [6]. The model includes an additional variable dead-space, that can be switched in and out to simulate the re-breathing process. Four studies were performed to study: 1) errors produced under standard conditions, 2) effects of re-circulation, 3) effects of alveolar–proximal airway differences and 4) effects of rebreathing time.
RESULTS: Systematic errors are < 10% when the simulated PBF is between 3 and 6 l/min. (Fig 1) At 2 l/min PBF is overestimated by 35%. At 14 l/min PBF is underestimated by 40%. At PBF > 6 l/min re-circulation causes 60% of the systematic error, alveolar – proximal airway differences 20% and alveolar – arterial differences 20%. The standard re-breathing time of 50 s is shown to be excessive for PBF > 6 l/min. At PBF <3/min errors are caused by inadequate re-breathing time and alveolar-arterial gradients.
DISCUSSION: Simulated measurements in which we used constant mixed venous PCO_2 and PO_2 suggest that increases in mixed venous PCO_2 during re-breathing cause approximately 60% of the total systematic error in measured PBF at high cardiac outputs. $P_{et}CO_2$ differs from mean P_ACO_2, even in an ideal, single compartment homogenous lung, due to the time delay and mixing caused by the gas movement in the airways during tidal expiration. The alveolar-capillary PCO_2 gradient increases with cardiac output due to decreased capillary residence times, hence creating a systematic error in PBF that increases with PBF. Re-breathing times that at low PBF's are inadequate to achieve quasi-equilibrium in the alveolar compartment, are too long at high PBF's causing errors due to re-circulation. Our simulations suggest that errors can be reduced by using a variable re-breathing time, which should be increased at low PBF so that quasi-equilibrium in the alveoli can be achieved, and decreased at high PBF to reduce the effects of re-circulation.

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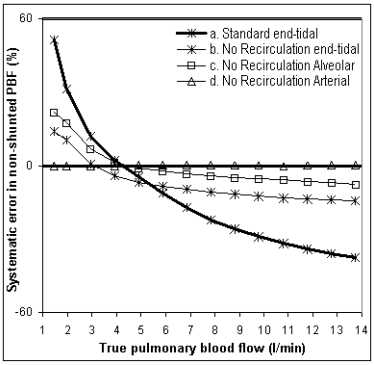

S-142

GAS COMPOSITION OF PNEUMOPERITONEUM DURING LAPAROSCOPIC GYNECOLOGIC PROCEDURES

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AFFILIATION: [1]CHU, Strasbourg, France, [2]LSMBO, Strasbourg, France.

INTRODUCTION: During laparoscopic surgery, the carbon dioxide (CO_2) insufflated into the peritoneal cavity constitutes a diffusion space for the nitrous oxide (N_2O) used for anesthetic maintenance. This study was designed to confirm and to quantify, in a clinical setting, this phenomenon previously reported in an experimental environment [1].
METHODS: With IRB approval and informed consent**,** ASA I/II adults scheduled for laparoscopic gynecologic procedures under general anesthesia (propofol TCI, sufentanil, rocuronium, 66% N_2O in O_2) were enrolled. Minute ventilation was adjusted to keep $P_{ET}CO_2$ between 34 and 36 mmHg. The abdominal cavity was insufflated to 14 mmHg, and leaks were compensated for, by CO_2 from the insufflator. Some of the procedures included a transvaginal operative approach, with exsufflated pneumoperitoneum (PNOP). Peritoneal gas samples (10 mL) were drawn every 2 min, starting 5 minutes after PNOP insufflation, until the end of the procedure, and analyzed for air, CO_2, and N_2O fractions (F_{PNOP}) (gas chromatograph P200; MTI Analytical Instrument, CA, USA).
RESULTS: Forty patients were included and one excluded for incomplete data. Eleven procedures involved a transvaginal step. The volume of CO_2 needed to establish the PNOP was 4.4 ± 2.1 L and the CO_2 flow necessary to maintain the PNOP pressure was 2.0 ± 1.5 L/ min. The duration of the insufflation (I) and exsufflation (E) / was 56.3 ± 21.2 and 32.9 ± 13.6 min. respectively. The highest peritoneal N_2O and air fractions recorded during the I and E periods are presented in table 1. No correlation was found between the leak flow, the I and E times and the highest observed values for N_2O fraction.

PNOP	highest $F_{PNOP}N_2O$ (%) median (min - max)	highest F_{PNOP} air (%) median (min - max)
Insufflated n = 39	1.7 (0.4 – 4.8)	Traces only
Exsufflated n = 11	5.6 (0.7 – 14.8) *	78.2 (18.4 – 95.2)

Table 1 *p<0,01, I vs E; Wilcoxon*

DISCUSSION: The results show a significant difference in $F_{PNOP}N_2O$ during insufflation and after exsufflation (when the laparoscopic procedure included a period of exsufflation). During insufflation, $F_{PNOP}N_2O$ remains low, because of the PNOP renewal induced by the surgical leaks. Conversely, after exsufflation the residual PNOP is no longer renewed. This allows for N_2O to accumulate into this residual PNOP (maximum observed $F_{PNOP}N_2O$: 14.8%), and for air to enter through the perivaginal peritoneal incision (maximum F_{PNOP} air: 95.2%). Despite usual low N_2O and air levels in the PNOP, higher values can be observed at times during surgery in humans. Clinical implications related to these findings must be further investigated, with a special focus on the potential risk associated with gas embolism.
REFERENCES:
1.Anesth Analg. 2000; 90:951-3

S-143

THE EFFECTS OF PATIENT POSITIONING ON RESPIRATORY MECHANICS ON SEVERE COPD PATIENTS DURING PNEUMOPERITONEUM

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INTRODUCTION: Chronic obstructive pulmonary disease (COPD) is generalised airways obstruction, particularly of small airways, associated with varying combination of chronic bronchitis, asthma and emphysema (1). In this study, the effects of patient positioning on respiratory mechanics are compared on COPD patients during pneumoperitoneum.
METHODS: After ethics committee approval and written informed consent from patients, 20 ASA III patients included in this study. All patients were diagnosed as having severe COPD according to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria (2). The standard anesthesia and monitorization has been used. During the operation, ventilation was controlled artificially. Tidal volume and ventilator frequency were kept constant throughout the operation. Gas insufflation was performed 2 L min-1 and the intraabdominal pressure was kept constant at 12 mmHg. VenTrak (novometrix,USA) respiratory mechanic device was used for measuring respiratory mechanics. The resistance of airway (Raw), the dynamic compliance (Cdyn), and the peak inspiratory pressure (PIP) were measured. Measurement was performed in four periods: after anaesthesia induction (induction), 5 minutes after insufflation of the peritoneum (pneuomoperitoneum), at 25° Fowler position (fowler),and 5 minutes after desufflation of the peritoneum (desufflation). Statistical analysis; Values are expressed as mean ± standard deviation. Statistical analysis was carried out using repeated measures ANOVA with Tukey Kramer post test to evaluate the differences between the established study points. A p value <0.05 was considered statistically significant.
RESULTS: During pneumoperitoneum and fowler position, respiratory compliance decreased, while respiratory resistance and peak inspiratory pressure increased (table 1). During the fowler position the respiratory compliance increased significantly again although it remained well below the post induction value. At the same time peak inspiratory pressure and respiratory resistance decreased.
DISCUSSION: It is suggested that fowler position has no significant advantages patients with COPD during pneumoperitoneum.
REFERENCES:
1)The Merck Manual, Berkow R (ed) Merck co. inc Rahway, NJ1987:636.
2) Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for chronic obstructive pulmonary disease. Curr Opin Pulm Med. 2002; 8: 81-86.

Table I: Respiratory mechanic values (mean±standard deviation)

Periods	Induction	Pneumoperitoneu	Fowler	Desufflation
Cdyn (mL cm H_2O-1)	41±6	27±4	28±4	37±7
Raw (cm H_2O L-1 sn-1)	17±4	22±4	21±4	19±3
PIP (mmHg)	21±5	25±4	24±4	21±4

S-144

VAGAL NERVE BLOCKADE INCREASES DEAD SPACE VENTILATION IN HUMAN

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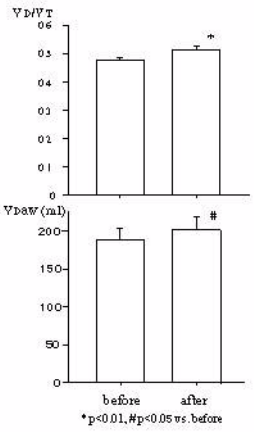
INTRODUCTION: Vagal nerve outflow is linked to respiration. Increased vagal outflow may result in tracheal and bronchial constriction and reduce anatomical dead space. The increase in vagal outflow in synchrony with expiration accentuates sinus arrhythmia which may improve the matching of pulmonary blood flow to lung volume during each respiratory cycle. We made an assumption that blocking vagal nerve activity with atropine in human would increase both anatomical dead space and alveolar dead space.
METHODS: 5 volunteers breathed at a given tidal volume and respiratory frequency (15/min) in synchrony with a metronome signal. The mean amplitude of the high-frequency component of R-R interval variation (RRIHF) from ECG signal was used as an index of cardiac vagal tone. Anatomical dead space (VDaw) , alveolar dead space (VDalv), physiological dead space ventilation/tidal volume (VD/VT) and pulmonary capillary blood flow (PCBF) were measured by NICOTM (Novametrix Inc.) before and after atropine administration (0.02 mg/kg).
RESULTS: Atropine increased heart rate and decreased the RRIHF. Atropin increased VDaw and VD/VT significantly ($p<0.05$) (Figure), but VDalv did not change significantly. PCBF decreased (~15%) after atropine administration, but the change did not reach statistical significance.
DISCUSSION: Vagal nerve blockade increased VDaw and VD/VT. The decrease in PCBF suggests that pulmonary blood flow contributing to CO2 excretion decreased as a result of the abolition of the vagally-mediated respiratory modulations in pulmonary blood flow, weakening the matching of pulmonary blood flow to lung volume during each respiratory cycle.
CONCLUSION: Blocking vagal nerve activity with atropine in human increased anatomical dead space. Vagal nerve activity may improve the efficiency of ventilation at rest in human, decreasing physiological dead space, at least anatomical dead space.



S-145

FLOW RESISTANCE OF THE BICORE VARFLEX FLOW TRANSDUCER

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INTRODUCTION: Bicore CP-100 monitor is using in many clinical studies of mechanical ventilation. VarFlex Bicore flow transducer accuracy has been already demonstrated. However there are not published data on transducer flow resistance. We measured inspiratory and expiratory resistance of this transducer at different levels of gas flow (GF).
METHODS: A constant GF delivered from a constant flow generator (precalibrated against a bell spirometer) was adjusted to 0.25, 0.5 and 1.0 L/sec. GF passed through a VarFlex flowmeter and proximal pressure was measured at each GF rate using a precalibrated Copal P-3000 (Japan) pressure transducer. Pressure drop was measured in both inspiratory and expiratory senses. GF rate delivered and proximal pressure were measured in quintuplicate. Resistance was derived from P/V× ratio.
RESULTS: Mean ± SD values obtained are shown in the table. Abreviations: Adjusted inspiratory flow, IFA (L/sec); Measured inspiratory flow, IFM (L/sec); Inspiratory proximal pressure, IPP (cmH_2O); Inspiratory resistance, IR (cmH_2O/L/sec); Adjusted expiratory flow, EFA (L/sec); Measured expiratory flow, EFM (L/sec); Expiratory proximal pressure, EPP (cmH_2O); Expiratory resistance, ER (cmH_2O/L/sec).
DISCUSSION: VarFlex measured resistance is almost constant for GF rate between 0.25 to 0.5 L/sec, but is near double for 1 L/sec GF. Resistance values are not significantly different ($p>0.05$) for both senses (inspiratory-expiratory). Resistance values for low to mean GF are almost negligible for clinical measurements. Nevertheless, for clinical investigations, resistance to high flows are to be considered because they reach 50% of normal airway resistance.

Table of results (see text)

IFA	IFM	IPP	IR	EFA	EFM	EPP	ER
0.25	0.3 ± 5E-3	0.7 ± 0.02	2.3 ± 0.07	**0.25**	0.24 ± 4E-3	0.7 ± 0.03	2.8 ± 0.16
0.50	0.6 ± 9E-3	1.3 ± 0.04	2.3 ± 0.09	**0.50**	0.3 ± 0.01	1.2 ± 0.05	2.4 ± 0.11
1.00	1.1 ± 5E-3	4.2 ± 0.04	3.9 ± 0.05	**1.00**	1.00 ± 5E-3	4.6 ± 0.04	4.6 ± 0.06

S-146

THE EFFECTS OF PNEUMOPERITONEUM AND POSITION CHANGES ON INTRAOCULAR PRESSURE

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INTRODUCTION: During laparoscopy increased intraperitoneal pressure could cause physiological changes that affect intra ocular pressure (IOP) (1). The aim of our study is to investigate the changes in IOP and its relationship with peak inspiratory pressure (PIP) and position changes during pneumoperitonium.
METHODS: ASA I-II, 50 patients (aged 42.46±12.8 years) undergoing laparoscopic cholecystectomy were included to our study after approval from the ethics committee of our institute. Anesthesia was induced with propofol 2 mg/kg and fentanyl 2 mgr/kg . All patients were intubated after receiving atracurium 0.5 mg/kg and ventilated mechanically with frequence:12/dk and tidal volum:8 ml kg–1. Ventilation parameters were kept constant throughout the study. Anaesthesia was maintained with isoflurane %1 vol and intraperitoneal insuflation of CO2 was maintained at 12 mmHg. Mean arterial pressure (MAP), heart rate (HR), IOP (measured with shiötz tonometer, Germany), peak inspiratory PIP and EtCO2 values were recorded: Before induction of anaesthesia (1), before pneumoperitoneum (2), in the horizontal position after the pneumoperitoneum (3), with a 150 head down tilt (4), with a 150 head up position(5) and just before the extubation(6). Data were analysed using repeated measures ANOVA with Tukey Kramer test. P value smaller than <0.05 were considered statistically significant.
RESULTS: IOP, MAP and HR were decreased with the effect of anaesthesia. While PIP, EtCO2 and MAP values showed a continual increase with establishment of pneumoperitoneum, an increase in IOP was only associated with the head down position and never exceeded preinduction levels (table 1).
DISCUSSION: Although IOP is influenced minimally from the pneumoperitoneum in deep anaesthesia, a special care should be taken with head down position.

Reference:
1) Effect of changes in PCO2 and body position on intraocular pressure during general anaesthesia. Acta Ophthalmologica 1981;59:465-75.

Periods	1	2	3	4	5	6
MAP(mmHg)	97.56	84.52	111.2	112	112	95.18
HR (beat/min)	82.96	79.1	77.12	78.76	78.26	72.56
IOP(mmHg)	16.41	14.11	14.67	16.75	14.78	14.42
PIP(mmHg)		19.38	24.01	25.48	23.3	19.82
EtCO2(mmHg)		26.74	29.26	30.62	30.9	28.22

S-147

DOES NASAL CAPNOGRAPHY IMPROVE PATIENT SAFETY DURING MAC?

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INTRODUCTION: Detection of apnea or airway obstruction is essential when potent sedatives are employed. Pulse oximetry, routinely used during monitored anesthesia care (MAC), is a reliable estimate of arterial blood oxygenation; however, detection of apnea or airway obstruction can be delayed, especially if patients are breathing supplemental oxygen.[1] Reliability of nasal capnography to monitor apnea and airway obstruction has not been examined in MAC/sedated patients breathing with and without supplemental oxygen.
METHODS: Patients scheduled to undergo procedures with monitored anesthesia care/sedation were studied after signing an IRB approved consent form. A cannula designed to administer nasal oxygen and sample both nasal and oral carbon dioxide (Smart CapnoLine™O_2, Oridion) was appropriately positioned to measure $P_{ET}CO_2$ with a handheld capnometer (NPB-70, Nellcor). Transthoracic impedance monitoring (970S, Respironics) was used to measure respiratory rate. Anesthesia provider had discretion regarding sedation regimen and employed monitors according to ASA practice guidelines for MAC, but was blinded to capnography and impedance data. Oxygen flow through nasal cannula was randomized at 0, 2, 4, and 6 L/min for 3min at each flow rate trial, with a repeat of randomized sequence every 12min. Data were collected at baseline, while patients breathed room air before sedation, and end of each trial until MAC was discontinued or apnea occurred. Apnea or airway obstruction for 20s, detected using transthoracic impedance monitoring, triggered an event. If apnea was undetected by routine monitoring, anesthesia provider was notified and patient was asked to breathe. If capnography did not detect apnea coincident with impedance monitor, position and patency of cannula and capnometer were checked. Data were summarized as percentage or mean±SD. Continuous data were compared with RM-ANOVA. Logistic regression analysis was used to examine potential moderators of apnea.
RESULTS: Ten (26%) of 39 patients experienced apnea, which were reliably detected by capnography. In only one case did SpO_2 decrease below 90%. Average SpO_2 of patients during apnea was 92±6%. There were no changes in variables reflecting cardiovascular function during apnea. Anesthesia provider detected no episodes of apnea. Mean time to apnea was 15±14min after onset of sedation. Variables reflecting cardiovascular function were statistically equivalent throughout study (Table: *P<0.05 v. Baseline; $^{+}$P<.05 v. 0 L/min). Oxygenation and $P_{ET}CO_2$ varied with oxygen flow rate. No independent variables predicted apnea.
DISCUSSION: Currently, capnography is not a mandatory ASA standard monitor for MAC procedures. This pilot study discovered apnea of at least 20s is relatively common during MAC, which was undetected with routine monitoring. By design, we only studied apnea episodes lasting 20s. Unrecognized episodes of much greater duration can occur without capnography, resulting in patient compromise. Technological improvements in measurement of end-tidal CO_2 may be important in improving safety in patients undergoing sedation.
REFERENCES:
1. *Anesth Analg* 1999;88:S39.

Variables	Baseline	Supplemental O_2 Flow Rate (L / min)			
		0	2	4	6
Episodes of Apnea	NA	2	4	3	1
SpO_2 (%)	97±2	97±2	98±2*	99±2*	99±3*$^{+}$
$PetCO_2$ (mmHg)	42±10	45±10	43±12	38±13	36±14*
Respiratory Rate (/min)	19±4	16±5	19±6	17±5	16±6
Heart Rate (/min)	77±10	78±13	78±15	77±12	77±13
Mean Arterial Pressure (mmHg)	95±24	96±16	96±20	96±17	97±16

S-148

OCCUPATIONAL EXPOSURE TO SEVOFLURANE: ASSESSMENT IN EXHALED BREATH

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INTRODUCTION: Evidence on potential health hazards arising from exposure to volatile anesthetics remains controversial. National public health authorities have implemented threshold values to minimise occupational exposure (1). Exposure may, in principle, be supervised by monitoring of ambient air or, alternatively, *in vivo* measurements (2). No investigations into volatile anesthetic kinetics in exhaled air of occupationally exposed persons have been conducted.
METHODS: Proton Transfer Reaction-Mass Spectrometry (PTR-MS) was employed to screen the breath of 10 OR staff members before OR duty, 0, 1, 2, and 3 hours after duty, and before commencing duty on the consecutive day. 15 persons not exposed to waste anesthetic gases were enrolled as controls.
RESULTS: Staff members exhibited significantly raised sevoflurane levels in exhaled air after duty, featuring a mean of 0.96 parts per billion (ppbv) as compared to baseline values of 0.23 ppbv ($p<0.05$). At all times, OR staff had exhaled sevoflurane levels greater than those of control persons ($p < 0.001$). Patterns of sevoflurane decay in exhaled air were depicted.
DISCUSSION: Using Proton Transfer Reaction-Mass Spectrometry, sevoflurane concentration patterns in exhaled air of operating room staff could be demonstrated. Exhaled air analysis may prove useful in short-term monitoring of occupational exposure and the excretion of volatile anesthetics.
REFERENCES
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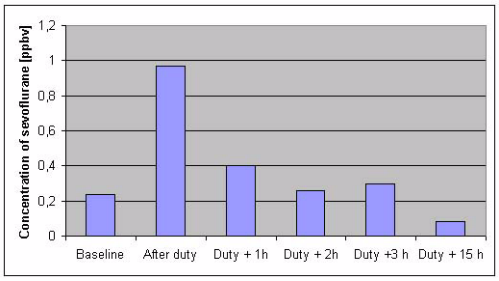
(2) Biomonitoring of exposure to nitrous oxide, sevoflurane, isoflurane and halothane by automated GC/MS headspace urinalysis. Int Arch Occup Environ Health 2001; 74: 541-548



S-149

THE COMPARISON OF DIFFERENT CALIBRATION METHODS FOR PNEUMOTACHOGRAPH

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INTRODUCTION: The pneumotachograph generates differential pressure approximately proportional to the flow and viscosity of the gas. As the viscosity varies with the gas composition, temperature, and humidity, flow-to-pressure conversion of a PT depends on all these factors. This report describes a new method for determining polynomial calibration curves from a number of syringe strokes and compares this new method with the conductance array method[1] of calibration.
METHODS: The experimental apparatus includes a 3-litre precision syringe, a screen pneumotachograph, a differential pressure transducer, a voltage carrier demodulator, a 6th order linear phase low pass filter, and a pressure transducer. With each syringe stroke, the differential pressure signals were recorded through a 12-bit analog to digital converter at the rate of 325Hz. The calibration and validation procedure consisted of 50 calibration and 70 validation strokes respectively. The volume of each stroke was evaluated by numerical integration. The Matlab optimization toolbox was used to obtain a parameter set that minimized volume errors for each polynomial. The conductance values were calculated using a Yeh's procedure[1]. Starting from a constant conductance for each stroke, the conductance values were updated using a weighted-averaging technique. The volume errors for the same set of calibration strokes and validation stokes were calculated using those conductance values and polynomial parameters.
RESULTS: Differences between conductance, linear, 2nd and 3rd order polynomial calibration curves and linear curve are plotted against differential pressure in Fig 1. When the coefficients are derived from calibration strokes and apply to the same set of strokes, the differences of the mean volume errors of the four methods are not significant, but variance was bigger for the linear group ($p<0.05$). When a separate set of 70 validation syringe strokes were used to assess the calibration curves, the volume errors were the smallest for 2nd and 3rd order polynomial compared to linear and conductance methods ($p<0.05$). For the 2nd and 3rd order polynomial methods the volumes are as accurate with 10 calibration strokes as with 50 calibration strokes, with average volume errors from 0.0000006% to 0.00032% and from 0.000069% to –0.0000349%, respectively in the calibration groups and from 0.009671% to 0.0016565% and from 0.01436% to 0.001014%, respectively in the validation groups.
DISCUSSION: Our study shows that the second and third order polynomial methods produce the best results for the calibration of a screen pneumotachograph, with a volume error as low as 0.009671%. Using 10 calibration strokes, we achieved similar accuracy as 50 strokes with second and third order polynomial methods. Second and third order polynomial methods are more accurate and efficient than either conductance or linear regression methods for the calibration of pneumotachograph.
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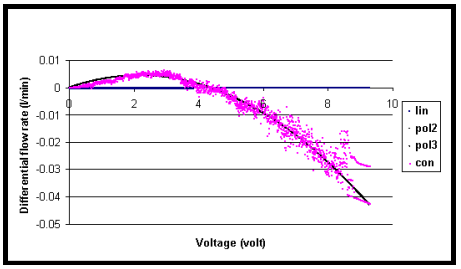

S-150

COMPARING ECGS GENERATED FROM A NOVEL STERNAL DEVICE TO TRACINGS PRODUCED BY THE BACKPAD ECG AND A STANDARD THREE LEAD ECG

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INTRODUCTION: When placing electrodes to generate an electrocardiogram (ECG) recording, Einthoven's triangle is typically thought of as a large area over the chest wall. There is no evidence to suggest shrinking the triangle to a region just over the heart itself would compromise the quality of the ECG tracings. Such a reduction would aid wire placement and ECG attachment using a single ECG pad (sternal pad). To assess the viability of this approach, we designed a sternal ECG pad and compared ECG tracings generated by a standard electrode setup and to those produced by the Backpad ECG, a single peel-off ECG pad placed on the back.
METHODS: The sternal ECG pad was designed by the PI and produced by ConMed® corporation of Utica, NY that also designed the Backpad ECG pad. Our pad consists of three leads positioned one inch apart forming an equilateral triangle. All three leads are contained in a small pad with a single peel-off sticker. This sternal ECG allows for easy placement and simplifies set-up, removal, monitoring, and re-attachment. After IRB approval, written consent was obtained from ASA I and II patients presenting for routine surgical procedures. After induction of anesthesia, standard, Backpad, and sternal ECG tracings were recorded successively. Each ECG tracing was read by three anesthesiologists unaware of the device used to generate the recording. The strips were evaluated for rate, rhythm, p wave, QRS, and t wave (10 patients). A weighted scale was developed for each of the five ECG components. Rate and rhythm were given a weight of 1, and .95 respectively. The QRS was weighted .7, p-wave .5, and t wave .2.
RESULTS: We describe the results of our pilot project. The means and standard deviations for the weighted score are: sternal ECG 9.2 (1.2), Back-pad 9.8 (0.74), and standard ECG 10 (0.16). We consider a score of 7.5 or less to be clinically unacceptable which would occur if one rater out of three were unable to read the rate, rhythm, and QRS (7.4) or none of the raters could read the rate, rhythm, or QRS on a single patient (2.1). (note: the sternal ECG received a score of 6.75 in one patient).
DISCUSSION: As Einthoven's triangle is traditionally thought of as a large triangle over the chest wall, this study suggests that shrinking Einthoven's triangle may have practical applications in anesthesiology, such as using a sternal ECG. The descriptive statistics suggest the sternal ECG and Backpad, while they simplify use, do not appear to compromise the quality of the ECG tracing. Continued investigation is warranted to increase the power of the study and determine if the sternal ECG pad can pick up evidence of myocardial ischemia or potential dysrrhythmias.

Total Affirmative Responses (3 evaluators rate 3 ECG methods on 10 patients)

(n=30)	QRS	Rate	Rhythm
1-Standard ECG	30/30	30/30	30/30
2-Backpad	30/30	30/30	29/30
3-Sternal ECG	30/30	29/30	28/30

S-151

RELIABILITY FOR ASSESSMENT OF HEPATIC FUNCTION USING ICG PULSE DYE DENSITOMETRY DURING HEPATIC TRANSPLANTATION

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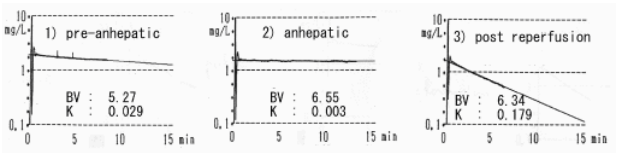
The Indocyanine green (ICG) elimination test is a reliable indicator for the liver function. Pulse dye densitometry (PDD) is based on the principal of pulse spectrophotometry and can measure the blood concentration of ICG continuously after its administration. The PDD can provide the measurement of blood volume and cardiac output as well as the ICG elimination rate. Then the effective hepatic blood flow is simultaneously estimated by the values of blood volume and ICG elimination rate constant (ICG_K). Therefore the measurements of ICG_K could be a simple, noninvasive and reliable method to monitor the liver function during hepatic transplant (figure). However the reliability for measurement of the PDD in the patient with the severe liver dysfunction has not been established. In this study, we simulated the effects of bilirubin and residual ICG on the values of ICG and ICG_K calculated by the PDD using the computer.
METHODS: (1) The ICG concentrations (12: the ratio of optical densities) corrected by bilirubin values in measurement of the PDD can be expressed by the following equation based on the Lambert-Beer's law and Schuster's: 12 = [{(Eh1+Ed1Cd/Hb+Eb1Bil/Hb)(Eh1+Ed1Cd/Hb+Eb1Bil/Hb+F)} - EX1] / [{(Eh2+Eb2Bil/Hb)(Eh2+Eb2Bil/Hb+F)} - EX2], where Eb is absorption coefficient of hemoglobin, Ed is absorption coefficient of ICG, Hb is concentration of hemoglobin, Cd is concentration of ICG, F is scattering coefficient, Ex is tissue constant, suffix1 is 805nm, suffix2 is 940nm, Eb is absorption coefficient of bilirubin, and Bil is concentration of bilirubin. Using this equation the effects of bilirubin in the range from 0 to 30 mg/dl on ICG concentrations were simulated at constant Hb level(14g/dl Hb). (2) The blood concentration time course of ICG were fitted to the following equation based on one-compartment model: $Cd(t) = \{Cdr + Cd(0)\} \cdot e^{-Kt}$, where k is the elimination constant, Cd (t) and Cd (0) are the blood concentration of ICG at time t and 0, and Cdr is the residual ICG concentration at time 0. The effects of residual ICG (1- 20 % of the initial concentration) on the K values (0.05-0.2) were simulated. All simulations were performed
RESULTS: (1) The ICG concentrations measured by PDD were 5.2, 3.6 and 11.8% at 10, 20 and 30 mg/dL of bilirubin, respectively, lower than those in the absence of bilirubin. (2) In the range of 0.05 and 0.2 on K, the error for K was less than 0.02 when more than 30min interval for measurement is allowed.
CONCLUSION: Since K value calculated from the elimination curve is little affected by high bilirubin concentration, PDD is reliable monitor for ICG_K in severe hepatic dysfunction.



S-152

ACCURACY OF NEEDLELESS SYSTEMS IN INTRAVENOUS ADMINISTRATION OF SMALL VOLUME DRUGS TO INFANTS AND CHILDREN

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INTRODUCTION: Health care workers sustain 600,000 to one million needle-sticks per year, resulting in at least 1,000 new cases of HIV, hepatitis C, or hepatitis B. More than 80% of needlestick injuries can be prevented through the use of safe devices. These include the use of stopcocks or valved injection ports (e.g. the Clave or SmartSite systems) for IV drug injections. Although the internal dead space of these devices is small, it can result in major inaccuracies when small volumes of drugs are injected; as typically happens in infants and small children. This study compared the accuracy of two needleless systems against the "gold standard" of a needle system when a small volume of IV drug is injected.
METHODS: A simulated clinical situation was created by injecting five different volumes of a standard 50% dextrose solution (0.1, 0.25, 0.5, 1 and 3 ml) into a running IV line delivering a measured 100 ml volume of distilled water into a measuring cup. The injections were performed using a 23-gauge needle into the side port of the IV tubing, into a stopcock, and into a valved needleless side port (Clave). All injections were again repeated with the injection site flushed after drug administration with a 1-ml volume of water. The difference between the measured dextrose concentration and the expected concentration in each 100-ml sample was determined. A difference of over 25% was considered unacceptable.
RESULTS: When very small volumes (0.1 and 0.25 ml) of "drugs" were injected, the needle system was consistently accurate. Injection through a stopcock was the least accurate, especially when no flushing was employed. The valved needleless Clave system delivered accuracy close to that of a needle, especially with flushing. The technique of flushing had a considerable effect on the ultimate amount of drug injected. If flushing is performed using the same syringe that delivered the drug, the additional trace of drug that is contained in the dead space significantly increased the actual delivered dose.
DISCUSSION: The Bloodborne Pathogens Standard of the Occupational Safety and Health Administration (OSHA) mandates the use of safer needlestick devices nationwide. Access sites for medication administration should be needleless, maintain sterility during multiple uses, and prevent leakage or backflow.
Although syringe/needle/tubing technology has been touted as simple and intuitive, it is a known cause of personnel and sometimes patient injury. The valved needleless system is an acceptable alternative for delivering small volumes of injected drugs. It is recommended that a separate syringe, not containing traces of the injected drug, be used for flushing. When using a stopcock for bolus dosing, a dilution of the intended dose to a minimal volume of 0.5 ml, followed by flushing, will ensure accurate dosing.

S-153

DELIVERY OF NORMOTHERMIC BLOOD AND FLUIDS TO PEDIATRIC PATIENTS USING A DRY HEAT WARMER

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INTRODUCTION: The disposable insert for the dry heat blood/fluid warmer, Ranger (Augustine Medical), can be distended with an additional 20ml bolus injection. Using a to-and-fro manual injection into the Ranger, we have utilized this distensability and warmed 10-15 ml volumes of cold (10°C) packed cells to 37°C to be used for rapid delivery to pediatric patients. We compared the speed and ease of preparation of 37°C volumes using our method with one previously described using the water bath warmer, Hotline (SIMS Level 1).[1]
METHODS: We recorded the time it took to turn on the heater, assemble the disposable components, wait for each heating unit to read 40°C and have each system deliver a 10-15 ml volume of 10°C packed cells warmed to 37°C. We also recorded the delivery time for subsequent normothermic aliquots. For Ranger, we used a blood administration set, a 20 ml syringe and a 3-way stopcock attached to the inflow tubing of a standard disposable warming set with a thermistor inserted into the inflow line. After 10°C packed cells flowed through the blood administration tubing, stopcock and disposable warming set, the outflow tubing was clamped off when blood began to exit the warming unit. Additional blood (15-20ml) was withdrawn from the blood bag into the syringe and then manually injected and withdrawn from the warming unit until the packed cells had been warmed to 37°C. For Hotline, we used blood tubing with a stopcock and 20ml syringe at each end of the disposable warming set. Once the heating unit reached 40°C, packed cells (10°C) were injected into the warming system and collected in a syringe after passage through an inline thermistor. Time to availability of 37°C packed cells was also recorded after each assembled system remained on for 15 minutes. Measurements were taken twice for each system and results were averaged.
RESULTS: It took 4.2 minutes for Ranger (measured from turning on the heater and including 7-8 to-and-fro injections) to produce 10-15ml of 37°C packed cells. It took 12.5 minutes for Hotline, mostly due to the slower warm-up time of the heater. With the units assembled and warm for 15 minutes, Ranger took 42 seconds to deliver normothermic packed cells while Hotline took 26 seconds. At flows greater than 60ml/min, Hotline did not deliver 37°C packed cells.
DISCUSSION: We have demonstrated that the dry heat blood/fluid warmer, Ranger, can be configured for rapid infusing of normothermic blood and fluids to pediatric patients and reducing the potential for hypothermia and bradycardia. The initial setup time to deliver aliquots of normothermic fluids is significantly faster with Ranger. Hotline is faster for subsequent normothermic deliveries but this difference is not clinically significant.
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S-154

DO VARYING LEAD LEVELS INTERFERE WITH COAGULATION: AN IN VITRO THROBELASTOGRAPHY (TEG) STUDY WITH WHOLE BLOOD

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INTRODUCTION: Lead levels in the toxic range have been noted in 2 of 1000 units of blood bank blood (1). We compared coagulation parameters using a TEG on whole blood with differing levels of added lead. Hemoglobin-based Oxygen Carriers have been tested for coagulation in conventional laboratory equipment by our team (2).
METHODS: Three mL of remainder sample blood was tested from 4 individuals and placed in a 3 mL blue top Vacutainer (Heparin). Baseline blood lead was measured in each sample using Zeeman-corrected atomic absorption spectrometry with graphite furnace. Prior to testing for each TEG, Heparinase, in the concentration used for routine TEG analysis, was used to reverse the heparin effect. Baseline TEG values (r, k, alpha angle, MA, EPL) and lead levels were measured. Then lead acetate was micropipetted into the TEG cuvette to produce the following lead concentrations (assuming baseline lead levels of 0): 10, 20, 50, and 70 µg/dL. A TEG was immediately performed. Blood lead levels were measured in each sample after addition of lead acetate. The effect of lead level on TEG variables was compared using an analysis of variance (ANOVA) for repeated measures.
RESULTS: Four blood samples were obtained for this study. See Table for data from five TEG assessments at different lead levels. With increasing lead in the blood, MA significantly decreased ($p<0.02$). Mean MA decreased from 69.6 mm at baseline to 48.5 mm ($p=0.035$) at a nominal blood lead level of 50 µg/dL.
CONCLUSION: The effect of lead exposure on platelet function has been unexplored. Our results suggest that lead worsens platelet function in ranges commonly encountered among industrially exposed populations, based on in vitro TEG MA values.

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TEG MA Values at Increasing Lead Levels (N = 4, [plusminus] SEM)

LEAD CONCENTRATION	1.8 mcg/dL	11.1 mcg/dL	20.3 mcg/dL	47.4 mcg/dL	65.9 mcg/dL
MA(mm)	69.6±3.7	63.4±1.1	57.0±3.7	48.5±3.9	49.3±4.3

S-155

ELECTRONMICROSCOPIC EVALUATION OF CLOT FORMATION ON THROMBOELASTOGRAM

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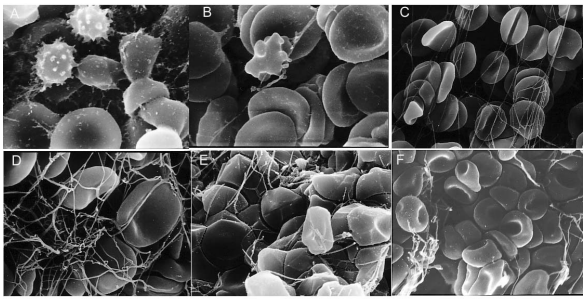
INTRODUCTION: Thromboelastogram (TEG) is a clinically useful coagulation monitor to guide transfusion of hemostatic products. Clot forms after activation of fibrin and platelets, but the exact sequence of TEG events has not been clearly described. We attempted to characterize the morphology of forming clot with scanning electronmicroscopy (SEMS).
METHODS: After institutional approval, blood samples were obtained from 6 healthy volunteers. 2-channel TEG (CTEG-3000T, Haemoscope, Niles, IL) was performed using 330 mcL recalcified blood samples (20 mcL of 0.2 M $CaCl_2$). First channel was used to obtain TEG variables: reaction time (R); amplitude; A 10 mm, A 20 mm, A 30 mm, maximum amplitude (MA), and second channel was used to obtain sub-samples for morphological examination by SEMS. Abciximab-modified TEG was also studied using c3E7 (Centocor) at final concentration (25 mcg/mL).
RESULTS: SEM images are shown in figures (A-F). At R point, coarse fibrin and budding of platelets are seen (fig. A). At A10 point, platelet shape change is observed (fig. B). At A20, fibrin strands are more clearly seen, and RBCs are somewhat bundled in-between fibrins and deformed (fig. C). At A30 point, RBCs are surrounded with thick mesh of fibrin strands (fig. D). At MA point, RBCs are squeezed together by fibrins (fig. E). With addition of abciximab, RBC shapes are still maintained at MA point (fig. F).
DISCUSSION: Our morphological evaluation of TEG agrees with conventional theory regarding TEG tracing, i.e., the amplitude of TEG reflects fibrin formation and platelet activation. Because RBCs are interspaced between forming fibrin and platelet bonds, hematocrit value may affect TEG results.



S-156

EFFECT OF HEAD POSITION ON CORMACK SCALE GRADING DURING LARYNGOSCOPY: IS 'SNIFFING POSITION' THE BEST?

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INTRODUCTION: Traditionally, 'sniffing position' is recommended during direct laryngoscopy. Recently, Adnet et al found the 'sniffing position' not superior to simple neck extension in their group of patients sedated with propofol.[1] Hochman et al found on the other hand the flexion position provided the best glottic exposure.[2] Our aim in this study is to determine if the 'sniffing position' provides superior laryngoscopic visualisation of the glottis compared to neck extension and flexion in elective anaesthetized paralysed patients.
METHODS: This was a randomized controlled prospective trial involving 51 adult patients of ASA class 1 or 2 scheduled for elective surgery in which general anaesthesia with IPPV was required. Exclusion criteria were patients at risk of aspiration or had conditions contraindicating intubation. After induction and paralysis, each patient was placed in the three intubating positions. The sniffing position was obtained by placement of a 7-cm pillow under the patient's head. The extension position was obtained by simple head extension while the flexion position had the patient's neck flexed to approximately 30 degrees by one of the investigators. Direct laryngoscopy was then performed by an independent observer at all 3 positions, and the laryngoscopic view was assessed using the Cormack scale without application of external laryngeal pressure.
RESULTS: The mean age was 39.8 ± 14 years while the mean inter-incisor and thyromental distances were 4.4 ± 0.8 cm and 6.0 ± 1.2 cm respectively. Median Mallampati score was 2. While median Cormack grading was 2 for all 3 positions, there were more patients with grade 1 exposure during sniffing and neck extension positions (22 and 23 patients respectively) as compared to flexion position (11 patients). There was no significant difference ($p<0.8$) in laryngoscopic view between the sniffing and extension positions while flexion position worsened glottic exposure as compared to the sniffing position in 39% cases ($p<0.002$) and did not alter laryngosopic exposure in 51% cases. There was no difference in exposure between flexed and extended positions in 53% cases, while in 37% cases flexion position worsened exposure as compared to extension position ($p<0.006$).
DISCUSSIONS: Routine use of sniffing position does not appear to offer any significant advantage over simple neck extension for tracheal intubation. However, neck flexion significantly worsens laryngoscopic visualization of vocal cords.
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S-157

AN EVALUATION OF ENDOTRACHEAL INTUBATION USING THE MACINTOSH VIDEO LARYNGOSCOPE

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INTRODUCTION: The Macintosh Video Laryngoscope (MVL) is designed to optimize visualization of the airway by projecting an enlarged video image of the laryngeal structures onto a monitor.[1,2] This study was designed to assess the effectiveness of the MVL by comparing the view of the glottic opening obtained with the (1) naked eye and (2) video monitor.
METHODS: This study was conducted on 102 anesthetized, paralyzed, apneic patients, ranging in age from 18-80, with no known abnormalities of the upper airway. Observations of the laryngeal structures were made by both a direct view of the oropharynx, and an image projected onto a video monitor using a size 3 MVL. Observations were categorized into the following classifications: full view of glottic opening (Grade I), partial view of glottic opening (Grade IIa), posterior portion of cords (Grade IIb), epiglottis only (Grade III), and neither epiglottis/glottis (Grade IV). The necessity of external laryngeal pressure was determined, applied if necessary, and optimal views again obtained.
RESULTS: The MVL displayed a Grade IIa or better classification in 99% of the patients (82% Grade I), in contrast to 52% of the patients (35% Grade I) with the naked eye (Figure 1). Thirty-three patients were thought to be possible difficult intubations. The possibility of a difficult intubation was noted when one or more of the following conditions were present: small mouth opening (<3 fingerbreadths), limited neck mobility, or a Mallampati III classification. Of these patients, the MVL revealed a Grade IIa or better classification in 97% (67% Grade I) on the monitor, compared to 3% (0% Grade I) with the naked eye.
DISCUSSION: The view on the video monitor provided a superior view of the laryngeal structures in comparison to the view obtained with the naked eye using the MVL. This study suggests that the MVL may be a practical device to aid in difficult intubation, yet further studies are warranted in this area.

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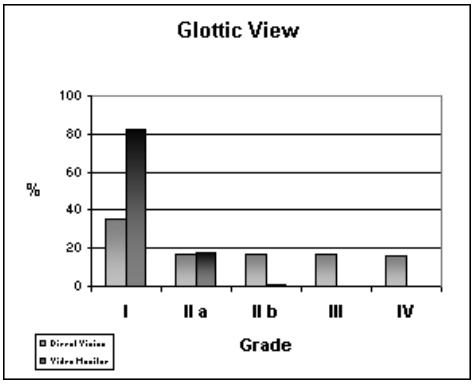

S-158

A PROSPECTIVE, RANDOMIZED, CROSSOVER STUDY TO ASSESS THE ENDOTRACHEAL TUBE CUFF INFLATION AS A MEANS OF IMPROVING SUCCESS RATE OF BLIND NASOTRACHEAL INTUBATION (BNI) UNDER VARIOUS CONDITIONS.

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INTRODUCTION: Cuff inflation seems to facilitate the passage of nasotracheal tube (NTT) during blind nasal intubation (BNI)[1] in apneic and spontaneously breathing patients[2-4] even in unskilled hands.[5] We hypothesized that the technique will be useful only for a beginner and not for a trained anesthesiologist.
METHODS: After IRB approval, this study was conducted in 80 ASA I/II patients aged 16years. Patients were randomized into apneic and breathing groups (n=40 each), then into trained and trainee subgroups (n=20 each) and finally to crossover between cuff-inflation first (CI) or cuff-deflation first (CD) (n=10 each). Patients' nostrils were decongested and they were premedicated with i.v. atropine 0.6mg, meperidine 0.5mg.kg^{-1}, and diazepam 5.0mg 15min before induction of anesthesia with i.v. thiopental 5mg.kg^{-1} and N_2O 66% and halothane in oxygen. The apneic-group patients received vecuronium 0.1mg.kg^{-1} i.v. The NTT (Mallinkrodt®) was introduced into the lubricated nostril and pushed to the nasopharynx and then further with either cuff deflated or inflated (with 15ml air till resistance was felt, when the cuff was deflated). Whenever it was felt that the tube had entered the trachea, its position was checked by laryngoscopy. In case the intubation failed, more attempts (maximum=3) were made. After intubation/failure by the first method, the patient's condition was stabilized and the second method attempted. When the trachea was intubated by the second method (or under vision if it failed), surgery was allowed to start. In breathing-group patients airway was topicalized after induction of anesthesia, the patients breathed spontaneously during the study period and the tube position was confirmed by capnography. The success rates and attempts with cuff-inflation and cuff-deflation were compared using the ^{2} test, and the time taken by unpaired t-test (P<0.05=significant).
RESULTS:

CUFF	**INFLATED / DEFLATED**			
Operator	Trainee		Trained	
Patient	Apneic	Breathing	Apneic	Breathing
Success (%)	40/45	45/35	55/65	85/85
Success time (sec)	29±16/ 60±47	43±24/ 56±53	38±18/ 59±32	31±24/ 39±21
Attempts for success	1.1±0.4/ 1.8±0.8	2±0.9/ 1.7±1	1.5±0.7/ 1.8±0.8	1.5±0.7/ 1.5±0.6
Failure time (sec)	69±34/ 127±41*	105±66/ 137±46	69±31/ 119±81	67±14/ 168±14#

Data as mean±SD. *P=0.014; #P=0.027 (Cuff Inflated v/s Deflated)
DISCUSSION: Cuff inflation does not improve the success rate of BNI for trained or trainee anesthesiologist. Although it lifts the tube away from the posterior pharyngeal wall, it probably pushes the tip more anteriorly than required in some cases and does not centralize it with respect to the lateral pharyngeal walls. However, it may be tried ahead of the usual BNI because, with similar success rates, the average time in cases of failure is consistently less (significantly so under two scenarios) than with cuff deflated.
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S-159

WARNING SYSTEM TO DETECT CONTACT WITH UPPER TEETH DURING LARYNGOSCOPY

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INTRODUCTION: Damage to the teeth is the most common complication during laryngoscopy (1) with an incidence of 0.02% to 0.7% (2)
METHODS:A size 3 Macintosh Laryngoscope blade was modified to incorporate a Force Sensing Resistor (FSR), connected by a wire to an integrated circuit that could activate a buzzer and two light-emitting diodes (LED). "Slight" pressure resulted in slow beeping and a yellow flashing light (warning signal) and greater pressure faster beeping and a red flashing light (crisis signal).
Ten intubations were performed on an training manikin by each of 21 Respiratory Therapy students and staff (RT) with a size 7 styletted endotracheal tube. The buzzer was switched on in random order for half the trials without the RT's knowledge. The signals (buzzer / light) per intubation were recorded, with successful intubation confirmed by inflating the lungs of the manikin using an Ambu bag. Data were analyzed using Chi-Square.
RESULTS: 199 of 210 trials resulted in successful intubation (mean time 12 sec. / intubation) with a contact signal (s) in 36.1%. Persistant pressure was significantly more frequent with the buzzer off ($p < 0.000$) [table 1]

Buzzer switch	**On**	**Off**
Number of trials with contact	35 (46%)	41 (53.9%)
Signal once / trial	14 (40%)*	11 (26.8%)
Signal twice / trial	12(34.2%)*	12 (29.2%)
Signals3 times or more / trial	9 (25.7%)*	18 (43.9%)
Total number of signals	69	105
Mean number of signals / trial	1.97	2.44
Number of warning signals	58 (84%)	66 (62.8%)
number of crisis signals	10 (14.4%)	19 (18%)
Number of signals with persistant pressure > 3 sec	1 (1.4%)+	20 (19%)

*p= 0.142 comparing single versus > 1 signal; + p < 0.000 comparing buzzer on / off

DISCUSSION: The modified laryngoscope appeared to successfully detect contact with the upper teeth. Persistent pressure occured only once with the buzzer on, significanly less than when the buzzer was off. Repeated contact occured in 73.1% and 59.9% with the buzzer off and on respectively with these inexperienced personnel, but this did not reach significance at the 5% level. The system showed promise for future use in clinical trials.
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S-160

A LABORATORY STUDY OF GAS DIFFUSION THROUGH AN ELLIPTICAL CUFF OF A LARYGEAL MASK AIRWAY

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INTRODUCTION: The purpose of this study was to examine basic gas diffusion properties of the elliptical cuff that is the mask component of the Laryngeal Mask Airway. Concern has been expressed that the use of nitrous oxide will increase the pressure within the cuff and potentially result in hypoperfusion of tissue in the posterior hypopharynx. Through a better understanding of the diffusion properties of the rubber elliptical cuff, potential risks of using the LMA may be minimized.
METHODS: Laboratory studies were used to evaluate Laryngeal Mask Airways (The Laryngeal Mask Company, Ltd), sizes 3, 4 and 5 using simple binary and more complex trinary gas mixtures. The compliance curves of the cuff were obtained for each size LMA. At the start of data collection LMAs were placed in pieces of PVC pipe of the appropriate size in order to simulate the constraints imposed on the cuff by the placement in the patient's oropharynx. The table below demonstrates the experimental protocol for each gas combination.

		Gas inside of the LMA Cuff		
		Oxygen	Nitrous Oxide	Air
Gas Outside of the LMA Cuff	Oxygen	LMA #3, #4, #5	LMA #3, #4, #5	LMA #3, #4, #5
	Nitrous Oxide	LMA #3, #4, #5	LMA #3, #4, #5	LMA #3, #4, #5
	Nitrous Oxide/Oxygen 80/20 60/40 20/60	LMA #3, #4, #5	LMA #3, #4, #5	LMA #3, #4, #5
	Air	LMA #3, #4, #5	LMA #3, #4, #5	LMA #3, #4, #5

The gas volumes within the cuff were 30 ml, starting from a completely deflated cuff volume, which mimics the clinical experience. Other volumes (15ml, 20ml, and 40 ml) were investigated under specific circumstances. Pressure in each cuff was recorded two times per second for 90 minutes using Labtech Notebook software (Laboratory Technologies, Andover, MA) running on a PC. At the end of 90 minutes, the gas concentrations within the cuffs were analyzed using the RAMS quadrapole mass spectrometer (GE Marquette, Milwaukee, WI).
RESULTS: Nitrous oxide diffusion far exceeded the diffusion of oxygen, which occurred faster than nitrogen. The volume of air used to inflate the cuff as well as the concentration difference between nitrous oxide inside and outside of the cuff, and oxygen inside and outside of the cuff, determines the magnitude of the pressure increase.The permeability of each gas through the rubber and the initial cuff volume determines the time constant for the pressure change.
DISCUSSION: Because oxygen diffuses faster than nitrogen, 100% oxygen surrounding an LMA cuff filled with air produces an increase in cuff pressure, which like nitrous oxide, may also be of concern clinically.This data supports the need to regularly monitor LMA cuff pressure even when nitrous oxide is not used.
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S-161

MANUAL VENTILATION OF A PATIENT TURNED 180° AWAY FROM THE ANESTHESIA MACHINE BY A SINGLE OPERATOR

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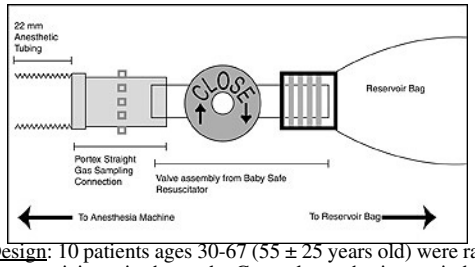
INTRODUCTION: At times the patient may be turned 180º away from the anesthetic machine and the anesthesiologist. We have used a modification of the OMAR slave[1] (personal communication 1970, Figure 1) which makes it possible, in the above circumstances, for one operator to stand at the head of the operating table both controlling the airway and manually ventilating the lungs.
METHODS: OMAR Circuit Construction: Our modification of the OMAR slave consists of a Portex Straight Gas Sampling Connection with a Luer port and cap[2] placed where the breathing bag is situated on a Narcomed 2B anesthetic machine[3]. This is connected to approximately 8 feet of 22 mm diameter anesthetic tubing extending to the head of the table and fitted with a valve with a bleed vent from a Baby Safe Resuscitator[4] (Fig 1).



Study Design: 10 patients ages 30-67 (55 ± 25 years old) were randomly selected to participate in the study. General anesthesia was induced and maintained in the normal manner. Data were obtained during 4 testing periods during general endotracheal anesthesia. 10-20 minutes after induction, mechanical ventilation was observed for 20 minutes (test period #1). Subsequently, the patient was manually ventilated using an OMAR circuit for 10 minutes (test period #2). Ten minutes of mechanical ventilation was again observed (test period #3), followed by 10 minutes of manual ventilation with the OMAR circuit (test period #4). During each testing period, end-tital CO_2 ($ETCO_2$), respiratory rate (RR), tidal volume (TV) and peak inspiratory pressures (PIP) were recorded.
RESULTS: The mean $ETCO_2$ among the four test periods (#1, 33.5±1.7; #2, 33.3±1.5; #3, 34.3±1.0; #4, 33.8±1.5) were not significantly different (P>0.3). The mean RR among the four test periods (#1, 6.5±0.5; #2, 8.3±0.5; #3, 6.5±0.6; #4, 8.3±0.5) were significantly higher in the OMAR circuit (test periods #2 and #4) (P<0.005). The mean tidal volumes among the four test periods periods (#1, 648±142; #2, 571±186; #3, 663±180; #4, 683±125) were not significantly different (P>0.3). Finally, the PIP among the four groups (#1, 20.5±1.7; #2, 17.3±2.2; #3, 20.8±1.9; #4, 16±1.6) showed that they were significantly lower in the OMAR circuit (test periods #2 and #4) (P<0.05).
DISCUSSION: Our results show that the OMAR circuit can be used by a single operator for manual ventilation of a patient turned 180º from the anesthetic machine while maintaining minute ventilation and $ETCO_2$ compared to mechanical ventilation. We believe this device may be useful to the lone anesthesiologist needing to control ventilation from the head of the bed turned 180º from the anesthetic machine.
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S-162

ENDOTRACHEAL LIDOCAINE WITH DISPERSION STEAM FOR AWAKE EXTUBATION

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INTRODUCTION: The aspiration of gastric content inside the tracheobronquial tree is a rare event during anesthesia. When it occurs, in about fifty percent of the cases, it is present during extubation due to laryngeal reflex inhibition caused by the residual effects of general anesthesia. Although, awake extubation constitutes a safe procedure, it is uncomfortable for the patient because of the hemodynamic changes, coughing and push that may occur. We have designed an dispersion steam, an instrument to administrate lidocaine directly into the trachea allowing a better tolerance to the endotracheal tube in the awakening phase of the anesthesia. The purpose of this study was to compare the tolerance to endotracheal tube and the hemodynamic changes during extubation after topical lidocaine administered through an dispersion steam versus intravenous lidocaine(1).
METHOD: Following IRB approval and informed consent, 60 ASA I-II adult patients S undergoing general inhalated anesthesia were enrolled in this randomized, prospective, single-blinded study. Study subjects were equally divided (n=30 each) into dispersion steam (DS group) and IV lidocaine group (L group). Anesthesia induction and maintenance were standardized. At the end of surgery and when the end-tidal isoflurane concentration was 0.2% the DS group received Lidocaine 1.5 mg/kg through a dispersion steam and the L group received lidocaine 1.5 mg/kg IV. In all cases the extubation was carried out with the patient awake responding to commands. Incidence of coughing, patient recall and discomfort, heart rate, blood pressure, and extubation time were recorded and analyzed by unpaired t-test, one-way ANOVA or Chi square as appropriate. $P<0.05$ was considered statistically significant.
The dispersion steam has a longitude of 32 centimeters, with an internal diameter of 0.5 millimeters, external of 1.2 millimeters; at its end, it has 12 lateral holes and one in the tip to distribute homogeneously the local anesthetic. This steam is introduced through the endotracheal tube, getting the distal end 3 centimeters under the tip tube (figure 1).
RESULTS: Demographic data were comparable between the two groups. The incidence of coughing was 27% and 64% for DS group and L group, respectively (P=0.001). Arterial blood pressure and heart rate increased significantly in the L group ($P < 0.001$). There was no difference in extubation time, patient recall or perception of discomfort during the procedure.
DISCUSSION: Our data shows that endotracheal lidocaine administered through a dispersion steam reduced the incidence of coughing and hemodynamic changes when compared to a similar dose of IV lidocaine. This technique makes extubation more comfortable, less traumatic, and allows patients emerging from anesthesia to tolerate an endotracheal tube while also affording airway protection with intact supraglotic reflexes.
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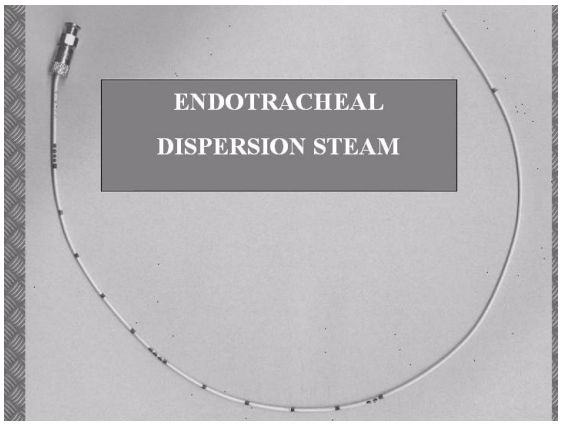

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DIFFERENT CONTINUOUS TOTAL INTRAVENOUS ANESTHESIA TECHNIQUE IS RECOMMENDED FOR WAKE-UP TEST (A PRELIMINARY STUDY)

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INTRODUCTION: Total intravenous anesthesia (TIVA) is one of the most recommended anesthetic method for wake-up test (1,2).
MATERIAL AND METHOD: Thirty eight (8 male, 30 female, ASA class I-II patients whose ages ranged 9y-31y, weight ranged 20kg- 85 kg) scolyosis surgery cases were received TIVA consist of midazolam, mivacurium, alfentanil infusions. Infusion rates were decreased in each surgery phase until wake-up (Table I)

INFUSION	PHASE 1 (EXPOSURE)	PHASE 3 (ROTE IMPLANTATION)	PHASE 4 (CORRECTION)	PHASE 5 (WAKE-UP)
Midazolam mg/kg/hour	0.225	0.15	0.075	0
Mivacurium mg/kg/hour	0.375	0.25	0.125	0
Alfentanil mg/kg/hour	0.03	0.03	0.03	0.03

At the surgeon's request midazolam and mivacurium infusions were discontinued, flumazenil was given, patients were asked to move hands and feet.
RESULTS: The median intraoperative wake-up times were 5.7 minutes. The protocol the authors set up allowed a very rapid intraoperative neurological examination without pain and no complication releated to the test was observed
CONCLUSION: Authors concluded that decreasing infusion rates of total intravenous anesthetics until wake-up test seems to be a safe and pratictical method. This report describes preliminary experience with this technique.
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MIDAZOLAM-FLUMAZENIL VERSUS PROPOFOL ANESTHESIA IN THE SCOLIOSIS SURGERY

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INTRODUCTION: Wake-up test is still useful test in the scoliosis surgery to ensure that spinal function remains intact.
METHODS: Intra-operative wake-up tests were performed in 60 patients randomized to either midazolam (M) or propofol (P) infusions for scoliosis surgery. Other anaesthetic medication was similar in both groups. At the surgeon's request, N2O was turned off and midazolam or propofol infusions were discontinued. In the M group, flumazenil was given in refracted doses. Patients were asked to move hands and feet.
RESULTS: The quality of intraoperative arousals was significantly better in the M group. Wake-up tests were smooth and also no patient recall of the test and no pain. All the patient in the P group had explicit recall of the test, but no pain. Two of these patients woke up violently. There were no neurological sequelae and no false negative results in both group.But, on the other hand the median intraoperative wake-up times were 5.7 min in the M group and 3.5 min in the P group($p<0.05$).
CONCLUSIONS: Wake-up tests can be safer and better with midazolam-flumazenil anesthesia compared with propofol anesthesia.
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Neuroanesthesia

S-165

DUAL EFFECTS OF DEXMEDETOMIDINE ON REACTIVE HYPEREMIA AND INFARCT SIZE FOLLOWING FOCAL CEREBRAL ISCHEMIA IN RATS

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BACKGROUND: It has been reported that a selective alpha 2 agonist, dexmedetomidine, causes cerebral vasoconstriction and decreases cerebral blood flow in vivo. Although neuroprotective effects of dexmedetomidine have been shown in some reports, little is known whether this direct cerebrovasoconstrictive action of dexmedetomidine deteriorates ischemic brain damage. Therefore, in this study, we examined the effects of dexmedetomidine on reactive cerebral hyperemia and cerebral infarct size following focal cerebral ischemia.
METHODS: Sixteen male Sprague-Dawley rats were used under an approval of Institutional Animal Care and Use Committee. After intraperitoneal injection of pentobarbital sodium (50mg/kg), rats were mechanically ventilated with air. We continuously measured left parietal cerebral blood flow (CBF) through the parietal cortex using laser Doppler flowmetry and mean arterial blood pressure (MAP) . At the end of preparations, continuous intravenous infusion of either high or low doses of dexmedetomidine (1 or 0.1μg/kg/min, n=8 each) was started. Focal cerebral ischemia was induced by the left middle cerebral artery occulusion for an hour using a thread with its tip coated by vinyl silicone. Reperfusion was made by withdrawing the thread. At the end, animals were sacrificed and the brain was dissected and its slices was soaked with 2,3,5 –triphenyl-tetrazolium-hydrochloride (TTC) to measure the cerebral infarct area. Results were expressed mean±SD. For statistics, ANOVA with Student-Newman-Keuls or X square significance test were used. A $p<0.05$ was considered significant.
RESULTS: At control, CBF was not significantly different between both groups of rats, whereas MAP was greater in rats with high dose of dexmedetomidine. In rats receiving the high dose of dexmedetomide (1μg/kg/min), CBF decreased to 27±9 % of control during ischemia, and increased to 139±29 % of control after reperfusion. In rats with the low dose of dexmedetomidine (0.1μg/kg/min), CBF decreased to 33±6 % of control (n.s. vs high dose), and increased to 160±19 % of control that was significantly greater compared to the rats with high dose. Cerebral infarction was confirmed in six out of eight rats infused with high dose of dexmedetomidine, while infarction was seen one out of eight rats with low dose of dexmedetomidine (significantly lower incidence). The calculated infarct size in the high dose rats was 12.5 folds of that in the low dose ($p<0.05$).
DISCUSSION: High dose of dexmedetomidine suppressed reactive hyperemia and increased infarct size following focal cerebral ischemia, while low dose of dexmedetomidine did not significantly alter them. This anti-neuroprotective effects of high dose of dexmedetomidine may be due to the direct cerebral vasoconstrictive effects. Therefore, it is suggested that high dose of dexmedetomidine should be avoided during cerebral ischemia. In contrast, low dose of dexmedetomidine may preserve reactive hyperemia and lessen infarct size, and thus it may be neuroprotective during cerebral ischemia.

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DEXMEDETOMIDINE SEDATION FOR AWAKE CAROTID ENDARTERECTOMY: RATIONALE AND SAFETY

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INTRODUCTION: Regional anesthesia for carotid endarterectomy (CAE) allows for the evaluation of cognitive function intraoperatively and is associated with a lower requirement for shunting. A cervical plexus blockade provides excellent analgesia for most patients undergoing CAE, but usually requires sedation. A combination of midazolam and fentanyl generally provides an adequate balance of sedation, cooperation and hemodynamic stability. Over and under sedation as well as an unacceptable level of hemodynamic and respiratory variability can, however, be a problem. Dexmedetomidine (Dex) is a highly specific alpha-2 adrenoreceptor agonist with sedative, analgesic and anesthetic-sparing effects. It is distinct from other sedative agents in that it does not depress respiratory function, and patients can be easily aroused (1). The objective of this study was to prospectively evaluate the safety an efficacy of Dex during regional anesthesia for CAE.
METHODS: 25 patients underwent CEA under deep and superficial cervical plexus blockade using 1.5% mepivacaine + epinephrine 1:200,000. An initial loading dose of 0.5 g/Kg/min of Dex was given over 15 min followed by a continuous infusion of 0.1 to 0.4 g/Kg/hr. The infusion rate was titrated to maintain a sedation level of 4 as measured by the Observer's Assessment of Alertness/Sedation Scale (OAA/S). The degree of pain, sedation and anxiety were self-assessed by the patients using a 10 point visual analogue scale (VAS). A motor function of the hand on the side contralateral to surgery was assessed to evaluate the adequacy of cerebral perfusion at the time of the carotid artery cross-clamping. Plasma levels of epinephrine and norepinephrine were measured preoperatively, 15 minutes after skin incision, and at the end of the procedure.
RESULTS: All patients reported acceptable analgesia from the block overall. Although readily aroused, patients reported a mean VAS sedation score of 3.1±2.6. Mean VAS for pain and anxiety were 1.8±1.9 and 1.2±2.0 respectively. Mean OAA/S was 4.2±0.5. P_aCO_2 levels were unchanged from baseline throughout the procedure. 4 patients required placement of a shunt due to mental status changes after cross clamping and 13 others required phenylephrine to maintain adequate blood pressure. Two patients required conversion to a general anesthesia. The plasma epinephrine concentrations did not change significantly during the procedure. Plasma norepinephrine concentration decreased by 31% ($p=0.04$) after 46±19 minutes of dexmedetomidine infusion and by 46% at the end of the procedure ($p=0.01$).
DISCUSSION: Dex sedation provides a stable and predictable anesthetic profile without hampering a mental status evaluation or causing respiratory depression. 52% of patients, however, were treated with phenylephrine to maintain systemic blood pressure within 20% of the baseline. The reduced level of norepinephrine may reduce the rate of cardiovascular complications. Thus, Dex may be an attractive alternative to standard sedation techniques during awake CEA.
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S-167

THE NEUROPROTECTIVE EFFECT OF XENON ADMINISTRATION DURING TRANSIENT MIDDLE CEREBRAL ARTERY OCCLUSION IN MICE

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INTRODUCTION: Xenon, a noble gas possessing anesthetic properties, is known to be an N-methyl-D-aspartate (NMDA) receptor antagonist (1). Neuroprotection has been demonstrated in several *in vitro* and *in vivo* models of brain injury but has not been studied in the setting of cerebral ischemia (2). The purpose of this investigation was to evaluate the neuroprotective effect of xenon in a mouse model of transient focal cerebral ischemia.
METHODS: Fasted mice (male, 8 week old C57BL/6) were anesthetized with isoflurane, intubated, ventilated and surgically prepared for right middle cerebral artery occlusion (MCAO). Mean arterial pressure and pericranial temperature (servo-controlled to 37°C) were continuously monitored. Following surgical preparation, the isoflurane was discontinued, all animals received fentanyl (50 µg/kg i.v. bolus; 50 µg/kg/hour i.v. infusion), and were randomized to one of three anesthetic groups (n=21 in each group): 70% Xe + 30% O_2; 70% N_2O + 30% O_2 and 35% Xe + 35% N_2O + 30% O_2. Sixty minutes of MCAO was then performed followed by 24 hours of reperfusion. The animals then underwent neurological evaluation by a blinded observer using two scoring systems following which they were euthanized with the brain removed for infarct volume analysis. Parametric data were compared amongst groups using ANOVA (followed by the Scheffe test) with non-parametric data analyzed using Kruskal-Wallis and Mann-Whitney U tests. A $P<0.05$ was considered significant.
RESULTS: The neurological scores and brain infarct volumes are summarized in the table below. The 70% Xe + 30% O_2 group had both improved functional as well as histologic outcome compared to the 70% N_2O + 30% O_2 group. The 35% Xe + 35% N_2O + 30% O_2 group had an intermediate outcome.

Group	Neurological Score		Infarct Volume (mm3)		
	General deficits	Focal deficits	Total	Cortex	Subcortex
70%Xe	9 ± 2†	12 ± 5†	45.2 ± 17.4*	24.1 ± 9.9*	21.0 ± 8.2†
70%N_2O	10 ± 2	16 ± 6	59.4 ± 11.5	35.5 ± 8.6	23.9 ± 4.8
35%Xe/ 35%N_2O	9 ± 2	14 ± 5	49.8 ± 14.3*	26.6 ± 8.9*	23.2 ± 6.9

Values are mean ± SD, n=21 in each group. †$P<0.05$ and *$P < 0.01$ compared to the 70% N_2O + 30% O_2 group.
DISCUSSION: In this model of transient focal cerebral ischemia, xenon improved both functional and histologic outcome. These findings are consistent with its action as an NMDA receptor antagonist (1) and with previous studies demonstrating reduction of NMDA-induced neuronal injury *in vitro* and NMA-induced hypothalamic arcuate nucleus injury *in vivo (*2).
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S-168

THE EFFECTS OF BETA-BLOCKERS ON CEREBRAL ARTERY BLOOD FLOW VELOCITY DURING ELECTROCONVULSIVE THERAPY

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INTRODUCTION: Electroconvulsive therapy (ECT) has an important role in the treatment of patients with severe depression or schizophrenia. ECT results in an acute cardiovascular response, characterized by tachycardia, hypertension, and increase in cerebral artery blood flow velocity (CBV)[1]. In patients with a history of hypertension mostly beta-blockers are administered pre- or post-ECT to prevent a further increase in blood pressure. In this study we evaluated the effects of beta-blockers on changes in CBV using Transcranial Doppler (TCD) measurements both in hypertensive and non-hypertensive patients.
METHODS: The study was approved by the IRB, and written informed consent was obtained. Eleven patients underwent 15 ECT's under general anesthesia, consisting of methohexital 0.5-1 mg/kg and succinylcholine (1 mg/kg). In case of pre-ECT hypertension (MAP > 100 mmHg) esmolol or labetolol were administered intravenously.
CBV, heart rate (HR) and arterial blood pressure (BP) were measured just before induction of anesthesia, and at 0.5, 5, 10 and 30 min post-ECT.
RESULTS: CBV increased significantly (90-100%) at 0.5, 5 and 10 min after ECT in patients not receiving beta-blockers pre-ECT. HR increased approximately 20 b/min at the same moments, but BP increased only after 10 min. Patients receiving esmolol pre-ECT followed the same pattern except for HR, which did not change. In patients receiving labetolol pre-ECT, CBV did not significantly change at 0.5 min, but at 5 and 10 min increased significantly, although BP did not change (table 1).
After 30 min all values had returned to pre-ECT baseline levels in all patients.

CONCLUSION: It is concluded that both labetolol and esmolol are effective in preventing hypertension in patients undergoing ECT, but that labetolol, and not esmolol, may attenuate the initial increase in CBV. Further studies have to elucidate if this finding is important as to the duration and quality of the seizures[2].
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typical pattern in three different patients

	No medication	No medication	No medication	Labetolol	Labetolol	Labetolol	Esmolol	Esmolol	Esmolol
	HR	BP	CBV	HR	BP	CBV	HR	BP	CBV
Baseline	95	129/76	50	67	150/74	44	70	135/85	73
0.5 min	110	174/90	102	85	160/95	44	68	151/85	150
5 min	130	140/86	90	74	160/85	60	66	160/95	89
10 min	120	140/75	50	74	160/85	73	69	160/85	70
30 min	107	125/85	50	76	155/80	43	76	120/68	68

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ASSOCIATION BETWEEN PLASMA CONCENTRATION OF NITRIC OXIDE PRODUCT (NITRATE & NITRITE) AND S100B PROTEIN AFTER SURGERY OF CEREBRAL ANEURSYM CLIPPING AND PATIENT OUTCOME

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INTRODUCTION: Despite the recent advances in brain imaging techniques, it is still difficult to quantify the extent of primary and ongoing secondary brain injury. The objective of this study was to examine the usefulness of plasma S100 and nitric oxide products concentrations (nitrate plus nitrite) (NOx) as markers of brain injury following clipping of cerebral aneurysm in patients with spontaneous subarachnoid hemorrhage (SAH).
METHODS: 15 patients with SAH and 10 control subjects (age matched healthy volunteers) were included in the study. Blood samples were obtained for estimation of plasma S100 and NOx at 10 minutes after clipping of cerebral aneurysm, 2, 6 and 12 hrs postoperatively and thereafter daily for 6 days**.** Outcome was assessed by using the Glasgow Outcome Scale.
RESULTS: The mean pre-operative plasma concentration of S100 in patients with SAH was increased (0.24g/l) compared to control group (0.18 g/l)(P=0.03). After clipping of aneurysm plasma S100 concentration increased in 11 (84%) patients at two hours (mean 0.34 g/l, median 0.28 g/l)(P=0.01) and in 12 (92%) patients at 12 hours (mean 0.31 g/l, median 0.02 g/l)(P=0.04) when compared to control group. The mean S100 concentration obtained in the poor outcome group (grade IV-V) was 0.45 g/l compared to 0.36 g/l (P=0.04) in the good outcome group (grade I-III) in the first 48 hrs postoperatively. The temporal profile of plasma NOx after clipping was a decreased plasma concentration at 12 hrs and thereafter an increased plasma concentration compared to control group. NOx concentration at 12 hrs postoperatively in patients with SAH was 9.61 mol/l compared to 12.37 mol/l in the control group (P=0.02). The mean value obtained in the poor outcome group and good outcome group was 12.56 mol/l and 13.7 mol/l respectively in the first 48 hrs postoperatively (P=0.4).
DISCUSSION: These findings suggest that S100 represents a better marker of cerebral injury and outcome after cerebral aneurysm clipping than nitric oxide product concentrations.
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S-170

DIFFERENTIAL EFFECTS OF BUPIVACAINE ON MITOCHONDRIAL RESPIRATION IN BRAIN AND HEART

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INTRODUCTION: Bupivacaine is known to be both cardiotoxic and neurotoxic since clinical overdose can result in cardiac arrest or seizure activity. Bupivacaine is also an uncoupler of oxidative phosphorylation. Mitochondrial respiratory ratio (RCR) is a measure of coupling, which reflects inner membrane integrity. The ratio describes the difference between mitochondria during ADP-supported oxygen respiration (state III) and resting state respiration (state IV). The purpose of this study was to compare brain and heart mitochondria in state III and state IV and to calculate RCR during bupivacaine treatment.
METHODS: These studies received animal care committee approval. Rats were decapitated, hearts and brains were harvested, tissue was homogenized and mitochondria were isolated by differential centrifugation. Oxygen concentration was measured in the mitochondrial suspension using a Clark oxygen electrode. Mitochondrial respiration was measured using pyruvate/malate as substrates. States III and IV were initiated using low concentrations of ADP. Bupivacaine concentrations were 0.5, 1.0 and 2 mM.
RESULTS: There was a decrease in state III respiration with increasing concentration of bupivacaine in brain but not heart mitochondria (table 1). State IV respiratory rates increased with increasing bupivacaine concentration, and this effect was greater in brain than heart mitochondria. RCR decreased with increasing concentrations of bupivacaine, and this effect was more pronounced in brain compared to heart mitochondria.
DISCUSSION: These results show that bupivacaine suppresses pyruvate-supported state III respiration in brain but not heart mitochondria. Bupivacaine may affect metabolite translocation in brain mitochondria by increasing inner membrane leakiness. State IV respiration was increased and RCR was decreased by bupivacaine more in brain than in heart, again indicating that membrane integrity was compromised. Disruption of mitochondrial membrane integrity is possibly one of mechanism of bupivacaine induced neurotoxicity.

Effect of bupivacaine on brain and heart mitochondria

	Brain			Heart		
Bupivacaine concentration (mM)	State III respiration (ng atoms O2/min/mg)	State IV respiration (ng atoms O2/min/mg)	RCR	State III respiration (ng atoms O2/min/mg)	State IV respiration (ng atoms O2/min/mg)	RCR
0	226	19.7	7.8	202	18.1	11.2
0.5	187	29.6	6.3	191	20.3	9.5
1.0	165	42.3	3.9	191	20.2	8.0
2.0	160	57.8	2.8	180	35.6	5.1

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EFFECTS OF INTRACELLULAR ACIDOSIS ON THE STEADY STATE RATES OF CREATINE KINASE IN RAT BRAIN SLICES

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INTRODUCTION: Intracellular acidosis is one of the cytotoxic mechanisms during ischemic brain injury. We showed in previously that pre-conditioning with intracellular acidosis could induce resistance to the fall in high-energy phosphate (creatinephosphate, PCr) during subsequent intracellular acidosis in rat brain slices[1]. In this study, we investigate the exchange flux in creatine kinase (CPK) reaction before and during intracellular acidosis induced by hypercapnia using the method of phosphorus nuclear magnetic resonance (^{31}P NMR) saturation transfer.
METHODS: Brain slices were obtained from male Wister rats (6-10 week, N=6). The slices were incubated in artificial cerebrospinal fluid (ACSF), bubbled with 5% CO_2, 60% O_2 plus 35% N_2 at 25°C for 1h. ^{31}P-NMR spectra were obtained using a Bruker AMX300wb spectrometer. After the steady levels of PCr and inorganic phosphate (Pi) were reached, intracellular acidosis was induced by changing gas mixture from 5% to 20-40% CO_2 and then returned to 5% CO_2. Intracellular pH (pH_i) was calculated from the chemical shift of Pi. The method of ^{31}P-NMR saturation transfer was according to the procedures of Shourbridge et al.(1982)[2] with modification
RESULTS: pHi decreased from 7.4 to 6.4 following increase of CO_2 in bubbling gas mixture from 5 to 40%. The level of PCr decreased rapidly and that of Pi increased at pHi less than 6.9. Pseudo-first order rate constant in forward reaction (kf) and flux (F) for CPK decreased during acidosis induced by hypercapnia as shown in Table 1.

Table 1. kf and F for CPK before and during acidosis (25degC)

	Control	Acidosis	Recovery
pHi	7.17	6.91	7.17
kf	0.12	0.06	0.14
F (micromol/g wet/s)	0.76	0.23	0.89

The forward direction of the CPK reaction is the direction of PCr hydrolysis. The flux calculations assume as in vivo [PCr] of 6.36 µmol/g wet wt.

DISCUSSION: It is reported that the optimal pH in the forward CPK reaction is 5-6 and in backward reaction 8-9. From the optimal pH data in CPK, it might be anticipated that forward reaction was accelerated by intracellular acidosis. However the rate in forward reaction was decelerated at pHi 6.91. Decreases in PCr and in the rate of backward reaction might be the major cause of the suppressed forward CPK rate. Pre-conditioning with intracellular acidosis might also modify the CPK rate constant
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S-172

CARDIOVASCULAR CHANGES DURING ENDOSCOPIC THIRD VENTRICULOSTOMY IN CHILDREN

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INTRODUCTION: Little attention has been paid to the cardiovascular changes during anesthesia and surgery for endoscopic third ventriculostomy (ETV). A negative correlation between bradycardia (B) and third ventricular pressure during ETV was reported (1). Blood pressure (BP) or tachycardia (T) were not discussed. More recently was stated that invasive blood pressure measurement is unnecessary during endoscopic surgery in pediatrics (2). Because this contrasts with our experience, we studied retrospectively the incidence of B,T, systemic hypertension and the occurrence of an increased intracranial pressure (ICP).
METHODS: After IRB approval, the anesthesia records of 37 patients who underwent an ETV during the last 12 years were examined. Anesthesia was induced and maintained with propofol, cisatracurium and remifentanil or alfentanil. A radial or femoral artery was cannulated with a 22 or 24G catheter to monitor beat to beat the BP. The heart rate was recorded continuously via the ECG. In children, we considered B or T to be present if the heart rate decreased below or increased above the range according to the age of the child. Hypertension was defined as a BP above the 95th percentile for age.
RESULTS: In 26 patients the procedure was uneventful. An isolated T or B was observed in 6 and 4 patients respectively. In 3 patients the T coincided with a systemic hypertension (table). In these patients an increase in ICP was likely present, due to a kinking of the irrigation fluid outflow tubule or a forceful inflow of the irrigation fluid to clear an obtunded view by blood.
DISCUSSION: Since B as well as T can occur during ETV, it is of outmost importance to monitor the BP beat tot beat invasively. In this way, the surgeons can be warned in the early fase of a Cushing response, when T and systemic hypertension are present (3). Waiting for a persistent B could result in a fatal asystole (4).

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	Cushing-group (n=3)		
variable	median	minimum	maximum
age	7 years	4 months	10 years
weight (kg)	30	6.3	30
heart rate/min (highest)	140	130	140
heart rate/min (lowest)	70	55	105
systolic BP (highest)	200	120	210
systolic BP (lowest)	85	75	100
diastolic BP	50	40	60

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SONOCLOT ANALYSIS IN NEUROSURGICAL PATIENTS

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INTRODUCTION: The Sonoclot analyzer, which has been used to monitor perioperative coagulation (1,2,3), has not been investigated in neurosurgical patients. As these patients may be at risk for either hyper or hypocoagulable chnages (4,5), we investigated changes in Sonoclot parameters in patients undergoing craniotomy.
METHODS: After institutional approval and informed consent, patients undergoing elective craniotomy were enrolled. Patients receiving any medication affecting coagulation or with abnormal baseline coagulation parameters were excluded. Blood was drawn from a central venous line for Sonoclot analysis (Sienco Inc., Broomfield, CO) after anesthetic induction, at 1 and 3 hours, at the end of surgery and after 24 hours. Parameters measured included: SonACT (Sonoclot activated clotting time [sec]-representing the liquid phase of coagulation up to initial fibrin formation); Clot rate (units/min [Sonoclot scale of signature anplitude/viscosity] - the slope of the signature during fibrinogen to fibrin conversion); Peak amplitude (units, signifying completion of fibrin formation and initial platelet interaction); and Time to peak amplitude (min, dependent on fibrin and platelet function). Patient demographics, hematology and coagulation results, estimated blood loss and blood product administration were recorded. Sonoclot parameters were compared by ANOVA with Bonferroni correction for multiple comparison (significance assumed with $p < 0.0125$).
RESULTS: 25 patients were enrolled (7 male, age 48.5 $\pm$ 11.9 years), undergoing aneurysm (14), AV malformation (3), tumor (2) or other intracranial surgery. Coagulation parameters remained withing normal limits. Sonoclot parameters (table) demonstrated a continual trend towards a decreased end of surgery and postoperative SonACT although this did not reach statistical significance.
DISCUSSION: Although the Sonoclot analyzer has been used in surgical patients at risk for altered coagulation (1,3), there is no data for neurosurgical patients. Our data in patients undergoing craniotomy with *normal* baseline coagulation suggest that the SonACT may be a useful monitor of accelerated peri/postoperative fibrin formation in this population, and supports prior findings of hypercoagulability in this patient group (4). Although changes in SonACT did not reach statistical significance, the trend in decreasing values ($\pm$ 40% from baseline to postop) may be of greater *clinical* significance. These findings suggest that investigation be continued to elucidate the role of the Sonoclot in neurosurgical patients, and in particular, for extension of monitoring to patients with pre-existing or developing coagulation abnormalities and those with traumatic brain injuries.

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Sonoclot parameters (n = 25)

	SonACT (sec) (p =0.08)	Clot rate (U/min) (p = 0.4)	Peak amplitude (U) (p = 0.5)	Time to peak amplitude (min) (p = 0.2)
After induction	141.5 $\pm$ 44.2	31.6 $\pm$ 15.5	87.6 $\pm$ 19.9	15.7 $\pm$ 6.3
After 1 hour	138.1 $\pm$ 34.3	28.9 $\pm$ 15.0	82.7 $\pm$ 19.9	12.3 $\pm$ 4.5
After 3 hours	139.5 $\pm$ 29.9	28.3 $\pm$ 12.6	82.6 $\pm$ 14.9	16.3 $\pm$ 7.0
End surgery	123.8 $\pm$ 26.0	27.3 $\pm$ 12.1	76.5 $\pm$ 17.5	14.0 $\pm$ 6.1
24 hours postop	107.9 $\pm$ 37.5	37.1 $\pm$ 13.5	83.9 $\pm$ 29.1	13.3 $\pm$ 3.8

S-174

EARLY MITOCHONDRIAL CHANGES IN RESPONSE TO ISCHEMIA-LIKE INJURY - EFFECTS OF BCL-X_L

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INTRODUCTION: Bcl-x_L is a member of the Bcl-2 family and blocks apoptotic and necrotic cell death. We have previously shown that it is effective in reducing glucose deprivation (GD) induced astrocyte death (1). Despite investigations in many labs the mechanism of protection remains unclear, but is likely to involve mitochondrial function.
METHODS: Primary mouse cortical astrocyte cultures were studied using the potentiometric dye TMRE to follow the time course of changes in mitochondrial membrane potential in live cells subjected to glucose deprivation. In addition, oxygen consumption was used to assess oxidative respiration as a measure of mitochondrial function. ATP and ADP levels were also measured.
RESULTS: As early as 3 h after removal of glucose mitochondria showed hyperpolarization and state III respiration decreased significantly. This is a time point well before cytochrome c is released. Damage to the electron transport chain is not responsible for this change because uncoupled respiration (measured after adding CCCP) did not change. At 5 h of GD when mitochondrial depolarization was observed, state IV respiration increased significantly. Bcl-x_L over-expression prevented both the decrease in state III respiration and mitochondrial hyperpolarization. The slight increase in state IV respiration in Bcl-x_L astrocytes was consistent with the slight gradual depolarization during 5 h of GD. The possibility that Bcl-x_L facilitation of ATP/ADP exchange could explain the differences in membrane potential was excluded by measuring cytoplasmic and mitochondrial ATP/ADP ratios.
DISCUSSION: Bcl-x_L protection is associated with maintaining normal state III and slightly increased state IV respiration. Although Bcl-x_L is associated with regulation of apoptosis the effects on mitochondrial function seen early in GD precede any evidence of apoptosis, such as release of cytochrome c from mitochondria. This work demonstrates Bcl-x_L effects on mitochondrial function during mild stress, suggesting direct effects on mitochondrial function independent of apoptosis.

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Obstetric Anesthesia

S-175

BISPECTRAL INDEX VALUES AT SEVOFLURANE CONCENTRATIONS OF 1% AND 1.5% IN LOWER SEGMENT CESAREAN SECTION

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INTRODUCTION: A bispectral index (BIS) of 60 appears to represent the threshold below which consciousness is unlikely [1]. Isoflurane 0.5% in 50% nitrous oxide is commonly used in lower segment cesarean section (LSCS) but does not reliably achieve BIS values <60 [2]. Inadequate hypnosis may therefore partly account for the increased risk of awareness in LSCS, especially since opioids are avoided prior to delivery of the neonate. Sevoflurane 1.0% has been shown to be equivalent to isoflurane 0.5% when used in this setting [3]. The aim of this study was therefore 1) to determine the BIS values achieved with an end-tidal sevoflurane concentration of 1.0%, and 2) to determine if a higher end-tidal concentration of 1.5% would consistently produce BIS values <60.
METHOD: Following institutional approval, 20 ASA 1-2 parturients requesting general anesthesia for elective LSCS were randomized into 2 groups. Group 1 was maintained at an end-tidal sevoflurane concentration of 1.0% throughout the operation, whilst Group 2 was maintained at 1.5%. Sevoflurane was administered in 50% nitrous oxide until delivery; thereafter nitrous oxide was increased to 66%. Thiopental 4 mg/kg and succinylcholine 1.0-1.5 mg/kg were used for induction. Morphine 0.1-0.15 mg/kg, and oxytocin 10 IU were given following delivery of the neonate. BIS values during anesthesia were recorded together with other indices of maternal and neonatal outcome. Patients were interviewed post-operatively regarding intra-operative recall. Results were analyzed using the Mann-Whitney *U*-test for BIS data, and Student's t test for other data. A p-value <0.05 was considered statistically significant* and <0.01 highly significant#.
RESULTS: Median BIS values in Group 2 were <60 at all times during the operation. Median BIS values in Group 1 exceeded 60 prior to delivery, except at intubation. BIS values were significantly different between Group 1 and Group 2 at skin incision (64 vs 52*), uterine incision (65 vs 39.5#), delivery of neonate (66 vs 42#) and 10 minutes after delivery (63 vs 42.5#). There were no significant differences between the 2 groups with regard to intra-operative hemodynamics, blood loss, neonatal Apgar scores, emergence times or recovery characteristics. None of the patients reported intra-operative recall.
DISCUSSION: End-tidal sevoflurane 1.5% reliably maintained BIS at levels <60 prior to delivery of the neonate in LSCS, whereas sevoflurane 1.0% did not. Prevention of awareness in LSCS may require an end-tidal sevoflurane concentration greater than 1.0% prior to administration of opioids.
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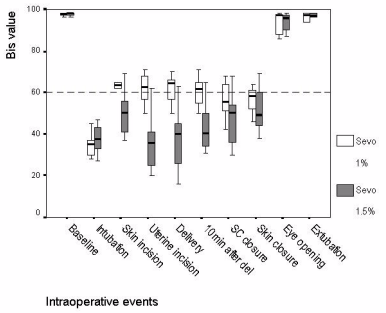

Figure 1. Intraoperative BIS values. Black bars = median, boxes = 25-75th percentiles, lines = 10-90th percentiles.

S-176

PROPOFOL PROVIDES BETTER ANESTHESIA THAN KETAMINE/DIAZEPAM SEDATION FOR TRANSVAGINAL OOCYTE RETRIEVAL WITHOUT ADVERSELY AFFECTING REPRODUCTIVE OUTCOME

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INTRODUCTION: Best anesthetic method for transvaginal oocyte retrieval for in vitro fertilization (IVF) is not established. Propofol is expected to provide adequate anesthesia with rapid recovery, but it may adversely affect reproductive outcome, because some *in vitro* animal studies have suggested its interference with blastocyst formation. Thus we compared the quality of anesthesia of propofol with ketamine/diazepam sedation as well as their effects on reproductive outcome in IVF.
METHODS: Our institutional review board approved the following two studies. *Anesthesia quality study.* Patients undergoing oocyte retrieval in the year 2000 were divided into three groups depending on the anesthetic agent according to the discretion of the anesthetist as follows: propofol only (group P), propofol-nitrous oxide (group PN), and ketamine/diazepam/atropine (group K). Incidence of intraoperative recall, pain, nausea, dizziness and dream were prospectively collected immediately after the procedure and two hours later at the time of discharge. *Reproductive outcome study.* Records of 1223 cycles for IVF from January 2000 to June 2002 were retrospectively reviewed in terms of dose of anesthetic agents, retrieval success rate, fertility rate, and pregnancy rate. The results were compared among the groups P, PN, K as described in anesthesia quality study, using Chi-square test.
RESULTS: *Anesthesia quality study.* The number of patients in each group were; P:87, PN:105, K:57. The dose of propofol between P and PN were not different (273mg vs.278mg, respectively). None of the patients in group P and PN had intraoperative recall, but 21% of group K had recall. Incidence of pain was significantly lower in group K(23.0%) as opposed to group P(51.7%) or group PN(57.7%) immediately after the procedure, but the difference resolved 2 hours later. Higher incidence of nausea was noted in group K(24.4%) than group P(9.4%) or group PN(2.0%) 2 hours later. Dizziness was two times higher in group K even when 2 hours had elapsed. About 20% of the patients in each remembered a dream, only one dream in group K was described unpleasant. *Reproductive outcome study.* The number of cycles in each group was; P(267), PN(812), K(144). The dose of anesthetic agent was; P(propofol 298±86.2g), PN(propofol 294±92mg, N2O 66%), K(ketamine 51.0±11.7mg, diazepam 10mg). Reproductive outcomes in group P, PN, K, respectively, were not statistically different with regard to retrieval success rate (98.8%, 99.3%, 98.6%), fertilization rate (90.6%, 94.7%, 96.4%), pregnancy rate (25.1%, 26.6%, 30.3%). However, when ICSI (intracytoplasmic sperm injection) cases were excluded, fertilization rate of group P was significantly lower than group PN (90.3% vs. 95.2%, P<0.05).
DISCUSSION: Propofol based general anesthesia for oocyte retrieval provides adequate anesthesia with good recovery profile, compared with the ketamine based sedation. However, analgesic supplementation may be warranted. Reproductive outcome is not worse when propofol is used for anesthesia in oocyte retrieval.

S-177

PERINATAL MANAGEMENT OF ANTENATALLY DIAGNOSED CONGENITAL DIAPHRAGMATIC HERNIA: SURVEY OF PRACTICE IN JAPAN

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INTRODUCTION: Neonates with congenital diaphragmatic hernia(CDH) remains to have high mortality rate despite antenatal diagnosis followed by elective Cesarean delivery. Recently, Japanese neonatologists advocated the deliberate delivery of a depressed, apneic neonate by Cesarean section in order to prevent gastric distension and PPHN. The preliminary report seems promising1). However, the safe and effective drug regimen or route of delivery (umbilical vein injection and/or maternal administration) for this purpose has not been established. There is also a concern for the maternal safety when general anesthesia is advocated for this practice. Thus we conducted the nationwide survey of perinatal management of CDH with emphasis on the anesthetic management for Cesarean section.
METHODS: After institutional review board approval, telephone survey was conducted to the chief anesthesiologist of 29 registered centers for maternal fetal medicine in Japan. Questions include mode of delivery, protocol of fetal anesthesia for deliberately depressing the neonate, type of anesthesia for Cesarean section and anesthetic agent. Opinion was also asked whether or not fetal anesthesia improved neonatal outcome. Neonatal management questions include availability of HFO, ECMO, NO.
RESULTS: All the centers responded to the survey. Chief anesthesiologist responded in all institutions except two, in which obstetrician or pediatric surgeon was considered more suitable for the survey. Four institutions lacked pediatric surgery service, thus the remaining 25 institutions were included in the analysis. 84% of the centers preferred elective Cesarean delivery. While only 53% had the protocol of fetal anesthesia at the time of survey, 72% of the respondents aimed for delivering the depressed neonate, the so-called "sleeping baby". For this purpose, 77% chose general anesthesia for Cesarean section. Maternally administered drugs include fentanyl, diazepam, propofol, sevoflurane. Direct umbilical vein drug administration, as originally proposed by Tamura, was practiced in only 3 centers in Japan, and they administer pancuronium and morphine. With regard to the neonatal outcome, half of the respondents had the opinion that this practice did not improve neonatal outcome. Availability of advanced neonatal management modalities was quite high except for ECMO; HFO: 82.7%, NO: 68.9%, ECMO: 37.9%.
DISCUSSION: This survey revealed that the concept of deliberately delivering depressed neonate by Cesarean section is widely accepted when CDH is diagnosed antenatally. However, still half of the respondents doubt its benefit. This may be due to the variable drug regimen with inadequate neonatal effect. Further refinement of the protocol and the follow up of outcome seems necessary before adopting this new idea of perinatal management for CDH.
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S-178

ENOXAPARIN THERAPY DURING PREGNANCY AND MANAGEMENT OF LABOR ANALGESIA

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INTRODUCTION: Low molecular weight heparin therapy (LMWH), especially when given with concomitant aspirin therapy, has been associated with bleeding and specifically with epidural hematoma in those patients receiving epidural anesthesia.
The purpose of this project was to determine the practice regimens and patient outcomes in parturients receiving LMWH and neuroaxial anesthesia for labor analgesia at our institution.
METHODS: With permission of the Institutional Review board, we reviewed patients' medical records over a period from 1998-2002. Using ICD9 billing codes, we identified those parturients with diseases associated with LMWH therapy, specifically Enoxaparin (EN). After reviewing the information, we entered the data into a computer database using Microsoft ACCESS™ software. Only those patients who received LWMH therapy during their pregnancy were included with the following data: date of birth, height, weight, maternal age, race, parity, maternal diagnoses, concomitant aspirin usage, maximum daily dosage of EN (mg), start and stop date of EN usage, hours between EN stoppage and insertion of regional, type of regional anesthesia, mode of delivery, apgar scores, birth weight.
RESULTS: We identified 50 patients who received LMWH during their pregnancy. The most common primary diagnoses were: Factor V Leiden deficiency (22/50), Systemic Lupus (4/50), Anti-Phospholipid Syndrome (4/50), Thrombophillia (4/50).The remaining diagnoses included embolic disease and coagulation disorders. Twenty- two out of the 50 patients studied took Aspirin 81 mg daily throughout their pregnancy in addition to the EN. The Obstetricians rountinely discontinued the EN during the third trimester and began unfractionated heparin therapy so that the patients could receive regional anesthesia during labor and delivery (Table). Factor Xa levels are not measured during EN therapy or when regional anesthesia is given. There were no bleeding complications nor were there any adverse maternal or fetal outcomes associated with the use of regional anesthesia in these patients (Table).

Enoxaparin Dosing Regimens and Fetal Outcomes

Daily Dose of Enoxaparin (EN) mg	Average =61.5	Min =40 Max =260
Weeks of Gestation EN Started (weeks)	13.4 +/- 8.08	
Weeks of Gestation EN Stopped (weeks)	34.3 +/- 5.36	
Hours Between Last EN dose and Regional Anesthesia (hrs)	370.68 +/- 447.54	min =6.75 max=1782
Birthweight (g)	2992.82 +/-896.58	
Apgar 1 min	7.91 +/- 0.39	
Apgar 5 min	8.89 +/- 0.47	

S-179

IS EPIDURAL-PCA ANALGESIA NECESSARY FOR A THIRD DAY POST CESAREAN SECTION PAIN?

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INTRODUCTION: Our practice has been to provide epidural-PCA ropivacaine 0.025% with fentanyl 3 mcg/ml & epinephrine 1 mcg/ml for most of our post cesarean section (C/S) patients for 48 hrs. Very often, patients requested to continue this treatment for another extra day.
METHOD: We determined if epidural-PCA analgesia is necessary for 3rd day post C/S. 112 pts who received epidural-PCA for post C/S pain for 48 hrs were included. The patients were given the option to continue this treatment for 72 hrs or to discontinue the treatment at 48 hrs and receive P.O. oxycodone 5 mg + acetaminophen 325 mg tabs along with ibuprofen 400 tab every 4 hrs PRN. Two groups were identified: G I: 78 pts preferred to continue the epidural-PCA treatment; G II: 34 pts preferred to discontinue the epidural-PCA treatment. Values are mean±SD.
RESULTS: The groups did not differ with age, weight, height or parity. The pts in GI received epidural infusion rate of 11.7 ± 7.0 PCA attempts of 24 ± 41 & PCA dose of 13 ± 13 ml. In G II 26 pts (76.5%) regretted their decision to discontinue the epidural-PCA treatment at 48 hrs. Overall satisfactions of the pain treatments were 9.3 ± 1.6 & 7.6 ± 2.3 ($p<0.00001$) for G I & II respectively.
CONCLUSIONS: During 48-72 hrs following C/S most pts still complained of pain & requested to continue the epidural-PCA ropivacaine-fentanyl-epinephrine which provided excellent analgesia with minimal side effects.

	Pain (rest at 72 hrs)	Pain (ambulation at 72 hrs)	Pain (cough at 72 hrs)	Sedation	Nausea	Pruritus
Group 1	1.3±2.0	2.5±2.3	3.8±2.8	7(9%)	5(6%)	23(29%)
Group II	2.7±2.6*	4.2±2.9*	5.2±3.0**	13(38%)*	5(15%)	1(3%)***

GII>I: *p<0.005, **p<0.03; ***GII<I, p<0.005.

S-180

DOES RESPONSE TME TO INITIATEEPIDURAL ANALGESIA FOR LABOR AFFECT PATIENT SATISFACTION?

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INTRODUCTION: As part of quality improvement, we instituted a patient evaluation survey designed to determine satisfaction with anesthesia services for labor and delivery (L&D). The questionnaire was used to determine the relationship between response time for labor epidural and overall satisfaction.
METHODS: All patients (n = 654) receiving epidural analgesia for L&D in a community hospital were surveyed for a 6 month period. The epidurals were performed by CA2 and CA3 residents supervised by an attending anesthesiologist using a standard technique. The questionnaire sought information as described in the table. Response time was calculated as the interval (in minutes) between request for epidural and bolus injection. Estimates of pain were made according to a 10 point visual analog scale (VAS).
RESULTS: Of the 446 evaluation forms returned, 53 (11.9%) were rejected as incomplete or inaccurate. The remaining 393 forms were submitted for data analysis. The table summarizes the responses. Data in the table appears as mean ± standard deviation followed by ranges or as counts followed by percent.
DISCUSSION: Most OB physicians (70.7%) discussed methods of pain relief during antenatal visits and half the patients recieved IM or IV butorphanol prior to an epidural. Epidural analgesia achieved a significant reduction in perceived pain ($P < .001$) and met or exceeded patients expectations in 80.8% of patients. Following epidrual, 73% of patients experienced little or no pain following epidural. These factors resulted in an overall satisfaction of 91.4%. Contrary to our original hypothesis, we found no relationship between mean response time and either timeframe satisfaction or overall satisfaction with labor epidural. Patient satisfaction is a multifactorial issue;[1-3] perhaps other factors (primigravida/multipara, previous anesthetics, etc.) not elicited from our survey, were also involved. In conclusion, patient satisfaction surveys yield valuable information and unexpected results. Although prompt response to requests for labor epidurals and adequate pain relief probably contributed to the high patient satisfaction, the factors contributing to dissatisfaction were not elucidated. Expanding the scope of the questionnaire may be necessary.

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Summary of Questionnaire Responses	
Age	26.3 ± 6.2 yrs
Prior discussion about pain relief	Yes = 266 (70.7%) No = 110 (29.3%)
IM or IV pain meds before epidural	Yes = 172 (50.3%) No = 170 (49.7%)
Pain prior to epidural (10 pt VAS)	8.0 ± 2.3 (0-10)
Pain after epidural (10 pt VAS)	2.8 ± 3.0 (0-10)
Was response time satisfactory?	Yes = 271 (73.8%) No = 96 (26.2%)
How often was pain moderate or severe after epidural	Always = 16 (4.2%) Almost Always = 19 (5.0%) Often = 63 (16.7%) Almost Never = 176 (46.6%) Never = 104 (27.5%)
Compared to expectations, how much pain was experienced after epidural	Much More = 38 (10.1%) Somewhat More = 34 (9.1%) As Much = 46 (12.3%) Somewhat Less = 113 (30.1%) Much Less = 144 (38.4%)
Overall Satisfaction	Very Satisfied = 236 (61.8%) Satisfied = 113 (29.6%) Neither = 20 (5.2%) Dissatisfied = 5 (1.3%) Very Dissatisfied = 8 (2.1%)
Response Time	30.9 ± 20.4 min (15-185 min)

S-181

PARTNER ANXIETY PRIOR TO ELECTIVE CAESAREAN SECTION UNDER REGIONAL ANESTHESIA IN AN AMERICAN TEACHING HOSPITAL

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INTRODUCTION: Over 90% of Caesarean sections at the University of Michigan are performed under regional anesthesia. A partner, relative, or friend usually accompanies the woman, which is helpful in reducing her stress level. The aim of this study was to measure the anxiety levels of the partners of women undergoing an elective Caesarean section with regional anesthesia and to assess whether there was any association between anxiety and the specific demographics of this group.
METHODS: One hundred partners of women undergoing an elective Caesarean section with regional anesthesia were recruited to this study over a nine-month period from August 2001 to April 2002. Each partner received both a verbal and written explanation of the study. Prior to the surgery, partners completed a questionnaire anonymously and without assistance (although a researcher was available to answer any questions). The questionnaire comprised four parts: (1) demographic data regarding age, gender, occupation, education, previous attendance during Caesarean sections, attendance at anesthetic assessment clinics, and relationship to patient; (2) the Leeds Self Assessment of Anxiety (SAA) scale [1]; (3) specific questions about possible sources of anxiety; (4) specific questions about potential relieving factors of anxiety. Additional comments were invited for the final two sections. The Leeds SAA scale has four possible responses to each question with the following associated points: not at all (0), not much (1), sometimes (2), definitely (3); possible overall scores range from a maximum score of 18 to a minimum score of 0. The scale uses a cut-off score of 7 to identify anxiety consistent with a pathological state. All scores were age-corrected using a standard formula [1]. Chi-Square tests and Fisher's Exact tests were used to determine differences between each of the demographic variables and level of anxiety among partners. A Student's *t*-test was used to determine differences in partner age in the anxious and non-anxious partners.
RESULTS: Twenty-eight percent of participants demonstrated anxiety scores consistent with a pathological state. No statistically significant associations between anxiety and demographic data were demonstrated.
DISCUSSION: We found the 28% figure for partner pathological anxiety recorded in this American study to be identical with the figure found for an equivalent study in the United Kingdom-28% [2]. The consistency of findings between these two observational studies warrants further investigation into how we can alleviate stress within this covert partner population. It is possible that this anxiety may be related to personal psychological vulnerability rather than any outside factors. It is interesting to note that the general anxiety caused by the terrorist attacks of 9/11 (which coincided with this study) appears to have had no effect on the level of partner pathological anxiety.
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S-182

PROSPECTIVE EXAMINATION OF EPIDURAL CATHETER INSERTION

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INTRODUCTION: It is generally accepted that inserting epidural catheter 4-5 cm into the epidural space minimizes complications. Complications can occur during epidural placement for women in labor. As many as 23% of epidural anesthesic may not provide satisfactory analgesia. The cause of this may be technical. This study was undertaken to determine the optimal distance that a multiorifice catheter should be theraded into the epidural space to maximize analgesia and minimize complications.
METHODS: Ninety healthy parturients were enrolled in this prospective, randomized, and double-blind study. Patients were randomly assigned to have the epidural catheter threaded 4, 6 or 8 cm into the epidural space. After placement of the catheter and administration of a test dose with 3 ml of 0,2% ropivacaine, an additional 10 ml of 0.2% ropivacaine was administered. Thirty minutes later, the adequacy of the analgesia was assessed by a blinded observer. The incidences of intravenous cannulation, unilateral sensory analgesia, and subsequent catheter dislodgment were recorder.
RESULTS: We found that epidural catheter insertion to 8 cm were associated with the highest rate of insertion complications while insertion to 4 cm was associated with the highest incidence of satisfactory analgesia. Epidural catheters inserted 8 cm required replacement more often than epidural catheters inserted 4 cm. Ninety-five percent and 50% of epidural catheters that resulted in unilateral sensory analgesia and intravenous cannulation, respectively, provided analgesia for labor and delivery after incremental withdrawal.
DISCUSSION: For women in labor who require continuous lumbar epidural anesthesia, we recommend threading a multiorifice epidural catheter 4 cm into the epidural space. Additionally, epidural catheters that result in intravenous cannulation or unilateral sensory analgesia can be manipulated effectively to provide analgesia for labor an delivery.

S-183

DOES SUTURING IMPROVE THE RATE OF SUCCESSFUL REACTIVATION OF LABOR EPIDURAL CATHETERS FOR POSTPARTUM TUBAL LIGATION (PPTL) SURGERY?

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92% of lumbar epidural catheters for labor pain remained in place until the time of PPTL surgery can be reactivated successfully until 24 h after they have been placed[1]. Suturing the epidural catheter in our previous study[2], reduced catheter movement, the need for re-insertion and provides a high success rate of epidural blocks.
We examined whether suturing the epidural catheter to the skin can further increase the success rate of reactivation of epidural catheters for PPTL.
METHODS: After obtaining IRB approval and informed consent, we studied 121 ASA I-II pts scheduled for PPTL with epidural catheter in place. Of 2400 pts who received epidural analgesia for labor pain and were randomized into 1200 pts who had the epidural sutured and 1200 that had catheter without suture, two groups were identified. GI (n=48) had their catheters sutured upon insertion. GII (n=73) had their catheters secured without suture. The epidural space was located at L2-3 using loss of resistance to air technique and a midline approach with the pt in lateral or sitting flexed position. An 18 gauge, closed end B Braun catheter was directed 5 cm cephaled and the pt's back was unflexed. For GI pts, the catheters were sutured with 3-0 vicryl suture at the insertion site and then looped downward 5 cm. GII pts had their epidural catheters looped downward 5 cm without being sutured.
RESULTS: Groups did not differ in age, weight, height, parity, distance of epidural space from the skin, position, history of previous neuraxial procedure, Bromage Score and maximum sensory level. Overall satisfaction was high in both groups, 9.6±0.9 vs. 9.5±1.0 for Groups I and II respectively. The length of catheter coiled under skin upon removal was 0.5±0.7cm and 0.2±0.6cm ($p < 0.05$ Student's unpaired test). The incidence of catheter movements and resulting complications and corrections are shown in Tables I & II. Of the 12 failed blocks in GII, 3 occurred within 4 to 12 h (4%), 7 within 12 to 24 h (10%) and 2 after 24 h (3%).
CONCLUSION: Suturing the epidural catheter for labor pain increased the success rate of reactivation of epidural block for PPTL,and may reduce catheter movement, need for reinsertion, the incidence of one-sided anesthesia and catheter puncture of epidural vessels.
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Table 1 Catheter Movement

	Outward	Inward	Catheter coiled Subcut. (cm)	Dislodged
Group I	7(14%)	4(8%)	0.5 ± 0.7	0
Group II	26(36%)	13(18%)	0.2 ± 0.6	11(15%)

Table II Incidence of Complications and Corrections

	Failed Block	One Sided Anesthesia	Blood Vessel Puncture	Readustment of Catheter	Reinsertion of Catheter	Catheter Kink
Group I	0	0	0	2	0	1
Group II	12(16%)*	5(7%)	1(1%)	4(5%)	0	1(1%)

Fisher's exact test, *$p < 0.01$

S-184

COMPARISON OF LEVOBUPIVACAINE 0,16% AND S-ROPIVACAINE 0,16% COMBINED WITH SUFENTANIL 0,5µG/ML FOR PARTURIENT-CONTROLLED EPIDURAL LABOR ANALGESIA

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INTRODUCTION: Pharmacological studies suggest that, compared to bupivacaine, the S(-)-enantiomer levobupivacaine has equal local anesthetic potency with reduced potential for cardiovascular and central nervous system toxicity (1). S-ropivacaine is chemically homologous to bupivacaine, but manufactured as the pure S-enantiomer. In vitro and in vivo studies demonstrated less motor block, less central nervous and cardiovascular toxicity (2) and a better neonatal outcome (3) compared to racemic bupivacaine. To date, no previous study has compared the analgesic efficacy of levobupivacaine and S-ropivacaine for parturient-controlled epidural analgesia (PCEA) in labor.
METHODS: After local ethics committee approval and written, informed consent, 40 parturients were included in the prospective, randomized and double-blinded study (ASA physical status I, 31.2±5.6 years, 167.1±5.7 cm, 79.9±11.7 kg, 39.2±1.9 weeks gestational age, cephalad presentation, singleton pregnancy). Epidural catheters were placed at the L2-3 interspace. The parturients were assigned to receive either ropivacaine 0,16% or levobupivacaine 0,16% combined with sufentanil. Thirty minutes after administration of a priming dose containing 16 mg ropivacaine or 16 mg levobupivacaine plus 10 µg sufentanil, PCEA was startet(background infusion 6 mL/h, lock-out time 20 min, bolus 3 mL, 0.5 µg sufentanil). The intensity of pain (visual analog scale, VAS, range 0-100 mm) as well as total drug dose administered, duration of labor and delivery, sensory and motor block characteristics, maternal satisfaction with the degree of pain relief and neonatal outcome (Apgar-score, umbilical cord blood analysis) were determined. Data are expressed as mean ± SD, a P-value of<0,05 was considered statistically significant.
RESULTS: No differences in parturients demographics, parity, induction of labor rate, total drug dose administered, duration of labor and delivery were observed. During PCEA, median sensory block level was T6 in both groups, maximum motor block according to the Bromage scale (4) was 1 in both groups. At no time there was a significant difference between VAScores among groups. Considering all VAScores over PCEA time, there were 72 time points in the S-ropivacaine group and 59 time points in the levobupivacaine group, respectively. In the S-ropivacaine group, VAScores were greater than 40 mm at 7 time points(9,7%) compared to 4 time points (6,8%) in the levobupivacaine group. This difference was not statistically significant. There was no evidence of neonatal depression.
DISCUSSION: Both local anesthetics combined with sufentanil provided excellent parturient satisfaction. Used epidurally for PCEA in labor, levobupivacaine 0.16% had the same clinical profile as S-ropivacaine 0.16%when combined with sufentanil.
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means±SD	S-Ropivacaine	Levobupivacaine
Duration of labor (h)	9:24±3:28	9:06±3:53
Duration of PCEA (h)	2:08±2:09	2:04±1:33
Cumulative local anesthetic dose administered (mg)	53.3±22.1	50.7±21.4
Cumulative sufentanil dose administered (µg)	16.7±6.9	15.9±6.7
Maternal satisfaction with the extend of pain relief (%)	100%	100%

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LEVOBUPIVACAINE COMBINED WITH FENTANYL ADMINISTERED INTRATHECALLY FOR CESAREAN SECTION: A COMPARISON WITH RACEMIC BUPIVACAINE

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INTRODUCTION & OBJECTIVE: Hyperbaric intrathecal (IT) *L*-bupivacaine(LB) has been shown to exhibit equivalent clinical efficacy to racemic bupivacaine (RB) in doses from 4 to 12 mg among healthy volunteers (1). For facilitating elective cesarean section, it has been recommended that IT LB 10-12.5mg could substitute for RB (2). The aim of this study was to compare IT LB with RB (both with added IT fentanyl) in parturients undergoing elective cesation section under spinal anesthesia.
METHODS: In this ongoing prospective, double-blinded trial, 24 patients has since been randomized to receive either hyperbaric 0.5% LB 9 mg + fentanyl 10 mcg (Group LB, *n*=14) or 0.5% RB 9 mg + fentanyl 10 mcg (Group RB, *n*=10). Sensory block (loss of pinprick sensation), motor block (modified Bromage scale), analgesic characteristics and post-block complications were evaluated. Statistical analysis comprised the Student's *t*-test, Wilcoxan ranked-sum test and Newman-Keuls test for post hoc comparison.
RESULTS: Patient characteristics in the 2 groups were not statistically significant. The time to regression of motor block to Bromage 0 was significantly shorter for LB compared to RB (146+/-29 min; 95% CI of 72-100 min *vs.* 155+/-26 min; 95% CI 137-179 min respectively). In addition, 3 (21%) patients in the LB groupdid not achieve a Bromage 3 score whereas all RB patients did.
CONCLUSION: The combination of 0.5% bupivacaine 9 mg (either LB or RB) with fentanyl 10 mcg provided for satisfactory analgesia in all study subjects. LB resulted in a faster resolution of lower limb motor power which may facilitate earlier postoperative ambulation.

Spinal block characteristics for the 2 study groups

	LB (*n*=14)	RB (*n*=10)
Highest dermatome reached	T3	T2
Time to reach highest dermatome (min)	9+/-2	12+/-4
Time to Bromage 3 (min)	7+/-3	6+/-3
Time to regression to T10 (min)	146+/-29	175+/-38
Time to regression to Bromage 0 (min)	86+/-26	155+/-25* (p<0.05)
Time to 1st sensation of pain (min)	108+/-28	140+/-32
Time to 1st request for analgesics (min)	910+/-147	284+/-87
Satisfaction score (VAS 0-100)	89+/-8	91+/-7

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S-186

BACKGROUND INFUSION ADDED TO PARTURIENT CONTROLLED EPIDURAL ANALGESIA DURING LABOUR AND DELIVERY - IS LESS MORE?

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INTRODUCTION: The use of a continious background infusion during parturient controlled epidural analgesia (PCEA) seems to reduce breakthrough pain [1, 2] during labor. Currently, 25 - 30% of the maximum dose as a continuous background infusion are recommended [1]. This study was designed to determine whether a 40% backround infusion results in less pain peaks than 25%.
METHODS: After local ethics committee approval and written, informed consent, 40 parturients were included in this study (ASA physical status I and II, >37 weeks gestational age, singelton pregnancy, cephalad presentation). After placement of an epidural catheter and administration of an initial bolus containing 16mg ropivacaine plus 10µg sufentanil, parturients were prospectively randomized into two groups. The PCEA-solution consisted of ropivacaine 0.16% plus 0.5µg/ml sufentanil. Group 1 received PCEA with 4mL/h background infusion plus an hourly maximum of 4 x 4mL boli on demand. Group 2 received PCEA with 6mL background infusion plus an hourly maximum3x3ml boli on demand. The intensity of pain (verbal analog scale VAS, range 0-100) as well as the overall drug doses administered, duration of labor and delivery, sensory and motor block characteristics, maternal satisfaction with the extent of pain relief and fetal outcome (Apgar-score, umbilical cord blood analysis) were determined at 30 and 60 min after start of PCEA and then hourly until delivery.
RESULTS: Demographics as well as duration of labor and delivery as well as sensory and motor block characteristics were comparable among groups. Pain peaks (VAS 40) in group 1 occurred at 6 of 91 time points (6.6 %) and in group 2 at 5 of 86 time points (5.8%). Bolus demand differed not significantly among groups. Mean PCEA-solution consumption in group 1 was 14.6 ± 7.3mL and in group 2 27.4 ± 14.9mL, being significantly higher (p=0.0018).

means ± SD	**Group 1**	**Group 2**	
duration of PCEA [min]	182.4 ± 132.58	205.35 ± 129.83	n.s.
cumulative sufentanil dose [µg]	7.32 ± 3.65	13.72 ± 7.45	0.0018
Apgar Score at 10mins	9.3 ± 0.3	9.8 ± 0.5	n.s.
satisfaction with the extent of pain relief [%]	100	100	n.s.

DISCUSSION: Although both regimens provided excellent pain control during labor and delivery, increasing the background infusion rate to 40% conferred no benefit. The regimen using less PCEA-solution yields identical results with respect to overall parturient satisfaction and pain relief. There was no evidence of neonatal depression.

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1. The role of continuous background infusions in patient-controlled epidural analgesia for labor and delivery. Anesth Analg 1994;79:80-84
2. Continuous background infusion plus demand dose is superior to demand - only parturient-controlled analgesia (PCEA) for labor and delivery IARS 76th Clinical & Scientific Conference 2002, Abstract S193

S-187

STATION OF THE PRESENTING PART VS CERVICAL DILATATION AT THE TIME OF EPIDURAL BLOCK AS PREDICTORS OF CESAREAN DELIVERY

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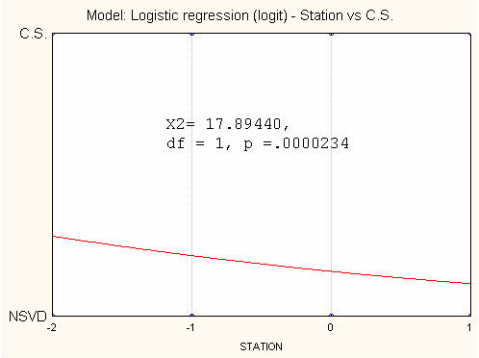
Epidural analgesia is implicated in increasing cesarean section (C.S). This reports whether the station of the fetal vertex or cervical dilataton at the time of epidural block is more frequenetly associated with cesarean section (C.S) section for dystocia.
The report is based on quality assurance database: Inclusion criteria: healthy parturients, nulliparity,singleton vertex presentation, oxytocin augmentaion, epidural analgesia with continuous infusion, birth weight >2.5 Kg. Results were expressed as mean (SD) and analyzed using X2 and logistic regression tests. Cervical dilatation and station of the vertex (-2, -1, 1 +1) were noted. A totalof 1554 parturients were included. No association between was seen between cervical dilatation and C.S.. However, C.S. was most likely to happen in patients at -2 station and least likely at +1 station (p=0.00002,Odds ratio for the range 9.8, Fig 1) The C.S. rate for dystocia was the highest at -2 station and the lowest at +1 (Table 1).
Our data show that the station of the presenting part in relation to the iliac spines is a btter predictor of C.S than cervical dilatation at the time of epidural block. This factor must be considered when evaluationg the effect of epidural analgesia on C.S rate.



Station vs C.S. rate

Station	Cervical Dilatation (cm)	Total cases (n)	C.S.%	p vs Station -2
-2	3.2(1.34)	209	26,8%	
-1	3.44 (1.23)	718	16.8	0.002
0	4 (1.72)	573	12.7	0.000
+1	4 (0.63)	54	9.2	0.01

Pain – Basic Science

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DEVELOPMENT OF A PRIMATE BEHAVIORAL NOCICEPTIVE ASSAY

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INTRODUCTION: Lacking the pain assessment tools that could differentiate different elements of a pain state would considerably hamper the ability to evaluate a distinct treatment outcome in the clinical setting(Mao J, pain 2002). We have established a rodent assay which allow for the separate assessment of nociceptive responses mediated by the activation of myelinated(A-) or unmyelinated (C) pain afferents (Yeomans, pain1996). However, prior to attempting novel analgesic treatment in humans, it is important to determine whether similar effects exists in non-human primates. This study is to develop a primate behavioral nociceptive assay such that we are able to separately assess heat-evoked withdrawal responses mediated by the two afferent types in stump-tailed macaques.
METHOD: Stump-tailed macaques were lightly anesthetized with IV propofol. Foot withdrawal latencies evoked by high (6.5 degree C/sec-A-) or low (0.9 degree C/sec-C fiber)rate radiant heating of the dorsum of the hindpaws are assessed. In some cases, the skin of the hindpaw are then treated topically with a solution of capsaicin which preferentially sensitize C fiber afferents. in some sessions, cumulative dose response for IV morphin are generated, as systemic morphin preferentially attenuate C, as opposed to A- mediated nociception.
RESULTS: The evoked foot withdrawal latencies similar to those observed in rats for both high (2-3 sec) and low (10-12 sec) heating rates. Capsaicin preferentially decreased foot withdrawal latencies for responses to the low rate heating. Morphin preferentially affected low vs. high rate heating responses.
DISCUSSION: In a non-human primate, responses to low rate skin heating are mediated by C fiber activation, whereas responses to high rate heating are mediated by A- activation. The principles determined in rodents with regards to differential testing of A- and C fiber mediated nociception are also applicable to the testing of non-humen primates. This primate nociceptive assay allows for differentiation of different elements of pain state and for better predictions of the clinic utility of novel approaches to the treatment of pain.
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S-189

ANALGESIC DRUG SENSITIVITY IN A NEW RAT MODEL OF POST-THORACOTOMY PAIN

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INTRODUCTION: The incidence of long-term pain after thoracotomy is 50% (1), usually along the distribution of the intercostal nerves. A recent clinical study has shown that rib retraction alone caused conduction block in the intercostal nerves on both sides of the retractor (2). In addition, a chronic pain syndrome can be produced in rats by inducing a chronic constriction injury (CCI) to the intercostal nerves with chromic gut sutures (3). The present study describes a combined rib-retraction/thoracotomy model and compares it to the CCI model. The effect of morphine or gabapentin on the mechanical allodynia elicited in these models was also tested.
METHODS: Following Animal Care Committee approval, male Sprague-Dawley rats were anesthetized with isoflurane and the right 4th and 5th ribs exposed. For the rib-retraction model, the pleura was opened between the 2 ribs and a small self-retaining retractor placed under the ribs and opened 8 mm. The retractor was left in place for 30 or 60 min. During this time, ventilation was mechanically assisted. For the CCI model, the pleura was also opened and 4-0 chromic gut sutures were loosely placed around the 4th and 5th intercostal nerves. At the completion of the surgery, air was aspirated from the pleural cavity before suturing the wounds. Starting at Day 2 post-surgery, animals were tested for mechanical allodynia using calibrated von Frey filaments applied to the dorsal skin around the incision site (3). Two weeks after surgery, animals were tested for reduction of allodynia with intraperitoneal injections of morphine sulfate 1-3 mg/kg or gabapentin 25-50 mg/kg. Responses pre- and post-injection were compared with the Wilcoxon signed-rank test.
RESULTS: With the CCI model, mechanical allodynia (withdrawal threshold < 4 gm) occurred in 60% of the animals, which is similar to the incidence reported in the original description of the CCI method (3). With the rib-retraction model allodynia was seen in 40% of the animals after 60 min of retraction, but only 17% when the retraction time was reduced to 30 min. Allodynia appeared by Day 9 in both the CCI and rib retraction models, and lasted at least 42 days. Morphine at 3 mg/kg, but not 1 mg/kg, and gabapentin at 50 mg/kg, but not 25 mg/kg, reduced allodynia (Fig.).
DISCUSSION: Rib-retraction in rats for 60 min produces a similar mechanical allodynia as in the CCI model. Allodynia in either model is sensitive to both morphine and gabapentin. Since rib-retraction in patients has been shown to affect intercostal nerve function, this new model presented here may be useful for devising techniques to treat and reduce long-term pain.
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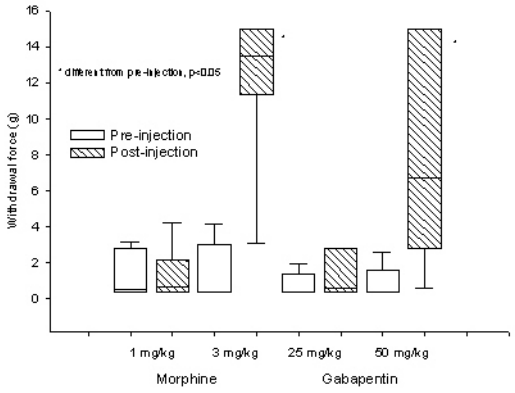

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INFLUENCE OF POST-OPERATIVE PAIN ON SPINAL CYCLOOXYGENASE-2 (COX-2) IN RATS

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INTRODUCTION: Peripheral inflammation elicits up-regulation of COX-2 (but not COX-1) mRNA and protein in the spinal cord (1,2). However, it is not known whether there are similar changes in spinal COX-2 following surgical incision. We have performed experiments with normal rats and rats 6 h after foot-incision surgery to determine if changes of COX-2 protein occur in the lumbar spinal cord postoperatively. The COX-2 protein was also compared to another group of rats who developed inflammation.
METHODS: Following Animal Care Committee approval, male Sprague-Dawley rats (300 g) were anesthetized with isoflurane, a 1 cm long incision made in the skin and plantaris muscle of the plantar hindfoot bilaterally, and then animals allowed to recover from anesthesia. This model produces post-operative pain within a few hours of the incision (3). Six hours after incision animals were sacrificed and the spinal cord rapidly ejected from the spine using a syringe with cold saline. The L3-L6 spinal cord segment was dissected free and quick-frozen. Spinal cords were also removed and dissected from normal control rats, as well as from a third group of animals that had kaolin-carrageenan injected into the knee, a technique known to produce an increase in COX-2 protein levels (4). The spinal cord sections were homogenized in lysis buffer and prepared for Western blot analysis. The total protein of each sample was adjusted to 2 mg/mL. Films were later analyzed with densitometry and experimental animals were compared to unoperated controls.
RESULTS: Western blot analysis of spinal cords showed two bands around 72 kD alongside that of the purified COX-2 protein standard (Fig.). In the foot incision animals, the optical density of the COX-2 protein band was increased 1.33-fold as compared to the control animals. In the kaolin-carrageenan animals (positive inflammatory control), COX-2 protein increased 1.44-fold.
DISCUSSION: This is the first study to demonstrate that post-operative pain leads to an increase in COX-2 protein levels in the lumbar spinal cord. We have previously demonstrated that a spinally administered COX-2 inhibitor contributes to pain relief in the same post-operative pain model (5) suggesting that COX-2 inhibitors delivered neuraxially may can have a role in the treatment of post-operative pain.
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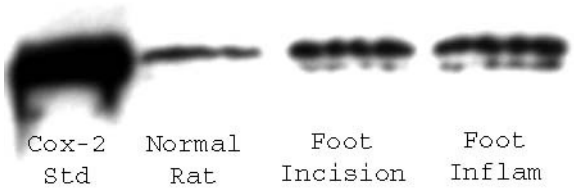

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OPIOID SENSITIVITY IN A RAT MODEL OF ADHESIVE LUMBAR ARACHNOIDITIS

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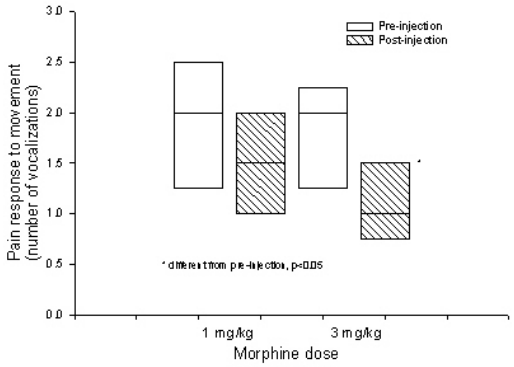
INTRODUCTION: Arachnoiditis is an intractable condition that is a known sequala of spinal surgery. Lumbar laminectomy in rats has been shown to produce adhesions around the lumbar-sacral nerve roots, especially with extradural kaolin application, and to produce pain related behavior in rats (1,2). The response to analgesic therapy, including opioids, is often equivocal in patients with post-surgical arachnoiditis, and there has been no systematic evaluation of opioid analgesia for this condition. In this study, we evaluated the rat post-laminectomy model as a method for testing pain responses after systemic opioid administration.
METHODS: Following Animal Care Committee approval, male Sprague-Dawley rats (300-350 g) were anesthetized with isoflurane and a laminectomy performed at the L5 and L6 vertebral level. Sterile kaolin powder, 5 mg, was applied to the epidural space. After 5 min, the wound was closed. Animals were monitored twice weekly for emergence of pain-related behavior: ambulation (rotating rod, 15 rpm, 300 sec max); pain response to movement (number of vocalizations in response to 5 consecutive extensions of the hindleg, average of left and right). After 6 weeks post-operatively, morphine sulfate (0.5 mL, i.p.) at either 1 or 3 mg/kg was administered and pain related behavior reevaluated 30 min later. Data were analyzed using the Wilcoxon signed-rank test.
RESULTS: Prior to surgery, all animals could remain on the rotating rod for 300 sec. At 6 weeks after the laminectomy, none of the animals could ambulate for the full 300 sec. Before surgery, rats did not vocalize when their hindleg was extended. At 6 weeks post-surgery, the animals vocalized 1.9 times out of 5 extensions. Morphine administration decreased the pain response to hip movement at 3 mg/kg, but not 1 mg/kg (Fig.).



Morphine at both doses improved time on the rotating rod (from 174 to 244 sec at 1 mg/kg; from 176 to 256 sec at 3 mg/kg).
DISCUSSION: Systemic morphine improved ambulation in rats with adhesive lumbar arachnoiditis, and also reduced the pain response to hip extension. This model should be useful for evaluating the efficacy of other drug treatments for post-laminectomy arachnoiditis.
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S-192

SPINALLY MEDIATED ANALGESIC INTERACTION BETWEEN CLONIDINE AND BUPIVACAINE IN ACUTE THERMALLY OR INFLAMMATORY INDUCED PAIN IN RATS

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INTRODUCTION: Intrathecal clonidine, an $_2$ adrenergic receptor agonist, showed synergistic analgesia with lidocaine in the tail-flick test in rats.[1] However, no studies were seen of the interaction between clonidine and local anesthetic in chronic or inflammatory pain. In addition, clinically bupivacaine is more often used than lidocaine in intrathecal or epidural analgesia because of longer duration of action. Therefore, we investigated the analgesic interaction between intrathecally administered clonidine and bupivacaine in inflammatory pain as well as acute thermal 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 clonidine (0.1 – 3 g) or bupivacaine (1 – 100 g). 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: ED_{50} values (g) are shown. ( ): 95% confidence interval.

	Tail flick	Formalin phase1	Formalin phase2
Clonidine	0.29 (0.19-0.41)	0.15 (0.09-0.21)	0.16 (0.09-0.23)
Bupivacaine	7.1 (3.9-10.5)	5.7 (2.5-8.1)	3.2 (1.7-5.1)
Combination (Clonidine)	0.11* (0.06-0.17)	0.009* (0.002-0.014)	0.012* (0.004-0.02)
Combination (Bupivacaine)	2.82* (1.74-4.35)	0.25* (0.08-0.33)	0.31* (0.09-0.41)

*: $P < 0.05$ vs. the value of each single agent.
Agitation, allodynia, motor disturbance and/or flaccidity were observed in the rats received clonidine or bupivacaine alone. However, the combination with the doses tested did not induce any observable side effects.
DISCUSSIONS: Intrathecal administration of the combination of clonidine and bupivacaine had significant synergistic analgesia for acute thermal or inflammatory induced pain in comparison with each single agent alone with decreasing motor disturbance and behavioral side effects in rats. These combinations might be useful in human pain management.
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S-193

CLINICAL AND EXPERIMENTAL EVALUATION OF THE MUSCLE RELAXANT EFFECT OF NEFOPAM HCL(A NON-NARCOTIC ANALGESIC)

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INTRODUCTION: Nefopam HCL is a potent non-opiate analgesic-that is chemically and pharmacological unrelated to any class of drugs presently known in analgesia. The mechanism of its analgesic action is not clear. It may potentiate the effect of some biogenic amines -have a weak atropine like action or may be a weak central nervous system stimulant. Nefopam possesses apparent muscle relaxant activity 5-10 times as potent as orphenadrine (1). However in contrast to this muscle relaxant property, it was reported that Nefopam HCL enhanced spinal motor neurone excitability and recovery and heightened stretch and flexion reflexes-in man. The aim of this study is to determine and evaluate the muscle relaxants effect of Nefopam HCL.
Table of Contents
METHODS: Clinical Study was carried out on 15 adult patients under going major abdominal surgery. Preparation of the hand with application of myotest (myograph 2000 Bioameter) was done. Continuous automatic record during the operation was done using traction transducer on the hand and setting up the apparatus. Nefopam HCL in a dose of 0.3-0.5 mg/kg was added to the IV infusion drip. Observation of the patient for the degree of relaxation in relation to the dose of Nefopam was done until a 90% reduction of the twitch was obtained by continuous recording of TOF. Patients were observed for the next 4 hours post operatively.
Experimental study of the neuromuscular transmission was carried out in vivo by using the gastrocenemius sciatic nerve preparation of 10 anesthetized cats. In vitro studies were done using isolated rat pherenic nerve diaphragm preparation and isolated Toad‘s rectus abdominis muscle.

RESULTS: TOF showed 90% reduction from the control which represent muscle relaxation, satisfactory for the surgery, in all cases and reversal at the end of the procedure was complete after prostigmine injection. There was no re-curarization and the mean postoperative tidal volume record was near to the preoperative one after prostigmine injection. Isolated animal study revealed that Nefopam HCI in a dose of 0.25-20 g/kg had no effect on height of contraction of cat gastrocnemius muscle. In vivo studies using rat phrenic nerve diaphragms and Toad's rectus abdominis muscle showed that small doses of Nefopam HCI (I0g to 640.g/50 ml bath) had no effect on the diaphragmatic response to nerve stimulations, while large doses of Nefopam HCI (1000-3000 g/50 ml bath) resulted in a dose related reduction in response to indirect stimulation with complete cessation 4 min. after addition of 3000 g/50 ml bath. Prostigmine 250 g/50 ml bath failed to prevent neuromuscular block caused by Nefopam HCI.
CONCLUSION: We concluded that Nefopam HCI offers adequate non-narcotic analgesia with a good muscle relaxant effect.
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S-194

MECHANICALLY ACTIVATED ION CHANNELS IN PAIN TRANSDUCTION

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INTRODUCTION: Currently, side effects limit the ability to manage acute and chronic pain states even if adequate pain relief has been achieved. Since the majority of pain originates in the periphery through the activation of primary afferent neurons that detect noxious stimuli (nociceptors), therapies that selectively block nociceptor activation could potentially block pain signaling at its origin. Our research supported by the IARS is focused on investigating the molecular basis by which mammalian organisms detect noxious mechanical stimuli. This new direction builds on previous work that led to the isolation of the "capsaicin receptor" now termed, vanilloid receptor subtype -1. Although "VR1" is activated by multiple noxious stimuli including products of inflammation and heat, it is insensitive to mechanical changes in membrane shape as occurs under either hypertonic (cell shrinkage) or hypotonic (cell stretch) conditions. Our initial aim is to test the hypothesis that: Ion channels activated by cell shrinkage function to transduce noxious mechanical stimuli in nociceptors. Thus far, we have focused on three main objectives: 1) Establish primary cultures of dorsal root ganglion (DRG) neurons to serve as a model system to characterize electrophysiologic and intracellular calcium responses following cell shrinkage or swelling under control / inflammatory conditions.
RESULTS: Using calcium-imaging techniques, primary cultures of rat sensory neurons showed a decrease in intracellular calcium in response to cell shrinkage whereas cell swelling produced an increase in intracellular calcium. 2) Constitute a high quality cDNA library derived from rat DRG to be used for cloning of mechanosensitive ion channels.
RESULTS: We have completed the subdivision of a rat sensory ganglion cDNA library with 140 individual pools containing approximately 10,000 recombinants /pool. In vitro RNA transcripts representing individual subpools were microinjected into oocytes and screened for mechanically induced inward current responses.
RESULTS: Hypertonic conditions elicited inward current responses in oocytes injected with a DRG cRNA library subpool greater than that observed in water injected oocytes. Additional characterization is underway. 3) Utilize alternative cloning strategies (differential display) to isolate candidate cDNAs that mediate mechanotransduction in nociceptors.
RESULTS: We have cloned, sequenced and partially characterized LRP157, a mRNA binding homologue that is regulated by NGF in nociceptors. We are testing the hypothesis that LRP157 binds to the 3' UTR of mRNA expressed in nociceptors and functions as a stability factor.
CONCLUSION: Using a combination of approaches including characterization of cultured primary sensory neurons activated by cell shape change, expression cloning, and differential display cloning techniques, we hope to isolate nociceptor specific ion channels and associated proteins that transduce or regulate mechanically induced pain and hyperalgesia.
Supported by a grant from the International Anesthesia Research Society.

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EFFECT OF CELECOXIB PREMEDICATION ON RECOVERY AFTER OUTPATIENT SURGERY: A DOSE RANGING STUDY

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INTRODUCTION: Celecoxib, a cyclooxygenase-2 (COX-2) inhibitor, has been reported to be comparable to acetaminophen[1] but less effective than rofecoxib[2] in the prevention of pain after surgery. However, these early studies evaluated a 200 mg dose of celecoxib. Recently, the FDA increased the celecoxib dosage recommendation to 400 mg for acute pain management. To date, no studies have directly compared the analgesic efficacy of different doses of celecoxib for the prevention of postoperative pain. This prospective, double-blind placebo-controlled study compared oral celecoxib 200 mg to 400 mg when administered for premedication of outpatients undergoing minor ENT surgery.
METHODS: 95 healthy outpatients undergoing nasal and sinus surgery were assigned to one of three study groups: Control (Placebo, n=31), Celecoxib 200 mg (n=30), or Celecoxib 400 mg (n=33). The study drug was given orally 30-45 min prior to surgery and all patients received a standardized general anesthetic technique. During the postoperative period, recovery times, the need for rescue analgesics, quality of recovery (0-100), patient satisfaction with pain management (0-100) and side effects were recorded. Pain was assessed using a verbal rating scale (VRS) with 0=none to 10=maximal in the Phase I (PACU) and II (DSU) recovery areas and at 24 hr. after surgery**.**
RESULTS: Celecoxib, 400 mg PO, was significantly more effective than placebo in reducing postoperative pain and the need for opioid analgesic medication. Although celecoxib 400 mg was more effective than celecoxib 200 mg in reducing the incidence of severe pain (VRS>6), no differences were observed between the study groups with respect to recovery times and outcome variables during the postdischarge period.
CONCLUSIONS: Oral premedication with celecoxib 400 mg was more effective than 200 mg in reducing severe postoperative pain and the need for rescue analgesic medication in the early postoperative period. However, even the 400 mg dose of celecoxib failed to facilitate the recovery process after outpatient ENT surgery

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	Control (Placebo)	Celecoxib (200 mg)	Celecoxib (400 mg)
Age (yr)	45±13	40±14	42±15
Anesthesia time (min)	90±36	90±40	87±43
PACU stay (min)	67±24	61±26	62±26
Actual discharge (min)	138±46	127±26	118±48
Peak Pain Score (n)	5 (2-10)	4 (0-8)	4 (0-7)
Patients with severe pain (%)	26	23	9*
Fentanyl rescue (g)	118±85	74±67	59±60*
Oral pain medication (n)	2±3	2±2	1±2
Peak pain score at home	2 (0-10)	2 (0-6)	2 (0-5)

* $p < 0.05$ vs Control t $p < 0.05$ vs celecoxib 200 mg

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ROLE OF SELECTIVE CYCLOOXYGENASE-2 INHIBITORS IN REDUCING NON-INCISIONAL POST-THORACOTOMY PAIN.

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INTRODUCTION: Non-steroidal anti-inflammatory drugs (NSAIDs) may be used to treat acute postoperative pain. NSAIDs inhibit the cyclooxygenase enzyme, reduce prostaglandin synthesis and alleviate inflammatory pain. Ketorolac has been used successfully to treat non-incisional post-thoracotomy (NIPT) pain (pleuritic chest pain, joint pain, shoulder tip pain)[1]. Selective cyclooxygenase 2 (COX-2) inhibitors may reduce NIPT pain. We report a series of nine patients in whom rofecoxib, a COX-2 inhibitor reduced NIPT and patient controlled epidural analgesia (PCEA) requirements.
METHODS: Six patients had lung resection, one had Nissen fundoplication and two had thoracoscopy. Thoracic epidural catheters were placed preoperatively in all patients. All patients received a combination of levobupivacaine 0.075% and hydromorphone 0.001% via epidural catheter. Verbal analogue scale (VAS) was used to evaluate patients for incisional and NIPT pain. Patients were evaluated by acute pain team immediately after surgery and twice daily afterwards. Epidural infusion rate was increased if patients had incisional pain. NIPT pain was treated with rofecoxib 50-mg orally once a day.
RESULTS: Epidural infusion was strarted in operating room. Immediately after surgery, epidural infusion was adjusted so as to reduce the incisional pain socre. On post-operative day one no patient had significant incisional pain (VAS= 0-2), however all patients complained of moderate to severe NIPT pain (VAS= 6-9). Patients who received rofecoxib 50mg orally, showed remarkable improvement in NIPT pain during evening evaluation. Patients had either complete relief (VAS=0 in seven patients) or more than 50% improvement (VAS= 3-4) within 12 hours of rofecoxib administration. On post-operative day two PCEA bolus requests were reduced by 60-80%.
DISCUSSION: Non-incisional post thoracotomy pain is common and can be severe. The cause is not completely understood but various mechanisms including pleuritic chest pain, phrenic nerve stimulation and positioning related stretch of shoulder girdle has been implicated. Diffuse nature of this pain makes it difficult to treat with epidural narcotics and local anesthetics. Ketoroalc, a non-selective cyclooxygenase enzyme inhibitor has been shown to be effective in treatment of non-incisional pain[1]. Our experience, suggests that rofecoxib, a selective cyclooxygenase 2 inhibitor is effective in treatment of NIPT pain and may reduce PCEA requirements and associated side effects. Placebo control, double-blinded studies are needed to further study the role of rofecoxib in thoracotomy patients. .
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S-197

ORAL DEXTROMETHORPHAN PREMEDICATION REDUCED POSTOPERATIVE ANALGESIC CONSUMPTION IN PATIENTS FOLLOWING UNILATERAL MANDIBULAR THIRD MOLAR EXTRACTION UNDER LOCAL ANESTHESIA

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INTRODUCTION: In order to prevent posttraumatic pain accompanying surgery, preoperative NMDA antagonists have been tried with a certain preferable effects, and which effect is called preemptive analgesia. Dextromethorphan is one of NMDA receptor antagonists and is reported to show preemptive analgesic effect when used in large doses (1, 2). And it has not been reported if dextromethorphan premedication has preemptive analgesic effect when it is used in small dose and in a dental surgery under local anesthesia. In this study, we tested if small dose dextromethorphan premedication might produce preemptive 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. Consecutive 111 ASA physical status I or II patients who underwent unilateral mandibular third molar extraction surgery were enrolled in this study, and were allocated into 3 groups. Group A (n=37) and B (n=38) patients were given dextromethorphan, 30 mg, and diclofenac, 25 mg, orally before surgery, respectively. Group C patients (n=36) were not premedicated. Surgery was completed within 30 min under inferior alveolar nerve block using a local anesthetic. Postoperatively the patients were allowed to take oral diclofenac, 25 mg, each time when they needed for postoperative pain relief. Postoperative pain was evaluated at the clinic on the first, 7th, 14th and 28th day after surgery, respectively, using visual analog scale (VAS) and verbal rating score (VRS). VAS, VRS and the number of diclofenac per a day they took were compared among the groups using Mann-Whitney U-test with statistical significance of $p<0.05$.

RESULTS: VAS and VRS scores were similar among the 3 groups during the study period, respectively. Total postoperative analgesic consumption was significantly less in Group A than in Group C (Figure 1, $p<0.05$).
DISCUSSION: The results of this study shows that small dose dextromethorphan showed preemptive analgesic effect after unilateral mandibular third molar extraction under local anesthesia. The reduced postoperative analgesic requirement brings patients major benefits in terms of the reduced incidence of the adverse effects induced by analgesics and the reduced cost. In conclusions, dextromethorphan premedication did not improve VAS and VRS scores, but reduced an analgesic consumption compared with control group.
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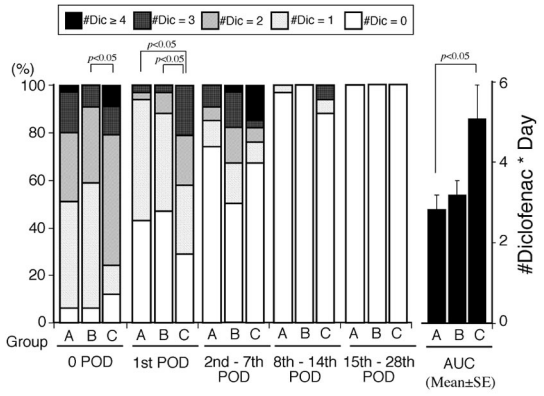

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PRE-ADMINISTRATION OF LOW-DOSE KETAMINE ATTENUATES TOURNIQUET PAIN IN HEALTHY VOLUNTEERS

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INTRODUCTION: The mechanisms of tourniquet pain are not well known. This study was designed to evaluate whether pre-administration of low-dose ketamine could attenuate tourniquet pain in healthy volunteers.
METHODS: The subjects of the study were ten healthy volunteers(males,22-50yrs). Tourniquet inflation was performed with pressure of 400mmHg at the thigh and concluded when the pain rose to a pre-determined level. Pain was assessed using a visual analog scale(VAS,0-100mm) until reaching maximum pain or maximum time of 60-min period. If the subjects recorded VAS100 before the end of 60-min period, they were assigned the maximum value for the rest of the time. Ketamine, 0.1mg/kg, or normal saline was given intravenously in a double blind fashion before tourniquet inflation(T0). Each subject recieved both of the test substances in a randomized order. Measurements included VAS, tourniquet time(from inflation to deflation), systolic blood pressure(SBP), and plasma concentrations of catecholamines(CAs). VAS and SBP were measured just after touniquet inflation(T1) and at 5-min intervals(T2-10), and plasma concentrations of CAs were measured before tourniquet inflation and just before tourniquet deflation. ANOVA and Student's t-test were used for statistical comparison. Data were shown in mean±SD.
RESULTS: All subjects could not tolerate tourniquet pain more than 45 minutes. Low-dose ketamine significantly reduced VAS compared to saline,i.e.,66.2±11.8 vs 90.0±10.3($P<0.0001$) at T1, 59.6±23.8 vs 79.3±16.1($P<0.05$) at T6 and 70.6±15.8 vs 86.7±15.5($P<0.05$) at T7, and significantly($P<0.01$) prolonged tourniquet time(33.6±6.6 min vs 28.3±5.7 min). SBP(124.6±6.4 mmHg at T0) significantly increased at T7(132.7±12.5 mmHg vs T0,$P<0.05$) and T8(143.3±5.1 mmHg vs T0,$P<0.05$) in the saline trial, while it showed no change throughout the time course in ketamine trial. The concentrations of CAs showed no change in either trial.
CONCLUSIONS: We conclude that pre-administration of low-dose ketamine attenuates tourniquet pain and prolongs tourniquet time in healthy volunteers. The activation of NMDA receptor might be involved in the tourniquet pain resulting from continuous stimulation of C-fibers.
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S-199

AXILLARY BLOCK WITH NEWLY DEVELOPED PENTAGON POINTED NEEDLE

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INTRODUCTION: The Axillary Block is a common anesthetic procedure for patients undergoing operations on an upper extremity. Because the Quncke pointed needle is so sharp, the anesthesiologist cannot easily sense the point of penetration through the axillary sheath.Therefore, obtaining the appropriate field of analgesia can be difficult.
The present study was designed to investigate how sensitively the anesthesiologist could feel the axillary sheath with the new Pentagon pointed needle (Dr.Japan Co,Tokyo,Japan)compared with the Quincke pointed. We also measured the penetration resistance of the axillary sheath using these two kinds of needles in human cadaver.
MATERIALS AND METHODS: STUDY 1.Seven patients aged 45 to 79 undergoing the elective orthopedic operations were informed consented about our study described below. All of them were premedicated. The induction of anesthesia was carried out with the propofol and they were insulted the laryngeal mask or intubated the tracheal tube. Subsequently, the anesthesiologist performed the axillary block. In the first instance, we penetrated the axillary sheath with the Quincke pointed needle, measured the sensation of resistance of the sheath using the four-grade scale(1.exellent,2 good,3.fair, 4.none) then, in the second instance, with the Pentagon pointed. After that we completed the injection of local anesthetic using the Pentagon pointed needle. Data were evaluated by ANOVA, followed by Mann-Whitney's U test. $P<0.05$ was considered as statistically significant.
STUDY 2. Using the axillary sheath from the cadaver, we measured the maximum resistance(mmHg) to complete the penetration, 5 times with each needle type. Data were evaluated by Student's t-test. $P<0.05$ was considered as statistically significant.
RESULT: STUDY 1. Axillery block was successful in all 7 patients without any neurological complications. Comparison between two needles: the anesthesiologist could feel the axillary sheath with the Pentagon pointed needle much better than with the Quincke pointed.(Table 1)($P<0.001$).
STUDY 2. The maximum resistance was significantly higher in the Pentagon pointed needle(45.41±16.38, n=5) than in the Quincke pointed (2.17±0.75,n=5) ($P<0.005$).
CONCLUSION: These results suggest that using the Pentagon pointed needle will allow the anesthesiologist to sense more precisely the exact penetration of the axillary sheath when performing the axillary block. We conclude that this newly developed Pentagon pointed needle is particularly useful and increases safty for the axillary block.

table 1:Comparison Between Two Needles with the Sensation of Axillary Sheath

needle type	exellent	good	fair	none
Pentagon pointed (n=7)	6	1	0	0
Quincke pointed (n=7)	0	0	2	5

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DOES PREEMPTIVE ANALGESIA REALLY WORK? A COMPARISON OF OXYCONTIN, ROFECOXIB AND PLACEBO IN PATIENTS UNDERGOING ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY

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INTRODUCTION: Recently, there has been renewed interest regarding the role of preemptive analgesia with long acting oral medication in the management of postoperative pain (1, 2). The purpose of this study was to compare the postoperative analgesic effects of Oxycontin, rofecoxib and placebo in patients undergoing outpatient laparoscopic cholecystectomy.
METHODS: Following approval from the Institutional Review Board, a randomized double blinded placebo controlled study was undertaken in ASA 1 and 2 patients. Group 1 (n=23) received 10 mg of Oxycontin, Group 2 (n=25) received 50 mg of rofecoxib, and Group 3 (n=23) received the placebo tablet. Exclusion criteria included patients less than 18 years or more than 65 years of age, patients with history of hypersensitivity to codeine, pregnancy, renal or hepatic disease, substance abuse, patients who had received any pain medications within 24 hours before surgery, and conversion to open cholecystectomy. All patients were administered their medications orally, approximately 60 minutes prior to surgical incision. Induction of general anesthesia was accomplished with propofol (1.5-2 mg/kg), fentanyl (2 mcg/kg) and cisatracurium (0.2 mg/kg) or rocuronium (0.6 mg/kg). Following intubation of the trachea, general anesthesia was maintained with O_2:N_2O (50:50) and isoflurane (0.6-1.2%), together with intermittent boluses of fentanyl and muscle relaxant. Patients did not receive any other analgesics during surgery, nor was any local anesthetic infiltrated at the sites of surgical incisions at any time during the procedure. In the postanesthesia care unit (PACU), pain and sedation levels were assessed every half-hour until discharge. Total dosage of morphine administered to each patient for breakthrough pain was recorded, and the number of patients requiring morphine treatment was documented in each group.
RESULTS: The average total dose of morphine required for each patient was 2.8 mg, 4.8 mg and 3.4 mg in the Oxycontin, rofecoxib and placebo groups respectively. However, using analysis of variance testing, no statistical difference was observed among the three groups ($p > 0.05$). With regards to incidence of breakthrough pain, 13/23 patients in Group 1, 7/25 in Group 2, and 10/23 patients in Group 3, did not require any supplemental morphine in the PACU. Furthermore, there was no obvious difference in pain scores among the three groups; however, there appeared to be a trend for greater morphine requirement in the rofecoxib group.
DISCUSSION: This study raises some questions regarding the efficacy of oral preemptive analgesia with Oxycontin (10 mg) or rofecoxib (50 mg) in the management of postoperative pain following laparoscopic cholecystectomy.
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S-201

A PROSPECTIVE, RANDOMIZED TRIAL OF THREE PERIOPERATIVE ANESTHETIC TECHNIQUES IN PATIENTS UNDERGOING BOWEL RESECTION

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INTRODUCTION: The principal factors preventing earlier discharge after bowel resection are ileus, pain, and postoperative nausea and vomiting. Opioids affect all of these; however, would the absence of opioids alone improve postoperative patient condition and allow for a more rapid recovery? The purpose of this study is to determine whether there are differences in return of bowel function and hospital stay in patients who undergo lower abdominal bowel surgery when using epidural local anesthetic regimens, with and without opioids.
METHODS: ASA Class I-III patients aged 18-80 years of age scheduled to undergo lower abdominal colon resection were studied. All patients received 2mg midazolam and 30mg ketorolac IV preoperatively. All patients received propofol for induction (1.5-2.5mg/kg) and maintenance of anesthesia titrated to a BIS of 40-60 and a rocuronium infusion to maintain 1-twitch in a train-of-four. Patients in Group 1 received no opioids during the intraoperative and postoperative period until return of bowel function and their analgesia was provided by 5ml 0.75% aliquots of ropivacaine intraoperatively. A continuous epidural infusion of 0.2% ropivacaine postoperatively was started at 6ml/h and titrated to patient response. Patients in Group 2 received the same epidural management intraoperatively but also received 1mcg/kg fentanyl with each ropivacaine aliquot. During the final 20 minutes of operation, patients were given 0.1mg/kg morphine intravenously. Postoperative pain was managed by ropivacaine 0.2% at 6ml/h and breakthrough pain was treated with an intravenous PCA infusion of morphine set to deliver no basal, 1mg demand with a 6-minute lockout. Patients in Group 3 did not receive an epidural but received fentanyl 3mcg/kg at induction and 1mcg/kg for breakthrough pain intraoperatively. Postoperative pain was treated with an intravenous PCA infusion of morphine set to deliver no basal, 1mg demand with a 6-minute lockout. All patients postoperatively received ketorolac 15mg IV q6h RTC until tolerating clear liquids for 4 hours, and then rofecoxib 50mg PO qAM was begun. Patients were evaluated every 6 hours and examined for bowel sounds, passage of flatus, PO tolerance, time to first passage of stool and discharge. Categorical data were compared with Pearson's chi-squared test. Continuous data were compared with an analysis of variance and Tukey's *post hoc* test.
RESULTS: There were no intergroup differences in age, gender distribution, or postoperative pain intensity. Outcome data are summarized in the table (Data are presented as mean ± SD; *$p < 0.05$ vs. Opioid Anesthesia).
DISCUSSION: Our preliminary results demonstrate that excluding opioids from the perioperative analgesic regimen in patients undergoing lower abdominal colonic surgery allows for a faster
return of bowel function with comparable pain relief. Factors other than return of bowel function delay patients hospital discharge.

Time to event (days)	Epidural Anesthesia		Opioid Anesthesia
	wo/opioids	w/opioids	
Bowel Sounds (n)	1.0 ± 0.5 (9)	0.9 ± 0.4 (8)	1.0 ± 1.1 (8)
Flatus (n)	1.3 ± 0.7 (9)*	2.1 ± 0.6 (8)	4.2 ± 2.1 (6)
Bowel movement (n)	2.6 ± 1.4 (7)*	3.8 ± 0.9 (8)	5.6 ± 1.7 (5)
Ingestion of clear liquid (n)	2.7 ± 1.0 (6)*	2.5 ± 1.5 (6)	5.2 ± 2.5 (5)
Hospital discharge (n)	6.1 ± 2.7 (9)	6.0 ± 1.2 (8)	7.7 ± 2.4 (8)

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PATIENTCONTROLLED INTRAVENUOUS ANALGESIA: MORPHINE VERSUS PIRITRAMIDE

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INTRODUCTION: Patientcontrolled intravenuous analgesia (PCIA) is a common method of providing control for acute postoperative pain. A number of different opioids have been tested and found to be useful alternatives (1). In some European countries the strong u-agonist piritramide (P) is the standard opioid for PCIA, in anglo-saxon countries mostly morphine (M). No controlled studies have compared P and M. Economical and practical considerations would favor M. From the available literature we hypothesed that P has less sedating and more nauseating effects than M.
METHODS: 42 patients (ASA I and II only) were studied after IRB approval and informed patient consent. 20 patients in each group were necessary to detect a clinically relevant difference of more than 20% for nausea and sedation. Patients were randomly assigned double-blinded into two groups (M and P). Only patients after elective "open" abdominal surgery were included. Patients with a history of motion sickness or postoperative nausea were excluded. All patients received identical anesthesia with fentanyl 2 ug/kg*hr and isoflurane as needed. Patients did not receive antiemetic prophylaxis. After arrival in the recovery room patients randomly received a PCA-pump (Graseby 9300) which delivers on demand a 4 ml bolus with either 1.5 mg M or 2 mg P with 10 min lock-out and without basic infusion rate. With NAS <= 3 patients were discharged from the recovery room. Pain, sedation and nausea were evaluated by a blinded observer at 6 times within the next 48 hours. Sedation and nausea were evaluated with categorial and analog scales.
RESULTS: Demographic data and type of surgery were not significantly different between both groups. Quality of analgesia and consumption of M and P (in ml) were identical at all times. On postoperative day 1 the incidence of nausea and "severe sedation" were higher ($p<0.05$) with P. Results did not differ for analog and categorical scales.
DISCUSSION: Identical pain intensity and cumulative use of opiods in ml at all times indicate that the choosen doses of M and P were equianalgesic. A ratio of 0.7 vs. 1.0 for P and M seems to be equivalent. Therefore the primary endpoints nausea and sedation could be evaluated. The prejudices against M could not be confirmed. M had lesser emetic and sedating effects than P. The specific pharmacokinetic profile (2) of P could be responsable for the better subjective tolerance of M. It is concluded that M is superior to P. Therefore, it would appear reasonable to replace P with M in clinical practice for PCIA.
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S-203

THE EFFECT OF ACUTE POSTOPERATIVE PAIN ON RANGE OF MOTION AT TIME OF DISCHARGE AFTER TOTAL KNEE ARTHROPLASTY

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INTRODUCTION: Improvement in surgical techniques, favorable outcomes and patient satisfaction after total knee arthroplasty (TKA) are closely associated with the range of motion (ROM) of the operated knee. About 60% of patients undergoing TKA experience severe acute postoperative pain, which hinders rehabilitation (1). This prospective study was conducted to determine if acute postoperative pain after TKA predicts subsequent ROM of the knee.
METHODS: Following IRB approval and informed consent, 49 patients scheduled for primary TKA were studied. All patients had a combined spinal (11.25 mg hyperbaric bupivacaine and 25 g fentanyl) - epidural anesthetic technique for the surgery. Patients had a standardized surgical technique of tourniquet and fixation of the bi-condylar components with methylmethacrylate. In the recovery room an epidural infusion of bupivacaine 1 mg/ml and fentanyl 10 g/ml at 6 ml/hr with a PCA mode of 1 ml every 15 minutes was commenced and titrated to achieve visual analog scale (VAS) 3-5 for 2 days. Immediately postoperatively VAS was measured every 4 hours and from postoperative day (POD) 1 it was measured daily till discharge (mean 4.7 days). On POD 2 patients were commenced on oral hydrocodone (4-6 tablets/day) for pain relief. All patients received physical therapy and ROM parameters were monitored. The active and passive flexion of the operated knee was measured goniometrically. Demographic data are expressed as mean ± SD. Pearson correlation coefficient was utilized to examine the relationship between VAS and ROM.
RESULTS: The mean age of the study group was 61.9 ± 9.5 years with a male: female ratio of 13: 36 and a mean weight of 202.1 ± 38.4 lbs. The mean VAS was 4.0 ± 3.1 on POD 1, which decreased to 3.0 ± 1.8 by POD 2 and to 2.2 ± 1.7 for POD 3-5 (discharge). Examination of the correlation matrix indicates that VAS is negatively related to ROM at discharge, with the 4 hours postoperative VAS most strongly correlated. A linear regression was used to evaluate the predictive power of VAS on both active and passive flexion. Linear regressions on both active and passive flexion produce r^2 values of 0.52 and 0.59 respectively (figure) and significant regression slope coefficients ($P<0.0001$). High scores on VAS, predict less flexion for both active and passive movements. Correspondingly, low VAS scores lead to higher degrees of flexion at time of discharge.
DISCUSSION: This prospective study demonstrates that lower pain scores on the first postoperative day is associated with an increase in both active and passive flexion on postoperative day 4 at the time of discharge. Effective pain management immediately after TKA appears to be associated with improved functionality at the time of hospital discharge.
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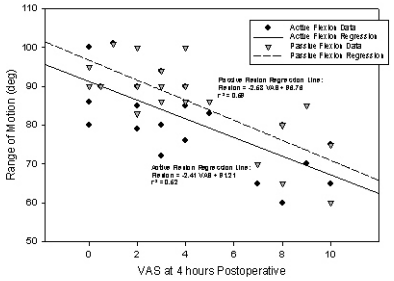

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FASCIA ILIACA BLOCKS FOR POST-OPERATIVE ANALGESIA IN TOTAL KNEE ARTHROPLASTY PATIENTS

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INTRODUCTION: The increasing utilization of new anti-coagulant drugs and early utilization of warfarin following orthopedic joint replacement has prompted anesthesiologists to adapt new strategies for the treatment of postoperative pain. Pain management in total knee arthroplasty (TKA) patients is challenging and often requires approaches beyond IV patient controlled analgesia, including regional blocks. We report the clinical results of using fascia iliaca blocks (FIB) in comparison with epidural analgesia after TKA.
METHODS: In our institution TKAs are typically performed under epidural/general anesthesia. We evaluated the clinical course of 406 consecutive patients undergoing TKA. Epidural analgesia was discontinued in the evening of postoperative day 1. All patients with pain scores >5 were offered FIBs. FIB is easily performed at the bedside with a 22g B bevel needle inserted 1cm below the junction of the lateral 1/3 and medial 2/3 of the inguinal ligament and anesthetizes the femoral and lateral femoral cutaneous nerves. The needle is inserted perpendicularly until two "pops" are felt (fascia lata and fascia iliaca). After negative aspiration, 20ml 0.25% bupivacaine with 200 mcgms epinephrine and 100 mcgms clonidine is injected. Pain scores (VAS) were compared before and after FIB and to VAS with epidural analgesia using the Mann-Whitney nonparametric test.
RESULTS: The first attempt success rate for FIB was 82%. All repeated attempts had 100% success. There were no complications with the 96 FIBs and 98% of these patients were satisfied. Pain scores 1 hr after FIB were reduced by an average of 3.86 ± 2.22 and similar to VAS in patients with epidural analgesia (3.04 ± 1.96 vs 2.68 ± 2.8 respectively). Quadriceps weakness was noted during the morning physical therapy (PT) visit but did not impede the patient's ability to accomplish the given tasks. By the afternoon PT visit no weakness was noted.
DISCUSSION: The ease of performing fascia iliaca blocks, the high degree of success and satisfaction, and the lack of complications make them useful adjuncts in managing the postoperative pain in TKA patients. Quadriceps weakness may be potentially beneficial since it can prevent spasm, a common cause of failure to progress in PT. We recommend the incorporation of FIBs into the traditional acute postoperative pain management for TKA This approach may be particularly useful for patients requiring regional analgesia in the face of anticoagulation.

S-205

EFFECT OF LOCAL ANESTHETIC WOUND ADMINISTRATION ON RECOVERY AFTER MAJOR ORTHOPEDIC SURGERY PROCEDURES

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INTRODUCTION: Controversy exists regarding the analgesic efficacy of local anesthetic wound instillation via either patient-controlled (1,2), or continuous infusion (3) delivery systems. The objetive of this study was to assess the effect of a local anesthetic infusion in preventing pain after major orthopedic procedures.
METHODS: 50 patients undergoing unilateral total knee of hip replacement surgery were enrolled in this randomized, prospective, double-blinded, placebo-controlled study. Upon completion of surgery, one multihole 20-ga. epidural catheter was placed under direct vision above the fascial layer prior to wound closure. Postoperatively, an On-Q™ infusion pump system (I-Flow Corporation) containing 270 ml of bupivacaine 0.25% (Bupi 0.25%), bupivacaine 0.5% (Bupi 0.5%), or saline solution (Control), was connected to the irrigating catheter, and the study medication was infused at a rate of 5 ml/hr. Patients' need for "rescue" pain medications, total dose of opioids analgesics (mg), pain scores (0=none and 10= highest) and satisfaction with pain management (0-100) were recorded at specific intervals for up to 1 week after surgery. Data was analyzed using ANOVA and 2 tests. P values <0.05 were considered significant (*).
RESULTS: Demographic data were comparable among the three treatment groups. The total dose of PCA morphine administered during the first 72 postoperative hours was significantly reduced in the 0.5 (vs. 0.25%) bupivacaine group (30±16 vs. 53 ±29 mg, respectively). However, pain scores and patients' satisfaction were not significantly different between the three groups up to 1 week after surgery.
CONCLUSIONS: Local anesthetic instillation at the surgical site failed to significantly improve pain control or facilitate recovery after major joint replacement surgery.

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	Control n=14	Bupi 0.25% n= 18	Bupi 0.5% n= 18
Age (yr)	56±14	58±13	63±10
Weight (kg)	89±20	90±2	89±26
Knee/hip surgery (n)	6/8	11/7	7/11
General/Spinal Anesthesia (n)	8/6	8/10	9/9
Intraoperative morphine (mg)	1.4±3	2.0±4	1.8±4
Intraoperative fentanyl (µg)	136±104	140±200	117±188
PCA morphine at 72 h (mg)	43±25	53±29	30±16*
Patient satisfaction at 72 h/7 d (0-100)	76±17/79±20	79±14/79±13	84±19/83±25
Pain score at 7 d (0-10)	4±2	4±2	3±3

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INTRATHECAL CLONIDINE DID NOT IMPROVE POSTOPERATIVE PAIN MANAGEMENT AFTER COMPLEX SPINE SURGERY.

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INTRODUCTION: Patients who undergo complex spine surgery have significant postoperative pain which is often difficult to manage. Treatment with large doses of narcotics often results in a high incidence of side-effects. Clonidine, an 2-selective agonist, has been used perioperatively both as a narcotic sparing agent and for the reduction in the hemodynamic responses to stressful stimuli. We previously demonstrated that intrathecal morphine improved postoperative pain management in these patients. In this pilot study we evaluated the addition of intrathecal clonidine.
METHODS: Ten patients with spinal deformities for elective anterior then posterior spinal fusions with instrumentation were randomly assigned to receive 15mcg/kg intrathecal morphine with (clonidine group) or without (control group) 1 mcg/kg clonidine (Duraclon®) through a 25G spinal needle prior to posterior instrumentation. All patients received the same 70% nitrous oxide, 0.3% isoflurane and 1-2 mcg/kg/h fentanyl general anesthetic. Postoperatively, pain was treated to a VAS (visual analog pain scale, 1-10) of 2-3 with i.v. dilaudid PCA and in the clonidine group a 0.1mg clonidine (Catapress®) patch.
RESULTS: There was no statistically significant difference between groups in patient demographics, the length of surgery, number of spinal segments fused or estimated blood loss (not shown). Both groups required almost identical quantities of i.v. dilaudid to maintain a VAS score of 2-3. The clonidine group received more i.v. crystalloid and two patients compared to none in the control group required naloxone for respiratory depression.
CONCLUSION: In this pilot study, there was no advantage to the addition of clonidine to the perioperative pain regimen. Furthermore, due its sedative and sympathetic effects, the addition of clonidine may result in increased fluid requirements and respiratory depression.

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Data for the first postoperative 24 hours.

	Control Group	Clonidine Group
Mean VAS	2.3±2.0	3.0±1.5
Postoperative LR (cc)	2600±600	3400±800
Dilaudid (mg)	26±18	26±22
Hypotensive patients (n)*	2	3
Treated vomiting (n)	1	2
Naloxone treated (n)	0	2

*Hypotension: SBP<100mmHg, treated.

S-207

ANALGESIC EFFECT OF A SINGLE 7.5 MG DOSE OF IV MORPHINE FOLLOWING TOTAL ABDOMINAL HYSTERECTOMY: COMPARISON TO PLACEBO

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INTRODUCTION: Patients undergoing total abdominal hysterectomy (TAH) often complain of moderate to severe pain in the immediate postoperative period. Morphine sulfate is a commonly used analgesic in this patient population. The initial dose of morphine is often institutionally fixed but usually ranges between 1-3 mg. The aim of this study was to evaluate the analgesic effect of a relatively large initial dose of morphine (7.5 mg IV) as compared to placebo in patients following TAH.
METHODS: Informed consents were obtained from 61 female patients with a mean age of 47 (9) years scheduled to undergo TAH under general anesthesia in this IRB approved study. Anesthetic management of the patients was standardized and consisted of fentanyl, propofol, nitrous oxide, muscle relaxants, and isoflurane. Patients with a moderate or a severe degree of pain in the PACU were randomly assigned to receive either a 7.5 mg bolus dose of morphine or placebo. Patients were encouraged to wait up to 15 min but had access to rescue medication at any time. Following the study administration subjects were frequently asked to rate their pain intensity (none, mild, moderate, and severe) as well as any pain relief (pain is worse, no pain relief, mild pain relief, moderate pain relief, or complete pain relief). Immediately before the first dose of rescue medication both subject and the investigator independently assessed their overall satisfaction with the analgesic efficacy of the study drug using a 5-point scale (poor, fair, good, very good, or excellent). Data was analyzed using 95% Confidence Interval and is reported as mean ± SD.
RESULTS: Twenty-five patients received morphine and 31 patients received placebo. There were no significant differences in any of the demographic data between the two groups. There was no significant difference in time to rescue between the groups. Patients in the morphine group were rescued 23± 15 min (range 5-55 min) after and those receiving placebo 18± 14 min (range 3-82 min) after the study drug administration. There was no significant difference in pain intensity between morphine and placebo at baseline, 2, 5, 10, or 15 minutes after the study drug administration. However, at 2 min the patients receiving morphine stated greater pain relief than those receiving placebo; these patients reported no significantly greater pain relief at any other time. Overall patients receiving morphine were more satisfied with pain relief than. The investigator's satisfaction with pain relief was the same in both groups.
DISCUSSION: A single initial high bolus dose of morphine (7.5 mg, IV) does not appear to significantly reduce the intensity of perceived pain in TAH patients. Patients, however, gave a significantly higher analgesic score to morphine. Dose titration to effect should replace fixed dose administration for better pain control.

S-208

ANALGESIC EFFECT OF A SINGLE 7.5 MG DOSE OF IV MORPHINE FOR THE TREATMENT OF PAIN AFTER RADICAL PROSTATECTOMY: COMPARISON TO PLACEBO

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INTRODUCTION: Patients undergoing radical prostatectomy often complain of moderate to severe pain in the immediate postoperative period. Morphine sulfate is a commonly used analgesic in this patient population. The initial dose of morphine is often institutionally fixed but usually ranges between 1-3 mg. The aim of this study was to evaluate the analgesic effect of a relatively large initial dose of morphine (7.5 mg IV) as compared to placebo in patients following prostatectomy.
METHODS: Informed consents were obtained from 27 male patients with a mean age of 56 (6) years scheduled to undergo radical prostatectomy under general anesthesia to participate in this IRB approved study. Anesthetic management of the patients was standardized and consisted of fentanyl, Propofol, nitrous oxide, muscle relaxants, and Isoflurane. Patients were frequently questioned in the PACU about the degree of pain using a 4-point verbal scale (none, mild, moderate, and severe). Patients with a moderate or severe pain were randomly assigned to receive either a 7.5 mg bolus of morphine or placebo. Following the study drug administration subjects were frequently asked to rate their pain intensity using the above 4-point scale as well as any degree of pain relief (pain is worse, no pain relief, mild pain relief, moderate pain relief, or complete pain relief). Patients were encouraged to wait up to 15 min but had access to rescue medication at any time. Immediately prior to the first dose of rescue medication both the subject and the investigator independently assessed their overall satisfaction with the analgesic efficacy of the study drug using a 5-point scale (poor, fair, good, very good, or excellent). Data was analyzed using 95% Confidence Interval and is reported as mean ± SD.
RESULTS: Twelve patients received morphine and 15 received placebo. There were no significant differences in any of the demographic data between the two groups. Patients in the morphine group were rescued 15± 9 (range 5-32 mi) min after and those receiving placebo 16± 13 min (range 5-51 min) after the study drug administration. Pain intensity was significantly lower in the morphine group at 5 min. Patients receiving morphine, however, stated a greater amount of pain relief at 2, 5, 10, and 15 min after its administration. Neither the patients nor the investigators gave a significantly higher score for morphine effectiveness as an analgesic agent.
DISCUSSION: A single 7.5 mg IV bolus dose of morphine does not appear to provide adequate reduction in the perceived pain intensity despite patients' experience of significantly more relief. Neither the investigators, nor the patients, gave a higher score with respect to analgesic efficacy in the morphine group. Dose titration to effect should replace fixed dose administration for better pain control.

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CARDIOVASCULAR AND RESPIRATORY EFFECTS OF A SINGLE 7.5 MG DOSE OF IV MORPHINE COMPARED TO PLACEBO IN POSTOPERATIVE PATIENTS

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INTRODUCTION: The initial dose of morphine for the treatment of postoperative pain is often institutionally fixed. To prevent a sudden change in cardio-vascular status initial doses in the range of 1-3 mg is often given. Higher doses are thought to significantly change hemodynamic stability or result in significant respiratory depression. In this study we report the hemodynamic and respiratory data following an initial high dose morphine (7.5 mg IV) in postoperative patients complaining of moderate to severe pain.
METHODS: Informed consents were obtained from 108 patients (80 females, 28 males) scheduled for lower abdominal surgeries to participate in this IRB approved study. Anesthetic management of the patients was standardized and consisted of fentanyl, propofol, nitrous oxide, muscle relaxants, and isoflurane. Patients with a moderate or a severe degree of pain in the PACU were randomly assigned to receive either a 7.5 mg bolus dose of morphine or an equal volume of placebo. All patients were on supplemental oxygen supplied by a nasal cannula with flows of 2 L/min. Vital signs were recorded at baseline and at 1, 2, 5, 7, 10, and 15 minutes after the study drug administration. Data was analyzed using 95% Confidence Interval and unpaired student t-test and is reported as mean ± SD.
RESULTS: Fifty patients (37 F, 13 M) received morphine and 58 patients (43 F, 15 M) received placebo. There were no significant differences in any baseline hemodynamic data between the two groups. The administration of morphine, or placebo, had no significant effect on systolic blood pressure, hear rate, oxygen saturation, or respiratory rate at any time during the time course of the study. Diastolic blood pressure was significantly lower in patients receiving morphine only at 5 min data collection time (68.3 ±15.3 mmHg vs. 74.2 ±12.4 mmHg, $P<0.05$). The mean percent drop in diastolic blood pressure at 5 min was approximately 9% in patients receiving morphine; those receiving placebo had no significant drop on diastolic blood pressure at this time point.
CONCLUSIONS: A single initial high bolus dose of morphine (7.5 mg, IV) does not appear to cause clinically significant alterations in cardiovascular or respiratory parameters. By giving a larger initial dose of morphine prompt control of pain can be achieved with minimum alterations in cardiovascular or respiratory parameters. Dose titration to effect using higher doses of morphine should replace fixed dose administration for better pain control.

S-210

PAIN MANAGEMENT FOR A PREGNANT PATIENT WITH UTERUS LEIOMYOMA - A LONG-TERM EPIDURAL INFUSION OF ROPIVACAINE

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INTRODUCTION: Abdominal pain in a pregnant patient with uterus leiomyoma often causes the premature labour. Therefore, a safe and effective pain management is required. IV or oral administration of opioids and/or NSAIDs might fail to achieve a complete pain relief and not be able to prevent the premature labour despite adverse effects. In this report, a pregnant patient with leiomyoma was successfully managed by continuous epidural infusion of plain ropivacaine. This is the first report of successful treatment of a pregnant patient with a long-term epidural analgesia. In this case, the effectiveness and the safety of this method were examined by measuring the maternal serum ropivacaine concentration, and inspecting the neurobehavioral testing.
METHODS AND RESULTS: A 32-year-old primigravida presented with lower abdominal pain at 25th week of gestation. On admission, conservative treatment with pentazocine and tocolytics was started but failed. Then, after informed consent had been obtained, continuous lumbar epidural infusion of ropivacaine at fixed rate of 5 mL/h was started. The infusion concentration was decreased by 0.05% according to the clinical symptom and visual analog scales (VAS) for pain during rest and movement. Maternal blood samples were collected at each infusion concentration and serum ropivacaine concentration was measured by the gas chromatography. Perinatal outcomes assessed were neonatal umbilical cord blood pH value and Apgar score. In addition, the newborn was evaluated by using the Brazelton and NACS neurobehavioral testing.Ropivacaine infusion was continued from 27th to 34th week of gestation, and infusion concentration was decreased gradually from 0.2%, and the final concentration was 0.05%. Throughout the intervention, the patient was allowed to continue to perform daily activities with minimal discomfort. No complications occurred such as local anesthetic toxicity, hypotension, motor weakness, or infection. The maximal serum concentration was 0.6microgram/ml. No analgesics were required after 34th week of gestation, and elective cesarean delivery was carried out uneventfully at 38th week of gestation. Apgar score for one and 5 minutes was 8 and 10 points, respectively and neonatal umbilical cord blood pH value was 7.363. The neurobehavioral testing on 4th postnatal day represented no abnormality.
CONCLUSION: There are the possible risks of delayed effects upon prenatal exposure to a given drug even if the organogenetic period has passed. In our case, however, maternal serum concentration of ropivacaine was extremely low, and perinatal assessment revealed no abnormality despite a long-term exposure. These findings support a long-term epidural analgesia in the case of a pregnant patient. An appropriately placed chronic epidural catheter and a titrated continuous infusion of ropivacaine provided adequate and safe analgesia for leiomyoma-associated abdominal pain and certainly improved quality of life in a pregnant patient.

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RELIEF OF UTERINE ARTERY ENBOLIZATION PAIN BY PATIENT CONTROLLED EPIDURAL ANALGESIA WITH DIFFERENT MIXTURES

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INTRODUCTION: Uterine Artery Embolization (UAE) is a nonsurgical treatment for uterine tumor that is gaining increasing acceptance. This procedure, however, is associated with considerable amount of postoperative abdominal cramp pain. The usual pain control is provided by the use of NSAID (non-steroidal anti-inflammatory drug) and parenteral opioid which in our experience frequently did not provide satisfactory pain relief. The present study was undertaken to evaluate the efficacy of patient controlled epidural analgesia (PCEA)with three different anaglesic mixtures in the relief of post UAE pain.
METHODS: After apporval from the Hospital Research Committee and informed consents eighty patients who were scheduled for UAE were randomly allocated into 4 equal groups: Group C (n=20) received nimesulide 100 mg PO at 1 hour before the procedure and meperdine 1 mg/kg IM q4h prn after the procedure; Group R-1 (n=20) received PCEA with a mixture of ropivacaine 0.2% + morphine 0.004%; Group R-2 (n=20) received PCEA with a mixture of ropivacaine 0.2%+morphine 0.004%+droperidol 0.005%; Group R-3 (n=20) received PCEA with a mixture of ropivacaine 0.2% + morphine 0.004%+droperidol 0.01%. All R groups had PCEA setting with loading dose of 6 ml +continuous infusion 2 ml + bolus 2 ml at lockout interval 10 min. VAS, Bruggman comfort score, Ramsay sedation score, sensory and motor block, vital signs and adverse effects were assessed for 48 hours.
RESULTS: Abdominal crampy pain was reported in 90% of the patients in Group C but in none of the patients in all the R groups and VAS were significantly higher in the C group than the R groups. Dose of ropivaciane and morphine were similar with no significant difference in the VAS scores among the three R groups. The addition of droperidol significantly decreased the incidence of nausea/vomiting in group R-2 and R-3 than R-1 and C with R-3 showing more sedation in 25% of the patients. Vital signs were stable and no patient had respiratory depression in all 4 groups.
DISCUSSION: Our study showed that PCEA with ropivacaine and morphine provided effective and safe analgesia to patients with UAE pain and the addition of droperidol to the epidural drug reduced the adverse effect of nausea/vomiting.

S-212

COMPARING QUALITY OF LIFE IN PATIENTS WITH CANCER-RELATED PAIN AND CHRONIC NONMALIGNANT PAIN USING THE TREATMENT OUTCOMES IN PAIN SURVEY (*TOPS*)

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INTRODUCTION: The *Treatment Outcomes in Pain Survey (TOPS)* is a comprehensive multidimensional tool developed by investigators at New England Medical Center, which measures physical and psychosocial outcomes in outpatients with chronic nonmalignant pain (CNMP).[1,2] The *TOPS* is comprised of 8 subscales derived from the *Medical Outcomes Study SF-36 Health Survey* and 14 *TOPS* domains. To date, no published reports have documented use of the *TOPS* with cancer-related pain. Therefore, we administered the survey to patients with cancer-related pain from advanced disease and compared their results to those of CNMP patients.
METHODS: Fifty-two subjects with advanced cancer reporting average pain levels of >3 (0-10 Numeric Rating Scale) were recruited from a hematology-oncology outpatient clinic and asked to complete the *TOPS*. Scores were computed and compared to those of 94 CNMP subjects who were new referrals to our Pain Management Clinic.
RESULTS: Psychometric properties of the *TOPS* were evaluated. Internal consistency reliability (Cronbach's alpha) was calculated for each of the 8 *SF-36* subscales separately for both groups. All *SF-36* subscales had coefficients of 0.70 or above and were remarkably similar for most subscales, with differences between groups no greater than 0.11. Social Functioning was the lowest subscale for the cancer group, 0.70. The *TOPS* domains also demonstrated acceptable reliability for both groups, except for Passive Coping which was 0.62 for the cancer group and 0.77 for CNMP subjects. Scores from the *SF-36* subscales and *TOPS* domains were compared using Student's t-tests. Subjects with cancer-related pain indicated less Body Pain ($p<0.001$), but poorer General Health ($p<0.01$). For the *TOPS* domains, the cancer pain group reported greater Health Care Satisfaction ($p<0.01$) and less Total Pain Experience ($p<0.05$). However, they experienced more Work Limitations ($p<0.05$) and reported poorer perceptions in Solicitous Response ($p<0.001$), which is a measure of the extent to which a spouse or significant other assumes role functions. The mean score for Perceived Family, a measure of the ability to perform family and social roles, was significantly better for cancer subjects ($p<0.05$). Interestingly, the CNMP group indicated much greater Pain Symptoms ($p<0.001$).
DISCUSSION: We conclude that the *TOPS* may have important contributions to the measurement of quality of life and treatment outcomes for persons with cancer-related pain. However, more studies are needed to establish its validity and sensitivity for evaluating physical and psychosocial dimensions of the cancer pain experience and to refine the instrument to reduce the item burden to persons with advanced cancer.
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S-213

SYMPTOMATIC TREATMENT OF CHRONIC LOW BACK PAIN: DETERMINATION OF OPTIMAL SIGNAL FREQUENCY AND PRELIMINARY EFFICACY OF A TARGETED NON-INVASIVE ELECTRONIC PAIN CONTROL DEVICE

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INTRODUCTION: The Biowave System (Biowave Corporation, Norwalk, CT) introduces two premixed high frequency wave forms (feed signals) through an electrode placed on the skin *opposite* the pain site (feed electrode). The electric field contains a low frequency component (beat frequency) equal to the difference between the feed signals. The feed signals pass *through* the body to a second electrode at the treatment site (pain site electrode). The feed signals mix, yielding an electric field equivalent to the beat frequency component, which is believed to interrupt transmission of pain impulses by preventing action potential propagation along pain fibers. This technology is being explored as a novel therapy for treating chronic, acute or post-surgical pain.
METHODS: Volunteers consented to undergo 3 treatment sessions in either of 2 phases with varying beat and feed frequencies separated by at least 24 hours. Criteria for inclusion: age 18-60, low back pain (below T12) for $\geq$3 months without radiation, and Visual Analog Scale (VAS) pain score of $\geq$40 at screening. Exclusion criteria were pregnancy, presence of a pacemaker or other implantable devices, cardiac arrhythmias, epilepsy, low back surgery, alcohol or drug abuse, or significant medical or psychological conditions. Subjects were connected to the Biowave device by application of a large hydrogel feed electrode (12.7 cm x 20.3 cm) to the abdomen and a smaller pain site electrode (5.1 cm diameter) to the lower back over the source of the pain. Subjects increased the power output of the device until tingling was felt; treatment continued for 20 min. Patients completed VAS pain assessments at baseline, after 20 min of treatment, and at 10 and 30 min after the device was turned off.
RESULTS: 29 patients were enrolled; 3 subjects completed each group. The only adverse reaction observed was skin irritation and minor blistering on one patient at the pain site electrode (n=1).

Feed Freq. (kHz)	Beat Freq. (Hz)	n	VAS Rating Baseline	VAS Rating @ 20 min	VAS Rating @ 30 min	VAS Rating @ 50 min
8	122	3	4.9±0.8	2.5±1.6	2.6±2.2	1.7±0.8
13.33	122	8	6.7±1.5	4.3±3.0	2.8±1.7**	2.6±2.2**
26.8	122	5	5.7±0.6	2.6±0.8**	1.6±1.3**	2.0±2.2**
8	90	7	5.3±1.0	2.3±2.1*	1.9±1.1**	3.3±2.5
8	122	3	5.0±1.3	1.6±0.7*	2.6±1.6	0.9±0.4*
8	150	3	5.9±1.8	3.6±2.7	1.8±2.5	0.9±1.1

*p<0.05, **p<0.01 vs. baseline by ANOVA with Dunnett's post-hoc test.
DISCUSSION: At a beat frequency of 122 Hz, all 3 feed frequencies tested produced comparable analgesia as evidenced by >50% reductions in VAS at the 3 time points tested. Variations in beat frequency at a feed frequency of 8 kHz showed significant reductions for 90 and 122 Hz. Analgesia persisted for at least 30 min after the treatments. Further studies are warranted to confirm the efficacy and safety of the system, as well as the duration of analgesia. The data suggest that the Biowave System is effective in the symptomatic treatment of chronic low back pain.
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PAMIDRONATE PRODUCES PAIN RELIEF FOR CHRONIC BACK PAIN IN GLUCOCORTICOID-INDUCED OSTEOPOROSIS

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INTRODUCTION: Pamidronate is an orally and intravenously active amino-substituted bisphosphonate which produces potent and specific inhibition of bone resorption. Clinical trials indicate that pamidronate is effective in a variety of conditions characterised by pathologically enhanced bone turn-over, including Paget's disease, hypercalcemia of malignancy, osteolytic bone metastasis, steroid-induced osteoporosis and idiopatic osteoporosis. We carried out a prospective study to assess whether intravenous pamidronate reduces the pain produced by glucocorticoid-induced osteoporosis. The primary purpose of the study was to determine the pain relief once a month after one year of treatment with pamidronate injected monthly. A secondary endpoint was to determine whether any differences in bone mineral density appeared after one year of the treatment.
METHODS: Twenty-two patients with a long-term glucocorticoid therapy (more than one year) and at least 10 mg daily of prednisona were studied. All of them had moderate or severe back pain (VAS >6) due to osteoporosis. After informed consent was obtained a blood sample was taken to analyse Ca, Phosphoro, hemograma, liver function (AST and ALT) and renal function (urea and creatinine). A bone hip and lumbar vertebral densitometry was done at the beginning of the study and after one year of the treatment in order to determine differences in bone mineral density. Sixty milligrams of pamidronate was administered intravenously once a week for one month followed by an infusion of sixty milligrams once a month during one year. Simultaneously patients were treated with 800 mg of calcium carbonate per day. We assesed monthly pain by VAS, pain relief, analgesic consumption and number of dreams hours. We also assesed any side effects. Subsequent blood samples were taken and analysed every month.
RESULTS: After the first month 80% of patients had a clinical relevant reduction (more than 20%) of pain intensity score measured by VAS. Three months later, in 60% of patients the pain score felt to 50%. Only twelve patients were treated with infusions during six months and their pain was nule or small. Every patient reduced analgesics consumption after three month of treatment and this reduction was higher after six months of infusions. None patients have been treated during one year, at this moment, to carry out the second densitometry. We are planning to do it in the next months in order to determine if the pain relief is accompanied with an improvement of mineral bone density.
DISCUSSION: Intravenous pamidronate seems to be a valuable treatment for chronic back pain due to glucocorticoid induced osteporosis.

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EFFECTS OF ELECTROACUPUNCTURE ON PAIN-RELIEF AND THE DISTRIBUTION OF LYMPHOCYTE SUBSETS IN PATIENTS WITH CHRONIC LOW BACK PAIN

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INTRODUCTION: Electroacupuncture (EA) has been used for the treatments of chronic pain (1), and it is reported that EA modulates immune responses in animal model (2). However, effects of acupuncture on pain-relief and immune-modulation remain in question. The purpose of this study was to assess the effectiveness of EA as a treatment for chronic low back pain. We also determined if EA affects the immune response, particularly changes in the proportion of lymphocyte subsets.
METHODS: Twenty patients with low back pain participated in this study. Patients who had back pain for more than 6 months and whose pain intensity more than 40 on a visual analog scale (VAS: 0-100) were chosen. Patients with the following diagnoses were excluded: pregnancy, osteomyelitis of spine, tumor, ankylosing spondylitis, vertebral fracture, and structural scoliosis. Participants received EA treatment on a twice-weekly schedule for 4 weeks (8 times). A certified acupuncturist experienced in its application stimulated the participants with needles. The stimulus was biphasic wave at a frequency of 2-4 Hz and was increased to the patient's comfortable level for 20 min. Pain level (VAS) was scored before the first, the forth, and the last treatments and also at one month after the last treatment. Blood samples were drawn before and after the first and the last treatment, and also at one month later. The distribution of lymphocyte subsets was analyzed. Data are expressed as mean ± SD. One-way analysis of variance or the Kruskal-Wallis test was used for statistical analysis. Values were considered statistically significant at $P < 0.05$.
RESULTS: Pain level was decreased significantly during treatments (before, 58 ± 10; the forth, 44 ± 12, $P < 0.01$; the last, 37 ± 14, $P < 0.01$), but pain level was returned to pre-EA value at one month after the end of treatment (51 ± 13). After the each treatment, the CD4+/CD8+ ratio increased significantly compared to values before the each treatment (Table 1). However, these parameters had all returned to pre-EA values before the next treatment.
DISCUSSION: EA treatment for 4 weeks (8 times) decreased pain score in patients with chronic low back pain during treatment, but pain-relief was not sustained for a long period. Although a little change was seen in the distribution of lymphocyte subsets after 20 min of EA, this effect was transient even after 8 times treatments. The duration and the indication of EA treatment should be further investigated.
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Table 1. Changes in Lymphocyte Subsets (n = 20, #P < 0.05 vs before)

	The first before	The first after	The last (8th) before	The last (8th) after	1 month later
B cells (%)	17.8±7.0	19.2±6.3	18.1±6.5	19.5±6.6	18.9±5.8
T cells (%)	67.2±8.5	69.0±8.3	66.9±8.0	68.5±8.3	66.0±8.1
CD4+ cells (%)	41.7±7.8	46.4±8.3	41.5±6.8	46.1±7.7	42.5±8.7
CD8+ cells (%)	25.5±4.5	21.4±5.4	25.5±4.0	22.5±4.6	23.5±4.1
CD4+/CD8+ ratio	1.7±0.5	2.4±0.9#	1.7±0.4	2.2±0.8#	1.9±0.6
NK cells (%)	15.0±4.9	11.8±5.3	15.0±4.2	12.0±4.3	15.2±5.4

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CONTINUOUS APPLICATION OF INTRATHECAL MORPHINE IN PHANTOM PAIN

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A 55 year old patient suffering from stump pain and allodynia in the area of his left knee and left shank for 14 years was treated with an intrathecal infusion. During the continuous intrathecal application of 6 mg morphine/day the pain level decreased from VAS 9 to VAS 5 in two days. After a intrathecal single shot of bupivacaine the pain didn't decrease. It took two weeks of continuous infusion to decrease the allodynia to VAS 1-2 and two weeks more to enable the patient to start walking with a prothesis. Testing the patient's response only by using single shot applications of epidural or intrathecal local anesthetics and/or opioids would have led to a negative conclusion. Only continuous application of morphine resulted in a modulation of the pain memory. We therefore conclude that testing of epidural or intrathecal drugs for the treatment of neuropathic pain should be performed continuously over several days and not using single shot applications.

S-217

INTERVENTIONAL PAIN MANAGEMENT ON POSTPOLIO SYNDROME(PPS)

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INTRODUCTION: This a case study of four non-paralytic postpolio syndrome (PPS) patients who were referred by primary care physicians to anesthesiology pain management consult. All four patients are female, age 50 to 59. Their chief complaints were daily aching and cramping pain due to physicla activity, mainly involve trunk, hip, upper and lower limbs. These pain symptoms has not responded to conservative treatments e.g. oral analgesic, alternative medicine, physical therapy and functional rehabilitation.
METHODS: After initial evaluation and then further workups as indicated, these four patients were found to suffer from myofascial spasm and pain syndrome, osteoarthritis, degenerative disc diease, facet arthropathy and sacroiliitis as common pain generators. Interventional pain treatment plans were recommended such as : trigger point injections, sacroiliiac joint injection, facet median branch block, and epidural steroid injection under fluoroscopic guidance. These four patients and family members were very apprehensive about making decision to take the interventional approach, because of the neurological sequelae due to polio and PPS. The risks and benefits of interventioal procedures were all discusse in detail.
RESULTS: There were noticeable pain relief and improvement in functional capacity following the diagnostic nerve blocks or injections. The radiofrequency neuroablation or other applicable interventional approach was then recommended as next step. Psychological evaluation and nonpharmacological pain coping strategies e.g. relaxation and biofeedback were initiated and proved beneficial. Anxiolytics and antidepresasants were popular choices in psychopharmacology regimens. As far as the pharmacological pain management is concerned, these four patients prefer to take long acting opioids and only use short acting analgesics for breakthrough pain as needed. The opioids requirement for optimal pain control were all decreased following individual interventional pain management treatments.
DISCUSSION: Increasing muscular atrophy and joint instability in the PPS patients leads to progressive muscle and joint pain, myofascial spasm, sacroiliitis, facet arthropathy and radicular pain. There has been series of reports on favorable outcome using physical therapy and exercise program, pharmacological or cognitive-behavior treatments on nonparalytic PPS pain management. Interventional pain management on PPS patiens has not been well studied or documented. However, with the advance in fluoroscopic gudied spine injection, botulinum toxins injection and radiofrequency neuroablation, PPS patients may have more options to help chronic pain management. These procedures will cause less side effects in comparison to pharmacological approach. We look forward to seeing more well designed interventional pain research in PPS patients. This progress will certainly reduce suffering and improve quality of life in PPS pain patients .
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S-218

THE EFFECT OF TERRORISM ON CHRONIC PAIN AND DEPRESSION

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INTRODUCTION: Individuals directly exposed to the terrorist attacks of September 11th, 2001 have a high probability of developing posttraumatic stress disorder. However, even individuals not directly exposed can experience a variable degree of trauma and stress (1). Stress leads to a state of hyper-arousal and increased sympathetic activity. This increased sympathetic activity can produce increased muscle spasms and exacerbate neuropathic pain syndromes. We sought to evaluate the effect of terrorism-induced stress on chronic pain patients.
METHODS: After IRB approval, data were extracted from medical records chosen from four epochs of time. The time period defining the post terrorist attack interval begins on September 12 and ends on October 11, 2001 (post 9/11/01). The immediately preceding time period is defined as August 12 to September 11 (pre 9/11/01). The two identical time intervals from the previous year (2000) were chosen for comparative purposes and to control for seasonal trends. Each interval comprises of 21 or 22 working days. Several variables, most notably, patient visits, gender, and presence of depression (clinically documented), were extracted and formed the basis of the analysis. A factorial analysis of variances with pre-planed comparisons was constructed to evaluate the data. Gender, depression (yes/no) and time category make up the factors of the three-factor ANOVA.
RESULTS: Two thousand thirty nine patient visits total were identify for all four time periods. Of those, 708 indicated depression as a symptom for that visit. Pre-planed contrasts indicate that the post-9/11/01 time category has a significantly higher mean visit rate compared to each other time category {pre 9/11/01, post 9/11/00, pre 9/11/00} ($P < 0.05$). The two-way interactions of depression by time and depression by gender were significant ($P<0.01$). Females were more greatly affected by depression after 9/11/01 then were males as seen by the larger visit rates as demonstrated in the figure.
DISCUSSION: Acute stress induced by world events is associated with an increase in visits to the chronic pain clinic in patients who have emotional and psychological issues of depression. This does not appear to occur in the absence of depression.
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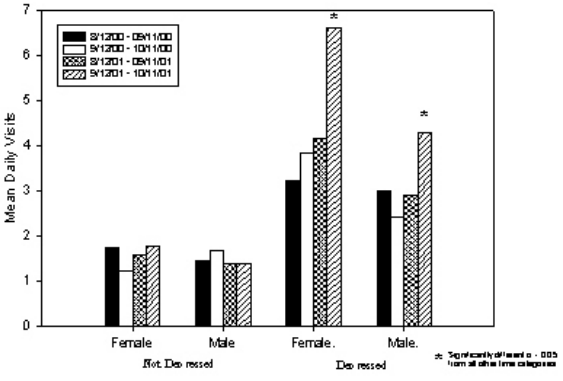

Pediatric Anesthesia

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NASAL ADMINISTRATION OF REMIFENTANIL IMPROVES CONDITIONS FOR INSERTION OF A LARYNGEAL MASK AIRWAY (LMA) FOLLOWING SEVOFLURANE INDUCTION IN CHILDREN

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INTRODUCTION: This study compares conditions for insertion of a Laryngeal Mask Airway (LMA) and airway response to LMA insertion (gagging, coughing and/or movement) after sevoflurane induction, with or without supplementary intranasal administration of one of three doses of remifentanil (1,1.5 or 2 mcg/kg) vs. saline in children 1-<7 yr. of age at 90 seconds following drug administration.
METHODS: Anesthesia was induced using nitrous oxide/oxygen and 8% sevoflurane. Sixty seconds later, nasal remifentanil (1,1.5 or 2 mcg/kg) or saline was administered. Anesthesia induction continued with 5% sevoflurane in oxygen, with the child breathing spontaneously. A principal investigator, who was blinded to the dose of remifentanil, attempted LMA insertion 90 seconds after nasal drug administration, and scored the response. End-tidal sevoflurane concentration was recorded immediately before and after LMA insertion in each patient. Following LMA insertion, ventilation was assisted using the same gas mixture until the respiratory rate returned to base-line value, or for a minimum of ten minutes, whichever occurred earlier.
RESULTS: To date, 52 patients have been studied. Good or excellent conditions for LMA insertion were seen in 93% of patients who received nasal remifentanil vs. 80% of controls. There was no difference in end-tidal sevoflurane or CO_2 concentration among patients in the four groups. Patients who received remifentanil had significantly lower respiratory rate from 5 until 10 minutes following nasal administration vs. saline controls. There were no complications associated with the nasal administration of study drugs. Serum remifentanil levels at the time of LMA insertion are pending.
DISCUSSION: Conditions for LMA insertion in adults following a single vital capacity breath of sevoflurane at 90 seconds compares favorably with those after propofol induction. Ninety seconds were chosen in adults (and used in this study) because it represented the time at which all patients would have completed their vital capacity breath. Remifentanil is commonly used by intravenous route to obtund the airway response to tracheal intubation or LMA insertion in adults, and more recently following IV induction in children. The use of the intranasal route to administer other lipophilic drugs (e.g. fentanyl and sufentanil) is well documented, especially before IV access is established. Our preliminary results indicate that nasal administration of remifentanil is a safe and potentially effective adjuvant technique to facilitate LMA insertion in children.
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S-220

AUSCULTATION OF BILATERAL BREATH SOUNDS DOES NOT RULE OUT ENDOBRONCHIAL INTUBATION IN CHILDREN

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INTRODUCTION: Auscultation of equal and bilateral breath sounds suggests the position of an endotracheal tube (ETT) to be above the carina ventilating both lungs. Absolute confirmation of the tracheal tube position is possible by fluoroscopy.
METHODS: Oro-tracheal intubation was performed in 72 consecutive patients undergoing cardiac catheterization. The ETT was taped at a level appropriate to the child's age based on standard formulae. Auscultation of bilateral breath sounds was confirmed. The relationship of the tip of the ETT to the carina was determined during fluoroscopy.
RESULTS: 49 patients (68.1%) were under 120 months, and 10 (13.9%) were infants under 12 months of age. By fluoroscopy the tip of the ETT was seen in the right mainstem bronchus in 11 patients (15.3%) and in a low position above the carina in 14 patients (19.4%). Out of the 11 patients with right mainstem intubation, 10 were children <120 months of age and 4 were less than 12 months of age. (Fisher's exact test P=0.040). There was a direct correlation between the age and weight of the patient and the incidence of low tracheal and right main bronchial intubation (P=0.005 and P= 0.004, respectively). There was no association between the experience of the anesthesia trainee and the incidence of right mainstem intubation.
DISCUSSION: Achieving appropriate ETT positioning in children is not always easy because the tracheal length of a child is shorter than that of an adult. Moreover, the position of the ETT is easily altered by head position, rotatory movements, and flexion as well as extension of the head. In one study, ETT malposition rates observed in ICU postintubation chest radiographs were 39.1% after positioning guided by clinical assessment alone.[1] Endobronchial intubation, or an ETT that is low enough to touch the carina, may precipitate coughing, bronchial spasm, arterial oxygen desaturation and patient's movement. The failure to diagnose main stem intubation by auscultation alone may be related to the use of Murphy eye ETTs. The Murphy eye was designed to allow ventilation of the lung when the bevel of the ETT is occluded. It has been demonstrated that the eye of the Murphy tube reduces the reliability of chest auscultation in detecting endobronchial intubation.[2]
Suggested measures for prevention of endobronchial intubation include increased awareness of the imperfection of auscultation, assessment of insertion depth by checking length scale on the tube, and minimizing patient's head and neck movement after intubation.
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S-221

DIRECTION OF THE NEEDLE INSERTION IN AN INTERNAL JUGURAR VEIN PUNCTURE, RADIOGRAPHIC CONSIDERATION

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INTRODUCTION: Placement of central venous line via the right internal jugular vein (RIJV) is widely practiced in anesthesia for open-heart surgery in infants and children. Direction of puncture needle is generally described as toward the ipsilateral nipple (1). We studied the relationship of this direction and right internal jugular vein anatomy.
METHODS: The protocol was approved by the local ethics committee and written informed consent was obtained from parents. Thirty-two patients scheduled for cardiac catheterization were studied. After routine cardiac catheterization, markers were placed on the insertion site of the RIJV puncture (high approach) and the right nipple, then right internal jugular venogram (2) was obtained. The anatomical relationship was examined on the film.
RESULTS: The age, weight and height of subjects were 0 month to 13 years, 3.5 kg to 50.4kg, and 51.3 to 153.2 cm, respectively. The angle between the line on the RIJV and the line drawn from the insertion site to the nipple was 30.6 ± 7.3 degrees. The RIJV run essentially parallel to the long axis of the body.
DISCUSSION: The line on the RIJV and the line from the insertion site to the right nipple were not identical at all. The direction of the puncture needle of the internal jugular vein could be parallel to the long axis of the body, i.e. the line on the internal jugular vein.
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S-222

ANESTHETIC IMPLICATIONS OF EPICARDIAL PACEMAKER PLACEMENT IN NEONATES WITH CONGENITAL COMPLETE HEART BLOCK

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INTRODUCTION: Congenital complete heart block (CCHB) carries high neonatal morbidity (58%) and mortality (7%)[1]. Placement of a permanent epicardial pacemaker (EPM) soon after birth may be necessary but can be associated with significant hemodynamic instability[2]; our experience in neonates with CCHB undergoing anesthesia for EPM placement is described.
METHODS: A retrospective chart review of neonates with CCHB who underwent anesthesia for EPM at Children's Hospital between 1988 and 2001 was performed. Demographic and perioperative data were examined; hypotension was defined as a 20% decrease from baseline.
RESULTS: Seventeen neonates were identified, 11 with structurally normal hearts (NH, 65%) and 6 with structurally abnormal hearts (AH, 35%; heterotaxy n=5, VSD n=1). Demographic data (mean) of NH vs. AH respectively included: gestational age 36.7 vs. 35.3 weeks, weight 2.9 vs. 2.5 kg, and age at surgery (day of life, DOL) 4.2 vs. 3.3. Mechanical ventilation and inotropic support were needed preoperatively in 8 patients (3/12 with NH (25%) and 5/6 with AH (83%)), and 2/8 were extremely premature (26 wks NH and 30.6 wks AH). Temporary epicardial pacing wires (TEPW), placed in the ICU via a small subxyphoid incision, were necessary for 4/6 (75%) of the AH group on DOL 1 because of low ventricular escape rate <40 bpm and clinical signs of a low cardiac output. All patients had a permanent epicardial VVI pacemaker placed through an extended subxyphoid incision. In the NH group, 7/11 received balanced general anesthesia - induction with ketamine (n=6) or thiopentone (n=1), and maintenance with N_2O/O_2 and volatile agent. The remaining 4 NH and all 6 AH neonates received a narcotic-based technique (fentanyl 12- 66 mcg/kg) supplemented with N_2O, midazolam and/or low concentrations of isoflurane. Intraoperative hypotension occurred in 4 patients, 2 with NH (16.7%) and 2 with AH (33.3%); 3/4 had clinical evidence of low cardiac output and did not receive inotrope preoperatively or in the operating room prior to the hypotension, and 1/4 (AH) developed hypotension despite preoperative intubation, inotrope and TEPW. 5/17 patients received atropine intraoperatively, without an increase in heart rate. The response to catecholamines was less than anticipated in 1 NH and 3 AH. Transcutaneous pacing was not used in any patient. There was one death (6%, 0/11 NH, 1/6 AH) and all other patients survived to discharge.
DISCUSSION: Patients with a structurally abnormal heart, baseline ventricular escape rate <40 bpm, low cardiac output state, and/or extreme prematurity pose the greatest perioperative risk for hemodynamic instability. When these factors are present, mechanical ventilation, invasive monitoring, inotropic support and temporary pacing should be considered early. Atropine appears to offer no benefit, and the response to catecholamines diminished.
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S-223

A RETROSPECTIVE REVIEW OF PERIOPERATIVE FRESH FROZEN PLASMA TRANSFUSION PRACTICE IN A CHILDREN'S HOSPITAL

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INTRODUCTION: Fresh frozen plasma (FFP) continues to be overused and also used inappropriately[1,2] despite its supply being finite. Moreover, medicolegal implications of transfusion-transmitted disease reinforce the need for recognized and defensible transfusion criteria. In 1997 Canadian Medical Association published recommendations for appropriate use of red cells and plasma transfusion in adults and children over 4 months of age.[3] As a part of quality assurance program we undertook this audit to determine how our perioperative practice of transfusion of fresh frozen plasma in children conformed with published criteria.
METHODS: From the guidelines published by the Canadian Medical Association we laid down the guidelines relevant in the perioperative period[3]. FFP perioperative transfusion episodes for 100 consecutive patients greater than 6 months of age admitted to our children's hospital for elective or emergency surgical procedure during the years 1999-2000 were evaluated. Each transfusion episode was rated as being similar, possibly similar or dissimilar to the guidelines. Transfusion episodes were also classified according to surgical specialty and by the time it was given i.e. preoperatively, intraoperatively and postoperatively.
RESULTS: The 100 transfusion episodes accounted for 170 units transfused to 82 children. Of the 100 transfusion episodes, 42 were judged similar, 11 possibly similar, 42 dissimilar to the guidelines and 4 had inadequate information to be judged. Of the 170 units transfused, 69(41%) were judged similar, 17(10%) possibly similar, 68(40%) dissimilar to the guidelines and 5% had inadequate information. Analysis of transfusion episode by specialty and time of transfusion is as follows

Specialty	Similar	Possibly similar	Dissimilar
Orthopedics	12	4	8
Cardiac	18	1	14
General surgery	8	4	7
Neurosurgery	1	2	3
Others	4	-	5
Time			
Preoperative	9	2	9
Intraoperative	16	4	15
Postoperative	17	5	18

DISCUSSION: Forty-two percent of the transfusion episodes were dissimilar to the guidelines. Unfortunately, such a high rate is similar to those reported in previous studies.[4-7] Since earlier studies use different guidelines and include adult population, the results of this study are not directly comparable. We were surprised to identify situations where FFP was inappropriately transfused. Guidelines for transfusion appropriateness, education of hospital staff and a monitoring system to ensure adherence to guidelines, are required.
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S-224

TO SWADDLE OR NOT: NOT ALL CHILDREN BECOME HYPOTHERMIC DURING MRI SCANNING UNDER GENERAL ANESTHESIA

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INTRODUCTION: The cool dry environment, circulating air within the magnet bore, and inability to use active warming devices characteristic of MRI scanning increases the risk of hypothermia during general anesthesia. Absorption of radiofrequency radiation during the scan, however, may counteract this effect. (1,2) As routine temperature monitoring is not possible due to the magnetic field, little is known about temperature fluctuations during MRI procedures. We sought to determine the incidence of hypothermia in children after MRI's under general anesthesia.
METHODS: With IRB approval, we prospectively studied 50 children who underwent MRI studies under general anesthesia. The ages ranged from 1 month to 18 years and weights from 1.4 to 89 kg. Induction and emergence occurred in a room adjacent to the MRI where the ambient temperature ranged from 22-24 C. 44 patients were induced with sevoflurane with LMA placement. 6 received propofol or ketamine for induction and were intubated. Maintenance was with sevoflurane with patients breathing spontaneously. The children were covered with a hospital gown and cotton blanket; no other heating device was used. Rectal temperatures were measured immediately after induction prior to MRI and after MRI prior to emergence from general anesthesia.
RESULTS: 21/50 children (42%) had post-scan rectal temperatures > 36.1 C. Patients with rectal temperatures > 36.1 C were older (7.2 +/- 3.7 vs 4.6 +/- 3.8 years) , had greater body mass (32.2 +/- 20.9 vs 22.2 +/- 17.2 kg), and shorter MRI scans (43.4 +/- 15.2 vs 63.4 +/- 22.9 minutes). The type of anesthesia and frequency of endotracheal intubation did not differ between groups.
DISCUSSION: Although the MRI environment and general anesthesia in children may increase the risk of heat loss, radiofrequency radiation may cause an increase in the heat gain by the patient. We found that nearly 42% of patients in our study did not become hypothermic (T> 36.1 C) even when only covered with a hospital gown and cotton blanket. Patients likely to stay warm were older, had a greater body mass and underwent shorter scans than those who became hypothermic. These results suggest that the absorption of energy during the scan may play a significant role in temperature fluctuations during general anesthesia for MRI procedures. (3) Further studies are needed to understand the mechanism of heat exchange in children during MRI procedures.
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S-225

EVALUATION OF AN OBSERVATIONAL DATABASE FOR OUTCOMES WITH EPIDURAL ANALGESIA IN PEDIATRIC POST-SURGICAL PATIENTS

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INFORMATION: Little is known about safety and effectiveness of continuous epidural analgesia for postoperative pain control in infants and children. McBride, et al.[1] evaluated 19 children (ages 4-17 years) receiving continuous epidural infusions, 17 via thoracic catheters, following pectus deformity repair. They reported excellent pain control and no catheter-related complications. We describe our experience with a larger number of patients, including children <4 years of age and those undergoing a variety of surgical procedures.
METHODS: We developed an observational database to monitor and track analgesia-related outcomes for a consecutive series of pediatric surgical patients followed by our Acute Pain Management Service. Information was recorded on clinical outcomes such as pain severity, sedation, nausea and vomiting (N/V), pruritis, respiratory depression, urinary retention and motor impairment, and practice variables (e.g., catheter level, epidural solution). Using nonparametric statistics, we examined outcomes from the entire sample (110 to date; 70 female) and by age groups [0-3 years (n=38), 4-9 (n=36), and 10-17 (n=36)], and compared severity of adverse effects using the Mann-Whitney U test.
RESULTS: The majority of subjects received continuous epidural infusions with bupivacaine 0.1%; 94.7%, 94.4% and 75%, respectively by age group. Most children >3 years underwent orthopedic procedures with a combination of regional and general anesthesia; level of catheter placement included thoracic (n=24), lumbar (n=49) and caudal (n=30). Eighty percent of patients <4 years had caudal catheters. Daily pain scores were similar between children 4-9 years and 10-17 years, with mean scores in the range of none to mild pain through postoperative day (POD) 2. No differences were observed for the severity of N/V, sedation, and pruritis, which if present, were mild. The majority of patients (75%) had Foley catheters immediately after surgery; however, 50% (n=19) of patients age 0-3 years did not have Foley catheters and were voiding spontaneously. Overall, respiratory depression, defined as a respiratory rate <10/min, was not detected in any patient immediately after surgery or on POD 1 and 2. Mild side effects from local anesthetic (e.g., metallic taste, tinnitis) were noted in 1 patient (0.9%). Pairwise comparisons with the Mann-Whitney U test revealed better motor strength on POD 1 and 2 for the 0-3 year group compared to those 4-9 years ($p<0.01$) and 10-17 years ($p<0.01$).
DISCUSSION: In a prospective evaluation of pediatric patients receiving epidural analgesia, we found no dural punctures or catheter-related infections. Assessments of children >3 years who were able to provide self-report data yielded no evidence of headache, pain at injection site, or new neurological deficits. Our findings show that epidural analgesia provides excellent pain control without significant risks for adverse side effects and complications.
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S-226

EFFICACY OF SOMATIC PARAVERTEBRAL BLOCK FOR POSTOPERATIVE PAIN RELIEF IN CHILDREN UNDERGOING OPEN APPENDECTOMY

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INTRODUCTION: Post operative pain relief is a major concern for pediatric anesthesiologists. Poor pain control causes patient and parent anxiety, dissatisfaction and delayed discharge. Pain management options include opioids, which may lead to vomiting and respiratory depression and adjuvant regional analgesia. Somatic paravertebral block (SPVB) has been used for analgesia in children (1-3). We conducted a chart review to assess the effectiveness of SPVB for postoperative pain relief in children undergoing open appendectomy.
METHODS: We reviewed 36 consecutive charts of children between the ages 3-16 years undergoing open appendectomy under general anesthesia in this case-control study. In both groups, rapid sequence induction of anesthesia was with IV propofol 2.5 mg/kg and succinylcholine 1.5 mg/kg. General anesthesia was maintained with isoflurane 1% in 70% N_2O and O_2 All patients were given fentanyl 2 mcg/kg IV, ketorolac 0.5mg/kg IV, and acetaminophen 20 mg/kg PR before incision. SPVB was performed by, or under supervision of, one of the investigators, at T_{11}, T_{12}, L_1 level using 22 G Touhy needle in left lateral decubitus position before incision. Ropivacaine 0.2% with epinephrine 1:200,000 in an amount of 0.25 ml/kg (maximum of 5 ml) was injected at each level. Charts were reviewed for the first 24 hours after surgery. In the postoperative period analgesia was provided with morphine 0.05 mg/kg IV q 2 hrs in a structured manner when VAS pain scores were greater $\geq$ 6/10. A record of time to the first dose of morphine required after surgery and total requirement of morphine in first 24 hr were recorded. Any adverse effects including nausea, vomiting or respiratory depression were noted.
RESULTS: Demographic data, such as age, weight, gender, and length of surgery, were similar. SPVB treated-patients required less total morphine during the first 24 hr, 0.12 ± 0.07 vs 0.34 ± 0.15mg/kg/24hr, mean$\pm$SD, $P<0.001$. The time to first dose of morphine after surgery was greater in the SPVB group, 7.1 ± 4.4. vs 2.5 ± 1.6 hr, mean$\pm$SD, $P<0.001$. Two patients in the SPVB-group and 5 control-patients vomited. None of the SPVB-treated patients had an adverse event secondary to their regional block.
CONCLUSION: This study shows that SPVB is an effective method of pain relief in children undergoing open appendectomy. SPVB can effectively increase postoperative analgesia and decrease the use of opioid medication that can obviate the incidence of undesirable side effects. A formal prospective investigation appears indicated.
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CAUDAL ANALGESIA MODIFIES THE EFFECT OF FLUMAZENIL ON RECOVERY FROM SEVOFLURANE ANESTHESIA AFTER ORAL MIDAZOLAM PREMEDICATION

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INTRODUCTION: Oral premedication with midazolam in children provides satisfactory anxiolysis before anesthesia (1), but delays recovery after brief sevoflurane anesthesia (2). Flumazenil, a potent benzodiazepine antagonist, can reverse the sedative effect of midazolam-induced anesthesia (3). So our first purpose was to evaluate the effect of flumazenil on recovery after sevoflurane anesthesia in children premedicated with midazolam orally. As we found that flumazenil shortened the recovery time without affecting the quality of recovery, our second purpose was to investigate if the effect of flumazenil is modified by caudal analgesia.
METHODS: 30 children (1-8 years, ASA physical status 1 or 2) undergoing lower abdominal procedure were randomly assigned to flumazenil group and control group. They were premedicated with 0.5 mg/kg midazolam orally approximately 30 minutes before the induction of anesthesia. Anesthesia was induced and maintained with sevoflurane (3-5%) and nitrous oxide (66%), in oxygen via a face mask with spontaneous breathing. Sevoflurane was discontinued at the beginning of skin closure, and then at the end of surgery nitrous oxide was discontinued and flumazenil 0.02 mg/kg or saline was injected. The time from discontinuation of anesthesia to grimacing at tactile stimulation (Recovery time) was recorded. At the time of discharge from operating room, a blinded observer evaluated the quality of recovery as Recovery score, which was sum of the three objective components: sedation (1 = awake; 2 = drowsy; 3 = asleep), crying (1 = panicky; 2 = moaning; 3 = not crying), and movement (1 = thrashing; 2 = restless; 3 = none). In other 30 children (1-8 years, ASA physical status 1 or 2) who had caudal analgesia with 1 ml/kg of 0.25% bupivacaine after anesthesia induction, the same protocol as above was performed and Recovery time and Recovery score were recorded as well.

RESULTS:

	Children without caudal analgesia		Children with caudal analgesia	
	Flumazenil group	Control group	Flumazenil group	Control group
Recovery score	5.0 ± 0.4	5.1 ± 0.4	5.3 ± 0.6*	7.7 ± 0.4
Recovery time	2.3 ± 0.4*	4.7 ± 0.6	4.3 ± 0.4*	6.1 ± 0.7

Values are means ± SEM, *p<0.05 vs control group
DISCUSSION: Recovery from sevoflurane anesthesia occurred earlier by flumazenil administration in children premedicated with midazolam regardless of the application of caudal analgesia. Flumazenil did not affect the quality of recovery in children without caudal analgesia but resulted in more agitated recovery in children with caudal analgesia.
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FELINE PULMONARY VASCULAR RESPONSES TO EPHEDRINE

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Pulmonary vascular responses to ephedrine, phenylephrine, and U46619, and their effects after administration of the non-selective $_1$ antagonist, prazosin, the $_1$B antagonist, chloroethylclonidine, and the selective $_1$D antagonist, BMY 7378, were investigated in the intact-chest under constant flow conditions in anesthetized cats. Ephedrine, phenylephrine, and U46619, a thromboxane A_2 mimic, all produced dose-dependent vasoconstrictor responses in the feline pulmonary vascular bed. After administration of prazosin, in a dose of 1 mg/kg iv, there was no significant change in U46619-induced vasopressor responses; however, there was significant attenuation of pulmonary vasoconstrictor effects induced by ephedrine and phenylephrine. The effects of the selective $_1$B antagonist chloroethylclonidine, in a dose of 0.3 mg/kg iv, were evaluated in a separate protocol. Pulmonary vasoconstrictor responses to ephedrine and phenylephrine were attenuated after the administration of chloroethylclonidine. However, no significant attenuation of the pulmonary vasopressor responses to U46619 was demonstrated. In a third protocol, the effects of the selective $_1$D antagonist BMY 7378, in a dose of 0.3 mg/kg iv, were evaluated. The vasopressor effects of ephedrine, phenylephrine and U46619 were unchanged after the administration of BMY 7378. These data suggest that ephedrine and phenylephrine induce pulmonary vasoconstriction in the cat and that this response is mediated, in part, by an $_1$ receptor-sensitive mechanism. Furthermore, this constrictor response is mediated by the $_1$B receptor and not the $_1$D receptor.

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ANALYSIS OF THE $GABA_A$ RECEPTOR AGONIST, MUSCIMOL, IN THE PULMONARY VASCULAR BED OF THE CAT

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Pulmonary vascular responses to a $GABA_A$ selective agonist, muscimol, bradykinin, and the potassium channel opener, pinacidil, and their effects after administration of the ATP-sensitive potassium channel blocking agent, glibenclamide (5 mg/kg iv), the nitric oxide synthase inhibitor, L-N5-(1-iminoethyl) ornithine (L-NIO) (1mg/kg iv), the cyclooxygenase inhibitor, meclofenamate (2.5 mg/kg iv), the $GABA_A$ antagonist, bicuculline (0.1 mg/kg iv), and the $GABA_B$ antagonist, saclofen (0.1 mg/kg iv), were investigated in the intact-chest cat under constant flow conditions. Muscimol, bradykinin, and pinacidil all produced dose-related decreases in lobar arterial pressure under high tone conditions after administration of an infusion of U46619, a thromboxane mimic. Following administration of glibenclamide, in a dose that significantly attenuated pinacidil-induced vasodepressor responses, muscimol and bradykinin were not significantly affected. Following administration of L-NIO, in a dose that significantly reduced bradykinin-induced vasodepressor responses, muscimol and pinacidil-induced vasodilatation was not significantly attenuated. After administration of meclofenamate, in a dose that significantly reduced arachidonic acid induced vasodepressor responses, pinacidil, bradykinin, and muscimol-induced vasodilatation was not significantly attenuated. After administration of the $GABA_B$ antagonist, saclofen, there was no alteration on muscimol, pinacidil, or bradykinin responses. Finally, after administration of the $GABA_A$ antagonist, bicuculline, there was no alteration on bradykinin or pinacidil responses; however, muscimol-induced vasodepressor effects were significantly attenuated. These data suggest that muscimol induces pulmonary vasodepressor responses in the pulmonary vascular bed of the cat and that this response is mediated, in part, by a $GABA_A$ receptor-sensitive mechanism and not the $GABA_B$ receptor.

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THE EFFECTS OF NOREPINEPHRINE IN THE PULMONARY VASCULAR BED OF THE CAT

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Pulmonary vascular responses to norepinephrine, phenylephrine, and U46619, and their effects after administration of the non-selective $_1$ antagonist, prazosin, the $_1$B antagonist, chloroethylclonidine, and the selective $_1$D antagonist, BMY 7378, were investigated in the intact-chest under constant flow conditions in anesthetized cats. Norepinephrine, phenylephrine, and U46619, a thromboxane A_2 mimic, all produced dose-dependent vasoconstrictor responses in the feline pulmonary vascular bed. After administration of prazosin, in a dose of 1 mg/kg iv, there was no significant change in U46619-induced vasopressor responses; however, there was significant attenuation of pulmonary vasoconstrictor effects induced by norepinephrine and phenylephrine. The effects of the selective $_1$B antagonist chloroethylclonidine, in a dose of 0.3 mg/kg iv, were evaluated in a separate protocol. Pulmonary vasoconstrictor responses to norepinephrine and phenylephrine were attenuated after the administration of chloroethylclonidine. However, no significant attenuation of the pulmonary vasopressor responses to U46619 was demonstrated. In a third protocol, the effects of the selective $_1$D antagonist BMY 7378, in a dose of 0.3 mg/kg iv, were evaluated. The vasopressor effects of norepinephrine, phenylephrine and U46619 were unchanged after the administration of BMY 7378. These data suggest that norepinephrine and phenylephrine induce pulmonary vasoconstriction in the cat and that this response is mediated, in part, by an $_1$ receptor-sensitive mechanism. Furthermore, this constrictor response is mediated by the $_1$B receptor and not the $_1$D receptor.

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MA HUANG VASOPRESSOR EFFECTS ARE MEDIATED BY AN ALPHA$_1$B RECEPTOR IN THE PULMONARY VASCULAR BED OF THE CAT

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Pulmonary vascular responses to the herbal stimulant, Ma Huang, phenylephrine, and U46619, and their effects after administration of the non-selective $_1$ antagonist, prazosin, the $_1$B antagonist, chloroethyl-clonidine, and the selective $_1$D antagonist, BMY 7378, were investigated in the intact-chest under constant flow conditions in anesthetized cats. Ma Huang, phenylephrine, and U46619, a thromboxane A_2 mimic, all produced dose-dependent vasoconstrictor responses in the feline pulmonary vascular bed. After administration of prazosin, in a dose of 1 mg/kg iv, there was no significant change in U46619-induced vasopressor responses; however, there was significant attenuation of pulmonary vasoconstrictor effects induced by Ma Huang and phenylephrine. The effects of the selective $_1$D antagonist BMY 7378, in a dose of 0.3 mg/kg iv, were evaluated. The vasopressor effects of Ma Huang, phenylephrine and U46619 were unchanged after the administration of BMY 7378. In a third protocol, the effects of the selective $_1$B antagonist chloroethylclonidine, in a dose of 0.3 mg/kg iv, were evaluated in a separate protocol. Pulmonary vasoconstrictor responses to Ma Huang and phenylephrine were attenuated after the administration of chloroethylclonidine. However, no significant attenuation of the pulmonary vasopressor responses to U46619 was demonstrated. These data suggest that the herbal stimulant, Ma Huang, and phenylephrine induce pulmonary vasoconstriction in the cat and that this response is mediated, in part, by an $_1$ receptor-sensitive mechanism. Furthermore, this constrictor response is mediated by the $_1$B receptor and not the $_1$D receptor.

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MODULATION OF VALERIAN ON BRAINSTEM GABAERGIC EFFECTS IN RATS

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INTRODUCTION: Valerian is an herb native to the temperate areas of the Americas, Europe, and Asia. Valerian is a commonly used herbal medicine to treat insomnia and anxiety (1), and thus, it may potentiate sedative effects of anesthetics (2). We hypothesized that there is an interaction between valerian activity and GABAergic mechanism in the brainstem neurons. In this study, we evaluated the effects of valerian and $GABA_A$ receptor agonist, muscimol, on brainstem neuronal activities.
METHODS: Experiments were performed on neonatal rats of 1 to 5 days old. After the animal was deeply anesthetized with halothane, a craniotomy was performed and the forebrain was ablated at the caudal border of the pons by transection. The caudal brainstem and cervical spinal cord were isolated by dissection in modified Krebs solution. The bathing solution was equilibrated with 95% O_2 and 5% CO_2 and adjusted to pH 7.4. Single tonic unitary discharges to valerian extract (from Lichtwer Pharma AG, Germany) were recorded in the nucleus tractus solitarius (NTS) in the brainstem by glass microelectrodes (3).
RESULTS: Muscimol, $GABA_A$ receptor agonist, inhibited the spontaneous activity of the majority of the NTS units. This inhibition (approximately 57% compared to 100% of the control level; IC_{50} = 30 M) could be antagonized by selective $GABA_A$ receptor antagonist, bicuculline (10 M). Application of valerian extract into the brainstem compartment of the preparation also significantly reduced the discharge rate of these NTS neurons (approximately 32% compared to the control level; IC_{50} = 1.0 mg/ml), and this reduction could partially be reversed by bicuculline (10 M). Pretreatment with 1.0 mg/ml valerian extract significantly decreased the NTS inhibitory effects (from 57% to 32%) induced by muscimol (30 M).
DISCUSSION: Valerian may act as a sedative via modulation of GABA neurotransmission and receptor function (4). Our results demonstrated the interactions of valerian extract with ligand-bindings of $GABA_A$ receptors and the modulation of the brainstem GABAergic mechanism by valerian. It seems that valerian may interfere with GABAergic neurotransmission, and presurgical valerian use may cause valerian-anesthetic interaction during perioperative care (2).
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THE RELATIONSHIP BETWEEN DOPAMINERGIC NEUROTRANSMISSION INNERVATION AND DEXAMETHASONE-INDUCE AGGRAVATION OF ISCHEMIC NEURONAL DAMAGE IN THE RAT STRIATUM

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INTRODUCTION: Glucocorticoids have been reported to aggravate ischemic neuronal damage in both humans and experimental animals. The agents also increase activity of the central dopaminergic system. Because excess release of dopamine in cerebral ischemia is closely related to the outcome of neuronal damage, the authors examined the relationship between dexamethasone-induced facilitation of dopaminergic activity and histologic outcome.
METHODS: Changes in the extracellular concentration of dopamine and its metabolites in the striatum produced by occlusion of the middle cerebral artery for 20 minutes were investigated by a microdialysis---high-performance liquid chromatography procedure and effects of intracerebroventricular administration of dexamethasone (10 μg) were evaluated in halothane-anesthetized rats. The histologic outcome was examined 7 days after ischemia by light microscopy. In another set of rats, the substantia nigra was lesioned 2 days before, and identical procedures were applied to these animals to assess the relationship between changes in ischemic release of dopamine and morphology.
RESULTS: The occlusion of the middle cerebral artery produced a marked increase in the extracellular concentration of dopamine in the striatum, the peak value being 240 times that before ischemia. The value returned to the basal level immediately after reperfusion. The preischemic administration of dexamethasone enhanced the increase in the dopamine level during ischemia, and the peak value in the dexamethasone group was 640% of that in the vehicle group. The value returned to the basal level 2 h after reperfusion. After 7 days, ischemic neuronal damage in the dexamethasone group was severe compared with that in the vehicle group. In rats receiving the substantia nigra lesion and dexamethasone treatment, ischemic release of dopamine was abolished, and aggravation of ischemic neuronal damage by dexamethasone was completely alleviated.
DISCUSSION: Because the striatum is predominantly innervated by dopaminergic fibers, the facilitation of ischemic release of dopamine by dexamethasone may be a contributing factor in the aggravation of ischemic in the striatum. The administration of glucocorticoids in cerebral ischemia may be harmful.

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LOW DOSE BUPRENORPHINE ENHANCE THE SPASTIC PARAPARESIS INDUCED BY INTRATHECAL MORPHINE AFTER NON- INJURIOUS INTERVAL OF SPINAL ISCHEMIA IN RATS

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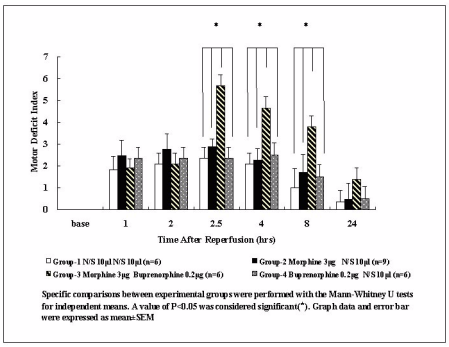
INTRODUCTION: We have recently reported that intrathecal (IT) injection of morphine (Mor) after non-injurious interval of spinal ischemia induced transient spastic paraparesis in rats(1). This effect was reversed by subsequent IT naloxone administration, suggesting that spinal opioid receptor play an active role in the spinal functional dysinhibition initiated by transient spinal ischemia. It was reported that Bup play some role in the analgesic actions of mu-opioid agonists in the spinal cord same as morphine(2). (3)However,we reported IT buprenorphine (Bup) 4micg did not induce spastic paraparesis after non-injurious interval of spinal ischemia (4). Therefore, we hypothesized that low dose IT Bup and Mor has interactive effect for the spastic paraparesis. The aim of this study was to characterize the interaction between low dose IT Bup and Mor after non-injurious interval of spinal ischemia in rats.
METHODS: In using rats implanted with IT catheter, the placement and subsequent inflation of a 2F Fogarty catheter in descending thoracic aorta induced 6 min of ischemia under halothane anesthesia. After ischemia rats were randomly divided into four groups and received intrathecal injections at 30min and 2hrs after reperfusion as follows: Group-1 saline 10micl and saline 10micl, Group-2 Mor 3micg and saline 10micl., Group-3 Mor 3micg and Bup 0.2micg, Group-4 Bup 0.2micg and saline 10micl. After injections rats were allowed to recover, and the motor function was periodically assesed using motor deficit index (MDI: 6=complete paraplegia, 0=complete normal) for 24hrs.
RESULTS: Neither IT 0.2micg Bup (Group-4) nor IT 3micg Mor (Group-2) could induce any spasticity same as IT saline (Group-1). On the other hand, the combination with IT 0.2micg Bup and 0.3micg Mor progressed a spasticity, resuting in complete paraparesis (Figure).



CONCLUSION: Our results demonstrated that low dose IT Bup enhance the spastic paraparesis induced by morphine after non-injurious interval of spinal ischemia in the rat. We suggest that the small dose morphine can induce spastic paraparesis in combined with buprenorphine.
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APROTININ REDUCES INTERLEUKIN-8 PRODUCTION AND LEUKOCYTE INFILTRATION AFTER CEREBRAL ISCHEMIA-REPERFUSION IN A RABBIT MODEL

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INTRODUCTION: Clinical and laboratory studies have shown that aprotinin can reduce interleukin-8 (IL-8) production and leukocyte activation after cardiopulmonary bypass (1,2). It is unknown if aprotinin can inhibit interleukin-8 production and brain tissue leukocyte infiltration after cerebral ischemia and reperfusion.
METHODS: Twenty-four New Zealand rabbits were randomly assigned into 3 groups (n=8 each). Complete cerebral ischemia was induced by the six-vessel model for 30 min followed by reperfusion for 4 hours in group A and B, while group C was sham operated without occluding the vessels and aprotinin administration. Animals of group A were given aprotinin at 30,000 KIU/kg through a peripheral vein for a duration of 10 min before inducing ischemia, followed by 10,000 KIU/ kg per hour throughout the experiment. Animals in group B and C received the same volume of saline. A catheter was inserted into the internal jugular bulb for blood samples. Serum concentrations of IL-8 and plasma malondialdehyde (MDA), a marker of lipid peroxidation, were measured at 15 min (T_0) before inducing ischemia, 30 min (R_1), 2 hours (R_2) and 4 hours (R_3) after reperfusion. After the completion of the experiment, cerebral cortex was obtained and processed with hematorylin and eosin staining to observe tissue leukocyte infiltration and neuron damage.
RESULTS: Serum IL-8 (0.48 ± 0.15, 0.39 ± 0.09 and 0.45 ± 0.11 ng/L) and plasma MDA (4.01 ± 0.21, 3.89 ± 0.83 and 4.12 ± 0.06 nmol/L) did not differ among group A, B and C at T_0. IL-8 and MDA of group C did not change over time during the experiment. Cerebral ischemia/ reperfusion was associated with significant increase of IL-8 (0.89 ± 0.10 ng/L, $P < 0.05$ vs T_0) and MDA (6.05 ± 0.80 nmol/L, $P < 0.01$ vs T_0) in group B at R_1 and onwards. IL-8 and MDA in group B were significantly higher than the corresponding values in group C and group A throughout reperfusion ($P < 0.05$, or $P < 0.01$). MDA did not significantly increase after reperfusion in group A. IL-8 in group A did not significantly increase after reperfusion until R_3 (0.80 ± 0.17 ng/L, $P < 0.05$ vs T_0), but was significantly lower than the corresponding value in group B (1.46± 0.23 ng/L, $P < 0.05$ vs group A). Cerebral cortex leukocyte infiltration and neuron damage were observed in group B under light microscopy after 30 min ischemia and 4 hours of reperfusion. These were significantly alleviated in group A.
CONCLUSION: Aprotinin attenuates IL-8 release after complete cerebral ischemia and reperfusion with concomitant reduction in tissue leukocyte infiltration and lipid peroxidation. The mechanism is dependent on the anti-protease activity of aprotinin.
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NEUROMUSCULAR BLOCK BY INFUSION OF TAAC3 IN THE PRIMATE

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TAAC3 is an ultra-short and ultra-fast-acting non-depolarizing neuromuscular blocking agent currently undergoing pre-human testing (1). Although it tends to depress blood pressure and cause cardiovagal block at high doses, it has acceptable pharmacological profile and superb neuromuscular blocking characteristics. Administration of the compound by infusion may ameliorate the side effects. However, long infusion may become uneconomical, and accumulation of metabolites may prolong the neuromuscular and cardiovagolytic effects. We evaluated TAAC3 for a 30-minute infusion in monkeys.
METHODS: Monkeys, macaca cyclopis (Swinhoe), 8-12 kg, of either sex, n = 5, were sedated with ketamine, induced and maintained with N2O and halothane (0.5%). Respiration was controlled via tracheal intubation for normocapnia. The ulnar nerve was stimulated (0.1 Hz, supramaximal, 0.2 ms) and the hypothenar electromyographic response was quantified. Blood pressure and pulse rate were monitored via arterial line. Normothermia was maintained. Boluses of TAAC3, i.v., was first administered to determine ED80. Twenty minutes later, an 80 % neuromuscular block was rapidly established and maintained for 30 minutes, after which spontaneous recovery was followed to completion.
RESULTS: On single bolus, the recovery index (25-75%) was 0.6 (0.04, SD) min. The ED80 was 0.096 (0.011) mg/kg. The infusion rate required to maintain an 80 % neuromuscular block was 0.049 (0.003) mg/kg/min, which did not change during the infusion. The recovery index after infusion was the same (not measurably different) as that of pre-infusion bolus. During infusion and after infusion, the blood pressure and heart rate remained the same as before infusion.
DISCUSSION: Cumulativeness of the neuromuscular blocking effect of TAAC3, if any, was less than what can be detected in this model. A faster stimulation rate may detect an increase in the recovery index of a few seconds; however, prolonged continuous 1Hz stimulation would bear no semblance to real clinical situation. No changes in blood pressure and heart rate were detected, either. If results in the primate model bear predictive value, infusion of TAAC3 for limited duration could be economically feasible and clinically advantageous.
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PERIPHERAL MUSCARINIC AND NICOTINIC RECEPTORS-MEDIATED EFFECTS OF TAAC3, A NEW ULTRASHORT ACTING MUSCLE RELAXANT IN THE RAT.

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INTRODUCTION: Several side effects of nondepolarizing muscle relaxants are attributable to their actions on certain muscarinic (m) and nicotinic (n) Acetylcholine (Ach) receptors (1,2). Therefore TAAC3, a typical representative of new, ultrashort acting tropinyl diester type muscle relaxants (3) was studied in rat experiments to explore its peripheral cholinergic receptor blocking spectrum of action.
METHODS: The following tests were used in anesthetized adult rats: 1) inhibition of the pressor response of the m M1 receptor stimulant, McN 343-A in spinal rats for the m M1 receptor mediated effect, 2) inhibition of the bradycardia -response to vagus nerve stimulation for the m M2 receptor mediated effect, 3)inhibition of the Ach induced hypotensive response for the m M3 receptor mediated effect, 4) inhibition of the nicotine -induced pressor responses in spinal rats for the n receptor mediated effect on sympathetic ganglia 5): inhibition of the twitch responses (by electromyography) of the anterior tibial muscle to sciatic nerve stimulation for the n receptors mediated effect on the neuromuscular junction.ED 50 (SEM) values (N=4-6) were calculated. Rocuronium (R) was used as a reference standard for comparison.
RESULTS: We found the following inhibitory effects [ED50 (SEM) mg/kg iv.] of TAAC3 and R against different m and n receptors-mediated responses: TAAC3: m M1: 1.1 (0.18), m M2: >1.3, m M3: >6, n (ganglionic): >3, n (neuromuscular): 0.19 (0.009); R: m M1: >3, m M2: 0.38 (0.015), m M3: >6, n(ganglionic): 0.97 (0.2), n (neuromuscular): 0.46(0.012).
DISCUSSION: TAAC3, relative to its NMB efficacy showed only negligible blocking effects on peripheral m and ganglionic n receptors-mediated functional responses. R. was less potent in blocking the m M1 receptors mediated effect than TAAC3. Hovewer, its was more potent in blocking the m M2 and n (ganglionic) receptors -mediated effects than TAAC3. Neither agents blocked the m M3 receptor mediated responses up to 6 mg/kg. Thus the peripheral cholinergic blocking side effects - profile of TAAC3 in the rat model seems to be favorable compared to that of R.
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EFFECTS OF PHENYTOIN ON ROCURONIUM-INDUCED NEUROMUSCULAR BLOCKADE ON RAT HEMI-DIAPHRAGM PREPARATION

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INTRODUCTION: Chronic anticonvulsant therapy with phenytoin antagonizes the action of nondepolarizing muscle relaxants. Rocuronium is a new non depolarizing muscle relaxant of rapid onset and intermediate duration of action. This study was designed to investigate the effects of phenytoin on rocuronium-induced neuromuscular blockade on the hemidiaphragm preperation.
MOTHODS: Male Sprague-Dawley rats (150-250g, n=70) were randomly allocated into control group (C, n=10), three phenytoin-non-pretreated group (PNP) and three phenytoin-pretreated group (PP). In phenytoin-pretreated group, phenytoin 50 mg/kg/day was administered intraperitoneally once a day for one day (PP_{1D}, n=10), one week (PP_{1W}, n=10) and four weeks (PP_{4W}, n=10). Animals were anesthetized with 40 mg/kg of thiopental sodium intraperitoneally and the hemidiaphragm with phrenic nerve was dissected and mounted in a bath containing 100 ml of oxygenated Krebs' solution at 32°C. The phrenic nerve was stimulated at the supramaximal intensity by stimulator through isolation unit and twitch responses were measured by precalibrated force displacement transducer and recorded. After stabilization of twitch response, rocuronium was added to the solution to obtain an initial concentration of 100 g. When a stable 3-5 twitch was obtained after the first dose, the concentration of rocuronium was increased in increments of 50 g to obtain more than 95% neuromuscular twitch inhibition at 0.1 Hz. In pheytoin-non-pretreated group,phenytoin 1 g/ml (PNP_1, n=10), 10 g/ml (PNP_{10}, n=10), 100 g/ml (PNP_{100}, n=10) were administered with initial dose of rocuronium simultaneously. Data were analyzed by probit and logistic models.
RESULTS: The dose-response curve of rocuronium was significantly shifted to the left in PNP_{100} group compared with control, PNP_1 and PNP_{10} group ($P < 0.05$). The dose-response curve of rocuronium was shifted to the right significantly in PP_{4W} group compared with control, PP_{1D} and PP_{1W} ($P < 0.05$).
CONCLUSION: The potency of rocuronium will be increased in the acute exposure to the high dose of pheyntoin. However chronic anticonvulsant therapy will be antagonized the action of rocuronium.
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Effective Dose of 5, 50, 90, 95% of rocuronium in non-treated and pretreated group (Mean ± S.D.)

	Control group	Phenytoin non-treated group			Phenytoin pretreated group		
		1 g/ml	10 g/ml	100 g/ml	1 day	1 week	4 weeks
ED5 (g)	250.6 ± 81.8	212.2 ± 75.8	245.7 ± 70.1	121.3 ± 26.3*	252.9 ± 67.5	183.8 ± 113.7	353.7 ± 82.0†
ED50 (g)	492.7 ± 81.8	432.7 ± 75.8	396.2 ± 70.1	179.0 ± 26.3*	476.7 ± 67.5	423.8 ± 113.7	640.0 ± 82.0†
ED90 (g)	681.3 ± 81.8	604.5 ± 75.8	513.5 ± 70.1	223.9 ± 26.3*	651.0 ± 67.5	610.8 ± 113.7	863.0 ± 82.0†
ED95 (g)	734.7 ± 81.8	653.2 ± 75.8	546.7 ± 70.1	236.7 ± 26.3*	700.4 ± 67.5	663.8 ± 113.7	926.3 ± 82.0†

S-239

CISATRACURIUM, BUT NOT MIVACURIUM, DECREASES SURVIVAL OF RAT SYMPATHETIC NEURONS IN VITRO

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INTRODUCTION: Cis-atracurium is a widely used neuromuscular blocking agent. Previous reports have indicated growth-inhibitory effects of isoforms cis-atracurium and atracurium on two human cell lines (Human umbilical vein endothelial cells and Human hepatoma G2 cells) in vitro (1). These effects were ascribed to oxidative stress elicited by acrylate esters formed during cis-atracurium breakdown via the Hofmann reaction (2). Mivacurium, not decomposed via the Hofmann reaction, did not impair growth. Rat sympathetic neuronal cells have been established as an in vitro model for neuronal survival (3). Therefore, the aim of the present study was to investigate the effects of cisatracurium upon neuronal cells. The hypothesis was that cisatracurium would not impair cellular survival.
METHODS: Sympathetic neuronal cells were excised from newborn rats and cultured in Roswell Park Memorial Institute (RPMI) medium plus Nerve growth factor (NGF, 1:000) on a poly-d-lysine-coated surface for three days. Following medium and NGF replacement, cells were incubated for 24 hours with cis-atracurium and mivacurium at concentrations of 0 (control), 1, 2, 5, and 10 mM dissolved in RPMI. All cell counts before and after incubation in each well were attained by the same author who was blinded to the incubation pattern.
RESULTS: A dose-dependent decrease in neuronal cell survival was caused by cisatracurium at concentrations of 5 and 10 mM cisatracurium, whereas mivacurium did not elicit a significant decrease in cell survival as compared to controls.
DISCUSSION: The dose-dependent decrease in cellular survival in the present study indicates the possibility of neuronal damage upon prolonged exposure to cisatracurium, as e.g. during long-term relaxation. This effect was observed at doses exceeding those achieved in clinical settings. Results from the present study should be followed up by morphological studies investigating the site of damage (e.g. growth cone).
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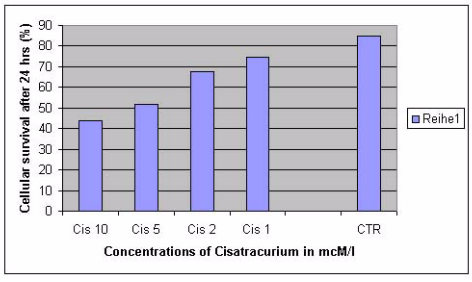

S-240

INTERACTIONS OF EDROPHONIUM WITH NEOSTIGMINE IN THE RAT TRACHEA

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INTRODUCTION: The muscarinic M3 receptor has both an orthosteric-binding site and an allosteric-binding site. Neostigmine at smaller doses would bind strongly to the orthosteric site of M3 muscarinic receptors, resulting in tracheal smooth muscle contraction through the activation of PI response (1). Neostigmine at larger doses would bind to the allosteric site, which inhibits the action of the orthosteric site of M3 muscarinic receptors, resulting in the attenuation of contraction through the inhibition of PI response (1). Although edrophonium itself does not affect the resting tension and PI responses of rat trachea (1-3), it at larger doses may bind to the allosteric site, resulting in the inhibition of the action of the orthosteric site of M3 muscarinic receptors. Thus, we examined the effects of edrophonium on neostigmine –induced contractile and PI responses of rat trachea.
METHODS: The studies were conducted under guidelines approved by the Animal Care Committee. Thirty Wistar rats (250-350 g) were used. The rats were anesthetized with pentobarbital, and the tracheas were rapidly isolated. The trachea was cut into 3-mm-wide ring segments or 1-mm-wide slices. Neostigmine (100 microM in final concentration) was added, and ring tension was examined by additions of edrophonium from 0 microM to 1000 microM in final concentrations. After the completion of the experiment, Krebs-Henseleit (K-H) solution containing both edrophonium and neostigmine (in the organ chamber) was changed three times with fresh K-H solution and the tension was recorded. Tracheal slices were incubated with [3H]myo-inositol and 100 microM neostigmine in the presence or absence of edrophonium. The [3H] inositol monophosphate (IP1), a degradation product of PI response, was measured with a liquid scintillation counter. Data were expressed as mean ± SE. Statistical significance ($P < 0.05$) was determined using ANOVA.
RESULTS: Neostigmine-induced tension was 2.02 ± 0.21 g, which was attenuated by edrophonium at doses of 100 microM or greater, and was 0.02 ± 0.09 g at a dose of 300 microM. This attenuation was reversed to 87% of control levels by washing with fresh K-H solution. Neostigmine-induced IP1 accumulation of rat tracheal slices was attenuated by edrophonium at a dose of 100 microM, and this attenuation was reversed by washing with fresh K-H solution. Decreases in IP1 accumulation at large doses were consistent with relaxation of rat tracheal rings.
CONCLUSION: Edrophonium at large doses would bind the allosteric site of M3 muscarinic receptors, resulting in the inhibition of the action of the orthosteric site of M3 muscarinic receptors.
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S-241

CHOLINESTERASE DEFICENCY: IDENTIFICATION OF A NOVEL MUTATION

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INTRODUCTION: A reduction of atypical cholinesterase (Butyrylcholinesterase = BCHE) activity leads to a prolonged duration of action of drugs metabolized by this enzyme, such as succinylcholine and mivacurium. As day-case surgery is becoming more frequent, short acting muscle relaxants - such as mivacurium - are increasingly important. A delay in inactivation of these drugs can lead to prolonged mechanical ventilation, which is not only unpleasant and potentially harmful for the patient but also increases health care costs. BCHE activity is biochemically determined and individuals are diagnosed as homo- or heterozygous on the basis of total activity, dibucain- and fluoride-inhibition. Recent molecular genetic investigations have proven this biochemical classification to be imprecise and frequently incorrect (1). We have therefore genotyped two patients with clinically prolonged duration of action of succinylcholine by investigating the DNA sequence of BCHE. The gene for BCHE is located on chromosome 3q26. The coding sequence is 1722 base pairs long and encodes for a polypeptide of 574 amino acids.
METHODS: Two patients with a history of prolonged neuromuscular block following succinylcholine and a biochemically determined BCHE activity of <50% were investigated. Blood samples were taken for DNA isolation. Primers for polymerase chain reaction (PCR) were designed to flank all 4 exons. A randomly selected DNA sample was used as control. PCR products were commercially sequenced and the resulting sequences compared with the sequence in the human genome database (http://www.ncbi.nlm.nih.gov/). If polymorphisms were identified, then they were confirmed by sequencing in the reverse direction.
RESULTS: We found a mutation in each of the two patients. The first mutations was a C -> T at position 551, resulting in a valine for alanine substitution, the second mutation was a G -> T at position 1294, resulting in a premature stop codon. Both mutations were heterozygous and and not present in a control sample.
DISCUSSION: Two mutations in the BCHE gene were detected in two patients with clinical and biochemical reduced BCHE activity. Mutation C551T has been described (2), mutation G1294T has not yet been published. In the latter a premature stop codon leads to a shorter protein and may explain the reduced BCHE activity. Our findings confirm the heterogenetic nature of reduced BCHE activity. If BCHE deficiency can be linked to certain mutations, then genetic investigations may in future be helpful in identifying those individuals and thus increase perioperative patient safety.
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S-242

NATRIURESIS GOVERNS THE DURATION OF THE EXTRACELLULAR VOLUME EXPANSION AFTER INFUSION OF HYPERTONIC SALINE IN SHEEP

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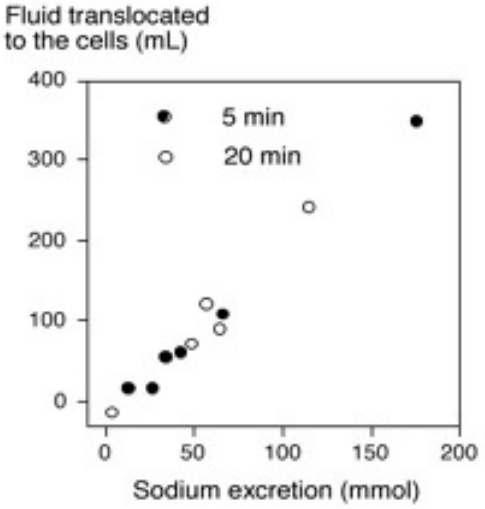
BACKGROUND: The mechanisms governing the duration of the extracellular fluid volume (ECF) expansion due to intravenous infusion of hypertonic saline solution are poorly understood. We hypothesized that the duration is closely related to the sodium excretion.
METHODS: Six conscious splenectomized ewes with a mean body weight of 30 kg were given an intravenous infusion of 4 mL kg-1 of 7.5% saline solution on two occasions, one over a period of 5 min and another over 20 min. Mass balance and volume kinetic calculations of the distribution and elimination of fluid were performed after repeated sampling of the plasma sodium concentration and the urinary excretion of water and sodium during 3 hours. The translocation of water from the cells to the ECF space was calculated based on the added osmolality, and the backward shift during the follow-up from the relationship between serum sodium and urinary sodium concentrations.
RESULTS: The amount of fluid infused was 119 ± 8 mL, and the fluid volume translocated from the intracellular space due to osmosis amounted to 564 ± 9 mL. Urinary excretion amounted to 228 ± 46 mL (mean ± SEM). The urinary sodium concentration increased gradually and exceeded the plasma sodium after 30 min. From this time onward, the sodium excretion produced a net uptake of fluid into the intracellular space, which finally amounted to 95 ± 30 mL. There were virtually no differences in these results between the groups. For the entire experiment, there were strong linear correlations between urinary excretion of fluid and sodium and the calculated uptake of fluid to the cells (see Figure).
The hypertonic saline increased the serum sodium level by 8%, which corresponded to a 10% dilution of the ECF space. Subsequent reductions of the ECF expansion could be estimated only if the sodium excretion was considered. This volume expansion decayed at an average rate of 20% per hour which, however, varied greatly in the animals, depending on their capacity to excrete sodium. Computer simulations indicated that a tripled natriuresis (up to approx. 750 mmol/L) would almost double the rate of elimination.
CONCLUSION: The sodium excretion was inversely proportional to the duration of the ECF volume expansion by 7.5% saline.



S-243

ROLE OF NALOXONE AND AUTOLOGOUS BLOOD TRANSFUSION ON THE RECOVERY FROM HEMORRHAGIC SHOCK IN DOGS

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INTRODUCTION: Opioid peptides, such as endorphins and enkephalins have been found in brain, peripheral tissues, blood, and were associated with the mediation of pain perception. They produce hypotension and the plasma levels of B- endorphin rise during stress (1). In the present work the possible inclusion of endogenous peptides in hemorrhagic shock and the possible reversal of the state of shock by injection of the morphine antagonist naloxone were investigated.
METHODS: Hemorrhagic shock was induced and maintained for 30 min. in dogs. In the control group (GI, 8 dogs) animals received only autologous blood transfusion. In another group of the experiment, (GII, 8 dogs), naloxone (1 mg/kg) was given immediately before autologous blood transfusion. The various cardiovascular parameters were recorded pre and post infusion of autologous blood transfusion
RESULTS: In GI, hemorrhage resulted in a highly significant drop in systolic, diastolic and pulse pressure, while the heart rate significantly increased. These average values were maintained for 30 min., during which two dogs died. With autologous blood transfusion the living animals recovered after 5 min. and gradually the heart rate returned to normal after 30 minutes, while the systolic, diastolic and pulse pressure returned to normal after 45 min. In GII, The systolic, diastolic and pulse pressure as well as the heart rate returned to the normal levels within 5 min.
CONCLUSION: These findings do not only indicate the possible role of morphine in post-operative shock but it may have the clinical implication of the role of naloxone in the management of hemorrhagic shock

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S-244

THE CHAOTIC ANALYSIS OF EEG CAN REFLECT DEPTH OF ANESTHESIA.

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Measuring depth of anesthesia has been an enigma ever since general anesthesia was clinically introduced 150 years ago. The most widely evaluated tool for assessing depth of anesthesia has been the electroencephalograph (EEG). The bispectral index (BIS), a value derived from the EEG, has been recently developed to measure anesthetic effects and has been rapidly accepted for clinical use in anesthesia. However, BIS monitoring can effectively reflect the hypnotic component of anesthesia but fail to respond to the analgesic component. This disadvantage of the BIS may arise from the limitations of linear science analysis such as frequency analysis, upon which BIS analysis is primarily based The EEG is a bio-signal from the complex systems and can be subject to rules of Chaos. Chaos theory is a typical mathematical theory for non-linear science and yields deterministic rules for signals. Using the chaotic theory, we analyzed the EEGs of the patients during anesthesia and compared them with the BIS.
METHODS: The EEGs were collected from the patients receiving sevoflurane-fentanil-N2O anesthesia. The EEG signal was acquired using Aspect A-1000 EEG monitor and Neuropack 8 monitor through the leads of Fp1 with CZ as the reference. Digitized raw EEG (sampling rate: 16 to 50 kHz, band pass: 0.1-850 Hz) was recorded into the personal computer and used for the chaotic analysis with off-line. As the chaotic parameters, the fractal dimension, Lyapunov index and trajectory parallel measurement (TPM) were analyzed for the EEGs during anesthesia The optimum embedding parameters for the EEG chaos analysis were determined by the local fuzzy reconstruction methods. All chaotic analyses were performed by the chaos analysis software, "meiChaos" (Meidensha Corp.).
RESULTS: For the EEG chaos analysis, the optimum embedding parameters were 3 for the detention, 2 for the delay and 9 for the neighborhood before, during and after anesthesia. The values of the fractal dimensions showed the non-integers between 2 and 8. The maximum Lyapunov index was positive and other Lyapunovs' were near 0. These results suggest that the EEG shows the chaotic characteristics both with and without anesthesia. The TPM values depicted 0.4 to 0.5 in awake and 0.2 to 0.3 during anesthesia, they shifted during anesthesia with the BIS level.
CONCLUSIONS: The EEGs can be the deterministic chaos and especially the TPM values may reflect the anesthetic depth.

S-245

REGIONAL CBF IS DECREASED IN DIFFERENT REGIONS OF THE BRAIN BY PROPOFOL AND THIOPENTAL AT EQUAL DRUG EFFECT

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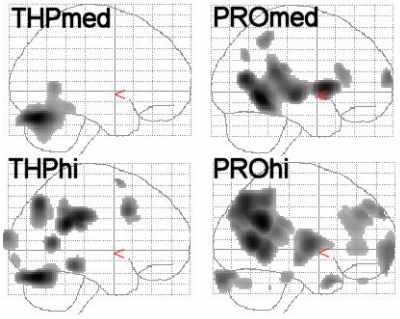
INTRODUCTION: Thiopental and propofol produce similar sedative effects, but propofol has a greater amnesic effect (1). Changes in regional cerebral blood flow (rCBF) induced by a drug may indicate the neuroanatomical location of drug effect, thus helping understand the mechanism of drug action (2). This study was undertaken to identify brain regions affected by propofol (PRO) different from those of the sedative control drug thiopental (THP) given at equivalent medium and high sedative concentrations. Significant decreases in rCBF were identified using SPM99 analysis of CBF images obtained using positron emission tomography with O-15 water (O-15 PET).
METHODS: Following informed consent, 8 right- handed male volunteer subjects (age 32.3 ± 11.5 yrs, weight 72.4 ± 7.7 kg) were randomized to receive THP (n=4) or PRO (n=4) using Stanpump software (S. Shafer; http://anesthesia.stanford.edu/pkpd) to target medium (THP 4 and PRO 1.2 ug/ml) and high (THP 7-9 and PRO 2.5-3 ug/ml) sedative concentrations. The high concentration was associated with unresponsiveness to voice. Bispectral Index was monitored using a standard clinical electrode montage (Ziprep Electrodes, Aspect 1050 monitor, Aspect Medical Systems, Natick, MA). Four CBF images were obtained during resting, auditory and tactile stimuli in baseline, medium and high drug conditions (total of 12 scans; 10 mCi radiotracer/scan). Between scans responsive subjects performed a reaction time task pushing a button upon hearing a tone. Decreases in rCBF were considered significant at a voxel-level p<0.001 (uncorrected).
RESULTS: BIS values decreased similarly in both groups (PROmed : 91.1 ± 6.1, PROhi 68.7 ± 5.6, THPmed : 89.7 ± 4.4, THPhi 75.3 ± 5.3; n.s. between groups). RT increased similarly in both groups (THPbase 258 ± 70 THPmed 398 ± 101, PRObase 213 ± 54 PROmed 325 ± 95 msec, no RT in high dose; n.s. between groups). The pattern of rCBF decreases was different for propofol and thiopental (see Figure).



SPM interaction analysis showed that propofol produced more effects in the frontal, orbito-frontal and temporal regions, located in the superior and medial frontal gyri (Brodmann's Area (BA) 8,9,10), the rectal gyrus (BA 11) and middle temporal gyrus (BA 37,39).
CONCLUSIONS: At equivalent levels of sedation propofol and thiopental affect different regions of the brain. Regions of the brain affected by propofol compared with thiopental may help identify the loci of the non-sedative effects of propofol, such as amnesia.
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S-246

CALORIMETRIC MEASUREMENTS OF BINDING OF VOLATILE ANESTHETICS TO SERUM ALBUMIN

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INTRODUCTION: Close correlation exists between oil/gas partition coefficients and potencies of general anesthetics. While this relation suggests that sites of action are hydrophobic, it does not imply that the binding is driven by hydrophobic interactions. On contrary, this simple correlation implies that, partitioning is enthalpy driven that require close contacts with the binding site(s). This study examines the binding of closely related haloethers (desflurane, isoflurane, enflurane, sevoflurane), a haloalkane (halothane), and an intravenous anesthetic (propofol) to bovine serum albumin.
METHODS: Heat produced or absorbed on binding of drugs to albumin was measured by isothermal titration calorimeter. Haloether data was fit to high and low affinity binding site (N=3) model, haloalkane data to a sequential model and propofol data to a single high affinity site model. Using standard nonlinear least squares regression models, number of drug molecules bound per macromolecule (N), equilibrium association constant (Ka), as well as the enthalpy and entropy of binding were determined.
RESULTS: The affinities (Ka) of the volatile agents were in the order: desflurane > isoflurane ≥ enflurane> halothane > sevoflurane. Competition studies indicated that anesthetics bind to the same high affinity site. We believe this represents the propofol/halothane binding lipophilic site (IIIA) identified on albumin (1). Interestingly, these binding constants were positively correlated (R2 = 0.86) with anesthetic potency (EC_{50}). All drugs produced significant heat generation with similar binding enthalpies of - 4600 to - 7600 cal/mol. The effects of temperature on enthalpy were evaluated in the range of 15º to 25ºC. In all cases, except isoflurane, increasing temperature increased the enthalpic contribution to binding. The results demonstrated a large excess negative dCp for all volatile agents (except for isoflurane), ranging from -1180 to -72 cal/mol/degree.

DISCUSSION: The results demonstrate that binding of volatile agents is driven by enthalpic changes that must involve close contact with binding site(s) in proteins. Selectivity for drugs is primarily entropic. Beyond the obvious chemical and stereochemical differences, the only general physical property that correlates with binding free energy is the lipole movement, R2 = 0.52 and 0.90 for high and low affinity binding respectively. This correlation suggests that the distributed lipophilicity of the drugs best explain their binding. The differences in excess heat capacity changes suggest a molecular selectivity with respect to protein conformation. Binding of anesthetics seems to produce specific changes in conformation, probably involving constraints to main chain movements, resulting in less overall contact with water. These changes could well involve a further shielding of hydrophobic side chains form solvent water; consistent with earlier reports of increased protein stability and excess heat capacity changes associated with binding of halothane to albumin (2).
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S-247

TEMPERATURE DEPENDENCE OF SOLUBILITY OF HALOTHANE, ISOFLURANE AND SEVOFLURANE

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INTRODUCTION: *In vitro* experiments with volatile anesthetics are often performed at temperatures other than encountered *in vivo*. There is very little data on the temperature dependence of the solubility of modern volatile anesthetics.We have therefore examined the effects of temperature on the solubility of halothane (H), isoflurane (I) and sevoflurane (S) in a physiologic salt solution.
METHODS: A modified Krebs solution (200 ml of Na^+ 137.5 mM, K^+ 5, Mg^{2+} 1, Ca^{2+} 2, Cl^- 124.5, SO_4^{2-} 1, acetate 20, MOPS 5, glucose 10, pH 7.4) was vigorously (>1000 ml/min) bubbled with 100% O_2 and anesthetic vapor (0.8% and 1.6% for H and I; 1% and 2% for sevoflurane) in a temperature-controlled water-jacketed glass chamber residing in a closed Lucite box at ambient pressure. Care was taken to avoid pressure and temperature changes in gas and liquid phases. Anesthetic gas concentration was measured continuously at different positions in the gas phase in the glass chamber (Ohmeda 5330 Agent Monitor). Anesthetic concentrations in the liquid phase were measured by gas chromatography (Hewlett Packard 5880A) after 30 and 60 min equilibration at each temperature. The Ostwald solubility coefficients = $C_{liq} * R * T_k / [(p_{amb}-p_{aqua}) * C_{gas} * 10]$ were calculated for data at 15ºC, 20ºC, 25ºC, 30ºC and 37ºC (n > 34 measurements for each anesthetic and temperature). From all data points of each anesthetic, the relationship between and temperature was fitted to the equation $= {}_{37} * [1 + (k/100)]^{T}$ to yield the temperature coefficient k and ${}_{37}$ (at 37ºC).
RESULTS: Liquid and gas temperatures were the same for each data set. Krebs/O_2 solubility coefficients at 37ºC were 0.33 (H), 0.48 (I), 0.19 (S) with temperature coefficients of -0.0491 (H), -0.0426 (I), -0.038 (S). Decreasing temperature increased more for halothane and isoflurane than for sevoflurane. There was no difference between measurements taken after 30 or 60 min of equilibration.

DISCUSSION: Sevoflurane is less sensitive to temperature than either halothane or isoflurane. Krebs/O_2 was isoflurane > halothane, whereas tissue solubility was halothane > isoflurane . This is the first report of Ostwald solubility coefficients (Krebs/O_2) of H, I and S collected in identical conditions with rigid control of pressure and temperature. The values are lower than those reported separately for individual anesthetics in various aqueous media. The temperature dependence is similar to that reported for tissue/gas solubilities . Support: USPHS GM36365, Mayo Foundation, IMF Muenster, Deutsche Forschungsgemeinschaft.
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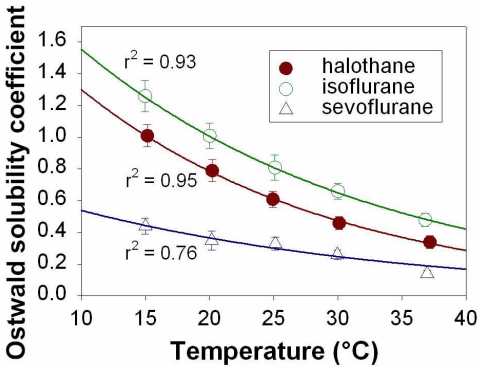

S-248

THE EFFECTS OF DIFFERENT ANESTHETIC AGENTS ON METASTATIC DEVELOPMENT AND NATURAL-KILLER CELL ACTIVITY: A COMPARATIVE STUDY IN RATS

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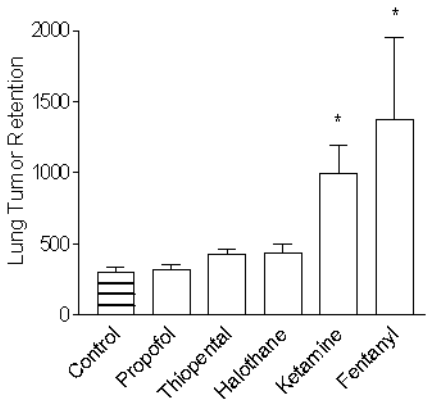
INTRODUCTION: Immunosuppression following surgery is partly ascribed to the effects of anesthesia, and may compromise patients' resistance to infection and metastasis. These effects may be mediated in part by suppression of natural killer (NK) cells – a subset of lymphocytes with special importance in host resistance against malignant and virally infected cells. The current study compares the effects of various anesthetic agents on the susceptibility to metastasis and on NK cell function.
METHODS: Fischer-344 rats (N=81) remained undisturbed in their home cages (Control), or were kept anesthetized for one hour using either inhaled halothane (via vaporizer) or one of the following intravenous anesthetics: Thiopental, Ketamine, Propofol, or Fentanyl. All anesthetics were given by titration to animal movement and respiration rate. Three hours later, blood was drawn for the assessment of NK-cell cytotoxic activity using ^{51}Cr release assay and the assesment of NK cell number using fluorescence-activated cell sorter (FACS) analysis. Concomitantly, the rats were inoculated intravenously with radiolabeled MADB106 mammary adenocarcinoma cells that metastasize only to the lungs. Twenty hours later, lungs were removed and their radioactivity measured to indicate lung tumor retention (LTR). Groups were compared using ANOVA, with Bonferroni post-hoc test used for pairwise comparisons. As a measure of cytotoxic activity, the number of lytic units (defined as 100 divided by the effector-to-target cell ratio required to lyse 20% of the target cells) was calculated from the cytotoxic assay curves using regression exponential fit method.
RESULTS: All anesthetic agents except propofol caused an increase in LTR compared to the control group (Figure), reaching statistical significance for fentanyl and ketamine (4.6 and 3.4 times control).



Fentanyl, halothane, ketamine, and thiopental decreased NK cytotoxic activity to 15%, 25%, 25%, and 33% of control levels, respectively. Propofol anesthesia was associated with a non-significant decrease in activity.
The number of circulating NK cells in the blood was significantly decreased by halothane (by 34% from the baseline), ketamine (36%) and thiopental (58%), but not by propofol. The effect of fentanyl was not assessed.
DISCUSSION: In the current study, most anesthetic agents, both volatile (halothane) and i.v. agents (thiopental, ketamine, fentanyl) increased the susceptibility to metastatic development and concomitantly suppressed NK-cell cytotoxic activity in the blood, partly by reducing the number of circulating NK cells. Propofol did not affect these immunological indices, favoring its use in cancer patients undergoing surgical procedures. We suggest that immunological aspects should be considered when choosing an anesthetic.

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SITE OF ACTION OF TIME-DEPENDENT INHIBITION BY LOCAL ANESTHETICS

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INTRODUCTION: Local anesthetics (LA) were shown to inhibit the signaling of G protein-coupled receptors (GPCRs) in *Xenopus* oocytes and human neutrophils (hPMNs) time-dependently [1,2]. This study aimed to characterize the possible site of action of this time-dependency in more detail.
METHODS: To define the site of action more specific, the effects of extracellularly applied (5mM) and intracellularly injected (42µM, $^1/_{10}$ of IC_{50}) QX 314, a membrane-impermeable lidocaine-analog, on control- and Gq-depleted (DNA antisense-knock down) *Xenopus* oocytes were studied. Therefore endogenous lysophosphatidic acid (LPA) receptors were stimulated (0.6 µM (EC_{50})) and Ca^{2+}-activated Cl^--currents ($I_{Cl(Ca)}$) were measured at different time points (10min - 48h) after LA-application, using 2-electrode-voltage-clamp-technique. Data are normalized to corresponding control responses and shown as mean±sd (n>22).
RESULTS: LPA-signaling in *Xenopus* oocytes was inhibited by intracellularly injected QX314 in a time-dependent manner (reduction to 40±7 % of control response after 24h), whereas no effects were observed when the LA was applied extracellularly or in the absence of the Gq protein. In contrast lidocaine attenuated LPA-signaling in Gq depletd oocytes significantly to 75 % of control, when applied extracellularly, but not time-dependently.
DISCUSSION: Our study shows that one possible site of action of the the time-dependent effect of GPCR-signaling inhibition by LA is located intracellular and critically dependent on Gq protein function. The non-time-dependent inhibition of LPA-signaling by lidocaine is explainable by an additional extracellular located binding site for LA. Thus, clinically relevant effects, based on GPCR signaling (e.g priming of hPMNs), might be attenuated more potent by continuous application of LA.

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S-250

MECHANISMS OF TIME-DEPENDENT INHIBITION BY LOCAL ANESTHETICS

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INTRODUCTION: Local anesthetics (LA) were shown to inhibit the signaling of G protein-coupled receptors (GPCRs) in a time-dependent manner [1]. The underlying mechanisms are not cleared in detail yet. We therefore studied to what extent this time-dependent effect of LA is affected by inhibition of various proteins within the signaling pathway and agonist independent stimulation of the G protein.
METHODS: *Xenopus* oocytes were incubated in either proteinkinase c (PKC)-antagonists (CT or BIM, 10 µM) or a phospatase inhibitor (okadaic acid, 1 µM), followed by application of bupivacaine (450 µM ($^1/_{10}$ of IC_{50})). Ca^{2+}-activated Cl^--currents ($I_{Cl(Ca)}$), induced by lysophosphatidic acid (LPA, 0.6 µM) or agonist-independent, using guanosine-5'-O-3-thiotriphosphate (GTPS, 1 mM) or aluminumfluoride (AlF, 100 µM), were measured at different time points (10min - 48h) after LA application, using 2-electrode-voltage-clamp-technique. Data are normalized to corresponding control responses and shown as mean±sd (n>22).
RESULTS: Inhibition of PKC enhanced LPA-signaling to 40 % and 20 % of control for CT and BIM, respectively, wheras the use of okadaic acid attenuated LPA induced responses to 70 % of control. In contrast neither inhibition of PKC nor phosphatase-activity affected the time dependent effect of bupivacaine on LPA signaling at all (13±3 % , 20±5 %, 11±4 % and 9±4 % of control for bupivacaine and in the presence of CT, BIM and okadaic acid, respectively, after 8 h). Similar results were obtained for GTPS and AlF induced $I_{Cl(Ca)}$, namely a time-dependent inhibition by bupivacaine to 29±10 % and 17±8 % of control after 4h of incubation.
DISCUSSION: LPA-signaling is based on a sensitive balance between phosphorylation and dephosphorylation. Modulation of one side or the other enhances or attenuates the signaling cascade but does not have any influence on time-dependent inhibition by LA. As agonist-independent stimulation of the G protein is inhibited by LA time-dependently as well, the underlying mechanism and the site of action seem to be located downstream of the G protein activation and independent from GDP/GTP-exchange.
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S-251

DIFFERENTIAL INHIBITION OF CYCLIC NUCLEOTIDE-GATED CHANNELS BY LOCAL ANESTHETICS

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INTRODUCTION: This study was conducted to investigate molecular mechanisms by which local anesthetics produce anesthesia. Experimentally, local anesthetics inhibit a variety of ion channels including voltage-gated Na channels, voltage-gated Ca channels, and K channels. Recently, tetracaine was reported to inhibit cyclic nucleotide-gated ion (CNG) channels[1]. These non-selective cation channels located in plasma membranes are activated by cAMP and cGMP. They are found in retinal rod cells, olfactory sensory neurons, brain, spinal cord, heart and other tissues[2]. In this study we tested the hypothesis that a variety of other local anesthetics also inhibit CNG channels.
METHODS: Experimental procedures were in accordance with the APS/NIH guidelines and were approved by our institutional Animal Care and Use Committee. Mature *Xenopus laevis* frogs were anesthetized, sacrificed, and retinas removed. The excised, inside-out configuration of the patch clamp technique[3] was used to record cGMP activated currents from individual rod cells, a rich source of CNG channels. Anesthetics were added to the cytoplasmic side of the membrane patches.
RESULTS: All twelve local anesthetics inhibited cGMP activated ion currents as shown in the figure. However, dyclonine (DY), tetracaine (TE), benoxinate (BX), dibucaine (DI), and pramoxine (PX) were potent blockers of the CNG channels. In contrast, lidocaine (LI), etidocaine (ET), mepivacaine (MP), procaine (PC), benzocaine (BZ), and bupivacaine (BU) were weak blockers. Mexiletine (MX) blocked with an intermediate potency.
DISCUSSION: All of the local anesthetics that we studied inhibit these channels; however, local anesthetics commonly used for topical anesthesia, i.e., dyclonine, tetracaine, benoxinate, dibucaine, and pramoxine, exhibited significantly greater inhibition of these channels. Inhibition of the CNG channels did not correlate with local anesthetic lipid solubilities. Dyclonine, a ketone local anesthetic, was the most potent inhibitor. Dyclonine is used exclusively for topical anesthesia. When compared with lidocaine for airway anesthesia, dyclonine produces a longer lasting and more intense topical anesthesia[4] . Lidocaine, an amide local anesthetic, was the least potent inhibitor of these channels. Although lidocaine is used topically for airway anesthesia and in a eutectic mixture with prilocaine for skin anesthesia, investigators have shown that other local anesthetics, i.e. dyclonine[4] and tetracaine[5] , which belongs to the ester family, provide more intense topical anesthesia. One explanation for this difference may be the greater inhibition of CNG channels.
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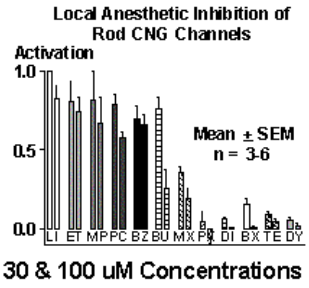

S-252

LOCAL ANESTHETICS INHIBIT THE 5-HT3 RECEPTOR VIA DIFFERENT MECHANISMS AND SITES OF ACTION

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INTRODUCTION: The 5-HT_3 receptors are diffusely distributed in the central and peripheral nervous system and are thought to be involved in physiological and pathological processes mediating peripheral and central nociception. To explore other analgesic actions of local anesthetics (LAs) than their blocking actions for voltage Na^+ channel, we investigated mechanisms and sites of action of LAs on recombinant wild-type and four mutant 5-HT_3 receptors.
METHODS: The cRNAs from human wild-type and four mutant 5-HT_{3A} subunit clones were synthesized *in vitro*. The homomeric wild-type and mutant 5-HT_{3A} receptors were expressed in *Xenopus* oocytes. Site-directed mutagenesis in N-terminal extracellular region, which involves the agonist binding domain, was carried out to make four mutant receptors. Tryptophan (W) at position 62 was replaced to tyrosine (Y), W at position 155 to Y, and glutamate (E) at position 101 to aspartate (D) or to asparagine (N), respectively. The electrophysiological recording was made by using the two-electrode voltage clamp technique and the peak currents induced by 5-HT (EC_{30}) in these receptors were measured and compared in the presence and absence of LAs. All data were expressed as mean±s.e..
RESULTS: All LAs inhibited 5-HT-induced currents in dose-dependent manners in the wild-type receptor. The half maximum concentrations (IC_{50}s) were 2.71±0.42 M for procaine, 22.6±2.67 M for tetracaine, 58.5±8.3 M for bupivacaine and 506±35.1 M for lidocaine. The rank order of potency for inhibitions of s by LAs was different from that for voltage-dependent Na^+ channel. Inhibitions of procaine and tetracaine were competitive whereas those of bupivacaine and lidocaine were both non-competitive and competitive. Four mutants (W62Y, E101D, E101N and W155Y) could all form the functional receptors. All mutant receptors exhibited drastic increase (> 10 fold) in the IC50s of procaine. The IC_{50}s of tetracaine, bupivacaine and lidocaine in mutant receptors increased 2-3 fold except that of tetracaine in W62Y receptor (6-fold).
CONCLUSION AND DISCUSSION: The ester type LAs, procaine and tetracaine may act at the different site and with different mechanism from the amide-type LAs. Procaine inhibits 5-HT_{3A} receptor most potently by acting the similar point of interaction to 5-HT with the binding domain.

S-253

VENTRICULAR FIBRILLATION IS LIKELY TO APPEAR AT THE MOMENT ON THE DECLINE OF THE BUPIVACAINE CONCENTRATION IN RABBITS - COMPARATIVE PHARMACODYNAMIC STUDY OF THE CARDIOTOXITY BETWEEN THE RACEMIC AND LEVO BUPIVACAINES

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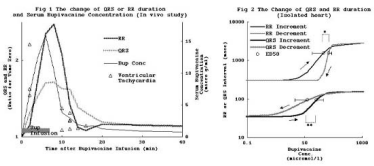
We studied the pharmacodynamics on the prolongation of QRS or RR intervals by bupivacaine in vivo model and isolated perfused rabbit heart to elucidate the phase of fatal cardiac arrhythmia. In vivo study; Eight male New-Zealand rabbits were anesthetized with pentobarbital and mechanically ventilated. Bupivacaine (1mg/kg/min, totally 7mg/kg) were infused. Electrocardiogram was recorded. Serum bupivacaine concentration of the samples (0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 30 and 40 minutes) was measured with HPLC. Result: The prolongation of QRS is delayed from RR. The frequency of ventricular tachycardia after the peak concentration was 100% and that before the peak concentration was 37.5%. (Fig 1)



Langendorff preparation; Fifteen male New-Zealand rabbits, were allocated randomly into three groups. The rabbits were anesthetized with pentobarbital. The animals were mechanically ventilated and after iv heparin injection, the heart was removed and was retrogradely perfused at a constant flow of 40 mL/min-1 with a Krebs-Henseleit buffer. Electrocardiogram was recorded using surface electrodes. After 10 minutes stabilization period drug infusion was begun by 6-min-step increments, and after maximum dose by 6-min-step decrements. Each group (n=5 each) received lidocaine (from 37 µmol/l to 123 µmol/l), bupivaicaine (from 3 µmol/l to 100 µmol/l) and levo-bupivacaine (from 62 µmol/l to 500 µmol/l). QRS and RR intervals were measured for each concentration at the end of a 6 min-step. Results are fitted to Emax model with computer software (SAAM II®) as follows. The change of EC50 between increment and decrement of the dose was evaluated with repeated-measures analysis of variance with the aid of the Scheffe post hoc method.
RESULTS: With bupivacaine, ventricular fibrillation (Vf) (n=4, 80%) was observed in the decrement slope. All the value of EC50 for QRS interval of decrement slope is significantly smaller than increment slope (Table 1) (*;$p < 0.05$, **;$p < 0.01$). EC50 for RR of decrement slope is significantly smaller than that of increment slope with lidocaine and levo-bupivacaine. However, EC50 for RR of decrement slope is significant larger than that of increment slope with bupivacaine (Table 2, Fig 2).
DISCUSSION: Bupivacaine in the decrement course was thought to minimize the differences between RR and QRS intervals and then is likely to cause fatal cardiac arrhythmia like as ventricular fibrillation. Compared with levo-bupivacaine and lidocaine, bupivacaine is more likely to lead to fatal arrhythmia with clinical possible dose in the concentration decrement slope. In conclusion, these results would make it possible to suppose the concentration of serum bupivacaine when the fatal arrhythmia occurs. Not only prolongation of QT interval but cardiac excitability may be concerned with the fatal arrhythmia by bupivacaine.

Table 1

QRS	Bupivacaine	Levo-Bupi	Lidocaine
Increment	25.4 ± 18.7	410 ± 298	232 ± 112
Decrement	12.2 ± 7.70**	174 ± 64.2*	121 ± 90.7**

Table 2

RR	Bupivacaine	Levo-Bupi	Lidocaine
Increment	52.0 ± 26.8	420 ± 236	241 ± 123
Decrement	66.4 ± 17.1*	189 ± 86.1*	134 ± 90.7**

S-254

MECHANISMS AND SITE OF ACTION FOR TIME-DEPENDENT INHIBITION BY LOCAL ANESTHETICS

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INTRODUCTION: Several beneficial effects of local anesthetics (LA) were shown to be due to inhibition of G protein-coupled receptor (GPCRs) signaling. Differences in exposure time might explain at least in part the discrepancies in concentrations of LA required to achieve these protective effects *in vivo* and *in vitro* (approximately 100 fold higher) [1]. We therefore studied time-dependent effects of LA on GPCR-signaling and characterized possible mechanisms and sites of action, employing *Xenopus* oocytes and human neutrophils (hPMNs).
METHODS: To assess LA effects on GPCR-signaling in oocytes and primed and and activated hPMNs, agonist-induced Ca^{2+}-activated Cl^--currents ($I_{Cl(Ca)}$) were measured at different time points (10min - 48h), using 2-electrode-voltage-clamp-technique, and superoxide anion production was determined by cytochrome c-reduction assay, respectively. Antisense knock down of Gq protein [2] and inhibition of various proteins within the signaling pathway served for defining mechanisms and sites of action more specific. Data are shown as mean±sd. Statistics: one-way ANOVA (Dunnett correction); $p<0.05$ was considered statistically significant.
RESULTS: LA attenuated GPCR-signaling in both models in a time-dependent and reversible manner (lidocaine reduced LPA-signaling to 19±3% after 48h of control response in oocytes and 25±2 % after 6h in hPMNs, respectively). Intracellularly injected QX 314, a lidocaine-analog, exerted similar time-dependent effects, whereas QX 314 applied extracellularly or injected intracellularly in Gq-depleted oocytes as well as inhibition of phosphatases or proteinkinases and agonist-independent G-protein stimulation, using guanosine-5'-O-3-thiotriphosphate (GTPS) or aluminumflouride (AlF) did not affect time-dependent inhibition by LA at all.
DISCUSSION: In summary our study could show that inhibition of GPCR-signaling by LA is time-dependent and reversible. Critically requiring Gq protein-function, this effect is located downstream of GDP-GTP exchange and not dependent on increased GTPase activity, phosphatases or proteinkinases. Thus, clinically relevant effects, based on GPCR signaling, might be attenuated more potent by continuous application of LA.
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PHARMACOLOGY - CLINICAL

S-255

CHARACTERIZATION AND MANAGEMENT DEXMEDETOMIDINE-RELATED HYPOTENSION FOLLOWING CABG

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INTRODUCTION: Dexmedetomidine (DEX), a new alpha-2 agonist sedative, may reduce blood pressure through centrally-mediated sympatholysis. This analysis, part of a large, prospective study of post-CABG sedation, was undertaken to quantify the nature of DEX-induced hypotension when compared to propofol (PROP).
METHODS: Following IRB approval at each center and informed consent, subjects were prospectively randomized to either DEX or PROP sedation post-CABG. Investigators determined whether a given blood pressure represented hypotension for each subject, after which any combination of the following were available for therapy: fluid bolus, patient repositioning, reduction of sedative infusion, reduction of concurrent vasodilator infusion, and initiation of vasopressors.
RESULTS: 308 subjects (DEX 153, PROP 155) were enrolled at 25 sites. Hypotensive events were more common in the DEX group (DEX 43 events in 36 subjects vs. PROP 28 events in 28 subjects); 26% of all events in the DEX group occurred within one hour of the 1 mcg/kg loading dose. A similar percentage of events in either group was successfully treated with a combination of fluids and repositioning: Dex 27% (11/43) vs. PROP 29% (8/28). Reduction of sedative and/or vasodilator infusions were successful in an additional 22% (10/43)of the Dex group vs. 15% (4/28) of the PROP group. Vasopressors alone or combined with other therapies were necessary for 51% (22/43) of the DEX group vs. 57% (16/28) of the PROP group. One subject in either group required cardioversion or pacing to restore normotension.
CONCLUSIONS: While hypotensive events occurred more frequently in the DEX group than in the PROP group, the PROP group had a slightly higher need for pressors. These findings suggest that the risk of refractory hypotension requiring pressors is similar among patients receiving DEX or PROP following CABG, and that modifications in the DEX loading dosing (total dose or rate of infusion) may be advisable to reduce the risk of hypotension.

S-256

INTRAOPERATIVE DEXMEDETOMIDINE INDUCED VASOCONSTRICTION

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INTRODUCTION: Alpha-2 adrenoceptor agonists have both centrally mediated sympatholytic and peripherally mediated vasoconstrictive effects. Dexmedetomidine, an alpha-2 agonist, causes peripheral vasoconstriction in young healthy volunteers during general anesthesia. The aim of this study was to determine the vasomotor effects of an intraoperative dexmedetomidine loading dose infusion during general anesthesia.
METHODS: After Human Research Committee approval and written informed consent 24 patients scheduled for elective surgery were studied in an open label design. Direct arterial blood pressure, heart rate and infrared light (nA) transmitted through the fingertip were monitored continuously, and recorded electronically every 10 seconds. An increase in transmitted light indicates a decrease in finger blood volume (i.e. vasoconstriction). A 1g/kg dexmedetomidine zero order infusion was administered over 15 minutes intraoperatively during general anesthesia. Maximum hemodynamic changes during infusion and values at the end of infusion were compared to pre-dexmedetomidine values by repeated measures ANOVA followed by Dunnett's post hoc test. We also compared values at the end of infusion to values 5 minutes after infusion using paired t-test.
RESULTS: Intraoperative dexmedetomidine infusion increased transmitted light through the fingertip ($p<0.001$) and systolic blood pressure ($p=0.004$), and decreased heart rate ($p<0.001$). Maximum increase in transmitted light through the fingertip was 29 ± 25 %. The increase was 29 ± 24 % at the end of infusion. Dexmedetomidine increased systolic blood pressure from 109 ± 16 mmHg to a maximum of 126 ± 18 mmHg. At the end of infusion systolic blood pressure was 115 ± 25 mmHg (p=NS). Dexmedetomidine decreased heart rate from 68 ± 14 bpm to a minimum of 62 ± 10 bpm at the end of infusion. In the first 5 minutes after the dexmedetomidine infusion, only heart rate and transmitted light through the fingertip decreased significantly ($p<0.05$). Systolic blood pressure remained unchanged.
DISCUSSION: In surgical patients under general anesthesia 1g/kg dexmedetomidine caused peripheral vasoconstriction (as measured by transmitted light through the finger) and a decrease in heart rate throughout the15 minute infusion. However, the increase in blood pressure was limited in duration. Intraoperatively, under general anesthesia we were able to observe vasoconstriction induced by dexmedetomidine with minimal interference from the sympatholytic effects on the drug.

S-257

THE EFFECT OF LISTENING TO HEMISPHERIC SYNCHRONIZATION ON THE AMOUNT OF INTRAOPERATIVE ANALGESIA REQUIRED

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INTRODUCTION: Innovative types of music are prevalent for relaxation and hypnosis. Surgical patients are able to process auditory input while under general anesthesia. (1,2) Hemispheric synchronization music (Hemi-Sync) is a stereophonic vibrato of two sounds, producing a binaural beat stimulating the thalamus and cortex, affecting awareness. (3) A previous study established that Hemi-Sync can successfully be used as an adjuvant to general anesthesia, but patients underwent a variety of procedures and requirement of analgesia was evaluated based on hemodynamics alone. (4) The current double-blind randomized study of 60 patients undergoing general anesthesia for either laparoscopic bariatric or lumbar surgery employed bispectral index monitoring (BIS) to ensure equivalent depth of hypnosis in addition to using hemodynamics as a determinant of analgesia requirement.
METHODS: Consented patients were randomized to hear either a blank tape or Hemi-Sync. The same physician anesthetized all patients undergoing a particular procedure. Following endotracheal intubation, headphones were applied. The patient was not disturbed for the first ten minutes of tape play to determine baseline heart rate and blood pressure. The concentration of inhalational agent was adjusted by increments of 0.3% every five minutes as needed to maintain BIS at a depth of 50 ± 10. Fentanyl was administered in boluses of 25 ug every five minutes if heart rate and/or systolic blood pressure were above baseline values by 15% and 20%, respectively. The headphones were removed at the time of instrument removal and the initiation of skin closure. Amount of fentanyl administered per kilogram, per minute, during the trial period was compared using a student's t-test.
RESULTS: Bariatric patients who listened to Hemi-Sync were given one-third less fentanyl than those listening to a blank tape (0.0152 ug/kg/min (0.00884) vs. 0.0242 ug/kg/min (0.00865)) ($p<0.01$). Patients undergoing lumbar procedures were given similar amounts of fentanyl regardless of whether they listened to Hemi-Sync or a blank tape (0.0147 ug/kg/min (0.00909) vs. 0.0124 ug/kg/min (0.0116)). Regression analysis showed no statistically significant correlation between age or sex and fentanyl requirement for either procedure.
DISCUSSION: Interestingly, there was a dichotomy in the results. Listening to Hemi-Sync intraoperatively decreased the amount of analgesia administered for bariatric surgery. In contrast, the amount of analgesia administered for lumbar procedures was not correlated with exposure to Hemi-Sync. The difference in analgesic requirement among the lumbar cases may not have been apparent because of an induction dose of 100 ug fentanyl which could have been excessive considering the low degree of surgical stimulation. Hemi-Sync was proven to complement analgesia in laparoscopic bariatric surgery and certainly deserves further evaluation.
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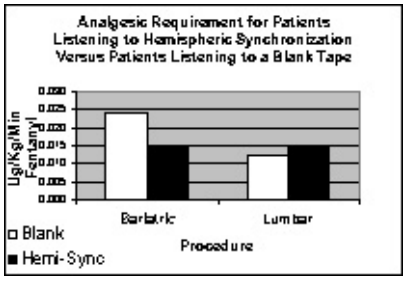

S-258

A NOVEL MIXTURE OF PROPOFOL, ALFENTANIL AND LIDOCAINE IN OBESE VS. NORMAL WEIGHT PATIENTS FOR SEDATION IN OPHTHALMIC PROCEDURES

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INTRODUCTION: IV sedation in obese patients presents clinical challenge because of difficulty in appropriate dose determination which can lead to over or under sedation. We studied a mixture of 6ml propofol (10mg/kg), 2ml alfentanil (500g/ml) and 2ml 2% lidocaine (A6-2-2) for IV sedation during regional block for ophthalmic surgery. With IRB approval, this retrospective review compared the effects of A6-2-2 mixture in obese patients vs those of normal weight.
METHODS: Obesity was defined as body mass index (BMI) >26. If patient was obese, weight for dosing was calculated as ideal body weight (IBW) plus 30% of (patient's weight- IBW). Bolus of A6-2-2 mixture was delivered by infusion pump based on alfentanil dose according to age. Age >74, 5g/kg; 65-74, 6g; 55-64, 7g; 45-54, 8g; and <45, 9g/kg. Following bolus, mixture was infused at 0.75 g/kg/min alfentanil until block completion. Block performed at 1 minute after bolus finished. All patients received O_2. They were monitored for vital signs, 3 signs of sedation including spontaneous eye closure(sec), sluggish speech(ss), and decrease in respiratory rate(drr), 3 responses to regional block including head movement(hm), eyebrow movement(ebm) and complaint of pain(cop), airway complication, N & V, pain to mixture infusion and recall. Patient and surgeon satisfaction (1-10) scored based on standardized questioning. Exact chi-square and T test or corresponding Wilcoxon rank sum test were used for statistic analysis. $P<0.05$ was considered significant.
RESULTS: 89 charts were reviewed. 40 of 89 patients were obese. There was no significant difference in age or gender between groups. The difference in BMI was significant ($P<0.0001$). No significant difference in % of patients presenting all 3 signs of adequate sedation and analgesia without 3 responses to block in both groups. No significant difference in incidence of apnea, oxygen desaturation, heart rate change, need for airway support, or recall between the 2 groups. No N&V or pain to mixture infusion in both groups. Systolic BP(SBP) was significantly increased from baseline with 17.04 ± 21.78 mmHg ($P<0.0000$) for non obese and 9.6 ± 23.98 mmHg($P=0.016$) for obese patients prior to IV sedation. After sedation and block, SBP was decreased comparing to the baseline, with –3.22 ± 20.73 mmHg ($P=0.28$) for non obese and –13.70 ± 22.37 mmHg ($P <0.001$, but < 10% from the baseline) for obese groups. See table for further results.

Group	# pt	BMI	Had Sec/ ss/drr	No hm/ ebm/cop	ebm only	Apnea with airway support	Brief O_2 desaturation	Patient & surgeon satisfactory score
Obese	40	30.93±3.58	31(78%)	31(78%)	3(8%)	1	3	9.81±0.53 9.64±0.7
Non obese	49	23.16±1.87 (P<0.0001)	40(82%) (P=0.79)	38(78%) (P=0.99)	8(16%) (P=0.33)	1	2	9.73±0.64 9.57±0.84

CONCLUSION: The effect of novel mixture of propofol, alfentanil and lidocaine (A6-2-2 mixture) in obese patients was comparable to non obese patients when dosage adjusted as described. This simple mixture provided excellent(no hm, ebm or cop) or good (ebm only) sedation/ analgesia for majority patients in both groups. The mixture also provided hemodynamic stability with similar low incidence of airway complication and no N&V or pain due to infusion.

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SEDATION WITH SEVOFLURANE OR PROPOFOL IN PATIENTS UNDERGOING REGIONAL ANESTHESIA FOR ORTHOPEDIC SURGERY

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INTRODUCTION: Sedation for surgical procedures performed under regional anesthesia has usually been accomplished with intravenous agents such as midazolam or propofol, whereas volatile anesthetics are rarely used for this purpose. Sevoflurane for sedation and induction of general anesthesia has been suggested because of its characteristics of non-pungency, rapid induction, and quick elimination. The purpose of this investigation was to compare the quality of sedation and recovery following use of either sevoflurane or propofol sedation during regional anesthesia.
METHODS: Thirty-seven patients undergoing orthopedic surgery with regional anesthesia were enrolled in a randomized investigation comparing sedation with sevoflurane (n=17) and propofol (n=20). Level of sedation was targeted to an Observer's Assessment of Alertness--Sedation score of 3 (OAAS=3, responds slowly to voice). Recovery from sedation was assessed objectively by Observer's Assessment of Alertness--Sedation, Digit Symbol Substitution Test (DSST) and memory scores.
RESULTS: All patients were assessable for efficacy and recovery data. Sevoflurane and propofol produced dose-related sedation. Recovery from sedation to OAAS 5 (fully awake) after surgery was similar between groups, 7±3 min and 8±3 min for sevoflurane and propofol, respectively (p=ns). Seventy-one percent (sevoflurane) of the patients compared with 60% (propofol) returned to baseline DSST at 30 min postoperatively (p=ns). Short and long term memory tests yielded similar results between the two groups (p=ns). Excitation was seen in seven of 17 patients receiving sevoflurane and three in those sedated with propofol. Discharge eligibility was deemed earlier with sevoflurane (48±7 min) than with propofol (55±9 min, $p<0.05$).
CONCLUSIONS: Sevoflurane for sedation produces similar recovery of cognitive function as measured by DSST and memory scores compared with propofol. Both agents can be recommended for sedation during regional anesthesia.

S-260

ROUTINE USE OF PREOPERATIVE BETA-BLOCKERS DOES NOT BLUNT STRESS (HEART RATE) RESPONSE TO IMPENDING SURGERY

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INTRODUCTION: b-blockers (BB) decrease post-operative cardiac morbidity and mortality1. Of the proposed mechanisms associated with their beneficial effects, a decrease in oxygen demand secondary to decreased chronotropy is hypothesized to play a major role. Recent ACC/AHA Guidelines recommend titrating preoperative BB to maintain resting heart rate (HR) between 50-60 bpm2. We recently showed that, despite beta-blocker use, only 38% of patients receiving routine BB had HR =60 bpm and 26% still had HR =70 bpm. This study was conducted to determine if routine use of BB blunts the stress response (HR) to impending surgery, as a measure of effective blockade.
METHODS: A retrospective review of the pre-anesthetic assessment record was conducted on 326 consecutive patients who were scheduled to undergo major vascular surgery (CEA, supra and infrainguinal bypass, thoracic and aortic abdominal aneurysm) and CABG between Jan 2001 to March 2002 at Yale-New Haven Hospital. Demographic data, medications, pertinent review of systems and resting HR and BP, while in the Pre-Admission Center, were obtained from the electronic records. Initial intraoperative HR and BP were obtained from chart review. Patients were grouped as: i) patients on BB (BB-patients), ii) patients not on BB (noBB-patients). Data are presented as mean ±SD and analyzed by unpaired t-test with Welch correction. $P < 0.05$ considered significant.
RESULTS: 60.43% (197/326) of patients scheduled surgery were on BB (mean PAT HR 65bpm ±14.85). 39.57% (129/326) were not on routine BB (HR 74.5bpm±0.71). Initial intraoperative HR in BB-Patients was 70.83bpm±2.83 and was significantly different from baseline PAT HR (p 70bpm nearly doubled (25.9% to 48.1%), while patients with HR rate <60bpm nearly halved (table). The difference in systolic and diastolic BP was not significantly different between BB-patients and noBB-patients.
CONCLUSION: Our study suggests despite routine preoperative beta-blocker use and reasonable preoperative heart rate, stress response to impending surgery is not effectively blunted. Prophylactic supplemental doses of BB may be required perioperatively even in patients who are on routine BB to blunt the HR response effectively in significant number of patients.

Patients	Age (mean) (SD)	Patients with HR <=6	Patients with HR >60 And <=70	Patients with HR >=71
BB Patient				
Pre-Op HR		75/197(38.05%)	71/197(36.04%	51/197(25.88%)
Initial HR	67.09 (7.07)	39/210(18.57%)*	70/210(33.33%)*	101/210(48.09%)
Non-BB Patients				
Pre-Op HR		16/129(12.04%)	43/129(33.33%)	70/129(54.26%)
Initial HR	69.12 (28.28)	18/138(13.04%)	29/138(21.01%)*	91/138(65.94%)*

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S-261

CHRONIC BETA-ADRENOCEPTOR BLOCKADE DOES NOT MINICK ACUTE MEDICATION IN ITS EFFECTS ON CARDIAC OUTCOME

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INTRODUCTION: A number of studies and RCT's have demonstrated an effect of acute -adrenoceptor blockade on perioperative cardiac outcomes in both high risk and other populations undergoing non-cardiac surgery (1-6). However there are fewer data on the efficacy of intercurrent chronic -adrenoceptor blockade (whether given for the treatment of ischemic heart disease or hypertension) with regard to cardiac morbidity and mortality in comparable patient groups.
METHODS: We conducted a MEDLINE search for papers evaluating the effects of chronic medication on cardiovascular outcomes. The terms used were 'perioperative care; postoperative complications; adrenergic antagonists; adrenergic beta-antagonists; myocardial ischemia; myocardial infarction; mortality and heart disease mortality', followed by hand searching of reference lists from the identified papers. We identified 8 studies (7 observational; 1 case-control [CC] linkage study with matched non -blocked controls). Various endpoints measured within 30 days of surgery were examined in the different studies - cardiac death plus/ minus major cardiac complications [n=4]; major complications alone [1]; postoperative myocardial infarction [1] and postoperative silent myocardial ischemia (SMI) [2].
RESULTS: Overall the studies encompass 6343 patients (1290 receiving chronic -adrenergic blockade; 20.3%). Individual odds ratios (and 95% CI) for the endpoints are shown in the table:
[Univariate odds ratios except * where adjustment made for possible confounders].
DISCUSSION: With the exception of Browner (13) (which examined in-hospital mortality), there were no significant differences from unity. This is in contrast to acute studies where most show significant reductions in morbidity and mortality with acute -adrenoceptor blockade (1-6). This leads to two important questions - what should be done for 'at-risk' patients presenting for surgery and already on -adrenoceptor blockade; or are there fundamental differences in the patient populations between the acute and chronic studies? Furthermore are there biochemical or pharmacological differences in the stress responses to anesthesia and surgery in patients receiving acute -adrenergic blockade compared with chronic medication?

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SMI postop	n	odds ratio
Hollenberg (7)	407	1.58 (0.78-3.14)
Sear (8)	453	0.67 (0.37-1.21)*
Major cardiac complications and death		
Browner (9)	474	2.4 (1.0-5.5)
Badner (10)	323	1.48 (0.56-3.97)
Lee (11)	2893	1.34 (0.71-2.51)
Boersma (12)	1351	0.59 (0.25-1.25)
Sear [CC] (13)	230	1.00 (0.41-2.44)*
Sear (14)	212	1.61 (0.65-3.76)

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THE EFFECTS OF ACETAMINOPHEN ON THE PHARMACOKINETICS OFORAL MIDAZOLAM.

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INTRODUCTION: The goal of this study was to characterize the interactions of acetaminophen with midazolam in humans. Acetaminophen and midazolam are metabolized by cytochrome P450 (CYP) 3A. Oral administration of midazolam results in significant CYP3A mediated-first pass metabolism (1). Since acetaminophen and midazolam will compete for CYP3A4, and this P450 plays a major role in the first-pass-metabolism; we have designed a study to ascertain the effects of acetaminophen on the pharmacokinetics of midazolam. The working hypothesis was that CYP3A4 mediated metabolism would be inhibited by acetaminophen and thereby increase Cmax and AUC of orally administrated midazolam.
METHODS: The protocol was conducted in the General Clinical Research Center of the Mount Sinai School of Medicine after Institutional Research Board approval was obtained. A double-blind randomized study of 16 human volunteers was performed to determine the pharmacokinetics, specifically Cmax and AUC, of oral midazolam in the presence of tacetaminophen or a placebo. Each volunteer underwent two testing periods, each at least 2 weeks apart. In a random sequence, each patient received one of the following combinations: I-Placebo (cherry syrup)* + Midazolam (0.3 mg/kg) or II-Dose 2 of acetaminophen syrup(15 mg/kg)* + Midazolam (0.3 mg/kg). Blood samples were acquired at 0, 15, 30, 45, 60, 90, 120, 180, 240 and 480 minutes. The blood was centrifuged and the plasma stored at –40ºC until analyzed. Blood samples were analyzed for midazolam by the method of Thummel *et al*. (2) using a Hewlett-Packard Model 5972 mass-selective detector (MSD). Results are expressed as the mean ± SD and were analyzed with a Student paired t-test (one tailed).
RESULTS: Cmax and AUC were estimated using PK **So**lutions 2.0 pharmacokinetics program (Summit Research Services, Ashland, OH). The co-administration of acetaminophen and midazolam had no effect on Cmax or AUC. Cmax's were 247 ± 258 and 242 ± 126 ng/ml ($p<0.45$) for control and the acetaminophen group, respectively. The AUC's calculated for the control and acetaminophen group were 93 ± 99 and 85 ± 64 ug-min/ml ($p<0.24$), respectively.
DISCUSSION: Since acetaminophen and midazolam are metabolized by the CYP3A4 in humans, it was hypothesized that acetaminophen might affect the pharmacokinetics of midazolam. The results show that acetaminophen had little effect on Cmax and AUC of midazolam. Although they are metabolized by the same P450, it has been previously shown that acetaminophen has a high Ki (3mM) for the inhibition of fentanyl metabolism (3). It appears that at the dose tested, acetaminophen has little effect of the disposition of midazolam.

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S-263

APPREARANCE OF ROFECOXIB, A SELECTIVE CYCLOOXYGENASE-2 (COX-2) INHIBITOR, IN CEREBROSPINAL FLUID FOLLOWING ORAL ADMINISTRATION IN PATIENTS

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INTRODUCTION: We have recently demonstrated in an animal model of post-operative pain that intrathecal COX-2 inhibitors can modulate hypersensitivity (1). Intrathecal COX-2 inhibitors can also reduce hypersensitivity in inflammatory animal pain models (2,3). Therefore, blood-brain-barrier penetration may be an important factor in the analgesic effectiveness of oral COX-2 inhibitors (4). Following oral administration of rofecoxib in rats, the compound appears in the cerebrospinal fluid (CSF) at a concentration 19-35% of the plasma level (5). The purpose of this study is to investigate the time course of rofecoxib in CSF when administered orally to patients undergoing total knee arthroplasty (TKA).
METHODS: Following IRB approval and informed consent, 11 patients scheduled for TKA received a dose of rofecoxib 50 mg both 24 h and just before surgery, as part of a analgesic regimen. All patients had combined spinal-epidural (CSE) anesthesia for the surgery, and CSF (100 L) samples were obtained prior to intrathecal administration of local anesthetic as part of the CSE technique. The range of time delay between the last oral administration and the CSF sampling ranged between 17-85 min. Rofecoxib concentration was assayed by HPLC.
RESULTS: For patients receiving oral rofecoxib, the CSF concentration was below 0.06 g/mL for the first 60 min after the post-surgery oral dose (Fig.). After 60 min, the CSF level was above 0.06 g/mL ($p<0.005$, Fisher's exact test).
DISCUSSION: Following oral administration, there is a 60 min delay before CSF rofecoxib levels increase. Oral rofecoxib (50 mg) has been shown to reduce post-operative opioid use following spinal fusion when given 60 min before anesthetic induction (6). Therefore, the timing of the rofecoxib administration, including the delay to reach CSF levels, may be one factor determining efficacy for this and other COX-2 inhibitors.
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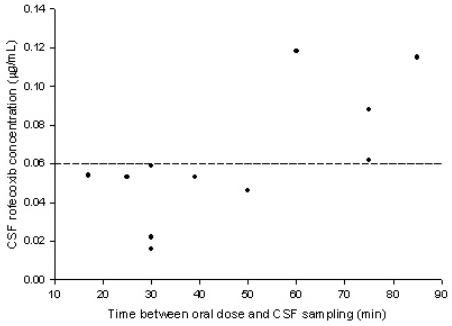

S-264

THE EFFECT OF FENTANYL ON RENAL TUBULAR FUNCTION AND NDOCRINE RESPONSE DURING THORACOTOMY

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BACKGROUND: Surgical stress produces various endocrine response including sympathetic hyperactivity and cytocaine release. Those are reported to associate with renal tubular damage during thoracotomy previously. Epidural analgesia with local anesthetics only couldn't prevent renal tubular damage and cortisol release. This study is assigned to evaluate the effect of fentanyl on those reaction.
METHODS: Thirty patients undergoing elective thoracotomy were divided into three groups at random. Control group was maintained under general anesthesia (GA). GA combined with epidural analgesia with 1% mepivacaine was used on epidural group. Fentanyl was administered by intravenous and epidural injection addictively on fentanyl group. Urinary output of N-acetyl-É¿-D-glucosaminidase (NAG) was measured as an indicator of renal tubular cell damage before and during the operation. Plasma cortisol and aldosterone were determined as indicator of the response to surgical injury.
RESULTS: NAG and cortisol increased significantly during thoracotomy from on control and epidural ($p<0.05$) but not fentanyl group. Aldosterone increased significantly by about three times on control and epidural group ($p<0.01$), less than twice on fentanyl group ($p<0.05$).
CONCLUSIONS: It was demonstrated that the administration of fentanyl suppress increase of NAG and cortisol completely and attenuate aldosterone release during thoracotomy. Those results suggest that fentanyl attenuate endocrine response and prevent renal tubular damage during thoracotomy.

S-265

IS THERE AN IDEAL APPROACH FOR RAPID SEQUENCE INDUCTION IN HYPERTENSIVE PATIENTS?

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INTRODUCTION: Hypertensive patients are more prone to exhibit an exaggerated hemodynamic response to laryngoscopy and tracheal intubation[1]. So far, the hemodynamic alterations associated with rapid-sequence induction of anesthesia in hypertensive patients has been under evaluated. This randomized, prospective trial was designed to examine the hemodynamic effects of four different rapid sequence induction protocols in hypertensive patients in order to determine the optimal approach for a smooth laryngoscopy and intubation.
METHODS: After IRB approval and patient consent was obtained; 120 hypertensive ASA II-III adult patients undergoing elective surgery were allocated to four groups at random by sealed envelope technique. Anticipated difficult airway, ECG evidence of heart block or congestive cardiac failure were the exclusion criteria. Patient's lungs were preoxygenated for 3 minutes, induction and tracheal intubation was performed in a 30° head-up position. At induction of anesthesia, group LS(n=30) received a bolus of lidocaine 1,5mg kg^{-1} over 30 s followed by thiopental 5-7 $mgkg^{-1}$ and a bolus of succinylcholine 1 $mgkg^{-1}$. Group LR (n=30) received the same induction agents as group LS with rocuronium 1$mgkg^{-1}$ for muscle relaxation. Group RS(n=30) received a bolus of remifentanil 1 $mcgkg^{-1}$ over 30 s followed by thiopental 5-7 $mgkg^{-1}$ and a bolus of succinylcholine 1 $mgkg^{-1}$. Group RR (n=30) received the same induction agents as group RS with rocuronium 1mg kg^{-1} for muscle relaxation. Hemodynamic data (heart rate, non-invasive blood pressure and peripheral oxygen saturation) were noted before induction (baseline), after induction, at intubation and at 1, 3, 5, 10, 20 minutes following intubation. 60 s after administration of muscle relaxant, endotracheal intubation was performed and intubation conditions were scored[2]. Anesthesia was maintained with isoflurane 1,5% and N_2O 50% in oxygen. ANOVA and chi square tests were used for statistical analysis. P value <0,05 was considered significant.
RESULTS: Demographic data and type of medication for anti-hypertensive treatment were similar in all groups. Systolic and mean arterial blood pressure (MAP) at intubation, 1 and 3 min after intubation were higher in group LS compared to groups RS and RR (p<0,01). MAP increased at intubation and 1 min after intubation compared to baseline in groups LS and LR (p<0.01). MAP was similar at all measurement intervals in group RS. Paramedian position of the vocal cords at intubation was higher in group LS(n=7) compared to other groups(n=1 for each group) (p<0.05).
DISCUSSION: Rapid sequence induction is generally used under emergent conditions. In this study an ideal approach to maintain cardiovascular stability during rapid sequence induction was searched for hypertensive patients. Remifentanil succinylcholine combination appears to be more beneficial in terms of hemodynamic stability. Remifentanil was found superior to lidocaine in attenuation of the response to laryngoscopy and intubation.
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S-266

LARINGEAL MASK AIRWAY INSERTION WITH REMIFENTANIL

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INTRODUCTION: Propofol is the commonly used anesthetic for the induction of anesthesia for insertion of laryngeal mask airway (LMA). When used alone, propofol may be inadequate to blunt undesirable airway responses (1,2). Increasing the dose to prevent these may cause hemodynamic disturbances. We conducted a study to find out the best conditions for LMA insertion with two different doses of remifentanil added to propofol and propofol administered alone.
METHODS: Following hospital clinical research ethics committee approval, 60 ASA I-II patients undergoing lower abdominal or urologic operations were included in the randomized double-blind study. All patients were premedicated with i.m. midazolam 0.2mg/kg and atropine 0.5mg/kg. Patients received i.v. 0.25mcgr/kg remifentanil (Group R1), 0.50mcgr/kg remifentanil (Group R2) or normal saline (Group P) in 60s.Then following 20mg lidocaine, propofol 2mg/kg were administered in R1 and R2 groups and 2.5mg/kg in P group. Ease of insertion of LMA was graded by 3-point scale and airway quality at first attempt was assessed either good or poor. Propofol 0.5mg/kg was added in inability to insert the LMA. Maintenance of anesthesia was provided with 50% N_2O–O_2 with 1.5-2% sevoflurane. Experience of the anesthesiologist, number of attempts of LMA insertion, apnea time, additional propofol requirement and heart rate, systolic (SBP) and diastolic (DBP) blood pressures was recorded before premedication, pre-induction (PI) and frequent intervals following the induction. Intra- and postoperative side effects were also assessed.
RESULTS: There were no significant differences in demographic data among the patients. Apnea time (mean ±SEM) was significantly shorter in P group (34.09±5.5 s) compared to R1 (82.5±12.7s) and R2 (87.2±6.6s) groups (p<0.05). Heart rate, SBP and DBP measured 2min. following the induction were significantly lower from baseline (PI) values in the R2 group (p<0.05), but only 2 patients received atropin. Ease of LMA insertion was found to be different between the groups (p<0.05). One hundred percent of patients were assessed as grade 1 in R2 group while 64.3% in R1 and 27.3% in P groups. No difference in airway quality was observed between the groups. More patients in P group required additional propofol compared to R2 group (p<0.05). Undesirable responses following LMA insertion; like limb, head movement or hiccup was observed in 54% of patients in P group.
DISCUSSION: Propofol given 2.5mg/kg alone is not a good agent for LMA insertion. Remifentanil used in both doses combined with propofol provides excellent conditions for insertion of LMA with minimal hemodynamic disturbances, especially in ASA I-II patients. More studies should be done to find out the proper dose of remifentanil for high-risk patients with unstable hemodynamia.
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S-267

SEVOFLURANE MAC AND CP50 FOR INSERTION OF PROSEAL VS CLASSIC LARYNGEAL MASK

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INTRODUCTION: A new laryngeal mask airway, ProSeal (PLMA) has a modified cuff to improve the seal and a drainage tube to provide access to the gastrointestinal tract. The PLMA is said to be more difficult to insert than laryngeal mask airway Classic (CLMA) during propofol anesthesia.(1) But there are no data using sevoflurane for insertion of PLMA vs CLMA. We investigate sevoflurane MAC and Cp50 for insertion of these LMAs.
METHODS: After written informed consent for the study was obtained, 34 elective unpremedicated adult female patients (ASA I-II), aged 20-50 were randomly assigned into PLMA (n = 18) and CLMA (n = 16) groups. Anesthesia was with sevoflurane in 100% oxygen. After the predetermined target end-tidal sevoflurane had been established and maintained more than 20 min using gas analyzer, venous blood was sampled and LMA insertion was attempted without neuromuscular blockade. The sevoflurane end-tidal concentration (ET Sevo), starting at 2% for each patient, was decided by up and down method with a 0.5% step. Data collection was continued until six crossover points were obtained for each group and analyzed using logistic regression to obtain the probability of no-movement versus ET Sevo and Cp Sevo to obtain MAC_{LMA} and $Cp50_{LMA}$ levels (proprietry software, JMP, SAS, Cary, NC) . Sevoflurane blood concentrations were measured using gas chromatography.
RESULTS: The ET Sevo crossover point of PLMA and CLMA were 2.92 +/- 0.41 and 2.42 +/- 0.26 %, respectively (p = 0.029; unpaired t-test). Logistic regression curves for probability of no-movement versus Cp Sevo and ET Sevo are shown in the figure. According to the figure, the values of MAC_{PLMA} and MAC_{CLMA} were 2.85 and 2.42%, respectively. $Cp50_{PLMA}$ and $Cp50_{CLMA}$ were 79.3 and 65.7mcg/mL. Both MAC_{PLMA} and $Cp50_{PLMA}$ were 17.8 and 20.7% higher respectively than those of CLMA.
CONCLUSION: The sevoflurane requirement for insertion of PLMA is higher than that required for CLMA.

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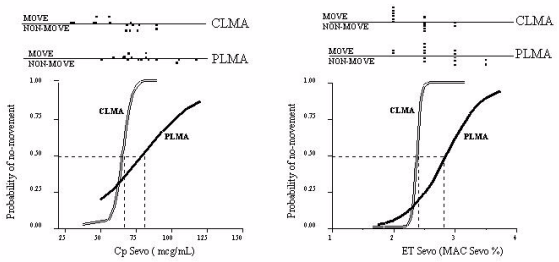

Fig.: Dose-response curves plotted from logistic regression of individual sevoflurane plasma concentrations (left) and end-tidal (right) to CLMA and PLMA insertion. In the upper part of the figure, individual observations are presented.

S-268

IS THE POST-TETANIC COUNT/TRAIN OF FOUR RELATIONSHIP FOR INTENSE CISATRACURIUM-INDUCED NEUROMUSCULAR BLOCKADE DOSE-DEPENDANT?

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INTRODUCTION: Recovery from intense neuromuscular blockade can be monitored by the post-tetanic count (PTC) and its relationship to the first response (T_1) of the train-of-four (TOF).[1] Schultz et al., demonstrated that this relationship is altered depending upon the dose of rocuronium.[2] Cisatracurium, in doses ranging from 0.1 to 0.2 mg/kg (2 – 4 x ED_{95}), has previously been used to facilitate tracheal intubation.[3] If this dose-dependent relationship also exists for cisatracurium, the initial dose must be taken into consideration when using PTC to assess the degree of neuromuscular blockade. The present study evaluates the PTC/T_1 relationship, onset time, and tracheal intubation conditions after administeration of 0.1, 0.15 and 0.2 mg/kg cisatracurium.
METHODS: After IRB approval, onset of neuromuscular blockade and recovery profiles were studied using an acceleromyographic sensor in 86 adult patients following either 0.1 (Group 1, n = 28), 0.15 (Group 2, n = 29) or 0.2 (Group 3, n = 29) mg/kg cisatracurium. Intubation conditions were graded two minutes after cisatracurium administeration using previously published criteria.[4] Intubation conditions were considered clinically acceptable if they were Excellent or Good and unacceptable if Poor or Impossible.
RESULTS: Increasing the dose of cisatracurium produced faster onset and prolonged the time to PTC_1 and the time to T_1. The time interval between a certain PTC and T_1 reappearance and the number of post-tetanic responses elicited when T_1 reappeared, however, were the same in the three groups (Table). Data in the table appears as mean ± standard deviation or as counts. At 2 minutes, clinically acceptable intubating conditions were obtained in all patients in Groups 2 and 3. Seven patients recieving cisatracurium 0.1 mg/kg (Group 1) had unacceptable intubating conditions (Poor = 6 and Impossible = 1) at two minutes.
DISCUSSION: Cisatracurium, in doses of 0.15 mg/kg or greater, provide acceptable intubating conditions by 2 minutes. The time to reappearence of T_1 when a certain PTC is elicited during recovery from intense cisatracurium-induced neuromuscular blockade is consistent and unchanged regardless of the initial dose used. This allows better predictability in the block course when monitoring such degrees of neuromuscular blockade even when different doses are initially administered.
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Onset and PTC/T1Recovery Profile

	Cisatracurium 0.10 mg/kg (n=28)	Cisatracurium 0.15 mg/kg (n=29)	Cisatracurium 0.20 mg/kg (n=29)	Significance *P* value
Onset Time (sec)	259.9 ± 21.0	207.7 ± 7.3	129.2 ± 5.7	< .0001
Time to PTC_1 (min)	24.5 ± 3.0	35.6 ± 7.5	47.1 ± 3.5	< .0001
Time to T_1 (min)	34.9 ± 2.8	46.9 ± 6.5	59.7 ± 3.3	< .0001
PTC_1-T_1 Interval (min)	10.9 ± 1.0	11.3 ± 1.9	11.6 ± 1.7	NS
PTC @ T_1	8 - 9	8 - 9	8 -9	NS

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OFFSET OF NEUROMUSCULAR BLOCK IS LONGER AT THE ABDUCTING LARYNGEAL MUSCLE THAN AT THE ADDUCTING LARYNGEAL MUSCLES IN HUMANS

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INTRODUCTION: This study investigates the onset and offset of Neuromuscular block (NRM) at the adducting and abducting laryngeal muscles in humans.
METHODS: After approval of the local Ethics Committee and informed consent, 10 patients were included. Intubation was performed without neuromuscular block using remifentanil/propofol and maintained using remifentanil/sevoflurane. Two small condenser microphones were inserted into the throat and placed lateral of the tube near the vestibular fold to record the response of the adducting laryngeal muscles (1) and behind the larynx to record the response of the abducting laryngeal muscle. Percutaneous stimulation of the laryngeal recurrent nerve was performed in routine fashion using superficial electrodes placed over the thyroid notch. Train-of-four stimulation was performed every 12 sec and supramaximal stimulation current determined. Mivacurium 0.1 mg/kg was injected IV. Onset, peak effect and offset of NMB was determined for both recording sites. Data presented as mean (SD) and compared using *t*-test, $P<0.05$.
RESULTS: Onset, onset 90, and peak effect were 118 (34) s and 142 (20) s, 89 (38) s and 105 (26), and 71 (18) % and 84 (18) %, respectively for the adducting laryngeal muscles and abducting laryngeal muscle without being statistically different. Recovery is presented in Figure 1, with offset of NMB at the abducting laryngeal muscle being significantly longer than at the adducting laryngeal muscles.
DISCUSSION: This is the first study in humans presenting a complete onset and recovery profile of NMB at the adducting laryngeal muscles and abducting laryngeal muscle. Offset of NMB after 0.1 mg/kg mivacurium is 4-5 min longer at the abducting laryngeal muscle. This is in contrast to previous findings in cats (2).
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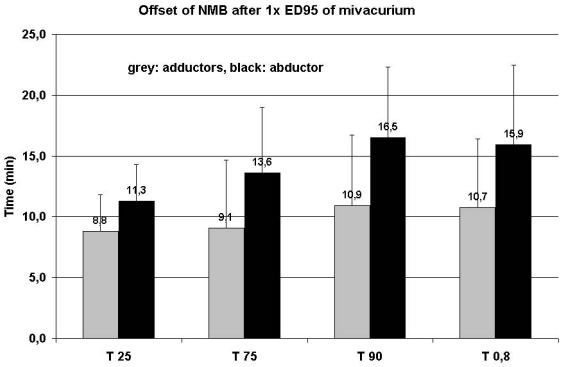

1 ASA 2002, A-985
2 Acta Anaesth Scand 2000; 44: 503-10

S-270

NEUROMUSCULAR EFFECTS OF ROCURONIUM IN PATIENTS WITH PARKINSON DISEASE

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INTRODUCTION: The effects of non-depolarising neuromuscular blockers could change in Parkinson disease (1,2). In this study we compared the neuromuscular effects of rocuronium in patients with Parkinson disease and normal patients.
METHODS: After ethics committee approval and written informed consent from patients, 30 ASA II-III patients included in this study. Patients with Parkinson disease were called in-Group Parkinson (n=15) and patients with not any sign of Parkinson were called in-group Control (n=15). Standard monitorization and anaesthesia induction were used. Rocuronium (0.6 mg/kg) was given for neuromuscular blockage. TOF Guard device (Organon tecnica, Belgium) was used for neuromuscular monitorization. Orbicularis oculi muscle with TOF (Train of Four) stimulation was used. The onset time of neuromuscular blockage (sec) (OT), neuromuscular block's recovery of % 25, %25-75 (recovery index) was recorded.
The intubating conditions were evaluated using a score described by Viby-Mogensen and his colleagues (3). The intubation scores were analysed using Chi-squared tests. The demographic data, and neuromuscular effects of rocuronium were analysed using unpaired Student's t-test. P value smaller than <0.05 were considered statistically significant.
RESULTS: There were no differences with respect to the age, sex, weight, intubation condition and neuromuscular effects between two groups.
DISCUSSION: The neuromuscular effects of rocuronium in Parkinson patients were not differing in normal patients.

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	Neuromuscular effects	
Groups	Group Parkinson	Group Control
Onset Time(sec)	59±7	64±15
% 25 recovery (min)	42±11	39±14
% 25-75 recovery (min)	12±4	9±7

S-271

THE EFFECT OF DOSAGE AND TIMING OF NEOSTIGMINE ADMINISTRATION ON REVERSAL OF VECURONIUM-INDUCED NEUROMUSCULAR BLOKADE INA REPITITIVE DOSE (VECURONIUM) MODE

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INTRODUCTION: To investigate the effect of dosage and timing of neostigmine administration on reversal of vecuronium-induced neuromuscular blokade in a repetitive dose (vecuronium) mode.
METHODS: Seventy patients were included in this investigation. Thirty of them were randomized into three groups-- N_{20}, $N_{40}$and N_{60}. When the T_1 recover to 10% after last dose of vecuronium administrated, neostigmine 20ug/kg (N_{20}), 40ug/kg (N_{40}) or 60ug/kg (N_{60}) were administrated. Then the time of T1 recovery to 90% (T_{90}), TOF recovery to 0.7 and 0.9 ($TOF_{0.7}$ and $TOF_{0.9}$) from neostigmine administrated, recovery index (RI) and time of TOF from 0.7 to 0.9($TOF_{0.7\text{-}0.9}$) were recorded. The other forty patients were randomized to four groups-- G_{5min}, $G_{T1\text{-}1\%}$, $G_{T1\text{-}10\%}$ and $G_{T1\text{-}25\%}$. The neostigmine 40ug/kg was injected when 5min after last dose of vecuronium administrated (G_{5min}), T1 recovery to 1%($G_{T1\text{-}1\%}$), 10% ($G_{T1\text{-}10\%}$) and 25% ($G_{T1\text{-}25\%}$) after last dose of vecuronium administrated. Then T1 recovery to 90% (T_{90}'), TOF recovery to 0.7 and 0.9 ($TOF_{0.7}$' and $TOF_{0.9}$') from last dose of vecuronium administrated, RI and $TOF_{0.7\text{-}0.9}$ were recorded.
RESULTS: There were no significant differences in the demographic data (age, sex, weight and height), surgical duration and vecuronium magnitude among groups. All parameters were significantly prolonged in N_{20} than N_{60}. $TOF_{0.9}$, RI and $TOF_{0.7\text{-}0.9}$ were significantly prolonged in N_{20} than N_{40}. $TOF_{0.7}$ and RI were prolonged in N_{40} than N_{60}. $TOF_{0.7\text{-}0.9}$ were significantly prolonged in G_{5min} than other three groups. RI was significantly shorter in $G_{T1\text{-}25\%}$ than other groups. $TOF_{0.9}$' was significantly prolonged in G_{5min} than $G_{T1\text{-}1\%}$.

	T_1 recovery to 90% (min)	RI (min)	TOF recovery to 0.7 (min)	TOF recovery to 0.9 (min)	$TOF_{0.7\text{-}0.9}$ (min)
"zero-point" : the time when neostigmine injected					
N_{20}(n=10)	15±7**	9±3** @@	17±7**	35±15 @@ ##	18±9 @@ ##
N_{40}(n=10)	11±5	6±2 ##	14±6 ##	25±9	11±4
N_{60}(n=10)	9±3	4±2	9±2	22±10	11±6
"zero-point":time when last dose of vecuronium administrated					
G_{5min}(n=10)	43±8	14±4	47±9	77±26 #	30±18
$G_{T1\text{-}1\%}$(n=10)	37±14	5±3 *	37±15	51±21	14±8 @
$G_{T1\text{-}10\%}$(n=10)	41±8	6±2 *	46±9	63±8	10±4 *
$G_{T1\text{-}25\%}$(n=10)	43±13	3±1 * # &	45±14	57±23	12±11 @

The symbols in table means: ** P<0.01 vs N_{60} ; ## P<0.05 vs N_{60}; @ @ P<0.05 vs N_{40} ; * P<0.01 vs G_{5min};@ P<0.05 vs G_{5min}; & P<0.01 vs $G_{T1\text{-}10\%}$; # P<0.05 vs $G_{T1\text{-}1\%}$.
DISCUSSION: In our study, we not only used the routine parameters but also set a new parameter—$TOF_{0.7\text{-}0.9}$. Because neuromuscular transmission was still impaired when TOFR was below 0.9, we think $TOF_{0.7\text{-}0.9}$ can reflect the "unstable duration after extubation". Our study shows the reversal of vecuronium-induced neuromuscular blokade was potentiate when neostigmine increased from 20ug/kg to 40ug/kg. But if neostigmine increased from 40ug/kg to 60ug/kg, only RI and $TOF_{0.7}$ were decreased, 2 and 5min respectively, which haven't clinical significance. In a single (vecuronium) mode, Bevan et al [1]found the timing of neostigmine administration didn't have significant effect on reversal of vecuronium-induced neuromuscular blokade if the time when vecuronium administrated was used as a "zero-point". In our repetitive (vecuronium) mode, the recovery of vecuronium-induced neuromuscular blokade were faster if neostigmine was administrated when T1>1%.
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S-272

NICOTINE AS A POTENTIAL ANTIEMETIC?

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INTRODUCTION: In a previous research we found that smokers have a significantly reduced incidence of PONV (1). The same results were published by Cohen et al in 1994 (2). Taking in consideration that smoke contains aproximately 4000 substances, the aim of this study was to see if nicotine, itself, has the same effects as the cigarette smoke.
METHODS: Following Ethics Comittee approval and after optaining informed written consent 75 pacients (ASA I and II) who underwent laparoscopic cholecistectomy under general anaesthesia were divided in 3 groups: group 1 (n=25) of nonsmokers, group 2 (n=25) of nonsmoking patients during the last five years witch received 16,6mg NICORETTE-patch and group 3 (n=25) of patients with a history of smoking. We decided to use 16,6 NICORETTE-patch after a pilot study with 4,15mg, 8,3mg and 16,6mg of NICORETTE-patch. The general anaesthesia was induced with thiopentone, fentanyl and atracurium and maintained with halothane, fentanyl and atracurium . For the profilaxy of PONV 1,25mg of droperidol were administrated to every patient during induction. The patch was maintened 16 hours and removed after. Postoperatively, nausea, retching, vomiting, the antiemetic medication and the degree of maximum pain (on VAS) were assessed for 24 hours. Statistical analysis used Chi-squared test and Student-T test for the demographic data.
RESULTS: PONV occurred in 19 patients (76%) in group 1; 5 patients (20%) in group 2 and 8 patients (32%) in group 3 (p1/2<0,05; p1/3<0,05).
The degree of maximum pain, on VAS, was 5,33 in group 1; 4,04 in group 2 and 2,8 in group 3 (p1/2<0,05; p1/3<0,05).
As side effects, 1 patient in group 2, developed dizziness, wich ceased after NICORETTE removal.
DISCUSSION: It is generally accepted that nicotine has emetic properties (3). In our study, application of Nicorette-patch significantly reduced the incidence of PONV after laparoscopic cholecistectomy, sugesting that among the numerous subatnces contained in the cigarette smoke, nicotine may have the most important antiemetic effect.

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S-273

COMPARISON OF ANALGESIC, ANTIEMETIC AND ANTI-HYPERTENSIVE MEDICATIONS IN THE POSTANESTHESIA CARE UNIT FOLLOWING USE OF REMIFENTANIL FOR MONITORED ANESTHESIA CARE VERSUS GENERAL ANESTHESIA

AUTHORS: **A. Kovac**, K. Picillo, C. Elliott
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INTRODUCTION: Remifentanil is an ultra-short acting opioid (half-life=9 min) found useful for General anesthesia (GA) and monitored anesthesia care (MAC). However, a potential drawback of remifentanil's short half-life can be pain, postoperative nausea and vomiting (PONV), and hypertension in the postanesthesia care unit (PACU).
Purpose: To evaluate correct intraoperative remifentanil use and end of surgery analgesic preparation during MAC versus GA in relation to pain control (analgesic use), PONV (antiemetic use), and treatment of hypertension in the PACU.
METHODS: Following IRB exempted protocol, over a 5-month period, 117 adult patients undergoing balanced GA with remifentanil and 50 adult patients undergoing MAC with remifentanil were retrospectively evaluated. In addition to demographic characteristics of age, weight, and ASA physical class, data was collected for intraoperative and PACU administration of antiemetics, analgesics (opioids), and treatment of hypertension. PACU intravenous (IV) administered opioids of fentanyl >100 g or morphine > 2 mg was considered to be a failure of end-of-surgery analgesic preparation.
RESULTS: Demographic variables were similar between groups. The most common MAC procedure was eye (cataracts) surgery, while the most common GA procedures were orthopedic, gynecologic, and general surgery. Significantly more patients having GA vs MAC anesthesia were treated for hypertension (11.96% vs 6%), PONV (14.5% vs 2.0%) and required more analgesic medications (42.7% vs 20.0%), respectively. The incidence of antiemetic use for PONV following GA was 14.5% (17 of 117) which was significantly more than in the MAC group (2%, 1 of 50). Thirty-one of 117 (26.5%) GA patients in the PACU required more than 2 mg of IV morphine or more than 100 g of IV fentanyl. This was also reflected in the fact that significantly more patients in PACU following GA versus MAC were treated for hypertension (11.96% vs 6.0%, respectively). Based on the need for additional analgesic medications in the PACU, end of surgery analgesic pain preparation was considered to be correctly administered for 100% of the remifentanil MAC patients and for 86 of 117 (73.5%) of the remifentanil GA patients.
CONCLUSION: Patients who received intraoperative remifentanil as a primary analgesic component of balanced GA were more likely to require treatment for postoperative pain, PONV and hypertension in the PACU compared to remifentanil MAC patients. It appears that remifentanil GA patients would benefit receiving a long acting analgesic and an antiemetic at the end of the operative procedure before admission to the PACU.

S-274

THE PROPHYLACTIC EFFECT OF DEXAMETHASONE ON POSTOPERATIVE SORE THROAT

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INTRODUCTION:The aim of this study is to evaluate the prophylactic effect of dexamethasone on postoperative sore throat.
METHODS:Two hundreds ten patients undergoing elective surgery under general anesthesia were enrolled in this prospective, randomized, double blined, placebo-controlled study and diveded three groups (n=70 in each three groups). Just after induction of anesthesia, Group 2 and 3 received 10mg and 20mg single dose of dexamethasone intravenously and Group 1 received placebo-normal saline. Postoperative follow-up was accomplished in all patients 2 hours and 24 hours after surgery using VAS.
RESULTS:The incidence and severity of sore throat were lower in Group 3 compared to Group 1.
DISCUSSION:Throat pain is one of most common complications after endotracheal intubation and trachel mucosa damage occuring at the cuff level is thought to an important cause. Dexamethasone is widely used as an antiinflammatory agent in otolaryngology, has strong action of relieving tissue edema and pain. So we hypothesized that dexamethasone is effective to reduce postintubation airway edema and symptoms and found 20mg of dexamethasone intravenous injection could reduce postoperative throat pain.

S-275

THE EFFECTS OF SEDATIVE DOSES OF PROPOFOL OR MIDAZOLAM AND HYPOXIA ON UPPER AIRWAY OBSTRUCTION

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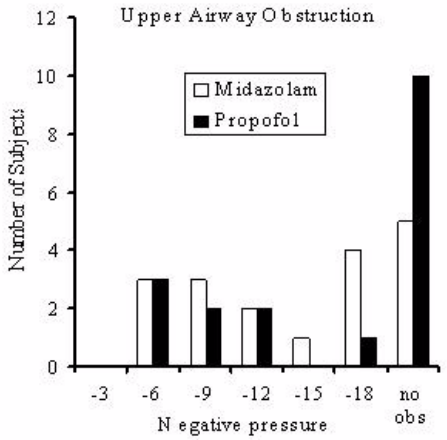
INTRODUCTION: Respiratory compromise and hypoxia is often due to upper airway obstruction (UAO) in sedated patients. We sought to determine if propofol or midazolam produced different degrees of UAO and whether hypoxia or gender influenced drug induced UAO.
METHODS: After IRB approval, informed consent was obtained from healthy adult volunteers. Study design was double blind and randomized. Standard monitors and an IV were used during the study. Dynamic Negative Airway Pressures (DNAP) of 3, 6, 9, 12, 15, and 18 cm H2O were applied as previously described (1) to quantify each individual's baseline propensity for UAO. Then, propofol or midazolam was administered via a computer assisted controlled infusion to the same clinical (Observer's Assessment of Alertness / Sedation Score of 2-3) and EEG (BIS value of 75 +/- 5) endpoints. During sedation DNAP was applied under hyperoxic (ET O2 = 150 mm Hg) and hypoxic (ET O2 = 57 +/- 2 mm Hg) conditions. Sedation was stopped and DNAP repeated 15 and 45 minutes later. UAO criteria included no airflow for 10 seconds or tidal volume <50 ml (measured via pneumotachograph) for 2 consecutive breath efforts. Respiratory inductive plethysmography documented the absence of central apnea. Subjects returned between 7 and 45 days later to repeat the study with the second drug.
RESULTS: Nine of 32 planned subjects (4 F, 5 M) have completed the study to date. With propofol, UAO occurred in 6 subjects during hyperoxia (1 F, 5 M) and in 2 subjects (0 F, 2 M) during hypoxia. With midazolam, UAO occurred in 7 subjects during hyperoxia (2 F, 5 M) and in 6 subjects (3 F, 3 M) during hypoxia. During recovery UAO occurred in 2 subjects (1F, 1M) at 15 minutes and 3 subjects (3 M) at 45 minutes after midazolam. No UAO occurred after stopping propofol sedation. The chart shows values of DNAP causing UAO. Results



presented at the meeting will include data from additionally studied subjects.
DISCUSSION: Knowledge of the propensity for sedative drugs to depress airway and ventilatory function, and of other factors that can influence UAO would help clinicians select and deliver safer sedation in numerous settings. Our preliminary findings suggest that males tend to have more UAO than females. This is similar to data with midazolam sedation from Masuda et al. (2). Our data also suggests that hypoxia might diminish UAO during sedation with propofol but not with midazolam. We also found delayed UAO occurred after midazolam but not propofol.
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S-276

A PRELIMINARY LOOK AT BETA2 ADRENERGIC POLYMORPHISMS AND UTERINE QUIESENCE

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INTRODUCTION: Preterm delivery is defined as delivery of an infant after 20 weeks but prior to 37 weeks gestation. Despite improved antenatal care, the incidence of preterm delivery in the United States increased from 9.5% in 1982 to approximately 11% in 1994.[1] Preterm delivery is associated with a large proportion of perinatal complications and deaths. The mechanisms of the initiation of labor, and the means by which these are jumpstarted in preterm labor, have yet to be fully understood. As well as the upregulation of an active system, labor may also involve the loss of quiescence. The downregulation of pathways that favor uterine quiescence by increasing cAMP formation, would result in a relative dominance of stimulatory receptors that increase IP_3/Ca^{2+} availabilty.[2,3] 2-adrenoreceptor agonists have been used to suppress labor in the preterm situation. This often limited grace period allows time for transfer of the mother or the action of steroids to promote fetal lung maturity. Myometrial dampening in response to agonists suggests that this system may be involved in the maintenance of the continuing pregnancy. There are four common 2 polymorphisms, Thr163Ile results in decreased receptor/G protein coupling. The polymorphisms at positions 16 and 27 alter agonist promoted receptor trafficking. In the 5' lead cistron polymorphism at position 19 leads to alteration in receptor expression. These polymorphisms have been associated with differences in disease severity and outcome, such as asthma and heart failure.[4] Our study looks at whether the presence of these polymorphisms in the pregnant population, perhaps by compromising quiescence, is associated with preterm labor
METHODS: Following IRB approval and written informed consent 200 women with preterm labor and delivery, and 200 women with term labor and delivery will have been recruited to the study. Venous blood is drawn, from which genomic DNA is derived using a standard kit (Puregene). Biotinylated PCR products are generated covering the regions 2-adrenoreceptor gene and its associated lead cistron that include the polymorphisms of interest. These products are genotyped by nucleotide extension in association with luciferase (Pyrosequencer).
RESULTS:

	Polymorphism Frequency	
	Gln27Glu	Thr163Ile
Preterm Delivery n=9	Glu/Glu-5, Glu/Gly-0, Gln/Gln-4	Thr/Thr-9, Thr/Ile-0
Term Delivery n=4	Glu/Glu-2, Glu/Gly-0, Gln/Gln-2	Thr/Thr-4, Thr/Ile-0

DISCUSSION: As yet numbers are insufficient to draw any conclusions, further recruitment and analysis is progressing.
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REGIONAL

S-277

EFFICACY OF CERVICAL EPIDURAL STEROID INJECTIONS IN PATIENTS WITH AXIAL AND RADICULAR PAIN

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INTRODUCTION: Epidural steroid injections (ESI) are commonly used for the treatment of axial and radicular pain of lumbar and cervical origin (1). While the literature is replete with studies that describe the results of ESI for treatment of lumbar spinal disorders, few studies have focused on the role of cervical ESI in non-operative management of neck and arm pain (2,3). The purpose of this study was to evaluate the efficacy of cervical ESI (CESI) in axial and radicular pain of cervical origin, and to determine if different disease processes have different treatment outcomes.
METHODS: Following IRB approval, 136 consecutive patients who received CESI between January and December of 2000 were retrospectively reviewed. From a comprehensive history, physical examination and imaging studies, patients were divided into three groups: axial pain, radicular pain, and combined axial and radicular pain. All patients received CESI with 80 mg of triamcinolone plus 4 ml of preservative free saline. Second and third injections were administered 2 weeks apart. Pain was assessed at the initial consultation and at each subsequent visit utilizing the visual analog scale (VAS). Patients were also evaluated at 2 weeks, 6 months and 12 months after the final injection. Statistical evaluation was done using Kruskal-Wallis test, Friedman's test, and Wilcoxon's signed-rank test.
RESULTS: Of the 136 patients reviewed, 38 patients were excluded secondary to co-morbidity and previous surgery. Two patients were lost to follow up. Five of the remaining 96 patients required surgical intervention during the study period. The remaining 91 patients had: axial pain (n=26), radicular pain (n=19), or combined axial and radicular pain (n=46). There was no difference in the baseline demographic data between the groups. Significant improvement in VAS was noted 2 weeks, 6 months and 12 months after the last injection in each individual group (Table). Some deterioration in axial neck pain was observed over time, but the reduction in VAS score at 12 months remained statistically significant. Improvement in arm pain was more sustained than neck pain, with VAS scores significantly lower for arm versus neck pain after 12 months.
DISCUSSION: The results from the current study show that patients with axial and radicular symptoms respond favorably to CESI. The improvement in neck VAS in patients with combined symptomatology is not as well sustained as for arm pain. We conclude that CESI remains a useful tool in the armamentarium of physicians for management of cervical disorders, and may obviate the need for surgical intervention in a sizeable number of patients.

	Axial Group	Radicular Group	Combined Group	
	Neck VAS	Arm VAS	Neck VAS	Arm VAS
Pre injection	7.35±0.88	5.60±2.49	6.79±1.59	6.56±1.66
2 weeks	3.31±3.12 *	2.35±2.04 *	2.67±2.64 *	2.27±2.72 *
6 months	3.50±2.85 *	2.35±2.19 *	3.38±2.75 *	2.35±2.90 *
12 months	3.81±2.84 *	2.60±2.28 *	4.29±2.74 *,#	2.44±2.86 *

* different from preinjection, $p<0.05$; # different from 2 weeks, $p<0.05$

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S-278

PROSTAGLANDIN D2 AS A MARKER FOR IDENTIFICATION OF CEREBROSPINAL FLUID DURING EPIDURAL ANESTHESIA: AN IN VITRO STUDY

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INTRODUCTION: Reliable identification/exclusion of Cerebrospinal fluid (CSF) is critical to avoid inadvertent subarachnoid injection of local anesthetics during epidural anesthesia. When aspirate from the epidural catheters yield fluid, it could be CSF, local anesthetics, saline or interstitial fluid. Currently, none of the clinical tests used (Thiopental precipitation, pH, glucose, temperature, Speed of flow from the catheter) can reliably differentiate CSF from other substances in all situations. For any test to be valid in the clinical setting, it should be specific, sensitive, non-toxic, quick and easy enough to perform for rapid bedside identification. Prostaglandin D2 synthase (PGDS) in brain is produced in the choroid plexus, leptomeninges, and oligodendrocytes of the central nervous system, and secreted into the CSF. PGDS catalyzes the isomerization of Prostaglandin H2 to Prostaglandin D2 (PGD). PGD accumulates in CSF, where it is shown to be an endogenous sleep-promoting substance (1). Both PGDS and PGD are being tested as immunological markers for the detection of cerebrospinal fluid traces (2). The aim of this study is to determine whether these markers have any predictive value when CSF is DILUTED with local anesthetics, saline and serum.
METHODS: After obtaining IRB approval and patient consent, CSF was obtained from patients and analyzed for PGD. CSF (n=5) samples were diluted with local anesthetic (Bupivacaine), normal saline and serum in the ratios of 1:5 and 1:10. PGD levels in the CSF samples were analyzed with a PGD-Methoxime (MOX) EIA Kit (Cayman Chemicals, MI). This assay is based on the conversion of PGD to a stable derivative, which is analyzed with antiserum specific for PGD-MOX.
RESULTS: Different concentrations of pure PGD-MOX conjugate were analyzed by EIA and a standard curve was derived. PGD levels in CSF and CSF with diluents were determined and the values were extrapolated onto the standard curve. Our results show a well-defined correlation for the presence of PGD in CSF samples. Even at 1:10 dilution of CSF with saline, anesthetic or serum, PGD was strongly detected.
DISCUSSION: PGD was reliably identified in CSF when diluted with local anesthetics, saline and serum. Assay of PGD can evaluate the presence of CSF and may be of great value to the clinician in safe conduct of epidural anesthesia. Though this is not yet available as bedside test, the possibility of development of such test in near future is very likely; as such a test is of great value not only for anesthesiologists but also to ENT and neurosurgical specialists.
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S-279

A COMPARISON OF THE COMPLICATION RATE ASSOCIATED WITH SUPERFICIAL VERSUS DEEP (OR COMBINED) BLOCK FOR CAROTID ENDARTERECTOMY

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INTRODUCTION: Carotid endarterectomy is often performed awake under cervical plexus block using the patient's neurologic status as a monitor of cerebral perfusion, and may offer advantages over general anesthesia (GA). Either superficial (SCPB) or deep (or superficial and deep combined, DCPB) block may be used (1,2). SCPB may be safer than DCPB (3). However, the two blocks have been compared in only two small randomised studies (1,2). The purpose of this study was to conduct a systematic review to assess the reported complication rates associated with the use of each block.
METHODS: A supplemented Medline search yielded 86 relevant publications in each of the following categories: randomised studies of SCPB vs DCPB (2 papers); randomised SCPB vs GA (1 paper); randomised DCPB vs GA (2 papers); non-randomised SCPB vs DCPB (0 papers); non-randomised SCPB vs GA (5 papers); non-randomised DCPB vs GA (21 papers); case series SCPB (11 papers); case series DCPB (35 papers); case reports SCPB (0 papers); case reports DCPB (11 papers). Each paper specified the total number of patients included in the study (the denominator). We defined the complications (numerators) in the following manner. A: any complication which was a potential threat to life arising directly from placement of the block (eg, intravascular, intrathecal injection, overdose, phrenic nerve paralysis); B: number of patients converted to GA; C: any other serious complications (eg, myocardial infarct, angina, stroke, transient ischaemic attack). A was the main study end-point. Data were analysed as previously described (4).
RESULTS: The 86 papers described 3032 SCPB and 7812 DCPB. The incidence of complications in both groups was low. There were 0/3032 cases of serious complications related to the block in SCPB vs 73/7812 with DCPB (odds ratio OR 9.44; P<0.001 ^{2} test; Fig. 1). Conversion to GA was lower with SCPB (18/3032 vs 127/7812; OR 2.74; P<0.001 ^{2} test). Perhaps surprisingly, incidence of cardiac and neurological events was also lower with SCPB (76/3032 vs 326/7812; OR 1.66; P<0.001 ^{2} test).
CONCLUSIONS: If SCPB and DCPB are equally effective (1,2), and if as suggested, the injectate with SCPB enters the deep cervical space (5), then there seems little advantage in performing a deep injection as part of the block. The higher DCPB complication rate is probably related to deep needle placement close to vital structures in the neck.
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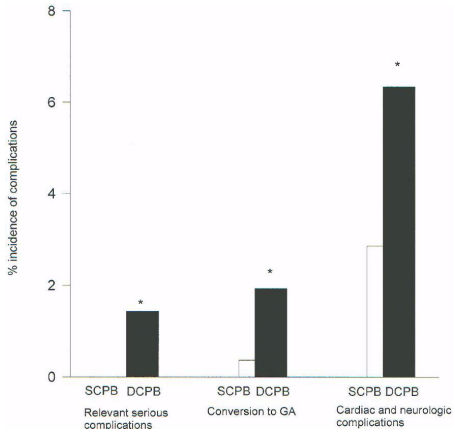

S-280

INTERSCALENE BLOCKS FOR OUTPATIENT SHOULDER SURGERY: A REVIEW OF EXPERIENCE WITH A SINGLE SURGEON IN A COMMUNITY TEACHING HOSPITAL.

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INTRODUCTION: While interscalene blocks (ISB) for shoulder surgery have become routine in many institutions, recent articles on safety and efficacy (1,2) have led to questions about the technique. To decrease the number of variables, and for surgical consistency, we retrospectively reviewed the charts of all outpatients receiving ISB and having shoulder surgery, by a single surgeon, over a 3-year period.
METHODS: The medical records of 93 consecutive outpatients undergoing shoulder surgery by a single surgeon were reviewed. The office records of each patient were also reviewed, as well as an interview with the surgeon, for long- term follow-up. All ISB were performed with the use of a nerve stimulator and a standard insulated blunt needle. A 1:1 mixture of alkalinized 2% lidocaine with epinephrine and either 0.5% or 0.75% bupivacaine was utilized. Blocks were performed by either residents under the direct supervision of, or personally by, attending anesthesiologists. Adjunctive general anesthesia (GA) was utilized in all cases. The need for immediate parenteral narcotics in PACU, and a pain score (PS) > 3 in PACU or ASU was used to indicate an inadequate block.
RESULTS: Of 93 scheduled outpatients, 87 patients received interscalene blocks. 8 patients met the criteria for inadequate block, for a success rate of 91%. Only 2 patients required admission for pain control. There were 3 other patients requiring admission, 1 for nausea, and 2 for pulmonary/cardiac monitoring. 21/87 outpatients had medication interventions for nausea in PACU (24%), and 22/82 (5 patients admitted) in 2nd stage recovery (27%). Only 5 patients in ASU received medication for pain, and all were oral tablets. 84 of 87 scheduled outpatients had no problems related to the ISB on their post-op report by the surgeon, with intact neurovascular status. 2 patients had residual numbness that resolved by their next visit (3 weeks later). One patient had neck pain, which resolved with a trigger point injection. Other demographic and data results are in the table.
DISCUSSION: Our experience with ISB, in contrast to recent reports (1,2) has been uniformly well accepted, with low morbidity, and excellent results. One factor not usually examined in reports on ISB, is that of the surgeon's experience. By analyzing data from a single surgeon's practice, we eliminate a potentially confounding variable. We conclude that we have found ISB to be effective and safe in this setting, and without sequelae on long term follow up. It is our contention that surgical experience, and surgeon acceptance of ISB, are important factors in determining whether or not to proceed with ISB for shoulder surgery.
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Variable	ISB
Height	67.6 ± 3.8
Weight	183.5 ± 36.1
Age	49.3 ± 14.4
Procedure Duration	62.6 ± 28.2
PACU Duration	71.8 ± 30.7
ASU Duration	129.7 ± 68.1

S-281

PERIBULBAR BLOCK FOR CATARACT SURGERY

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INTRODUCTION: Regional anaesthesia is the technique of choice for the majority of patients undergoing cataract surgery. The purpose of this study was to compare peribulbar block with ropivacaine 1% and bupivacaine 0'5% + lignocaine 2%.
METHODS: Fifty patients (60 – 85 years old) were enrolled and assigned randomly to two group. The group 1 (25 patients) received 8 ml of ropivacaine 1% + hialuronidase 150 IE and the group 2 (25 patients), 8 ml a mixture of bupivacaine 0'5% and lignocaine 2% + hialuronidase 150 IE.
The following variables were evaluated:
1. Haemoynamic parameters: systolic and diastolic blood preasures and heart rate.
2. Surgical conditions: very good, good, acceptable, bad and very bad.
3. Time of surgery.
4. Postoperative analgesia.
Data were analysed using Wilcoxon and Fisher tests.
RESULTS: No differences were found in haemodynamic variables, surgical conditions, time of surgery and postoperative analgesia between the two group.
DISCUSSION: Ropivacaine 1% is an effective alternative to bupivacaine 0'5% for peribulbar anaesthesia, when combined with lignocaine and hyaluronidase.

S-282

EXPERIENCE REDUCES VARIABILITY IN DETERMINATION OF POINT OF NEEDLE INSERTION IN PERIPHERAL NERVE BLOCKS

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INTRODUCTION: Accurate identification of surface landmarks is essential for successful performance of peripheral nerve blocks.[1] We hypothesized that there is a learning curve to successfully identifying skin surface markings, which is vital in accurately identifying the point of needle insertion. The variability between experienced and inexperienced practitioners has not previously been studied.
METHOD: A male volunteer (90 kg, 178 cm, Body Mass Index=28) was positioned in the left lateral knee-chest position. A large clear adhesive dressing was placed over the volunteer's back and buttock area. All anesthesia residents and attendings in the OR on a random day were giving a textbook description and photograph of how to perform a posterior lumbar plexus block.[2] They were asked to identify the point of needle insertion by identifying the landmarks as described in the textbook. X and Y coordinates were measured in millimeters for the point of needle insertion. All skin markings were erased from the dressing after each attempt. In addition the level of experience in performing regional anesthesia was ascertained for each anesthesiologist. Those who had performed more than 30 lumbar plexus blocks in the past year were classified as experienced. The data were analyzed using unpaired t tests with Welch's correction and the F test for equality of variance.
RESULTS: 37 anesthetists (16 experienced, 21 inexperienced) took part in the study. The mean (SD) [Range] values for the X, Y coordinates in millimeters were 81 (12)[62-108], 65 (12)[46-86] and 92 (24)[49-150], 63 (26)[0-131] in the experienced and inexperienced groups respectively. While the differences in the mean values approached significance (p=0.07) the variance between the 2 groups differed significantly (p<0.01).
DISCUSSION: There was considerably more variability in the point of needle insertion in the inexperienced group (Figure 1). This may help explain the difficulty experience by some anesthesiologists in performing peripheral nerve blocks. We conclude that with increasing experience there is reduced variability in determining point of needle insertion using skin landmarks.
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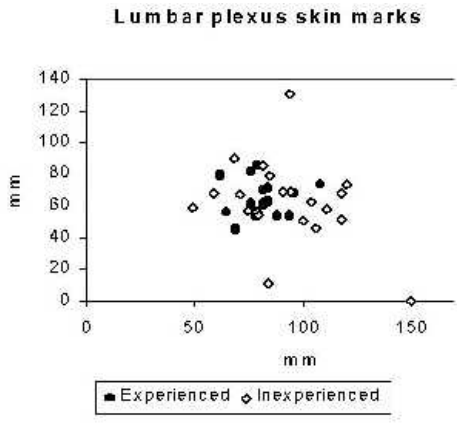

S-283

TUMESCENT LOCAL ANESTHESIA

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Tumescent local anesthetic (TLA) technique is a very useful way of infiltration anesthesia. It was first described in December 1993 by a plastic surgeon for use in Liposuction and other cosmetic procedures to reduce blood loss , and uses higher doses of lignocaine per kilogram body weight. In this study TLA has been tested in adjunct to other forms of anesthesia and as a sole form of anesthesia to study tolerance to the combination of drugs used, subjective assessment of blood loss and to assess compatibility with other forms of anesthesia.
METHODS: In a period between, Sep.1998 to March .2000, diverse cases which presented for surgery, in which normally blood loss is anticipated were chosen for trial with this technique.
The compositon of the fluid that was used for injection was as follows
ØNormal saline /
Ø Ringer lactate - 500ml
Ø Lignocaine 2% - 25ml
Ø Adrenaline - 1ml (1:1000)
Ø 7.5% NaHCO3 - 10ml
Ø Hyaluronidase - 1500 iu(1 vial)
The volume of injection used was 10-15 ml/kg body weight using the multiple injection technique. The tissue contact time was 10-15 minutes. 420 cases with diverse surgical procedures, emergency and elective, adult and pediatric were studied. They included Post burns contracture neck, Soft tissue swellings of the neck, Hemangiomas, Craniotomy, laminectomy, Incisional and recurrent inguinal hernias and Breast lesions. Informed consent was obtained for all patients
RESULTS: All patients tolerated the injection well. It could be combined safely with other forms of anesthesia.Subjective assessment revealed superior operating field in terms of clarity of tissue plane dissection, scanty blood loss, reduced intra-operative and post operative analgesic anesthetic requirements. No adverse outcome with reference to its constituents or wound healing was recorded.
DISCUSSION: Tumescent local anesthesia is a technique which deserves further investigation as it appears to offer advantages such as conservation of blood, avoiding of transfusion hazards and decreasing operating time. It can be used alone or as an adjunct to any form of anesthesia with very few contra-indications.
Literature on this technique is seen mainly pertaining to cosmetic plastic surgery and it is the endeavor of the author to evoke debate and consensus on the use of this technique in routine surgical practice

S-284

EFFECT OF SPINAL ANESTHESIA ON PROCESSED EEG

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BACKGROUND: Centroneuraxis blockade has been known to have a sedative effect (1) thereby decreasing the need for inhalational and intravenous anesthetic agents (2). The BIS monitor has been used previously to quantify sedation during spinal anesthesia (3). In the present study, quantification of sedation following spinal anesthesia was investigated using a relatively new and more sophisticated analysis of processed EEG (Patient State Analyzer, PSA 4000 monitor).
METHODS: Eighteen unsedated patients were scheduled to undergo urologic and orthopedic surgeries under spinal anesthesia. All received 1.5 ml (11.25 mg) of hyperbaric bupivacaine 0.75% intrathecally. Monitoring included a 2-lead electrocardiogram, pulse-oximetry, and non-invasive blood pressure (NIBP). A 4-lead EEG tracing with two reference leads (PSA 4000) and Observer's Assessment of Alertness/Sedation Scale (OAAS) score were obtained to evaluate the depth of sedation. Baseline recordings were obtained for a period of 3 min prior to surgery and every 2 minutes during the surgical procedure. Data are expressed as mean±SD and were evaluated by Wilcoxon signed rank test for non-parametric data.
RESULTS: The patients were 69±16 years of age. Surgical procedures lasted 65±34 min. Sedation scores measured by PSA decreased from previously 98±2 to 76±10 at 33±15 min into the spinal anesthetic ($p<0.05$). OAAS decreased from formerly 5 to 4±1 at the time of the lowest PSA scores (p=ns). Following spinal anesthesia to a dermatomal level of $T_{8\pm2}$, the systolic/diastolic BP decreased from baseline 143±20/82±11 mmHg to 104±11/62±10 mmHg at the time of the lowest PSA score ($p<0.05$).
DISCUSSION: In this elderly patient population, spinal anesthesia induced changes in the processed EEG with reduction in PSA scores without affecting substantially OAAS. The reduction in systolic and diastolic blood pressures following spinal anesthesia was within the range of cerebral autoregulation. Most likely, the reduction in afferent input to the CNS due to spinal anaesthesia contributed to the reduction in the PSA scores. These results indicate that spinal anesthesia reduces the need for sedative agents in an elderly patient population.
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S-285

SPINAL CHLOROPROCAINE

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INTRODUCTION: The choice of local anesthetic agent for spinal anesthesia in the ambulatory surgery patient remains a problem. Lidocaine is plagued by the frequent symptoms of transient radicular irritation (TRI). Bupivacaine often produces an excessively long block, even in markedly reduced doses. Chloroprocaine is avoided because of reports in the 1980s of neurotoxicity after unintentional intrathecal injection of large volumes of preservative-containing solutions intended for the epidural space (1). However, a preservative-free formulation of 2-chloroprocaine (Nesacaine-MPF, AstraZeneca LLC) is now available. When first introduced in 1951, Foldes described the successful use of preservative-free chloroprocaine for spinal anesthesia in 214 patients (2). As chloroprocaine is known to be of shorter duration than lidocaine, we investigate the dose-response effects of the new preservative-free formulation of 2-chloroprocaine in a human volunteer model, as a possible alternative for outpatient spinal anesthesia.
METHODS: This randomized, blinded study is designed to initially investigate 2 doses of hyperbaric 2-chloroprocaine (45 and 60 mg), with or without the addition of 0.2 mg epinephrine, using a previously described cross-over methodology (pinprick anesthesia, tolerance to transcutaneous nerve stimulation and thigh tourniquet, and motor strength assessments) in 12 volunteers (3). If the duration or density of anesthesia is not clinically suitable, an additional 6 volunteers will receive 75 mg. 2-chloroprocaine, with or without epinephrine.
RESULTS: As this investigation is ongoing and still blinded, the preliminary combined results from the first 14 spinal anesthetics, in which volunteers received either 45 or 60 mg of 2-chloroprocaine (with or without 0.2 mg epinephrine), are presented. Successful spinal anesthesia was attained in all subjects, with complete return of neurologic function within 200 minutes of injection. No signs or symptoms of neurotoxicity have been observed. No symptoms of TRI have been reported. Peak block height averaged T4 (range C5 – T11, Figure 1). Regression of 2 segments and to the L1 dermatome averaged 49 ± 11 (mean ± SD)(range: 35 – 80) minutes, and 91 ± 24 (range: 50 – 150) minutes, respectively. The thigh tourniquet was tolerated 63 ± 21 (range: 28 - 107) minutes. Full lower extremity muscle strength returns at 110 ± 35 (range: 70 - 190) minutes. Time to complete sensory regression (and the ability to ambulate) averages 142 ± 30 (range: 100 - 200) minutes.
DISCUSSION: Initial results suggest that hyperbaric spinal 2-chloroprocaine may have an anesthetic profile appropriate for use in the surgical outpatient. As some of the spinal anesthetics attained high dermatome levels (C5), it will not be necessary to study the previously planned higher dose (75 mg), but the investigation of a lower dose (30 mg) is warranted.
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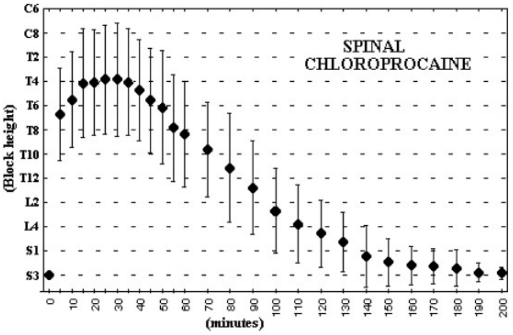

S-286

BLOOD VOLUME INCREASE BY HYPERTONIC SALINE ADMINISTRATION PREVENTS SYSTEMIC HYPOTENSION AFTER SPINAL ANESTHESIA

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INTRODUCTION: Indications for hypertonic NaCl infusion for maintenance of arterial hypotension (AH) after subarachnoid anesthesia (SA) are still being investigated.[1,2] We examined the effect of NaCl 10% on blood volume and resultant arterial blood pressure changes in clinical conditions.
MATERIALS AND METHODS: In HS group (n=30) NaCl 10%, 1 ml/kg/bw was administered before and after SA. The NS group (n=32) was given NaCl 0.9 % 5-7 ml/kg/bw. Administration of NS continued up to a total of 1500 ml. AH was defined as a decrease in MAP of more than 30%. Blood pressures were measured for an hour in 5 min. intervals. Changes in blood volume were determined according to unicompartmental model.[3] Other parameters monitored included serum Na, K, Hg, time for prehydration and mean corpuscular volume (MCV) of RBC. Treatment groups were compared using repeated measures mixed models, which included main effects for baseline values and treatment group and a cubic polynomial for time. Wilcoxon rank-sum test was utilized for blood volume, retained volume, MCV, Na, and Hg. Results are presented as medians and 95% confidence intervals (95%CI) with significance level 0.05.
RESULTS: Treatment group was not a significant predictor of AH, MAP, SBP, or DBP. The NS group had significantly larger increases in blood volume during surgery than did the HS group (0.83 L vs. 0.33 L, 95% CI 0.08 to 0.71, P=0.011). Retained volume of HS was higher in the HS group than in the NS group (217% vs. 55%, P=0.002). In the NS group, MCV increased significantly during surgery (0.8 fL, 95% CI 0.1 to 1.0, P=0.008). A transient increase of serum Na was observed after HS (7.5 mmol/L, 95% CI 4.0 to 11.0 mmol/L, P<0.001). Hemodilution was observed in the HS group at 10 min. post SA (Hg, NS 14.2 g/dL, HS 13.2 g/dL, P<0.001). At the end of the observation period, treatment groups did not differ significantly on Na or Hg. Time for prehydration was significantly lower in HS group than in the NS group (5.0 vs. 25.5 min, 95% CI 19 to 23 min, P<0.001).
CONCLUSION: Our results indicate that a single bolus dose of NaCl 10% administered preoperatively might be a safe alternative to a normoosmolar crystalloid. HS was not significantly less effective than much larger volumes of NS in maintaining arterial blood pressure. HS infusion requires significantly less time for prehydration. Although the clinical relevance of these results in patients with different co-morbidities should be established in future studies, application of HS should be considered as a practical option to the standard prehydration practices.
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S-287

CONTINUOUS SPINAL ANESTHESIA WITH TWO DIFFERENT CATHETERS IN ELDERLY

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INTRODUCTION:The purpose of this retrospective study was to compare the technical problems in elderly patients after CSA using catheter in side the needle (CIN) and the catheter over the needle (CON) techniques.
MATERIAL AND METHOD: Forty elderly patients (ASA I-II) ranging from 80-92 yrs old and undergoing hemiarthroplasty surgery were assigned to CIN (n:20) and CON (n:20) group. Technical difficulties of both techniques , side-effects and complications were recorded.
RESULTS: In CON group; inadequate anesthesia, difficulty threating catheter and poor cerebro-spinal fluid (CSF) flow was seen in 1,2, and 3 patients, respectively.So that; technical problems occured more frequent in CON group ($p< 0.05$) but none in CIN group. No neurologic sequelae and PDPH occured in both groups. The catheter functions and postoperative results were similar with the two catheters.
CONCLUSION: CSA using catheter in side the needle technically more easy than using the catheter over the needle and also there are no differency with side- effects and complications (PDPH etc.) between two different catheters in the elderly.
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S-288

CONTINUOUS SPINAL ANESTHESIA WITH HYPERBARIC BUPIVACAINE 3MG+ FENTANYL 10µG FOR HEMI-ARTHROPLASTY IN THE ELDERLY

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INTRODUCTION: Three mg of hyperbaric bupivacaine + 10 µg fentanyl produces a reliable spinal anesthesia(1,2). We hypothetized that continuous spinal anesthesia with same dose agents will allow hemiarthroplasty surgery in the elderly.
MATERIAL AND METHOD: Thirty ASA II-III patients,all older than 85 yr who underwent hemiarthtroplasty were randomly assigned to receive either 5 mg hyperbaric bupivacaine (Group B)(n:15) or 3 mg hyperbaric bupivacaine + 10 µg fentanyl (Group BF)(n:15). We used " catheter over needle continuos spinal anesthesia technique" for all cases. The sensory level was assesed by the pinprick test. To maintain mean arterial pressure within %25 of initial value, incremental doses of ephedrine were given iv.
R**ESULTS:** Twelve patients (80.0%) in Group B and one patient (6.6%) in GroupBF required fractional reinjection of local anesthetic via spinal catheter($p<0.001$). More patients in the Group B(13 vs 2)(86.6% vs 13.3%)($p<0.001$) required ephedrine. All patients in both groups developed a level of anesthesia not higher than T6.
CONCLUSION: Three mg of hyperbaric bupivacaine + 10 µg fentanyl produces a reliable continuous spinal anesthesia for hemiarthropasty in elderly.
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S-289

INFLUENCE OF THE PATIENTS POSITION DURING INDUCTION OF COMBINED SPINAL-EPIDURAL ANESTHESIA FOR TOTAL KNEE ARTROPLASTY

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INTRODUCTION: We wish to compare the anesthetic protocol for total knee artroplasty done by combined spinal-epidural anesthesia just changing the patient position while puncture.
METHODS: 40 patients of both sexes over 60 years were evaluated during the intervention. All of them were randomly allocated in two groups: group A (n=20) and group B(n=20). The patients in group A were sat when they had the puncture and the insertion of the epidural catheter. Patients in group B went to the same anesthetic procidia, in lateral decubitus on the side of the knee that was going to be operated. All the patients, 20 minutes before the surgery were administered 500cc of lactated Ringers's solution. All of them were administered bupivacaíne 0,5%, 10 mg. + fentanyl 20 g by spinal application, leaving the epidural catheter for post surgery pain control. The cardiac frequency, arterial pressure, oxygen saturation, need for efedrin administration, vomit sensation, vomits, sweat, if there was any punction by the catether of blood vessels were evaluated. It was also evaluated patient's sensation of comfort or disconfort before starting surgery.
RESULTS:

Symptom	Group A (Sitting position)	Group B (Lateral decubitus)
Hypotension	54%	38%
Sweating and vomiting sensation	47%	32%[a]
Efedrin needed for hypotension control	35mg +/-8mg	20mg+/-5mg
Duration of hypotension	7min+/-3	4min+/-2
Vessels punctured	6[b]	5[b]

a. Also better tolerated. b. In three of the cases reported in group A, the catheter could not be left due to spinal blockade in the 5 cases of group B even if the spinal blockade appeared the correct placement of the epidural catheter could be done.
DISCUSSION: In the Combined Spinal-Epidural (CSE) anesthetic technique, the lateral decubitus position presents less incidence and duration of hypotension, higher tolerance of vomiting sensation and less failure of the technique while puncturing a vessel with the catheter.

S-290

THE EFFECTS OF EPIDURAL ANESTHESIA WITH 0.25 % BUPIVACAINE ON THE NEUROENDOCRINE RESPONSE TO MAJOR ABDOMINAL SURGERY

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INTRODUCTION: The simultaneous administration of epidural local anesthetics with general anesthetics is frequently used in major abdominal surgery (1,2).To determine the ability of epidural anesthesia with 0.25 % bupivacaine to attenuate the surgical stress response.
METHODS: Thirty ASA I-II patients undergoing major abdominal surgery were randomized to receive either general anesthesia (n = 15) or combined regional/general anesthesia with intraoperative epidural catheter anesthesia using bupivacaine to the T10 dermatome level (n = 15). The stress response was quantitated by blinded measurement of baseline and postoperative (0, 2, 6, 24 hours) serum cortisol, glucose, interleukin (IL)-6, C-reactive protein (CRP), malonildialdehide (MDA), nitric oxyde (NO), super oxyde dismutase (SOD).
RESULTS: IL-6 and NO levels (table I) were less predictable and undetectable in the Group G-Epi ($p<0.05$). There was no difference in any of the stress response indices between those patients receiving patient-controlled or epidural catheter anesthesia.
Discussion:The neuroendocrine response to major surgical stress is propagated normally despite epidural blockade.

nitric oxyde (pg/ml) and interleukin levels(mikromol/L)				
Periods	0. hour	2. hour	6. hour	24. hour
Group G: IL-6	15.0±3.4	46.9±8.3	57.0±8.0	46.1±8.2
Group G-Epi: NO	17.4±3.5	35.3±7.2	45.2±5.6	35.5±4.8
Group G: NO	22.95±3	31±3	34.3±4	29.95±4
Group G-Epi: NO	21. 5±4	33.2±3	30.1±2	27.2±3

REFFERENCES:
1) Use of epidural anesthesia and spontaneous ventilation during transabdominal colon and rectal procedures in selected high-risk patient groups. Dis Colon Rectum 1997 ; 40: 339-43.
2) Influence of postoperative epidural analgesia with bupivacaine on intestinal motility, transit time, and anastomotic healing. World J Surg 2002; 26: 303-6.

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THE INFLUENCE OF EPIDURAL ANESTHESIA ON THE INTRAVENOUS INDUCTION WITH PROPOFOL

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INTRODUCTION: Epidural anesthesia has been reported to the decrease requirements for general anesthesia (1), suggesting the general anesthetic effects of epidural anesthesia. Therefore, epidural anesthesia possibly modulates the intravenous induction with propofol. Epidural anesthesia and propofol intravenous anesthesia have circulatory interactions, which may affect the circulatory changes during the anesthesia induction. There is little information about the influence of epidural anesthesia on the propofol induction using target controlled infusion (TCI). This study was designed to assess the induction time and circulatory changes on the intravenous induction with propofol following the epidural anesthesia.
METHODS: After obtaining IRB approval, twenty ASA status I-II patients received epidural and general anesthesia. Ten patients (Group E) were received 3mg/kg of 1.5% lidocaine and another patients (Group C) received the same volume of saline via thoracic epidural catheter. All patients were induced general anesthesia with propofol using TCI 15minutes after epidural injection. The target concentration of propofol was set on 3g/ml. Loss of consciousness (LOC) was assessed the time to drop a holding syringe. Bispectral Index (BIS) scores and mean arterial pressure (MAP) and heart rate (HR) were measured after induction following baseline measurement with the interval of 5 seconds, 2 minutes and 2minutes, respectively. Statistical differences were analyzed by Mann-Whitney U-tests or non-paired t tests or one-factor ANOVA with Scheffe's S procedure. P value less than 0.05 was considered as statistically significant.
RESULTS: There were no differences in demographic data between groups. The time until LOC assessed by dropping the syringe was significantly shorter in Group E compared with group C (mean 84s ± 21 vs. mean 143s ± 61). BIS scores in the group E tended to decrease more rapidly than that in the group C. The decreases in MAP were significantly greater in the group E during induction of general anesthesia. MAP and HR increased significantly in the group C after tracheal intubation, but did not in the group E (table).
DISCUSSION: Epidural anesthesia shortens the time until LOC with propofol and diminishes MBP and HR changes caused by tracheal intubation. The results suggest that the epidural anesthesia combined with the propofol anesthesia may contribute the rapid induction with little circulatory changes caused by tracheal intubation.
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(1) Anesthesiology 1999; 91:1687-92

Table: circulatory changes following induction with propofol
(*P<0.05 vs. baseline, †P<0.05 vs. 6min)

	baseline	4min	6min	post intubation
MBP (mmHg)				
Group E	90.6±14	62.9±11*	57.3±9*	77.4±18
Group C	98.3±13	78.1±8	75.1±8	127.5±19†
HR (/min)				
Group E	73.2±16	61.1±11	60.9±11	74.8±8
Group C	73.8±11	70.0±10	69.8±11	91.4±13†

Mean ± SD

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AN ANALYSIS OF CLINICAL OUTCOMES WITH EPIDURAL ANALGESIA IN ADULT POST-SURGICAL PATIENTS

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INTRODUCTION: While effectiveness and safety of postoperative epidural analgesia have been demonstrated with prospective and retrospective reviews,[1] few studies explore the influence of practice pattern on clinical outcome. Here, we present an analysis of epidural analgesia-related outcomes to examine how practice variables (e.g., catheter placement, combinations of epidural solutions) affect pain and adverse effects.
METHODS: We tracked analgesia-related outcomes in 980 consecutive patients receiving epidural infusions for postoperative pain control over 18 months. Information was collected on pain diagnosis, surgical service, type of anesthesia, catheter level, and epidural solution. Serial measurements of pain severity, sedation, nausea/vomiting (N/V), pruritis, motor impairment, urinary retention, and respiratory depression were recorded for duration of therapy. Data were analyzed using descriptive, parametric and nonparametric and correlation statistics, and recursive partitioning.
RESULTS: Table 1 shows the summary statistics for the sample and the most common epidural solution combinations. No differences in severity of adverse effects (sedation, N/V, pruritis, motor impairment) were found by epidural solution in the PACU. Increased severity of nausea and vomiting occurred with solution BH compared to BF ($p<0.01$) and PB ($p<0.05$) on postoperative day (POD) 1. Pruritis was worse with BF compared to FB ($p<0.05$) and PB ($p<0.01$), and BH compared to PB ($p<0.01$) on POD 2. The incidence of respiratory depression, rate <10/min, for the entire sample was 0.5% in the PACU, 0.1% on day 1 and 0.2% on POD 2, limiting the ability to detect meaningful differences by epidural solution. Mild local anesthetic side effects (e.g., metallic taste, tinnitus) were observed in 0.4% of patients on POD 1 and 0.3% on POD 2. Higher catheter level and younger age were significant predictors of less pain on day 1 ($p<0.01$), but catheter level and increase infusion rate accounted for lower pain scores on day 2 ($p<0.01$). Recursive partitioning confirmed that adequacy of pain management in the PACU was the principal determinant of pain on POD 1. Overall, rates of infection and new neurological deficits (e.g., weakness, numbness) were 0.2% and headache 0.6%.
DISCUSSION: Adequacy of pain management in the PACU, age, and catheter site predict postoperative pain levels, whereas epidural solution influences the occurrence of side effects. Practice pattern variation does affect clinical outcomes for patients receiving continuous postoperative epidural analgesia. Studies with larger numbers of subjects may reveal measurable differences in other adverse effects with epidural solutions.
REFERENCES:
[1] Wheeler M, et al.: J of Pain, 3(3):159-180, 2002.

Key: FB - Fentanyl 4 mcg/mL + Bupivacaine 0.0625%; BF - Fentanyl 4 mcg/mL + Bupivacaine 0.125%; BH - Bupivacaine 0.125% + Hydromorphone 15 mcg/mL; PB - Bupivacaine 0.1%

Age (yrs)	Gender (M/F)	Weight (Kg)	Average Pain Level (0-10)	Surgical Service*		Epidural Solution in PACU*		Catheter Level	
				Service	n	Solution	n	Level	n
56.5 ±17.4	489/ 491	90.2 ±32	PACU 2.2±3.4 n=965 POD 1 1.9±2.6; n=890 POD 2 1.2±1.9; n=679	Orthopaedics General Vascular GYN/OB Cardiothoracic Urology	374 299 109 86 69 33	FB BF BH PB	137 566 99 35	T1-T8 T8-L1 L1-L5	169 274 499

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OUTCOMES AFTER ACL RECONSTRUCTION: THE EFFECT OF FEMORAL NERVE BLOCK ANALGESIA

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INTRODUCTION: We are studying the influence of nerve block pain management on outcomes after outpatient anterior cruciate ligament (ACL) reconstruction. Our hypothesis is that patients undergoing nerve block analgesia (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 (from anesthesia) and extent of reported pain, and to determine whether the use of nerve block analgesia is associated with impairment of quadriceps femoris torque output. Comparisons were performed to determine the better dosing strategy for these patients of the following 3 treatment groups: (i) single-shot femoral nerve block and nerve sheath infusion with levo-bupivacaine, (ii) single-shot block with levo-bupivacaine and infusion with saline, and (iii) single-shot sham block and infusion with saline.
METHODS: Consented patients (n=62) undergoing ACL reconstruction received conventional spinal anesthesia and were randomized to receive one of the 3 nerve block treatments. Patient-reported recovery outcomes throughout the first week after surgery were compared across treatment groups using validated health status measures suitable for daily assessment (Verbal Pain Score, SF-8, and the Quality of Recovery [QoR-40] Score [1]). One and 3 weeks after surgery, goniometry with electromyography (EMG) data were collected to test postoperative range of motion in extension, and to determine quadriceps femoris torque output. Assessments at 3, 7, and 12 weeks were performed with 2 validated patient-reported outcome measures (SF-36, Knee Outcome Survey).
RESULTS: Verbal pain scores with activity, QoR-40, and SF-8 physical component summary scores were significantly different between treatment groups on POD#4. At 12 weeks, there were significant differences between groups with respect to the SF-36 physical component summary and the Knee Outcome Survey Sports Activity Scale. There were no significant differences with respect to cumulative opioid requirements during the first 4 postoperative days, any other verbal pain scores during the first 3 weeks, or other measurable physical function outcomes (by self-report or in the physical therapy laboratory).
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.
REFERENCES:
[1]BJA 84:11-15, 2000
[2]Rheum Dis Clin North Am 25:283-298, 1999.

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Self-Reported Outcomes after ACL Reconstruction Based On Nerve Block Treatment Group

Treatment Group	*POD#4 VPS with Movement*	*POD#4 QoR40 Total Score*	*POD#4 SF-8 PCS*	*Wk#12 SF36 PCS*	*Wk#12 KOS SAS*
A	3.0	176	28	41	43
B	4.0	183	34	48	59
C	2.0	189	37	49	74
Sample Size	n=58	n=55	n=57	n=38	n=26
P value	0.015	0.032	0.004	0.019	0.016

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