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Supplement to

ANESTHESIA & ANALGESIA®

IARS

Abstracts of Posters Presented at the 81st Clinical and Scientific Congress of the International Anesthesia Research Society

Orlando, Florida

March 23–27, 2007

This Supplement will Appear Online Only

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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

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Abstracts of Posters Presented at the International Anesthesia Research Society 81st Clinical and Scientific Congress Orlando, Florida March 23-27, 2007

IARS 81st Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Ambulatory

(S-1) Stierer, T.L., Saturday 10:15
(S-2) Sweitzer, B., Saturday 10:15
(S-3) Goy, R.W., Saturday 10:15
(S-4) Reuben, S.S., Saturday 10:15
(S-6) Kim, J.T., Saturday 10:15
(S-7) Ogunnaike, B.O., Saturday 10:15
(S-8) Spatz, R., Saturday 10:15

Bleeding

(S-9) Camporesi, E.M., Saturday 10:15
(S-10) Lee, C.C., Saturday 10:15
(S-11) D'Alonzo, R., Saturday 10:15
(S-12) Nobari, M.M., Saturday 10:15
(S-13) Taketomi, T., Saturday 10:15
(S-14) Pivalizza, E.G., Saturday 10:15
(S-15) Dote, K., Saturday 10:15
(S-16) Witte, B.F., Saturday 10:15

Cardiothoracic & Vascular - Basic Science

(S-17) Shirozu, K., Saturday 1:00
(S-18) Laurito, C.E., Saturday 1:00
(S-19) Tse, J., Saturday 1:00
(S-20) Gillmann, H., Saturday 1:00
(S-21) Mizuno, J., Saturday 1:00
(S-22) Hirsh, R.A., Saturday 1:00
(S-23) Swintek, A.U., Saturday 1:00
(S-24) Strum, D.P., Saturday 1:00
(S-25) Frenzel, T., Saturday 1:00
(S-26) Chao, W., Saturday 1:00
(S-27) Pagel, P.S., Saturday 1:00
(S-28) Hahnenkamp, A., Saturday 1:00
(S-29) Cruchley, P.M., Saturday 1:00
(S-30) Merkel, M., Saturday 1:00
(S-31) Hagiwara, S., Saturday 1:00
(S-32) Okusa, C., Saturday 1:00
(S-33) Frenzel, T., Saturday 1:00
(S-34) Göbel, U.M., Saturday 1:00
(S-35) Liu, Y., Saturday 1:00
(S-36) Kaczmarek, D., Saturday 1:00
(S-37) McEvoy, M.D., Saturday 1:00
(S-38) Mizuno, J., Saturday 1:00
(S-39) Monreal, G., Saturday 1:00
(S-40) Lanckohr, C., Saturday 1:00

Cardiothoracic & Vascular - Clinical

(S-41) Cooper, L., Sunday 8:00
(S-42) Dejonckheere, M., Sunday 8:00
(S-43) Souissi, R., Sunday 8:00
(S-44) Vigoda, M., Sunday 8:00
(S-45) Howard-Alpe, G.M., Sunday 8:00
(S-46) Olivier, J., Sunday 8:00
(S-47) Vigoda, M., Sunday 8:00
(S-48) Rheaume, J., Sunday 8:00
(S-49) Kakinohana, M., Sunday 8:00
(S-50) Murphy, G.S., Sunday 8:00
(S-51) Hemmerling, T.M., Sunday 8:00
(S-52) Feinleib, J.L., Sunday 8:00
(S-53) Nguyen, P.B., Sunday 8:00
(S-54) Insler, S.R., Sunday 8:00
(S-55) Reich, N.T., Sunday 8:00

Critical Care Medicine & Trauma

(S-57) Enohumah, K.O., Sunday 3:00
(S-58) Enohumah, K.O., Sunday 3:00
(S-59) Patel, S., Sunday 3:00
(S-60) Nunnally, M., Sunday 3:00
(S-61) Achari, R., Sunday 3:00
(S-62) D'souza, G., Sunday 3:00
(S-63) Souissi, R., Sunday 3:00
(S-64) Arezki, F., Sunday 3:00
(S-65) Nguyen, H., Sunday 3:00
(S-66) Larmann, J., Sunday 3:00
(S-67) Pentyala, S., Sunday 3:00
(S-68) Souissi, R., Sunday 3:00
(S-69) Asakura, Y., Sunday 3:00
(S-70) O'Hara, J.F., Sunday 3:00
(S-71) Terao, Y., Sunday 3:00
(S-72) Batchinsky, A.I., Sunday 3:00

Economics; Education and Patient Safety

(S-73) Strum, D.P., Monday 10:15
(S-74) Chelly, J.E., Monday 10:15
(S-75) Chelly, J.E., Monday 10:15
(S-76) Anannab, K., Monday 10:15
(S-77) Roskoph, J.A., Monday 10:15
(S-78) Cobos II, F.V., Monday 10:15
(S-79) MacDougall, P., Monday 10:15
(S-80) Holt, N., Monday 10:15
(S-81) Powell, T.E., Monday 8:00
(S-82) Silverman, R.B., Monday 8:00
(S-83) Barach, P., Monday 8:00
(S-84) Malik, A.M., Monday 8:00
(S-85) Malik, A.M., Monday 8:00
(S-86) Barach, P., Monday 8:00
(S-87) Roth, S., Monday 8:00
(S-88) Barach, P.,Monday 8:00
(S-89) Wischmeyer, P.E., Monday 8:00
(S-90) Burden, A., Monday 8:00
(S-91) New, D., Monday 8:00
(S-92) Wilson, J., Monday 8:00
(S-93) Cassingham, S.F., Monday 8:00

IARS 81st Clinical and Scientific Congress
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(S-94) Schell, R., Monday 8:00
(S-95) Vezina, D.P., Monday 8:00
(S-96) Chau, D.F., Monday 8:00
(S-97) Glassenberg, R., Monday 8:00
(S-98) Yamaguchi, H., Monday 8:00
(S-99) Mantha, S., Monday 8:00
(S-100) Shaffer, R., Monday 8:00
(S-101) Cobos II, F.V., Monday 8:00
(S-102) Kumaraswami, S., Monday 8:00
(S-103) Handley, L., Monday 8:00
(S-104) Barach, P., Monday 8:00
(S-105) Christo, M., Monday 8:00
(S-106) Zafirova, Z., Monday 8:00
(S-107) Singbartl, G., Monday 8:00
(S-108) Meng, J., Monday 8:00
(S-109) Vezina, D.P., Monday 8:00
(S-110) Asnis, J., Monday 8:00
(S-111) Fuller, S.M., Monday 8:00
(S-112) Cohen, J., Monday 8:00

Equipment/Monitoring

(S-113) Kelling, J., Monday 1:00
(S-114) Cohen, J.B., Monday 1:00
(S-115) Singbartl, G., Monday 1:00
(S-116) Torjman, M.C., Monday 1:00
(S-117) Macknet, M.R., Monday 1:00
(S-118) Takayama, W., Monday 1:00
(S-119) Maroof, M., Monday 1:00
(S-120) Ahmed-Nusrath, A., Monday 1:00
(S-121) Hofer, C.K., Monday 1:00
(S-122) Vadivelu, N., Monday 1:00
(S-123) Xin, Z., Monday 1:00
(S-124) Harris, S.N., Monday 1:00
(S-125) Inagawa, M., Monday 1:00
(S-126) Greenwald, S., Monday 1:00
(S-127) Setoguchi, H., Monday 1:00
(S-128) Mori, Y., Monday 1:00
(S-129) MacLeod, D., Monday 1:00
(S-130) Fenson, B.J., Monday 1:00
(S-131) Suzuki, A., Monday 1:00
(S-132) Mora, B., Monday 1:00
(S-133) Loushin, M.K., Monday 1:00
(S-134) Moore, R.M., Monday 1:00
(S-135) Rosenbaum, A., Monday 1:00
(S-136) Goy, R.W., Monday 1:00

Genetics/Genomics

(S-137) Yang, Z., Monday 10:15
(S-138) Novalija, E., Monday 10:15
(S-139) Murthy, A., Monday 10:15
(S-140) Fung, E., Monday 10:15
(S-141) Tampo, A., Monday 10:15
(S-142) Zaugg, M., Monday 10:15
(S-143) Hamiel, C., Monday 10:15
(S-144) Singleton, K., Monday 10:15

Liver/Transplantation

(S-145) Saner, F.H., Monday 10:15
(S-146) Schmidt, R., Monday 10:15
(S-147) Beebe, D., Monday 10:15
(S-148) Aggarwal, S., Monday 10:15
(S-149) Jones, D.T., Monday 10:15
(S-150) Oravitz, T.M., Monday 10:15
(S-151) Aggarwal, S., Monday 10:15
(S-152) Matsusaki, T., Monday 10:15

Neuroanesthesia

(S-153) Roth, S., Monday 3:00
(S-154) Cheng, H., Monday 3:00
(S-155) Hoffman, W.E., Monday 3:00
(S-156) McLaren, A.T., Monday 3:00
(S-157) Kramer, D.C., Monday 3:00
(S-158) Roth, S., Monday 3:00
(S-159) Bennett, H.L., Monday 3:00
(S-160) Dauber, M.H., Monday 3:00

Obstetric Anesthesia

(S-161) Mantha, V.R., Monday 3:00
(S-162) Mantha, V.R., Monday 3:00
(S-163) Glassenberg, R., Monday 3:00
(S-164) Enohumah, K.O., Monday 3:00
(S-165) Fujino, Y., Monday 3:00
(S-166) Souissi, R., Monday 3:00
(S-167) Iwakiri, H., Monday 3:00
(S-168) Souissi, R., Monday 3:00

Pain - Basic Science

(S-169) Kroin, J.S., Saturday 3:00
(S-170) Sharar, S.R., Saturday 3:00
(S-171) Niinomi, K., Saturday 3:00
(S-172) Buvanendran, A., Saturday 3:00
(S-173) Xu, L., Saturday 3:00
(S-174) Hagiwara, S., Saturday 3:00
(S-175) McDonald, J.S., Saturday 3:00
(S-176) Nagatani, H., Saturday 3:00

IARS 81st Clinical and Scientific Congress
Abstract Presenter Presentation Schedule

Pain - Clinical

(S-177) Reuben, S.S., Saturday 3:00
(S-178) Viscusi, E.R., Saturday 3:00
(S-179) Chelly, J.E., Saturday 3:00
(S-180) Sweitzer, B., Saturday 3:00
(S-181) Noguera Chia, E.M., Saturday 3:00
(S-182) Nielsen, E.T., Saturday 3:00
(S-183) Buvanendran, A., Saturday 3:00
(S-184) Foss, J.F., Saturday 3:00
(S-185) Dreier, J., Saturday 3:00
(S-186) Gogia, S., Saturday 3:00
(S-187) Sabia, M., Saturday 3:00
(S-188) Fujii, H., Saturday 3:00
(S-189) Overdyk, F.J., Saturday 3:00
(S-190) Salomone, M.M., Saturday 3:00
(S-191) Shibata, Y., Saturday 3:00
(S-192) Abraham, Y., Saturday 3:00
(S-193) Sloan, P.A., Saturday 3:00
(S-194) Ishikawa, S., Saturday 3:00
(S-195) Kim, D., Saturday 3:00
(S-196) Sumitani, M., Saturday 3:00
(S-197) Kim, D., Saturday 3:00
(S-198) Gallagher, M., Saturday 3:00
(S-199) Yamaguchi, S., Saturday 3:00
(S-200) EL-Shammaa, N., Saturday 3:00

Pediatric Anesthesia

(S-201) Loepke, A.W., Saturday 10:15
(S-202) Patel, A., Saturday 10:15
(S-203) Robinson, P., Saturday 10:15
(S-204) Chhabra, A., Saturday 10:15
(S-205) Dalal, P.G., Saturday 10:15
(S-206) Galiza, C., Saturday 10:15
(S-207) Foley, R.T., Saturday 10:15
(S-208) Ramsdell, R., Saturday 10:15

Pharmacology - Basic Science

(S-209) Alkire, M.T., Saturday 8:00
(S-210) Wise-Faberowski, L., Saturday 8:00
(S-211) Robinson, P., Saturday 8:00
(S-212) Alkire, M.T., Saturday 8:00
(S-213) Alkire, M.T., Saturday 8:00
(S-214) Nishikawa, K., Saturday 8:00
(S-215) Wang, J.Q., Saturday 8:00
(S-216) Angelotti, T., Saturday 8:00
(S-217) Westphal, M., Saturday 8:00
(S-218) Angelotti, T., Saturday 8:00
(S-219) Mori, T., Saturday 8:00
(S-220) Ueno, T., Saturday 8:00
(S-221) Durieux, M.E., Saturday 8:00
(S-222) Hemmings, H., Saturday 8:00
(S-223) Durieux, M.E., Saturday 8:00
(S-224) Camporesi, E.M., Saturday 8:00
(S-225) Urano, A., Saturday 8:00
(S-226) Schmidt, R., Saturday 8:00
(S-227) Diemunsch, P.A., Saturday 8:00
(S-228) Schmidt, R., Saturday 8:00
(S-229) Roesslein, M., Saturday 8:00
(S-230) Hanazaki, M., Saturday 8:00
(S-231) McEvoy, M.D., Saturday 8:00

Pharmacology - Clinical

(S-232) Fan, Q., Sunday 10:15
(S-233) Shields, C.H., Sunday 10:15
(S-234) Ng, S.Y., Sunday 10:15
(S-235) Gin, T., Sunday 10:15
(S-236) Tufanogullari, B., Sunday 10:15
(S-237) Steinberg, D., Sunday 10:15
(S-238) Carter, R., Sunday 10:15
(S-239) Gupta, D.K., Sunday 10:15
(S-240) Steinberg, D., Sunday 10:15
(S-241) Nigrovic, V., Sunday 10:15
(S-242) Shah, P., Sunday 10:15
(S-243) Bhatt, S.B., Sunday 10:15
(S-244) Steinberg, D., Sunday 10:15
(S-245) Steinberg, D., Sunday 10:15
(S-246) Steinberg, D., Sunday 10:15
(S-247) Mathews, D.M., Sunday 10:15
(S-248) Lee, K., Sunday 10:15
(S-249) Shadle, C.R., Sunday 10:15
(S-250) Kasuya, Y., Sunday 10:15
(S-251) Markewich, S., Sunday 10:15
(S-252) Steinlechner, B., Sunday 10:15
(S-253) Tufanogullari, B., Sunday 10:15
(S-254) Chen, B.L., Sunday 10:15
(S-255) Samhan, Y.M., Sunday 10:15

Regional

(S-256) Williams, B.A., Sunday 3:00
(S-257) Roth, S., Sunday 3:00
(S-258) Neumann, K.J., Sunday 3:00
(S-259) Sheen, M.J., Sunday 3:00
(S-260) Patel, S., Sunday 3:00
(S-261) Kerner, M.B., Sunday 3:00
(S-262) Swenson, J., Sunday 3:00
(S-263) Tanaka, T., Sunday 3:00
(S-264) Burns, D.A., Sunday 3:00
(S-265) El-Sayed, G., Sunday 3:00
(S-266) Salomone, M.M., Sunday 3:00
(S-267) Ito, H., Sunday 3:00
(S-268) Acalovschi, I., Sunday 3:00
(S-269) Fujiwara, Y., Sunday 3:00
(S-270) Duggan, E., Sunday 3:00
(S-271) Morris, A.H., Sunday 3:00

Ambulatory Anesthesia

S-1.

PROPENSITY FOR OBSTRUCTIVE SLEEP APNEA AND PERIOPERATIVE OUTCOME IN AN AMBULATORY SURGICAL POPULATION

AUTHORS: T. L. Stierer[1], D. Cohen[2], C. Wright[1], A. George[1], C. Wu[1], R. H. Brown[1];
AFFILIATION: [1]Johns Hopkins Medical Institutions, Baltimore, MD, [2]Johns Hopkins School of Public Health, Baltimore, MD.

Introduction: Patients with obstructive sleep apnea (OSA) are thought to be at higher risk for adverse perioperative outcomes. We undertook a prospective study using a previously validated self-report tool to measure the propensity for OSA in an ambulatory surgical population to determine whether the diagnosis of or the increased propensity for OSA are associated with unplanned admissions or adverse outcomes after surgery.
Methods: Consecutive patients presenting for ambulatory surgery at Johns Hopkins Hospital from May 2004 to April 2006 completed a self-administered questionnaire to assess demographic, medical history, and sleep symptoms. The anesthesia teams and surgeons were blinded to the results of the questionnaire. Intraoperative data included anesthetic technique, changes in anesthetic plan, difficulty with endotracheal intubation, and vasoactive medications administered. Postoperative data included need for supplemental oxygen to maintain oxygen saturation >95%, cardiac arrhythmias, need for assisted ventilation, reintubation, unplanned admission and death. Propensity to OSA was determined by logistic regression analysis combining the results of the aforementioned questionnaire data with the Epworth Sleepiness scale to predict the probability of having an apnea-hypopnea index > 10 events/hour.
Results: To date, data on 1,278 patients have been analyzed. The study population had an average body mass index of 26.1 kg/m2. Fifty-two patients (4.1%) carried a previous diagnosis of OSA. In addition, 2.6% of the remaining patients had a greater than 70% propensity for OSA but had not yet been diagnosed. There were no unplanned admissions for patients who carried a formal diagnosis of OSA. Furthermore, there was no association of OSA propensity scores with patients requiring unplanned admission. In contrast, difficult intubation and poor view of vocal cords with direct laryngoscopy (p-value <0.0006), and prolonged supplemental oxygen or lower post operative oxygen saturation (p-value<0.001) were associated with higher OSA propensity scores. 27% of patients with a previous diagnosis of OSA received intraoperative intravenous ephedrine, and there was a positive correlation of patients with a higher propensity to OSA with those who required intraoperative ephedrine (p-value <0.001) and labetolol (p-value0 .003). .
Discussion: A significant number of patients presenting to an ambulatory surgery can have OSA either diagnosed or undiagnosed. We found no relationship between unplanned admission, life threatening events such as reintubation, cardiac arrhythmia or death and patients with either a diagnosis or higher propensity for OSA. However, there remains an increased risk of potentially serious perioperative events such as increased difficulty of intubation, increased need for supplemental oxygen, and use of medications to correct hemodynamic derangements in patients with OSA. Therefore, our data suggest that patients with OSA can be treated safely in an ambulatory care center; however, they may require additional perioperative interventions.
Supported in part by the IARS 2005 Clinical Scholar Research Award.

S-2.

INTRAOPERATIVE METHADONE SUPERIOR TO FENTANYL FOR POST-DISCHARGE PAIN IN AMBULATORY SURGICAL PATIENTS

AUTHORS: B. Sweitzer, K. Tomfohrde, M. Drum;
AFFILIATION: University of Chicago, Chicago, IL.

Introduction:
Pain control with minimal side effects are important in ambulatory surgery. Apfelbaum determined that 79% of ambulatory surgical patients have pain post-discharge with most reporting moderate to severe pain (1). Use of short-acting opioids is driven by concern over delayed discharge. Evidence suggests morphine offers superior pain relief compared to fentanyl without significantly delaying discharge. (2) We postulated that intraoperative methadone compared to fentanyl would decrease postoperative pain without increasing time to discharge in ambulatory patients.
Methods: Wth IRB approval we recruited 67 same-day surgery patients expected to require postoperative analgesics. After informed consent, patients were randomized to receive either 10 mg of methadone or 200 mcg of fentanyl (diluted in 10 cc saline) intra-operatively in divided doses (on induction and 30-45 minutes later). Anesthesia providers were blinded to the study groups. No additional analgesics were given intraoperatively.
Upon PACU arrival, a nurse blinded to opioid group evaluated pain, side effects, and discharge eligibility using a Postanesthetic Discharge Scoring System (3). Discharge readiness was achieved with a score of ≥ 9 out of 10. Fentanyl was given (25-50 mcg) q5 minutes as needed. Surgeons prescribed post-discharge analgesics per their normal routine. Postoperative opioid analgesics were converted to morphine equivalents. Patients were contacted after discharge to determine the amount of oral analgesics consumed and pain in the 24-hour period following discharge.
Morphine equivalent and acetaminophen doses and pain scores were evaluated with Wilcoxin's rank sum test. The two-sided two-sample t-test evaluated time to discharge. Analysis was conducted on an intent-to-treat basis.
Results:
62 patients completed the study (33 fentanyl and 29 methadone). After discharge, methadone patients used significantly less morphine-equivalent analgesics (median 3.0 mg vs 9 mg, p=0.016) and significantly less acetaminophen (median 600 mg vs 1800 mg, p=0.006). There was no difference in ibuprofen dose between groups. Fentanyl patients reported significantly higher "least pain" (median: fentanyl 2, methadone 0; p=0.04) and marginally higher "worst pain" (median: fentanyl 5, methadone 4; p=0.06). Average pain scores were not significantly different (median: fentanyl 4, methadone 2; p=0.12). There was no difference in time to discharge between groups.
Discussion:
Intraoperative methadone compared to fentanyl in ambulatory surgery patients decreased postoperative pain and resulted in a lower requirement for oral analgesics post-discharge. Methadone did not cause significant adverse effects and did not delay discharge. Methadone given during surgery offers superior pain control post-discharge in an ambulatory surgical population.
References:
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S-3.

IMPACT OF PERSISTENT POSTOPERATIVE PAIN ON THE QUALITY OF RECOVERY FOLLOWING AMBULATORY SURGERY

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Introduction: Traditional indicators of day surgery performance e.g. incidence of unanticipated ward admission, time to discharge from unit do not take into account patients' perception of their own recovery. The impact of persistent pain on health outcomes after ambulatory surgery is unclear. Using a validated instrument, the Quality of Recovery Score 40 (QoR-40)1, we aim to study the effect of persistent postoperative pain on less well defined parameters of postoperative recovery i.e. physical discomfort, dependence, emotions and feelings of need for support.
Methods: After institutional board review and written informed consent, 525 adult patients, ASA status I and II, presenting for elective ambulatory surgery under general anaesthesia were recruited. The use of the QoR40 questionnaire (40 questions based on a 5-point Likert scale, min 40 - max 200) was explained to all patients prior to induction. The choice of intraoperative analgesics was left to the discretion of the attending anaesthetist. Patient demographics, intraoperative data and recovery characteristics were documented. After surgery, the patients were discharged from PACU when they met standard discharge criteria and oral analgesics (paracetamol, NSAIDS, tramadol) were prescribed for self-administration. The QoR questionnaire was applied to each patient by two trained interviewers at 3 points: discharge from PACU, 24 hours and 7 days after surgery (telephone interview).
Results: Complete response rate was 96%. 133 (25.6%) and 78 (15.5%) patients reported persistent moderate-severe pain (defined as pain VAS>40) at the 24-hour and 7-day review. Anterior cruciate ligament reconstruction, knee arthroscopy and laparoscopic hernia repair were commonly associated with unresolved pain. Patients with persistent moderate-severe pain reported poorer global QoR scores (median 173, min-max 133-184) as compared to those with mild pain (median 181, 140-185) ($p<0.001$). Pain VAS correlated negatively with poorer recovery indices ($p<0.001$, $r=-0.6$). Unresolved pain resulted in greater physical discomfort and dependence, more emotional upheavals and feeling of less support ($p<0.001$). Predictors of poor recovery at 24 hours include longer duration of anaesthesia, higher pain VAS in recovery and poorer global QoR at discharge ($p<0.01$). There was no difference in satisfaction scores between the two groups ($p>0.05$).
Discussion: Unresolved pain can significantly reduce the quality of anaesthetic recovery. This is especially important in patients undergoing ambulatory surgery as objective measures of patient recovery is terminated upon discharge. QoR score before discharge from PACU may be used as a tool to identify patients who are at risks of greater postoperative pain and poorer recovery. As more invasive procedures are performed in ambulatory surgical units, management strategies should be focused on the control of postoperative pain.
References:
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S-4.

EVALUATING THE ANALGESIC EFFICACY OF CELECOXIB AS A COMPONENT OF MULTIMODAL ANALGESIA FOR OUTPATIENT ACL SURGERY

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Introduction: A multimodal approach is recommended in treating pain in anterior cruciate ligament (ACL) reconstruction (1). The perioperative administration of NSAIDS play an important role in this multimodal management of pain (2), but are also associated with decreased platelet aggravation and increased bleeding time (3). Celecoxib, a COX-2 specific NSAID, has no effect on platelet aggregation or bleeding time (4) and has recently demonstrated analgesic efficacy following major orthopedic surgery (5). The goal of this study is to assess the analgesic efficacy of utilizing celecoxib in a preventative multimodal analgesic technique for patients undergoing outpatient ACL surgery.
Methods: 200 consecutive patients were randomized to receive acetaminophen 1000 mg and either celecoxib 400 mg or placebo 1-2 hours prior to surgery. Before awakening, all patients were administered 20 mL intraarticular bupivacaine 0.25% and morphine 5mg and an external cooling system was applied to the operative knee. In the PACU patients were asked to rate their pain on a numerical rating scale (NRS) from 0 - 10; with 0 representing no pain and 10 representing the worst imaginable pain every 15 minutes. After discharge patients were instructed to take acetaminophen 1000 mg every 6 hours and either celecoxib 200 mg every 12 hours or matching placebo (according to randomization) for the first 14 days postoperatively. In addition, patients were instructed to take oxycodone 5-10 mg every 3 hours for an NRS ≤ 3. All patients were enrolled in an accelerated rehabilitation program. While at home patients were asked to record their daily NRS pain scores and oxycodone use in a diary. Pain scores were recorded both at rest and with movement.
Results: There were no differences between the two groups with respect to demographic variables, operative times, or number of requiring admission or re-admission to the hospital. Patients in the celecoxib group were more likely to experience less pain in the PACU ($p < 0.01$) and require less opiods ($p < 0.001$) for postoperative analgesia. These patients reported a lower incidence of PONV ($p < 0.05$) and were discharged home earlier ($p < 0.05$). While at home, patients in the celecoxib group reported lower pain scores both at rest ($p < 0.05$) and with movement ($p < 0.01$), and utilized less oxycodone at all postoperative time intervals.
Conclusions: The administration of celecoxib as an adjunct in the multimodal approach for ACL reconstruction results in significant analgesic efficacy with a reduction in pain, opioid use, and PONV. In addition, patients receiving celecoxib were discharged home sooner.
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2007; 104; S-1–S-271

S-5

WITHDRAWN

S-6.

LAVENDER OIL ALLEVIATES POSTOPERATIVE PAIN IN MORBIDLY OBESE PATIENTS UNDERGOING LAPAROSCOPIC GASTRIC BANDING.

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Introduction
The standard practice in our institution is to treat postoperative pain after gastric banding surgery with ketorolac (an NSAID) and morphine. The side effects of opioids include nausea, constipation, sedation, and respiratory depression, which are especially problematic in morbidly obese patients. Adverse renal, gastrointestinal, and haemostatic effects may limit the use of ketorolac. Complimentary non-pharmacological treatments may decrease the requirements for both drugs, hence reducing the incidence of perioperative complications.
Aromatherapy is one of the methods to reduce postoperative pain. Lavender oil has been particularly attributed with mood-enhancing and analgesic properties in experimental nociception. The aim of this study was to examine whether the use of postoperative lavender aromatherapy reduces narcotic demand after gastric banding surgery.
Methods
With IRB approval, 56 consented ASA I-III patients scheduled for gastric banding surgery were randomly assigned to receive either lavender aromatherapy or placebo (scented baby oil). The anesthestic induction agents included fentanyl 1.5 ug/kg and propofol 2-2.5 mg/kg. Sevoflurane was used for the maintenance of anesthesia. The patients receive ketorlac 60 mg. IM at the end of the case. Upon arrival in the PACU, patients received 2 drops of either 2% lavender oil or placebo applied to the inside surface of the face mask. VbAS score, total amount of analgesics, as well as discharge time from the PACU were recorded. Patients were assessed on arrival to the PACU, and at 5, 30, 60, and 90 minutes. Differences in demographic data and perioperative drug use between groups were analyzed by unpaired Student's t-test. The proportion of patients reporting pain and postoperative analgesic requirements were analyzed using a chi-squares test. A $P<0.05$ was considered significant.
Results
The two groups were comparable with regard to patients' characteristics, intraoperative medication use, and duration of surgery. Significantly more patients in placebo group (78%) versus the lavender group (46%) requested supplemental postoperative narcotics ($P<0.034$). Among the patients who did request postoperative narcotics there was no significant difference in the amount needed for pain relief in the placebo vs. the lavender group (5.5 mg vs. 5.3 mg of morphine SQ.).
Discussion
Lavender oil aromatherapy significantly reduced the proportion of patients that were treated with narcotics after gastric banding surgery. It could be recommended as an adjunct therapy in the perioperative period, considering the innocuous nature of this treatment. Interestingly, opioid requirements were similar among the patients who did require postoperative analgesia. We believe that patients who do not respond to lavender would have had a reaction similar to a placebo. Our previous study showed that lavender does not have a direct analgesic action, but only a perceived effect (1).
Reference
1. Kim J, et al. Pain Practice 2006

S-7.

DOES COCAINE ABUSE ALTER ANESTHETIC REQUIREMENTS IN HUMANS?

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Introduction: It is generally thought that chronic cocaine (C) abuse causes central nervous system neurotransmitter (serotonin, dopamine, and norepinephrine) alteration (1,2). This variation in neurotransmitter concentration is considered to be the mechanism for the change in anesthetic requirements (MAC) of inhaled anesthetic agents in animals (3). Chronic C abusing patients (identified by history and a positive urine test for C metabolites) commonly present for elective surgery in our Day Surgery Unit.
Methods: Following IRB approval, forty urine C positive patients were compared to an equal number of drug free controls in a prospective, non-randomized, blinded analysis. Mean ± SD end-tidal concentrations (%) of sevoflurane (S), total dose of fentanyl (µg), duration of anesthesia (min), and intraoperative volume (ml/Hr) of infused crystalloid were recorded and compared. Standard monitors routinely used for general anesthesia and end-tidal gas analysis](S/5 Anesthesia Monitor, Datex-Ohmeda, Finland) were applied. A standard general anesthesia protocol for all patients included induction with propofol (1.5-2.0 mg/kg) and maintenance with fentanyl (1-5 µg/kg), and S in 50% N_20 in oxygen. The end-tidal concentration of S (mean concentration throughout the surgical procedure) was averaged over 15-minute increments. Unpaired Student's T- test was used to compare the C group against the control group, P-values of 0.05 or less defined significance.
Results: Intraoperative end-tidal S concentration, total fentanyl dose, duration of anesthesia, and crystalloid infused of the C group was not significantly different when compared to an ASA matched drug-free control group (Table 1).
Discussion: These results demonstrate that chronic C abusing patients have similar anesthetic requirements to drug-free controls. C-induced changes in the minimum alveolar anesthetic concentrations (MAC) of S(3) was not suggested from our data.
References:
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Table 1.

	Cocaine Group (n=40)	Control Group (n=40)	p-value
Number of males	23	24	0.82
Age (yrs.)	37.6 ± 4.1	44.3 ± 4.9	0.01*
Weight (Kg)	83 ± 5	86 ± 5.8	0.02*
End-tidal sevoflurane Concentration (%)	2.02 ± 0.5	1.95 ± 0.3	0.45
Total fentanyl dose (µg)	202±20	210±19	0.07
Intraoperative crystalloid Volume infused (ml/Hr)	722 ± 63	698 ± 71	0.11
Post-anesthesia recovery Room stay (min)	58.5 ± 5	61.3 ± 8	0.06
Duration anesthesia (min)	114±19	118±21	0.37

All values are mean ± SD. *denotes significant p-values

S-8.

PRE-OXYGENATION ROLE ON HEMODYNAMIC STABILITY AND OXYGEN SATURATION DURING ELECTROCONVULSIVE THERAPY

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In spite of passive oxygenation with a nasal canula during electroconvulsive therapy (ECT) as a treatment for severe depression and other psychiatric disorders, a marked degree of hypoxemia was noted during the procedure in most of the patients with effects on their hemodynamic stability(1,2). No clear guidance is given in the literature concerning the ventilation management of the patient receiving ECT under general anesthesia.
The aim of the present study is to demonstrate the efficacy of our technique in pre-oxygenation of 100 patients undergoing electroconvulsive therapy.
Patients were classified into two groups. Patients in Group 1 (n=50) received 4 liter .min-1 100% wall oxygen through a nasal canula with voluntary inspiration prior to induction. Fifty patients (Group 2) were ventilated with 4 liters min.-1 100% wall oxygen attached to an (Ambu) bag with 3-4 assisted full ventilations prior to induction. Anesthesia was induced with methohexitone (0.5-1.0 mg.kg-1) and succinylcholine (0.75-1.5 mg.kg-1). The electric shock was administered by a psychiatrist using the Thymatro TM system IV, Somatics, *INC*.
A baseline oxygen saturation, respiratory rate, MAP and heart rate were recorded and continuously monitored. These parameters were recorded on starting oxygenation, before, during and 5 minute after ECT. The oxygen saturation reading was taken from the patient s index finger using a pulse oximeter (Ohmeda Biox III). Statistical analysis was with the unpaired t-test, the Chi squared test and analysis of variance (ANOVA). Our results showed that Patients in group 1 (without Ambu bag ventilation) had a statistically significant reduction in SaO_2 during ECT ($p<0.002$) while patients in group 2 showed a non significant decrease in SaO_2. The decrease in SaO_2 during the ECT period was significant between the two groups ($p<0.002$). The mean respiratory rate was significantly decreased during ECT ($p<0.001$) in both groups with no significant change between both of them. The means of MAP and heart rate were significantly decreased during ECT in both groups ($p<0.05$) with non significant increase after 5 minutes in patients in group1.

We concluded that the anesthetic technique utilizing methohexital as an induction agent and succinylcholine as a muscle relaxant in doses recommended by the Royal College of Psychiatrists and American Psychiatric Association, together with our pre-oxygenation technique utilizing 4 liters/minute and an Ambu bag using assisted deep ventilation is the safest method in patients undergoing ECT. There were no incidence of complications, minimal decrease in oxygen saturation during induced convulsions and a better hemodynamic stability.
References
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2. Kadar AG, Ing CH, White PF, et al. Anesthesia for electroconvulsive therapy in obese patient, *Anesthesia Anal 2002; 94:360-1*

Bleeding/Blood Product Conservation

S-9.

SIMILARITY OF BRAIN BLOOD FLOW RESPONSES DURING HEMODILUTION WITH TWO PERFLUOROCHEMICAL SUBSTITUTIONS IN SPRAGUE DAWLEY RATS

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Introduction: Hemodilution and reduction of circulating red blood cells result in a decrease in oxygen transport to the brain. A compensation mechanism is the redirection of oxygen supply from the systemic circulation to the brain, resulting in an increase in cerebral blood flow (CBF)1. Oxygent(Alliance Pharmaceutical Corp.) and Oxycyte® (Synthetic Blood International) are artificial perfluorochemical (PFC)-intravascular oxygen carriers that are more efficient at delivering oxygen to tissues than red blood cells. The purpose of this study was to compare the effect of the two PFC emulsions on CBF after hemodilution.
Methods: Sprague-Dawley rats were subjected to isovolemic hemodilution under isoflurane anesthesia, while ventilated with 100 % O_2, with serial blood gas monitoring. This was performed by withdrawing 4ml of arterial blood, replacing blood with 4 ml of human Albumin (control groups 1 and 2, each at n=8) or PFC (2ml) plus Albumin (2ml) (experimental groups 3 (Oxygent®) and 4 (Oxycyte®), each at n=8) every 20 minutes. Serial hemodilutions continued until hematocrit values were reduced below 10%. Supplemental continuous phenylephrine infusion was used to maintain stable mean arterial blood pressure. Cerebral blood flow was measured using a laser doppler flow (LDF) probe (Moorlab Inc.) in the striatum region of the brain. CBF was compared at different hematocrit levels for each control and each experimental PFC group.
Results: Cerebral blood flow at hematocrit values of less than 15% was significantly higher in the albumin group than in the rats receiving the Oxycyte® perfluorochemical solution. Similar results were found in the Oxygent® perfluorochemical solution, as cerebral blood flow was significantly higher in the albumin group than the perflurochemical group at hematocrits below 17%. Once below these hematocrit ranges, the difference between the albumin control group and experimental perfluorochemical group increased as hematocrit was allowed to decrease to extremely low levels for both Oxygent® and Oxycyte®.
Discussion: These data suggest that both perfluorochemical-based blood substitutes significantly maintained a stable cerebral blood flow to the striatum at low hematocrit levels after isovolemic hemodilution. This is likely a consequence of the increased oxygen delivery to the brain with both PFCs, a characteristic of perfluorochemical substitutions that are marketed for their increased loading, delivery, and extraction of oxygen to the tissues.
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S-10.

APROTININ USE IN COMPLEX ADULT SPINAL DEFORMITY

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Introduction: Aprotinin has been shown to reduce intraoperative blood loss and reduce transfusion requirement in pediatric spine and cardiac surgery populations. Previous literature (prior to 2006) has not reported acute renal failure as a potential complication. This study was designed to examine the efficacy of Aprotinin in reducing operative blood loss following long spinal arthrodesis in adult spinal deformity patients and analyze complications.
Methods: Adult spinal deformity patients undergoing long spinal arthrodesis at one institution between 2001 and 2005 were analyzed. Patients were matched according to age and type of procedure performed. 40 patients received high-dose Aprotinin (Group A) intraoperatively and 41 patients matched as controls (Group NA) who received no Aprotinin. Outcome variables included intraoperative blood loss, intraoperative transfusion requirement, early postoperative blood loss and transfusion requirement, and postoperative complications.
Results: Average blood loss for Group A was 906 ml and 1.3 L for Group NA. The difference was statistically significant with a $p< 0.05$. Complications seen in Group A included four cases of acute renal failure (ARF) requiring dialysis and one DVT. In Group NA, there was only one case of acute renal failure (presumed to be secondary to inadvertent gentamycin overdose) and one case of pulmonary embolus. The four Group A patients with ARF were female, aged 61-73 years old, with various comorbidities. All required inpatient hemodialysis, and three averaged two months of continued outpatient dialysis before resolution of renal compromise. One patient is on chronic dialysis.
Discussion: In long spinal arthrodesis in complex adult spinal deformity surgery, Aprotinin does reduce intraoperative blood loss but also substantially increases the risk of acute renal failure. Strong consideration should be given to the use of other blood conserving medications including tranaxemic acid and aminocaproic acid.
References:
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S-11.

ANESTHETIC MANAGEMENT OF ROBOTIC ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMIES

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Introduction: Robotic assisted laparoscopic radical prostatectomies (RALPs) have recently gained popularity and are becoming more frequent. In 2004, RALPs accounted for 10% of all prostatectomies in the US.1 It has been estimated that 25% of all prostatectomies in 2006 will be RALPs. Surgical groups have published data concerning surgical management and outcomes for patients undergoing RALPs,2 but little data exists concerning anesthetic outcomes and management of these patients. This current study presents a retrospective perioperative comparison of patients who presented to our institution for either a RALP or a radical retropubic prostatectomy (RRP).
Methods: Data from 541 patients was obtained from the electronic database beginning 1/2003 until 6/2006. The data included 283 RRP patients and 253 RALP patients who had their surgeries performed under general anesthesia. Patients who received an epidural were not included in the study. The database was queried for information concerning patient demographics, fluid management, hemodynamic parameters, pain management, and anesthetic management. Data were analyzed by Student's t-test and Fisher's exact test. P <0.05 was considered significant.
Results: There was no difference in patient demographics between the two groups. The length of RALP surgery was 295 ± 78 min compared to 175 ± 73 min (mean ± SD) with RRP surgery (p<0.0001). Intraoperatively, the mean estimated blood loss (EBL) was significantly higher (1027 ± 829 mL) for the RRP patients compared to the RALP patients (285 ± 317 mL), p<0.0001. Likewise, 24% of the RRP patients received red blood cell (RBC) transfusion intraoperatively, while only 1.2% of RALP patients received RBC transfusion (p<0.0001). Seven RRP patients also received fresh frozen plasma transfusions. RALP patients received less crystalloid (2584 ml versus 3185 ml, p=0.00016) and colloid (438 ml versus 727 ml) infusions compared to RRP patients. Interestingly, compared to the RRP group, the RALP patients received anti-hypertensive medication more often (37% compared to 21%, p<0.0001), and less vasopressors (63% compared to 78%, p<0.0001). The two groups had similar morphine equivalent narcotic use intraoperatively (51.8 mg RALP, 50.3 mg RRP, p=0.49). In the post-anesthesia care unit (PACU), less RALP patients required narcotic medications (74% versus 86%, p=0.04) with less average morphine equivalent narcotic consumption (11.3 mg versus 14.9 mg, p<0.0001). They also reported decreased maximum post-operative pain scores (3.7 versus 5.6 out of ten, p<0.0001) in PACU. The duration of PACU stay was significantly shorter for RALP patients compared to RRP patients (161 vs.196 min, p<0.0001).
Discussion: In summary, RALP received more intraoperative anti-hypertensive agents, had less EBL, and had longer surgical times, but lower pain scores, less narcotic consumption, and a shorter duration of PACU stay compared to the RRP patients.
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S-12.

PRE-OPERATIVE FACTORS ASSOCIATED WITH BLOOD PRODUCT TRANSFUSION IN ORTHOTOPIC LIVER TRANSPLANTATION USING THE PIGGYBACK HEPATECTOMY TECHNIQUE: A REGRESSION ANALYSIS

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Background
Orthotopic liver transplantation (OLT) may be associated with massive blood loss related to the coexistence of varices, thrombocytopenia or other coagulopathies, or portal hypertension. Piggyback hepatectomy (PGB) is a surgical technique increasingly utilized in OLT to avoid veno-venous bypass and vena cava clamping. We evaluate the factors associated with blood product transfusion in PGB hepatectomy.
Methods
We retrospectively reviewed the anesthesia pre-operative and operative notes, and laboratory values, for all adult cadaveric OLTs over a 30 month period (n=399). Ninety-eight percent of transplants were performed using a standard piggyback approach with no use of veno-venous bypass. Univariate and multivariable regression analyses were performed with a direct entry method. P<.05 was considered significant.
Results
Blood loss and transfusion data were available for 368 OLT recipients (92%). Median blood loss was 1000cc with median transfusion rates being packed cells 3 units, plasma 8 units, and platelets 6 units. Factors associated with increased packed cell transfusions on univariate analysis included male recipient with higher MELD score, increased BMI, previous major upper abdominal surgery, increased serum creatinine, increased INR and reduced starting hemoglobin. Significant predictors in the multivariable regression model included gender, BMI, MELD score, and starting hemoglobin. These results correspond with a mean 1.0 additional unit for males than females, an additional 0.6 unit for each g/dL Hgb below 11.9, an additional 0.7 unit for each 5 MELD points above 17.8, and an additional 0.6 unit transfused for each 5 unit increase in BMI above 28.1.
Conclusions
These results demonstrate that, similar to previous reports using venovenous bypass or clamping of the vena cava, certain factors predictably increase the likelihood that blood products will be administered during OLT. Overall, the piggy back technique, typically requiring less surgical and warm ischemia time, may represent a safer and cheaper alternative to the conventional approach.

Linear regression model for transfused PRBCs during liver transplant using piggy-back technique

Model (*Predictors*)	**Beta**	**Std error**	**Significance**
Constant	7.154	2.435	0.004
Gender (male 0)	-1.090	0.578	0.060
BMI	0.113	0.054	0.037
MELD	0.140	0.042	0.001
Pre-op hemoglobin	-0.653	0.132	0.000

S-13.

THROMBIN TIME WITH THROMBELASTOGRAPHY IS USEFUL FOR EVALUATION OF ANTICOAGULANT EFFECTS OF DIRECT AND INDIRECT THROMBIN INHIBITORS

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Introduction: Thrombin inhibitors are clinically important therapeutic agents for vascular thromboses. For heparin contraindications, direct thrombin inhibitors (DTIs) as well as dermatan disulfate (Intimatan) are alternative anticoagulants. DTIs directly bind to thrombin, whereas Intimatan mediates heparin cofactor II (HCII) dependent thrombin inhibition (1, 2). There are differences in the mode of thrombin inhibition among these agents, and conventional assays (*e.g.*, activated clotting time) may not be well suited for monitoring their anticoagulant effects. We hypothesized that whole blood thrombin time on thrombelastography (TEG®) would be more useful in evaluating therapeutic responses to both direct and indirect thrombin inhibitors.
Methods: After institutional approval and written informed consent, whole blood was obtained from 6 health volunteers in a glass tube containing 3.2 % sodium citrate and corn trypsin inhibitor (CTI; final concentration of 100μg/ml) to minimize contact activation. Intimatan (Celsus, OH), bivalirudin (Medicines company, NJ), Argatroban (Daiichi, Japan), recombinant Thrombin (Zymogenetics, WA) were used in this study. In the presence of citrate and CTI, endogenous thrombin generation is minimal, and only exogenously added thrombin affects thrombin inhibitors, and uninhibited thrombin would induce clotting on TEG®. Thrombin (100 nM) was added to TEG® cups immediately before adding blood samples. We tested 4 types of samples (n=6 each); control (no inhibitor), Intimatan (20 μg/ml), argatroban (3.75 μg/ml), and bivalirudin (15 μg/ml). Three variables of TEG® were obtained; R time, angle, MA (maximum amplitude). In this test, R time represents the whole blood thrombin time.
Results: Compared to controls without anticoagulants, thrombin time was prolonged significantly with thrombin inhibitors in the order of bivalirudin>Intimatan>argatroban. TEG® -angle was also reduced in the order of Intimatan>bivaliridin=argatroban. Only Intimatan effectively reduced TEG® -MA. Data are summarized in Table (mean±SD, *p<0.05).
Conclusions: At therapeutic concentrations to conduct heart surgery, three thrombin inhibitors prolonged thrombin time on TEG®. Bivalirudin prolonged thrombin time (R time) most, however, clot developments were only reduced with Intimatan. Our findings clearly indicate that bivaliridin and argatroban are reversible thrombin inhibitors. HCII mediated thrombin inhibition with Intimatan seems to be more effective in preventing clot development. In conclusion, modified thrombin time using TEG® could be useful in predicting the kinetics of thrombin inhibition with direct or indirect thrombin inhibitors.

References:

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Thrombelastography Variables with Thrombin at 100nM

	R(min)	angle(degree)	MA(mm)
WB(control)	0.8±0.03	60±1/0	51±0.2
WB+bivalirudin15mcg/ml	17±1.3*	24±2.2*	55±1.3
WB+argatroban3.75mcg/ml	7.3±0.2*	22±1.7*	44±1.9
WB+intimatan20mcg/ml	11±1.8*	4.6±0.8*	5.1±1.0*

S-14.

PREOPERATIVE PLATELET DYSFUNCTION IN LIVER TRANSPLANT RECIPIENTS

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Introduction: Patients presenting for liver transplantation (LT) have multiple risks for impaired hemostasis, including thrombocytopenia. In addition, *qualitative* platelet defects, previously documented by aggregometry, may be present in cirrhotic patients (1) and after reperfusion during LT (2). ThrombelastographR (TEGTM) indices of platelet function are described and validated in LT patients (3). We investigated platelet function in LT patients with a new FDA-approved Platelet Mapping (PM) assay (4).
Methods: After IRB approval, consecutive LT patients were enrolled. Prior to incision or blood product transfusion, blood was obtained from an arterial line (non-heparin containing) for analysis. PM measures platelet function as % reduction in maximum amplitude (MA), measuring contributions of fibrin only, thrombin, ADP and arachidonic acid (AA) in simultaneous samples. After thrombin inhibition in a heparin tube, MA is measured in the presence of an activator, and with added ADP, and compared to the kaolin-activated MA. This data may be more specific for platelet function than traditional indices of platelet function (maximum amplitude [MA] and G [mathematically derived from MA]).
Results: This preliminary adult cohort demonstrated anticipated defects in hemostasis by laboratory (INR 1.9 ± 0.7, platelet count 96.3 ± 63.3 x 103/mm3) criteria with minimal abnormalities in TEG criteria (Table 1), as well as mildly impaired renal function (BUN 18.1 ± 9.5 mg/dl, Cr 1.6 ± 1.3 mg/dl). In the absence of anti-platelet pharmacotherapy (aspirin or clopidogrel), there was a *significant* inhibition of baseline pre-incision platelet function in response to ADP (84.3 ± 24.6 % inhibition), much greater than expected from the borderline changes in TEG MA and G.
Conclusions: In addition to the anticipated defects in hemostasis in patients presenting for LT, including thrombocytopenia, the TEG-PM assay, which offers a specific assessment of platelet function, identified significant inhibiton of ADP-mediated platelet aggregation in this small, heterogenous population. Continued investigation is indicated to corroborate these initial findings and investigate for possible associations with renal dysfunction, severity of hepatic dysfunction, bleeding and blood product administration and possible therapeutic implications, including platelet administration.

References: 1. Ordinas A et al. Hepatology 1996; 24: 1137-42.
2. Himmelreich G et al. Transplantation 1992; 53" 582-6.
3. Gillies BS. Semin Thromb Hemost 1995; 21S4: 45-9.
4. Tantry US et al. J Am Coll Cardiol 2005; 46: 1705-9

Baseline TEG data

	LT patients (8)	Normal
R time (min)	8.2 ± 3.0	4-8
K time (min)	3.0 ± 1.3	1-4
Angle (^{0})	55.9 ± 9.9	47-74
MA (mm)	55.7 ± 13.7	55-73
G (Kdyne/sec)	7.4 ± 4.2	6-13.2

S-15.

NEW THERAPEUTIC STRATEGY FOR MUSSIVE PULMONARY THROMBOEMBOLISM. (FIVE CASES TREATED WITH PERCUTANEOUS TRANSLUMINAL ASPIRATION UNDER PERCUTANEOUS CARDIOPULMONARY SUPPORT)

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INTRODUCTION : Massive pulmonary thromboembolism is usually fatal if not treated aggressively, but management is not standardized (1). Even the open heart surgery was required for mussive pulmonary thromboembolism, we experienced five cases of massive pulmonary thromboembolism, which were treated with percutaneous transluminal aspiration of pulmonary thrombi under percutaneus cardiopulmonary support. We summarized these five cases.
METHOD : We performed a retrospective chart review of the five cases. All five cases developed into shock. As administration of catecholamines and mechanical ventilation failed to improve the shock, percutaneous cardiopulmonary support (PCPS), a kind of extracorporeal membrane oxygenation widely available in Japan (2), was introduced. After that, percutaneous transluminal aspiration using percutaneous transluminal coronary angioplasty (PTCA) catheter was performed to remove the pulmonary thromboemboli. And their hemodynamic parameters became stable. The treatment with PCPS was continued several days.
RESULTS : All five patients discharged with no complications. The average duration of PCPS was 3.4 ± 0.9 days (range 1 - 4), and the average duration of mechanical ventilation was 10 ± 4days (range 4 - 15), and the average of hospital days in cardiac division was 39 ± 10 days (range 27 - 50). The average of cost was 4356 ± 964 dollars (range 3092 - 5700).
CONCLUSION: Our experiences suggest that this combined therapeutic strategy, percutaneous transluminal aspiration under percutaneous cardiopulmonary support, improve the prognosis of massive pulmonary thromboembolism.
REFERENCES
(1) Ann Thorac Surg 2001; 72: 266-7
(2) Perfusion 2000; 15: 527-9

S-16.

PLATELET STORAGE POOL DEFICIENCY DURING PREGNANCY AND REGIONAL ANESTHESIA

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Introduction: Platelet storage pool deficiency is a bleeding disorder in which platelet granules are decreased in number or absent. The alpha and delta platelet granules are responsible for storing chemical mediators to facilitate platelet aggregation. The occurrence of this disease during pregnancy has rarely been reported. There have been few documented cases of the anesthetic implications of this disease and the use of regional anesthesia (1,2). Understanding this rare disease and the regional anesthetic implications makes this case important for presentation.
Case Report: A primigravida patient with a diagnosis of platelet storage pool deficiency presented to the labor and delivery ward for a scheduled cesarean section. She requested regional anesthesia. Extensive laboratory testing was performed, including coagulation status, thromboelastogram (TEG) and platelet function assay (PFA-100). Eight units of platelets were transfused and extensive risk/benefit counseling was completed. A single shot spinal anesthetic with a 27-gauge whitacre needle was administered without complication. Close attention to neurological checks followed for three days postpartum and the patient was discharged without incident.
Discussion: Most authors advocate general anesthesia for patients with platelet storage pool deficiency, however, none of the reported cases involved pregnant patients. Because general anesthesia in a parturient carries increased risk, regional techniques have become standard practice for cesarean section. A patient with platelet storage pool deficiency presents unique bleeding tendencies secondary to decreased platelet aggregation. This presents a risk for regional anesthesia in addition to intraoperative hemostasis. We demonstrate that adequate preparation with platelet transfusion coupled with the use of modern platelet function tests can lower the risk of regional techniques. Through minimizing the bleeding risk, regional techniques may become a safe anesthetic option in parturients with this disease.
References:
1. Australian and New Zealand Journal of Obstetrics and Gynaecology: 43:171-172, 2003
2. Canadian Journal of Anesthesia 47:12, 1224-1229, 2000

Cardiothoracic & Vascular - Basic Science

S-17.

MECHANISMS BEHIND THE ACTION OF ETOMIDATE ON VASCULAR REACTIVITY IN ISOLATED RAT MESENTERIC RESISTANCE ARTERIES

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Introduction: Etomidate, when administered in higher doses for cerebral protection (i.e., electroencephalographic burst suppression), produces immediate decreases in systemic arterial pressure. The aim of this study was to investigate the direct action of etomidate on systemic resistance arteries and its underlying mechanisms.
Methods: Isometric force was recorded to examine the effects of etomidate (1-300 μM) on contractile response to noradrenaline (NA) or KCl in endothelium-intact or endothelium-denuded strips prepared from rat small mesenteric arteries. In some experiments, changes in the force and intracellular Ca2+ concentration ([Ca2+]i) were simultaneously recorded in the fura-2-loaded, endothelium-denued strips. All experiments were performed in HEPES-buffered (pH 7.35, 35°C) physiological salt solution. ANOVA, Scheffe F test, contrast, Student's t-test and Welch's t-test were used to determine significance ($P<0.05$), as appropriate.
Results: In the endothelium-intact, fura-2-nonloaded strips, etomidate enhanced ($p<0.05$, n=7-8) contractile response to NA (2 μM [~EC_{50}] , 10 μM) and KCl (40 mM) only at a low concentration (3 μM), but inhibited ($p<0.05$, n=7-8) at higher concentrations (10-300 μM). In the endothelium-denuded, fura-2-nonloaded strips, etomidate (10-300 μM) inhibited ($p<0.05$, n=7) contractile response to NA (0.5 μM [~EC_{50}], 10 μM) and KCl (40 mM) without exerting any enhancing action. In the endothelium-denuded, fura-2-loaded strips, etomidate (10-300 μM) inhibited ($p<0.05$, n=6-7) increases in both force and [Ca2+]i induced by NA (10 μM) or KCl (40 mM). Etomidate (10-300 μM) also inhibited ($p<0.05$, n=3) the NA-induced increase in [Ca2+]i after depletion of the intracellular Ca2+ stores with ryanodine. However, etomidate did not influence ($p>0.05$, n=5) NA- or caffeine-induced increase in [Ca2+]i in the absence of extracellular Ca2+. In addition, etomidate did not influence ($p>0.05$, n=6) Ca2+ uptake into the intracellular Ca2+ stores. Finally, etomidate did not influence ($p>0.05$, n=5) the [Ca2+]i-force relation during stimulation with NA or KCl at lower concentrations (10-30 μM), but caused ($p<0.05$, n=5) its rightward shift at a high concentration (100 μM).
Conclusion: The action of etomidate on contractile response to NA or KCl consists of two components: an endothelium-dependent enhancing component and an endothelium-independent inhibitory component. Etomidate, at lower concentrations (10-30 μM), directly inhibits the vascular reactivity by inhibiting plasmalemmal Ca2+ influx and thereby reducing [Ca2+]i in vascular smooth muscle cells, while the direct vasodilator action of higher concentrations of etomidate is probably due to reductions of both [Ca2+]i and myofilament Ca2+ sensitivity in vascular smooth muscle cells. Since the plasma concentrations of etomidate necessary for cerebral protection are approximately 10-30 μM, systemic hypotension caused by etomidate used as a neuroprotectant is presumably due, at least in part, to its direct inhibitory action on vascular smooth muscle cells of mesenteric resistance arteries.
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S-18.

RESISTANCE TO HIGH CO2 IN NAKED MOLE-RATS, ANIMALS THAT NATURALLY LACK VASOACTIVE NEUROPEPTIDES FROM THEIR RESPIRATORY TRACT

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Introduction: Naked mole-rats congenitally lack Substance P (SP) and Calcitonin Gene Related Peptide (CGRP) from their skin and respiratory tract. In all other mammals including humans, these neuropeptides are thought to function in (1) central sensitization from inflammatory pain (2) peripheral wound healing and (3) CO2 induced pulmonary edema. As a selective “natural knockout” for these neuropeptides, we can use the naked mole-rat model to study these phenomena in new ways. In recent studies on the skin, we showed that naked mole-rats are insensitive to inflammatory pain stimuli. Here we present initial findings from experiments focusing on the respiratory system. In other mammals, high concentrations of atmospheric CO2 trigger pulmonary edema and death via local release of vasoactive neuropeptides (eg SP and CGRP). We hypothesized that the lack of neuropeptides in naked mole-rats might make them resistant to these effects.
Methods: Awake naked mole-rats and standard laboratory mice were exposed to different concentrations of CO2 for 15 minutes in an atmosphere chamber. The O2 level was always maintained at 20%. Animals were video recorded, and the time to loss of voluntary movement was noted. Immediately after exposure, the animals were decapitated and the lungs removed and weighed (wet weight). The lungs were again weighed after desiccation (dry weight). The wet to dry lung weight ratio was then calculated as an indicator of pulmonary edema.
Results: Both the behavioral and the anatomical results indicate that naked mole-rats are much more resistant to the adverse effects of high atmospheric concentrations of CO2 compared to mice. At 50% CO2, naked mole-rats maintained voluntary movements for 100 seconds, whereas mice lost voluntary movements at 20 seconds. Lung measurements showed that mice suffered significant edema at CO2 concentrations as low as 15%, with maximum edema (wet/dry ratio = 7.6) at concentrations ≥ 20%. In contrast, naked mole-rats showed no edema even at 50% CO2.
Discussion: The preliminary results presented here support a role for the neuropeptides SP and/or CGRP in pulmonary edema evoked by high concentrations of atmospheric CO2. To further test this hypothesis, our next goal is to test animals after applying gene therapy techniques to up-regulate neuropeptides in mole-rat lungs and down-regulate neuropeptides in mouse lungs. Naked mole-rats have a unique ecology - they are fully subterranean and live together in very high numbers. Hence, the atmosphere in their living space has chronically high concentrations of CO2. Presumably, these conditions have led to the adaptive loss of neuropeptides which would normally be released from exposure to high CO2 levels. Experiments that exploit the unique features of the naked mole-rat, like those presented here, are helping us better understand basic pulmonary physiology.
References: International Association for the Study of Pain Proceedings, 235-243, 2003.

S-19.

NEGATIVE INOTROPIC EFFECTS OF NATRIURETIC PEPTIDES ARE ATTENUATED IN ISOLATED MYOCYTES FROM THYROXINE-INDUCED HYPERTROPHIC HEARTS IN RABBITS

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Introduction: It has been shown that cardiac hypertrophy increased atrial natriuretic peptide expression in rats1. However, the negative inotropic effects of C-type natriuretic peptide was attenuated in pressure-overload-induced ventricular hypertrophy in mice2. We tested this hypothesis using myocytes isolated from thyroxine-induced hypertrophic rabbit hearts and also studied the probable molecular mechanism.
Methods: Ventricular myocytes were isolated from control (n=8) and thyroxine (T4)-treated (0.5 mg/kg SQ/day x 16 days, n=7) rabbits using collagenase. Myocyte contraction was measured via a video edge detector. Myocyte functions were examined at basaeline and after addition of brain natriuretic peptide (BNP 10-7, -6 M) or C-type natriuretic peptide (CNP 10-7,-6M) in the absence or presence of zaprinast (specific cyclic GMP phosphodiesterase inhibitor 10-6M). Soluble (sGC) (±0.1 mM S-nitroso-N-acetyl-penicillamine, SNAP, a nitric oxide donor) and particulate (pGC) (±0.1% Triton X-100) guanylyl cyclase activities and cyclic GMP (cGMP) levels were measured in myocyte homogenates. ANOVA was used for statistical analysis. A value of $p<0.05$ was accepted as significant. Data were presented as mean ± S.E.M.
Results: Baseline functions were similar in the control and T4 myocytes. Percent shortenings were significantly reduced by both concentrations of BNP (10-6M: 5.7±0.2 to 4.3±0.1%) and CNP (10-6M: 5.7±0.4 to 4.2±0.2%) in the control. These reductions were not observed in T4 myocytes (10-6M BNP: 5.7±0.6 to 5.6±0.6%: 10-6M CNP: 5.6±0.4 to 5.5±0.5%). The responses to BNP and CNP were similar in the presence of zaprinast in both groups. There was no difference in baseline cGMP levels between the control and T4 myocytes, however, BNP increased cGMP in the control but not in T4 myocytes. The basal activities of pGC were similar in the control and T4 myocytes. Triton-stimulated pGC activity was significantly lower in T4 myocytes compared to the control (Figure 1). Both basal and SNAP-stimulated sGC activities were similar in the control (4.4±1.3, 30.6±5.5 pmol/mg protein/min) and T4 (4.9±0.2, 37.0±7.5) myocytes.

Discussion: The data showed that the negative inotropic effects of natriuretic peptides were blunted in thyroxine-induced cardiac hypertrophy. This blunted response could be due to the decreased natriuretic peptide-induced cGMP level and the decreased total particulate guanylyl cyclase activity in hyperthyroid myocytes.
References: 1. Circ Res 73:184, 1993. 2. Aneth Analg 100:s-65, 2005.

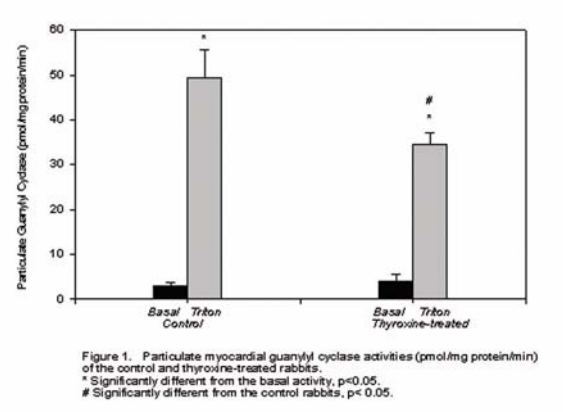

Figure 1. Particulate myocardial guanylyl cyclase activities (pmol/mg protein/min) of the control and thyroxine-treated rabbits.
* Significantly different from the basal activity, p<0.05.
# Significantly different from the control rabbits, p< 0.05.

S-20.

THE LECTIN-LIKE DOMAIN OF THROMBOMODULIN GOVERNS VENTRICULAR REMODELLING IN AFTERLOAD-INDUCED HYPERTROPHY IN MICE

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Introduction: Hypertensive cardiomyopathy is a frequent cause for perioperative cardiovascular complications. Thrombomodulin not only plays an important role for thrombin inactivation and protein C activation but is, through it's lectin-like domain (TMLeD, a powerful modulator of inflammation (1)We hypothesized that because of its central position in between haemostasis and coagulation TMLeD may also have an effect on myocardial remodeling phenomena and set out to test this hypothesis by subjecting mice with a knock-in mutation of TM lacking TMLeD to transversal aortic constriction-induced left ventricular hypertrophy (TAC).
Methods: With approval of the IRB, the aortic arch of WT- and TMLeD/LeD mice was constricted by ligating a 6-0 silk suture over a 26G cannula between the brachiocephalic artery and the left carotid, inducing a trans-aortic gradient of about 40 mmHg. Echocardiographic exams were conducted before and 14 days after TAC, before necropsy left ventricular mass was assessed, collagen expression was quantitated by realtime PCR and immunohistochemical analysis of myocyte area, leukocyte recruitment and collagen deposition was perfomed. Data are mean±sem. Non-parametric tests were performed to detect differences at $p<0.05$.
Results: No baseline differences were detected between WT and TMLeD/LeD. Left ventricular mass and myocyte area increased slightly more in TMLeD/LeD compared to WT (WT 193 mg vs. TMLeD/LeD 223mg, n=10, p<0,05 and (WT 365 µm² vs. TMLeD/LeD 402 µm², n=6, p<0,01).). Echocardiographically a 30% increase in LV enddiastolic diameter was detected in TMLeD/LeD compared to concentrically hypertrophied WT-LVs. While only few leukocytes were detectable was maladaptive remodeling associated with an increase in CD45-positive cells and collagen deposition at mRNA and protein level: CD45-pos x-fold vs. sham: WT 2,3±0,96 vs. TMLeD/LeD 10,3±6,0, n=5, p<0,05; collagen staining: x-fold vs. sham; WT vs. TMLeD/LeD; 0,9±0,2 vs. 1,2±0,3, n=6, p<0.05; RT-PCR: x-fold vs. control: WT 8,1±2,6 vs. TMLeD/LeD 20,1±4,4, n=3, p=0,05).

Discussion: An increase in afterload induces hypertrophy in WT mice, while mice lacking TMLeD display increased leukocyte recruitment, fibrosis and LV dilatation. TMLeD thus seems to play a role, possibly by altering inflammatory pathways, for myocardial remodelling in hypertrophy and may thus be a valuable target to prevent maladaptive remodelling in patients at risk.
Reference:
1) Conway et al. JExpMed 2002: 196(5):565

S-21.

SUPERIOR LOGISTIC FITTING FOR DECAY OF CA2+ TRANSIENT IS INDEPENDENT OF ONSET IN MURINE LEFT VENTRICULAR PAPILLARY MUSCLE

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Introductions: A decrease in myocardial intracellular calcium concentration (Ca2+) precedes relaxation. We found that a logistic function has been shown to better fit the isometric relaxation force curve (1) and the isovolumic relaxation left ventricular (LV) pressure curve (2, 3) than the conventional monoexponential function. However, the monoexponential function has been used to fit for the decay of the Ca2+ transient. In the present study, we compared the logistic and monoexponential fittings for the decay of the Ca2+ transient.
Methods: We measured the twitch isometric force curve and the Ca2+ transient using the aequorin method in 15 isolated murine LV papillary muscles. We analyzed the decline of the Ca2+ transient from four different starting points: the Ca2+ levels relative to peak Ca2+ level of the same rate as the tension at the maximum negative time derivative (dF/dt_{min}), and the 10, 20, and 30% lower-developed tensions relative to peak isometric tension (0%SP, -10%SP, -20%SP, -30%SP). We evaluated the decay of the Ca2+ transient, using the logistic: $Ca(t) = Ca_A/[1 + \exp(t/C\tau_L)] + Ca_B$ and monoexponential functions: $Ca(t) = Ca_0\exp(-t/C\tau_E) + Ca_\infty$. We compared the goodness of the logistic and monoexponential fittings with correlation coefficient (r) and residual mean squares (RMS).
Results: Table showed the r and RMS values (mean ± SD) of the logistic and monoexponential fittings for the four declines of the Ca2+ transient from 0%SP, -10%SP, -20%SP, and -30%SP. The r values of the logistic fittings were always significantly larger than the monoexponential fittings (* $P < 0.05$). The RMS values of the logistic fittings were always significantly smaller than the monoexponential fittings (# $P < 0.05$).

Table. Correlation coefficient (r) and residual mean squares (RMS) of logistic and monoexponential fittings for declines of Ca2+ transient at 4 onsets

	0%SP	-10%SP	-20%SP	-30%SP
Logistic r	0.9957 ± 0.0033*	0.9948 ± 0.0647*	0.9937 ± 0.0051*	0.9921 ± 0.0069*
Monoexponential r	0.9939 ± 0.0036	0.9929 ± 0.0046	0.9917 ± 0.0055	0.9900 ± 0.0072
Logistic RMS $(\mu mol/l)^2$	0.00067 ± 0.00056#	0.00063 ± 0.00055#	0.00061 ± 0.00056#	0.00057 ± 0.00056#
Monoexponential RMS $(\mu mol/l)^2$	0.00092 ± 0.00065	0.00083 ± 0.00060	0.00078 ± 0.00061	0.00073 ± 0.00060

Discussions: Superiority of the logistic fitting to the monoexponential fitting for the decline of the Ca2+ transient is independent of onset in the murine LV papillary muscle. Logistic function fitting more reliably characterizes the decay of the Ca2+ transient. Simultaneous analyses by the logistic function for myocardial lusitropism and the decline of the Ca2+ transient might be a useful strategy for speculating myocardial calcium handling.
References:
1) Jpn J Physiol 50: 479-487, 2000
2) Circulation 92: 2318-2326, 1995
3) Anesth & Analg 102: 1032-1039, 2006

S-22.

STROKE VOLUME PER UNIT EJECTION INTERVAL AS A NON-INVASIVELY MEASURABLE PROXY TO DP/DT MAX, A MEASURE OF MYOCARDIAL CONTRACTILITY, IN PIGS

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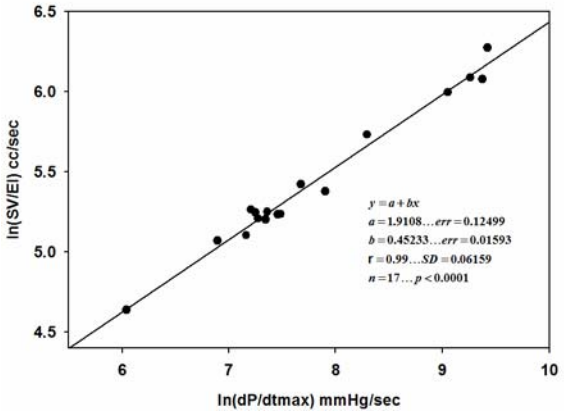
Introduction: Myocardial contractility, as a parametric determinant of stroke volume (SV), is not presently monitored perioperatively because the measurement of dP/dtmax requires a hazardous, invasive LV catheter. This work shows why the quantity SV/EI, the average rate at which the SV is ejected from the LV into the aorta during the ejection interval (EI), is a useful, non-invasive substitute for dP/dt max.
Methods: Under general anesthesia an adult pig had right femoral Swan-Ganz and arterial line catheters inserted. A 16 gauge catheter was placed through the chest wall, directly into the LV. EKG, femoral arterial, and left ventricular pressures were recorded simultaneously. Dobutamine, nitroglycerine, and phenylephrine were infused to create 17 distinct steady hemodynamic states with large variations in preload, afterload, and contractility. Thermodilution cardiac outputs were measured at functional residual capacity (FRC) in rapid sequence while 60 seconds of hemodynamic data recorded at each steady state. Using averaged CO and averaged cardiac cycle period T, average SV was obtained for each steady state. SV and EI were used to calculate mean SV/EI (cc/sec) over the ejection interval.
Results: The results are summarized in fig. 1.



Over a large range of LVEDP and SVR. A and B are empirical constants. Equation 1 applies in the absence of respiratory variation, with the lung at FRC. Fig. 1 reveals that with varying conditions of preload and afterload, eq. 1 yields a correlation coefficient of 0.99 ($P<0.0001$). Eq. 1 applies over 3.5 log units with respect to dP/dt max, and nearly 2 log units with respect to SV/EI. LVEDP, as a metric of preload, varied from 1.183 to 19.974 mmHg. SVR, as a metric of afterload, varied from 421 to 12,390 dyne*sec*cm^-5.
Discussion: SV/EI could be measured as a proxy for dP/dt max to provide a real time, non-invasive index of myocardial contractility. The relation between SV/EI and dP/dtmax appears independent of preload and afterload. Constants A and B may be predictable functions of anthropometric parameters.

S-23.

DYNAMIC HIGH RESOLUTION POSITRON EMISSION TOMOGRAPHY TO ASSESS BIODISTRIBUTION OF F-18-FDG LABELED CELLS IN MICE

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Introduction: Today, many pathophysiological studies of cardiovascular diseases rely on in-vitro experiments. However, being able to assess molecular and cellular pathways in living animals is expected to further improve the relevance of these studies, especially if it comes to translational research from mice to men. Here, we demonstrate the feasibility of following the biodistribution and fate of intravenously injected cells using a labelling technique with F-18 fluorodesoxyglucose (FDG) in combination with dynamic small animal positron emission tomography (PET).
Methods: Immortalised mouse endothelial cells (f.End5) were cultured in DMEM with 5% glucose 5% CO_2 in air at 37°C. After 3 days cells underwent different incubation periods (15-90 min) with 100 MBq F-18-FDG in a glucose free buffer containing 1-3 I.U. of insulin. Simultaneously, fluorescent staining cells were stained with near infrared fluorophor (NIRF) DiR for microscopic confirmation of cell associated signals in vivo. Experiments were varied in temperature and duration of incubation as well as insulin concentration in order to establish optimal conditions for F-18-FDG uptake. After incubation cells were trypsinized, washed twice and resuspended in 300µl 0.9% saline supplemented with 1% mouse serum. Trypan-blue exclusion was used to assess viability. Intracellular 18-FDG was measured and 1x106 cells were injected intravenously in isoflurane anesthetized swiss mice. A dynamic PET scan for 3 hours was initiated on a sub-millimeter-resolution, dedicated animal PET (quadHIDAC, Oxford Positrons Ltd.). Mice were sacrificed and 10µm cryosections were prepared from FDG-positive tissues. Cell-associated DiR-signals were registered by NIRF microscopy.
Results: Cell viability depended on incubation time, but FDG-uptake was independent of the insulin dose. An optimized protocol of 30 min FDG-incubation at 37°C and 1 I.U. insulin in the buffer solution yielded a cell viability of 98% and FDG uptake of 0.53-1.8 % of the incubation dose. Dynamic small animal PET using the quadHIDAC, being uniquely able to image the whole mouse in 3D space over time, detected F-18-FDG labeled cells in the lungs within seconds after intravenous injection, later on in kidney and bladder with high temporal and spatial resolution. Background signal was little to none. Correlative histological analyses also demonstrated the expected corresponding fluorescence DiR signal in lung tissue.
Discussion: Small animal PET with F-18-FDG-incubated endothelial cells is able to assess biodistribution/homing of intravenously injected cells. To our knowledge this method is used here for the first time to detect F-18-FDG-labeled cells in mice in vivo. Further establishing this method should provide a mean to dynamically follow different cell types in mice in vivo with many potential applications in animal models of tissue injury or inflammation such as myocardial infarction and atherosclerosis.

S-24.

REGIONAL PHASE ANGLE ANALYSIS OF ISCHEMIA-INDUCED DYSSYNCHRONOUS MYOCARDIAL CONTRACTION IN DOGS

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INTRODUCTION: Regional dyssynchrony is common in patients during normal and abnormal cardiac function, but is not easily quantified (1). We described previously a model using esmolol-induced regional dyskinesis for quantifying left ventricular (LV) dyssynchrony that referenced regional amplitude and phase angles to global LV systole (2). Esmolol may not represent a clinically relevant model for regional ischemia however, thus our goal was to validate our regional phase angle analysis in a canine model of regional ischemia.
METHODS: With institutional approval, we studied 10 anesthetized open-chested dogs. Regional and total LV volumes (conductance catheter) and regional shortening (sonomicrometer crystals) were compared before, during, and following systemic dobutamine infusion, esmolol-induced regional apical dyskinesis, and matched apical ischemia. Regional phase angle of contraction (α) was defined as the relative distance (measured in degrees) that regional minimum volume differed from global end-systole (minimum total LV volume). Regional dyskinesis was induced by bolus of 750ug/kg of esmolol into a LAD coronary artery catheter or by ligature occlusion of the LAD artery (LAD coronary artery perfusion zone 29.7 ± 1.7 g; total LV 136.7 ± 7.5 g; n = 10).
RESULTS: Systemic dobutamine advanced apical contraction and decreased heterogeneity of regional α with respect to baseline while esmolol and ischemia delayed apical contraction and increased the heterogeneity of regional contraction relative to baseline. Systemic blood pressure was elevated during dobtamine and decreased during regional esmolol and apical ischemia relative to baseline.

End-systolic phase angles (degrees) of regional volumes relative to global end-systole.

Treatment	Conductance Catheter Region					Sonomicrometer	
Group	Apex	Papillary	Chordal	Base	Global	Apex	Base
Baseline	12.4±8.9	6.1±4.7	3.7±4.5	2.1±3.9	0	53.6±7.2	26.6±8.6
Dobutamine	1.0±13.2	-5.0±4.2*	-5.0±2.9*	8.5±11.1	0	4.2±10.3*	26.6±14
Esmolol	27.4±9.6*	17.5±6.5	-0.7±6.4	-6.0±2.7*	0	67.7±8.0*	33.3±11.1
Ischemia	54.2±10.3*§	28.2±9.6*	-13.8±7.6*	-14.7±6.9*	0	87.9±5.3*	26.4±16.3

* Values differ from baseline ($P < 0.05$). § Values differ from esmolol ($P < 0.05$). Values are mean ± SEM; n=10. End-systole is defined as the minimum value with respect to time signal for each region. Abbreviation: LV = left ventricle.
CONCLUSIONS:
Changes in regional α and its associated phase angle analysis are more sensitive than global measures of LV performance at quantifying regional dyssynchrony. We validated phase angle analysis as an effective model to describe and quantify regional dyssynchrony induced by regional ischemia. Potentially, phase angle analysis may prove an effective measure to identify and quantify the beneficial effects of resynchronization therapies on myocardial function.

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S-25.

UROKINASE-TYPE PLASMINOGEN ACTIVATOR RECEPTOR (U-PAR) DEFICIENCY REDUCES INFARCT SIZE AND IMPROVES NEUROLOGICAL OUTCOME AFTER FOCAL CEREBRAL ISCHEMIA AND REPERFUSION IN MICE

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Introduction: Reperfusion injury after focal cerebral ischemia is characterized by leukocyte recruitment and the release of cytotoxic mediators and oxygen-derived radicals inducing necrosis and apoptosis in previously unaffected cells.1,2 Strategies to abolish leukocyte recruitment have not demonstrated any treatment benefit with respect to clinical endpoints.3 Urokinase-type plasminogen activator receptor (u-PAR) modulates integrin activation during leukocyte-endothelial cell interactions.4 We tested whether modulation instead of abolishment of leukocyte recruitment by genetic ablation of u-PARwould (1) render brain injuries smaller and (2) improve neurological functional recovery after focal cerebral ischemia.
Methods: Adult male u-PAR knock out (KO, n=10) and wild type (WT, n=11) mice underwent 45 minutes of transient middle cerebral artery occlusion (tMCAO) using an intraluminal suture followed by 24 hours of reperfusion. Cerebral blood flow (CBF) was monitored using a laser Doppler flowmeter. Infarction volume was assessed using a cresyl violet staining. Inflammatory cells were identified using CD45 and myeloperoxidase (MPO) immunohistochemistry. Motor-function was tested using a five-point score. Data are presented as mean±SEM.
Results: No cerebrovascular abnormalities, including common carotid artery, internal carotid artery, external carotid artery, Circle of Willis or microvessels were detected in u-PAR KO mice compared to WT mice. There was also no difference in baseline blood glucose levels and blood gases. There was no difference in CBF in the ischemic core before, during tMCAO and after 24 hours of reperfusion between u-PAR KO and WT mice ($p>0.05$). Infarction volume was significantly smaller in u-PAR KO mice compared to WT mice (0.21±0.2 vs. 1.26±0.4mm3, $p<0.05$, un-paired t-test). Motor-function was better in u-PAR KO compared to WT mice (3.0±0.2 vs. 1.7±0.4, $p<0.05$, rank sum test). Immunostaining showed fewer CD45 and MPO positive cells in the ipsilateral hemisphere of u-PAR KO mice than that in WT.
Conclusion: Decrease of infarction size and improvement of neurological outcome after tMCAO in the u-PAR KO compared to WT mice suggested that abrogation of u-PAR function is neuroprotective. CD45 and MPO positive cells were attenuated in the ischemic region in u-PAR KO mice, suggesting u-PAR plays an important role in the ischemia induced inflammatory response.
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S-26.

TLR4 PROTECTS CARDIOMYOCYTES FROM APOPTOSIS AND REDUCES MYOCARDIAL INFARCTION IN A MOUSE MODEL OF ISCHEMIA-REPERFUSION INJURY

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Introduction: The innate immune response to ischemia-reperfusion injury (IRI) is the most common cause of myocardial inflammation. Recent studies have shown that Toll-like receptor-4 (TLR4), a critical component of innate immunity, may play an important role in mediating tissue inflammation and cell survival in non-infectious injury. The goal of this study is to examine the role of cardiac TLR4 in protecting cardiomyocytes from apoptosis and IRI.
Methods: *Mouse ex-vivo model of IRI:* After 10-min of control perfusion, isolated mouse hearts were exposed to 20-min of global ischemia followed by 30-min of reperfusion. The hearts were then removed, sliced, and incubated with 1% TTC. Infarct and total LV areas were measured using Adobe Photoshop. *In vitro model of apoptosis*: Neonatal mouse cardiomyocytes were subjected to serum-deprivation (SD) or hypoxia for 24-hours. Apoptosis was examined using multiple methods including DNA laddering, DNA-histone ELISA, TUNEL-staining. *Cardiomyocyte function*: Sarcomere shortening and [Ca2+]i transients were recorded on an IonOptix system in adult mouse cardiomyocytes loaded with fura-2 and electrically paced.
Results: SD or hypoxia induced a significant increase in the number of apoptotic cardiomyocytes. Lipopolysaccharide (LPS), a TLR4 agonist, activated TLR4 signaling and led to significant reduction in apoptosis and improved cellular function of surviving cardiomyocytes with enhanced Ca2+ transients and cell shortening. We found that both TLR4 and MyD88 are required for the LPS-induced beneficial effects as demonstrated by improved survival and function in wild type (WT) but not in TLR4-/- or MyD88-/- cardiomyocytes. Moreover, genetic deletion or pharmacological inhibition of NOS2 abolished survival and functional rescue of cardiomyocytes treated with LPS. Importantly, in isolated mouse hearts, global IRI induced 19±8% infarction (MI/LV) in WT mice and 38±18% in TLR4-/- mice (mean±SD, n=8) (P=0.02).
Discussion: These data suggest that TLR4 activation mediates a direct anti-apoptotic effect and improves cardiomyocyte function. Both MyD88 and NOS2 are essential for these benefits. Moreover, "loss of function" studies in the *ex-vivo* model of IRI, a system devoid of *extra-cardiac* inflammatory cells often associated with *in vivo* IRI, suggest that *cardiac* TLR4 may represent an intrinsic cardio-protective mechanism against ischemic injury.
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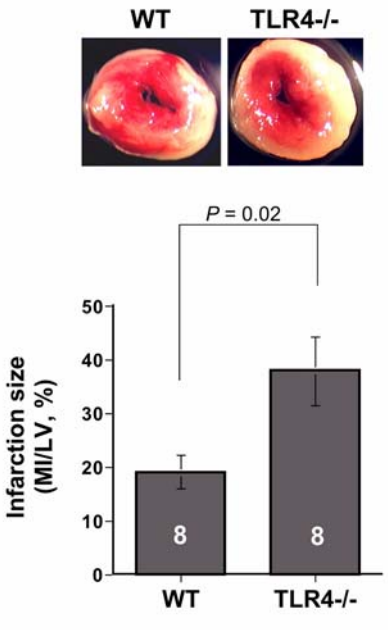

S-27.

REACTIVE OXYGEN SPECIES AND MITOCHONDRIAL KATP CHANNELS MEDIATE HELIUM-INDUCED CARDIOPROTECTION IN RABBITS

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Introduction: Our laboratory recently demonstrated that brief administration of a noble gas without anesthetic properties (e.g., helium, neon, and argon) before prolonged coronary artery occlusion and reperfusion protects myocardium against infarction by activating prosurvival signal transduction and inhibiting mitochondrial permeability transition(1). Reactive oxygen species (ROS) and mitochondrial KATP (mitoKATP) channels are important mediators of anesthetic and ischemic preconditioning(2,3), but whether ROS or mitoKATP channels play a role in noble gas-induced cardioprotection is unknown. We tested the hypothesis that ROS and mitoKATP channels mediate helium preconditioning in vivo.
Methods: Rabbits were anesthetized with sodium pentobarbital (30 mg/kg), acutely instrumented for the measurement of systemic hemodynamics, and ventilated using positive pressure with an air-oxygen mixture (FiO_2 = 0.30). All rabbits were subjected to a 30 min left anterior descending coronary artery occlusion followed by 3 h reperfusion. In separate experimental groups, rabbits (n=4 to 7 per group) were randomly assigned to receive 0.9% saline (control), three cycles of 70% helium-30% oxygen administered for 5 min interspersed with 5 min of the air-oxygen mixture before coronary artery occlusion, the ROS scavengers N-acetylcysteine (NAC; 150 mg/kg) or 2-mercaptopropionyl glycine (2-MPG; 1 mg/kg/min over 60 min), or the selective mitoKATP channel antagonist 5-hydroxydecononate (5 mg/kg) in the absence or presence of helium pretreatment. Myocardial infarct size was determined using triphenyltetrazolium chloride staining. Statistical analysis was performed with analysis of variance followed by Bonferroni's modification of Student's t-test.
Results: Systemic hemodynamics, arterial blood gas tensions and acid-base status, and arterial oxygen saturation (pulse oximetry) were unchanged during administration of helium with or without NAC, 2-MPG, or 5-HD pretreatment. Body weight, left ventricular mass, area at risk weight, and the ratio of area at risk to left ventricular mass were similar between groups. Helium significantly ($P<0.05$) reduced myocardial infarct size [23±4% of left ventricular area at risk (mean±SD)] as compared to control (46±3%). NAC, 2-MPG, and 5-HD alone did not affect infarct size (49±5, 44±7, and 45±3%, respectively), but these drugs abolished helium-induced cardioprotection (45±4, 45±1, and 44±3%, respectively).
Conclusions: The results confirm that brief, repetitive exposure to helium before coronary occlusion and reperfusion reduces myocardial infarct size in rabbits. The results further demonstrate that ROS and mitoKATP channels mediate this helium preconditioning in vivo.
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S-28.

ORALLY BIOAVAILABLE S1P-ANALOGUE MOBILIZES ENDOTHELIAL PROGENITORS AND PROTECTS AGAINST MYOCARDIAL ISCHEMIA IN MICE

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Introduction: Therapeutic strategies to protect the heart from reperfusion injury following restitution of blood flow after ischemia are currently not available. We recently demonstrated that HDL and its constituent S1P (sphingosine-1-phosphate) acutely protect the heart against ischemia/reperfusion injury in vivo via a S1P3- mediated and NO-dependent pathway (1). The novel immunemodulator FTY720 is a structural analogue of S1P and activates several of the S1P receptors. We tested whether FTY720 evolves protective effects against ischemia/reperfusion injury and whether its influence on mobilization of regenerative CD117+/flk1+ stem cells (SC) from bone marrow into the blood is part of this protective effect.
Methods: MI/R: To induce ischemia the LAD of C57Bl6-mice fed or not FTY720 (Cayman Chemical, Estonia) for 4 weeks via the drinking water (0,01 mg/L) was ligated over PE10 tubing for 30 minutes and reperfusion for 24h. In coomassie blue and TTC stained sections area at risk and infarct size were planimetrically delineated. Data are presented as percent infarcted tissue per area at risk. Mobilisation of endothelial progenitor cells (EPC) was flow cytomerically analyzed using antibodies anti-CD117+ and anti-Flk1+ in whole blood before and 24h after MI/R.
Results: We observed that FTY 720 dramatically attenuated infarction size by 36% (sd=14, n =6 with FTY, n= 8 control) respectively. While baseline mobilization of EPC was comparable (WT = 4644± 1788 cells/ml n=11 , WT/FTY = 4041± 1094 cells/ml n=9) EPC increased after MI/R only slightly in the WT control but markedly in WT/FTY (WT= 7045±1218 cells/ml n=8, WT/FTY = 17807± 4472 cells/ml n=8, $p<0,05$).
Discussion: It has been demonstrated that the immunomodulator and S1P receptor agonist FTY720 exerts direct effects on the vascular endothelium. FTY720 potently induced vasodilation in mouse aortae by activating the Akt/eNOS/NO pathway through the $S1P_3$ receptor (2). These findings already suggested that, unlike conventional immunosuppressive drugs, FTY720 may have beneficial effects on vascular structure and function and prevent cardiovascular morbidity and mortality. Our data now demonstrate that FTY720 protects the heart against ischemia/reperfusion injury in vivo and that this effect might interestingly be due to EPC mobilisation. Therefore a new therapeutic intervention of FTY720 may be beneficial in patients at high risk of acute myocardial ischemia.
References:
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S-29.

EARLY VS MODERATELY-LATE EXTUBATION FOLLOWING CARDIAC SURGERY: ARE THESE THE SAME PATIENTS?

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Introduction: Since Hickey's group1 described the benefits of early extubation (EE) in CABG, EE has become standard. Despite detailed protocols, a tendency exists for health care providers (HCWs) in CVICUs to delay extubation, often for non-essential clinical reasons: busy unit, newer staff, family visits, nursing breaks. We postulated that these "non-clinical" issues, not patient differences, were the determinants of intubation time (IT) across the cohort of potential EE patients.
Methods: Our patients sign consents for the use of their data entered into our database. We reviewed our most recent 70 patients, undergoing all types of cardiac surgery. We divided the patients into three groups: those extubated by four hours (group A), those extubated after four but less than eight hours (group B), and those extubated at eight hous or later. We assumed patients intubated longer than eight hours were not candidates for EE - they are not assessed further here. We compared IT, length of ICU and hospital stay and rates of reintubation, return to CVICU, transfusion, reexploration and MI for the two groups. We also reviewed the two groups for type of surgery, urgency classification, LV grade and time of day of case start. Differences were compared using Chi2 and t-test with significance set at the $p<0.05$ level.
Results: See Table. There was no difference in hospital LoS , age, gender or urgency score, nned for hemodynamic support or complications (data not shown).

Table

	Group A	Group B	p
n	24	34	
intubation time (hrs)	3.0 ± 0,3	5.5 ± 0.9	<0.001
ICU length of stay (hrs)	30.2 ± 13.9	48.1 ± 29.9	<0.04
% CABG only	45.8	85.3	<0.01
% 2nd case	52	85.3	<0.02
% LV grade>2	41.6	76.4	<0.02
% non-elective	52	63.4	NS

Discussion: Despite strong efforts and protocols, some "extubatable" patients are extubated later than others. The assumption is that these are failures of the HCW team. We show them to be a different group of patients: they were significantly more likely to have had *CABG only* surgery, a poorer LV grade and been started later in the day. Previous studies2.3 showed no pre-operative differences between the EE vs not-EE patients, but these were carefully selected for the study, were sometimes only CABG, or were dropped if certain complications arose. Larger numbers will need to be followed to determine if our trends persist, as this may lead to further modification of pre- and post-operative care to improve outcome.
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S-30.

GENDER DIFFERENCE OF OPIOID-INDUCED CARDIOPROTECTION IS INFLUENCED BY ESTROGEN

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Introduction: Pretreatment with opioids results in protection against ischemia-reperfusion injury (I/R) in male animals (1). Estrogen activates cardioprotective signal pathways similar to opioids (2). It is unknown if this results in an additive or inhibitive interaction of opioid-induced cardioprotection (OICP). Therefore, we tested the hypothesis that there is a gender difference in OICP and that the presence of estrogen reduces the magnitude of OICP in females.
Methods: Post-natal day 7 murine cardiomyocytes were isolated by collagenase digestion, cultured for 24 hours, and subjected to 90 min hypoxia and 180 min of reoxygenation at 37°C. Met5-enkephalin (ME 100 microM) was given for OICP 15 min prior to hypoxia. Cell death was assessed by propidium iodide. More than 300 cells were examined for each treatment. Tests were performed in hormone-free (control/ME; n=5 replicates), hormonally active 17-β-estradiol (10nM) and hormonally inactive 17-α-estradiol (1 microM) containing medium (n=3 replicates) in male and female cardiomyocytes.
Results: In male cardiomyocytes both 17-β-estradiol and 17-α-estradiol reduced cell death during simulated I/R comparable to ME alone. In addition, ME pretreatment in the presence of both stereoisomers increased male cell death compared to ME or hormone alone. Female cardiomyocytes were also protected against simulated I/R by 17-β-estradiol and, to a lesser degree, by 17-α-estradiol. ME plus 17-β-estradiol increased female cell death compared to estrogen alone, whereas 17-α-estradiol had no effect on OICP in female cardiomyocytes.

h	Control		ME		17-β-E2		17-β-E2+ME		17-α-E2		17-α-E2+ME	
	M	F	M	F	M	F	M	F	M	F	M	F
0	26±0.9	27±0.3	23±0.6*	23±0.7	22±0.5*	21±2.9*	21±0.7*	22±3.1	22±1.0*	22±2.7	23±0.3*	21±1.2*
1	38±1.2	39±0.7	27±0.7*	26±0.7*	28±0.5*	29±1.9*	29±2.2*	32±4.8*	29±1.5*	31±3.1*	30±1.2*	24±0.9*
2	49±0.7	52±0.9	31±1.1*	30±0.2*	31±1.4*	36±1.8*	36±0.6#	38±3*#	34±0.8*	39±1.9*	36±1.0$	29±1.6*
3	62±0.8	64±0.1	33±0.4*	33±0.5*	35±0.7*	39±0.6*	42±0.7#	47±1.8*	36±1.3*	49±1.7*	39±1.1$	32±1.2*

2-way RM ANOVA: ($p<0.05$) * vs control; # ME vs 17-β-E2+ME; $ ME vs 17-α-E2+ME
h= time [hours] of reperfusion; ME=Met[5]-enkephalin; 17-β-E2=17-β-estradiol; 17-α-E2=17-α-estradiol; M=male;F=female

Discussion: There is a gender difference in the interaction between estrogen and OICP in vitro. The cardioprotective effect of both estrogen stereoisomers in males suggests an estrogen-receptor independent mechanism that abolishes OICP. In contrast, the observation that 17-β-estradiol, but not 17-α-estradiol, diminished the ability of OICP to protect female cardiomyocytes indicates an estrogen-receptor dependent mechanism in females. These findings suggest that opioids, commonly used for cardiac high risk patients, will not be protective in women, and support the need for a gender-specific approach in cardiac anesthesia.
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S-31.

ISOSORBIDE DINITRATE (ISDN) PROTECTS RAT HEART AGAINST ISCHEMIA-REPERFUSION INJURY

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Introduction: One of the mechanisms for adapting ischemic stress is ischemic preconditioning (PC). Ischemic PC was first described as an immediate adaptation of the heart to ischemic stress after brief sublethal ischemia in a dog. Ischemic PC protects against not only myocardial infarction but also myocardial stunning, therefore, ischemic PC is significant in clinical studies. Some drugs can induce cardioprotective effect mimicking ischemic PC, and preoperative administration of NO donor prevents arrhythmia during percutaneous transluminal coronary angioplasty (PTCA). Heat shock protein (HSP) 70 has cellular protective effects as molecular chaperone. We investigated that NO donor, isosorbide dinitrate (ISDN), induces HSP 70 expression in the heart, and it plays an important role in ischemic PC.
Methods: Seven-week-old Wister male rats were administered ISDN of 4 μg kg1 h1 (ISDN group) or saline (control group) for 24 h, and following experiments were performed 24 h after administration. 1) Confirmation of HSP 70 expression in the heart using western blotting technique. 2) In vivo ischemia-reperfusion model: The rats were anesthetized and incubated, and then underwent a 30-min ischemia and reperfusion of the left anterior descending coronary artery territory. Moreover, hearts were excised and infracted area was determined by incubating with triphenyltetrazolium chloride, 24 h after the operation. Infarct size was analyzed as a percentage of area at risk. 3) Isolated perfused heart experiments: Rat hearts were excised and perfused retrogradely by Langendorff method. A water-filled latex balloon was inserted into the left ventricle (LV). After 20 min equilibration, normothermic no-flow global ischemia was performed for 60 min, followed by reperfusion for 30 min. LV pressure was monitored with a pressure transducer, and the measured parameters are as follows: LV developed pressure (LVDP) is the difference between the LV systolic and diastolic pressure, the peak positive and negative first derivatives of LV pressure (dP/dt_{max} and dP/dt_{min}), and heart rate (HR). Results were shown as mean ± standard error, and statistical analysis was performed with one-way ANOVA.
Results: Cardiac expression of HSP 70 was significantly increased in the ISDN group in comparison with the control group. However, the infarct size was significantly reduced in ISDN group in comparison with the control group. No significant difference in each parameter was observed between the control and ISDN groups at the baseline. During no-flow ischemia, all parameters immediately decreased to zero. The recovery of LVDP and dP/dt was observed in both the groups during reperfusion period; however, the recovery was greater in the ISDN group in comparison with the control group. The recovery of HR was same degree in both the groups.
Discussion: These results suggest that preoperative administration of ISDN shows a preconditioning effect by inducing HSP 70.

S-32.

ANESTHETIC PRECONDITIONING BY 2% SEVOFLURANE IS LOST WITHIN 1 HR AFTER A BRIEF EXPOSURE IN ISOLATED GUINEA PIG HEARTS

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Introduction: Recent evidence indicates that sevoflurane exerts a cardioprotective effect which mimics ischemic preconditioning. To achieve this effect, the duration between sevoflurane exposure and sustained ischemia (washout time; acute memory phase) is crucial. It has been reported that isoflurane has an acute memory phase with the duration of at least 30 min (1). It is unknown how long the duration of washout time can be extended to exert a cardioprotective effect in sevoflurane-induced preconditioning. The purpose of this study was to define the critical limits of efficacy of sevoflurane-induced preconditioning by varying the duration of washout time.
Methods: Isolated perfused guinea pig hearts were subjected to 30 min global ischemia and 120 min reperfusion (I/R) in all groups. Anesthetic preconditioning (APC) was elicited by administration of 10 min of sevoflurane (1 MAC; 2%) before ischemia. The duration of washout time were 10 min, 30 min, 60 min and 90 min. The contractile recovery was monitored by left ventricular developed (LVDP) and end-diastolic (LVEDP) pressures. Infarct size (IS) was determined by triphenyltetrazolium chloride (TTC) stain. Coronary flow (CF) was measured by collecting effluent from the right ventricular outflow tract.
Results: After 120 min reperfusion, infarct size was significantly reduced by APC compared with control for the duration of washout time of 10 and 30 min, but not 60 and 90 min (control:39 ± 2, 10 min:19 ± 2, 30 min:25 ± 2, 60 min:37 ± 4, 90 min: 43 ± 4, respectively, $p<0.05$). LVDP was increased by APC compared with control for the duration of washout time of 10 and 30 min, but not 60 and 90 min (control:38 ± 4, 10 min:63 ± 3, 30 min:57 ± 2, 60 min:50 ± 5, 90 min: 51 ± 2, respectively, $p<0.05$, at 40 min reperfusion). LVEDP was decreased by APC compared with control for the duration of washout time of 10 and 30 min, but not 60 and 90 min (control:45 ± 7, 10 min:21 ± 3, 30 min:20 ± 2, 60 min:32 ± 2, 90 min: 37 ± 4, respectively, $p<0.05$, at 40 min reperfusion at 40 min reperfusion). CF was similar among all groups throughout the experiment.
Discussion: Although sevoflurane-induced preconditioning protects against infarction, this cardioprotective effect in this model is restricted to a range of durations of acute memory phase of less than 60 min.
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S-33.

NON-INVASIVE IN VIVO OPTICAL TRACKING OF MACROPHAGE RECRUITMENT TO ATHEROSCLEROTIC INJURIES USING FLUORESCENCE MEDIATED TOMOGRAPHY IN MICE

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Introduction: Cardiovascular diseases (CVD) are the leading cause of death in the western world.1 Recruitment of macrophages into atherosclerotic lesions is a powerful marker of plaque vulnerability.2 Information on dynamics of leukocyte recruitment in a clinical setting would significantly ease diagnosis, therapeutic decision-making and control of therapeutic efficacy. Non-invasive means to image macrophage homing to vulnerable plaques *in vivo* are not available.3 We tested the feasibility of fluorescence mediated tomography (FMT), providing 3-dimensional information, to track macrophage homing to atherosclerotic plaques *in vivo* using cells labeled with near-infrared fluophors (NIRF).
Methods: Thioglycollate elicited peritoneal macrophages from GFP-transgenic mice were stained with lipophilic NIRF-dye DiR. Adult ApoE deficient mice on a cholesterol-rich diet were subjected to guidewire-injury (GWI) of the left carotid artery. The right carotid artery served as negative control. On day 7 10x106 DiR-GFP-macrophages were injected IV. FMT was conducted 7 days after macrophage injection. FMT data were quantitated as mean DiR-fluorescence (nMol) in the region-of-interest. Carotid arteries were harvested for fluorescence reflectance imaging (FRI) and fluorescence microscopy. FRI data were quantitated as mean peak fluorescence in injured and non-injured arteries. Target-to-background ratio was calculated.
Data are presented as mean±SEM and tested non-parametrically.
Results: Macrophages homed to lung, liver and spleen. Double-labeling with DiR and GFP confirmed a macrophage-associated DiR-signal.
In mice with GWI injected with macrophages FMT resolved fluorescence projecting in all 3 planes on the injured carotid *in vivo*. FMT measurements showed no difference between SHAM and control (71±8 vs. 42±9, n=4/5, p>0.05), but showed a significant signal increase in GWI compared to SHAM or control (126±23 vs. 71±8 vs. 42±9, GWI vs. SHAM vs. control, n=5/4/5, p<0.05).
FRI and fluorescence microscopy confirmed macrophages to injured carotids in GWI, but FRI showed no signal difference between SHAM and control (5.3±1.39 vs. 1.5±0.12 vs. 1.3±0.12, GWI vs. SHAM vs. control, n=5/4/5, p<0.05).
Discussion: FMT is feasible to track homing of DiR-labeled macrophages to atherosclerotic lesions *in vivo*, which was confirmed by FRI and fluorescence microscopy.
Optical Imaging using FMT to track NIRF-labeled inflammatory cells is a powerful tool to specifically assess and localize cell-trafficking in CVD. This methodology may potentially allow to assess cellular inflammatory responses not only in atherosclerosis but in all disease-states associated with leukocyte recruitment. FMT may allow to estimate the vulnerability of plaque and thereby guide diagnosis and therapy.
References: 1. 2004 NHLBI Morbidity and Mortality Chartbook, 9. 2. Circulation. 1995 Sep 15;92(6):1565-9. 3. Stroke. 2005 Dec;36(12):2764-72.

S-34.

CARBON MONOXIDE INDUCES ANTIINFLAMMATORY RESPONSE IN LUNGS DURING CARDIOPULMONARY BYPASS SURGERY IN PIGS

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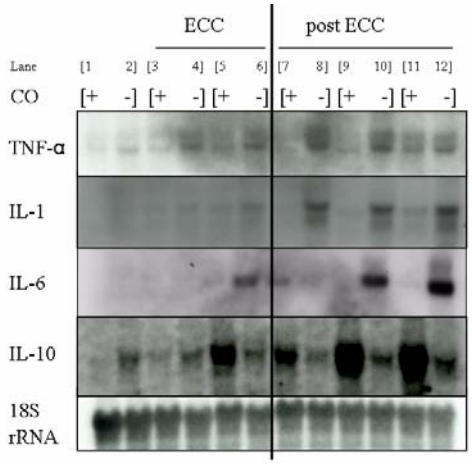
Introduction: During extracorporeal circulation (ECC) a pulmonary inflammatory response is induced, which leads to acute lung injury and functional impairment [1]. We hypothesized that carbon monoxide (CO), a known antiinflammatory agent [2,3] would reduce pulmonary cytokine formation during ECC.
Methods: Pigs were randomized to sham operation [n=3], standard cardiopulmonary bypass (CPB) [n=7] or standard CPB with preoperative inhalation of CO [n=7] (250 ppm; 1h). Blood gases (ABG) and hemodynamics were continuously monitored. Cytokine expression (TNF-α, IL-1, -6, -10) in lung tissue was examined by northern blot and enzyme-linked immunosorbent assay. The activation of transcription factors (NF-κB, AP-1, CREB) was analyzed by bandshift assay.
Results: Hemodynamics and ABGs showed no differences between groups. CO inhalation induced NF-κB, AP-1 and CREB binding activity. IL-1, IL-6 and TNF-α mRNA expression of showed significantly higher levels in the ECC compared to the CO group. In contrast, IL-10 levels were strongly elevated in the CO treated animals (Fig.1). In analogue, protein expression of TNF-α, IL-1, and IL-6 were significantly higher in the CPB compared to the CO group (Tab.1). IL-10 protein expression was significantly higher after ECC in the CO compared to the standard CPB group (Tab.1).

Table 1: Cytokine Protein Expression (* = p<0.05 CO vs. CPB [n=7])

pg/ml	Baseline CO vs. CPB	120 min post ECC CO vs. CPB
TNF-α	298±27 vs. 289±78	474±82 vs. 868±94*
IL-1	249±87 vs. 147±88	278±82 vs. 1591±90*
IL-6	121±27 vs. 125±37	279±156 vs. 898±61*
IL-10	95±32 vs. 54±70	594±143* vs. 69±18

Discussion: CO inhalation inhibited the ECC-mediated activation of proinflammatory cytokines. The induction of transcription factors such as NF-κB, AP-1 and CREB suggest a protective role of CO inhalation during CPB-mediated lung injury.
References: 1. Brix-Christensen V. et al., Acta Anaesthesiol Scand 2001; 45: 671-679 2. Otterbein LE. et al., Nat Med 2000; 6: 422-428 3. Lavitrano M. et al., FASEB J 2004; 18: 1093-1095



S-35.

HIGH-DOSE MORPHINE IMPAIRS ANGIOGENESIS AND MOBILIZATION OF ENDOTHELIAL PROGENITOR CELLS IN A MOUSE MODEL OF EXCISIONAL WOUND INJURY

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Introduction: Morphine is one of the most commonly prescribed analgesics in controlling of postoperative wound pain, burn scald and cancerous wound pain. At high dose, morphine mediates cytotoxic and pro-oxidant effects on different cell types. We have also recently shown that high-dose morphine impairs vascular endothelial function via increased production of superoxide anions. Since endothelial cells are also significantly involved in the process of angiogenesis, we therefore tested the hypothesis that high-dose morphine impairs angiogenesis and mobilization of endothelial progenitor cells (EPC, premature endothelial cells that contribute to angiogenesis) in a mice model of excisional wound injury.
Methods: A full skin-thickness excisional wound was created on the dorsum of anesthetized mice (C57BL/6J). Following the procedures, animals were randomly assigned to control or morphine-treated group and received normal saline or morphine (20 mg/kg/d, i.p.) injection for 14 consecutive days, respectively. Degrees of wound healing were compared by measuring the unhealed wound ratio. Generation of reactive oxygen species (ROS) in the wounds was determined under confocal microscope. Circulating polymorphonuclear leukocytes were isolated and quantified for the numbers of EPC (defined as CD34+/AC133+ cells) using the Ficoll assay. The Matrigel assay was used to determine levels of angiogenesis in mice with excisional wound, and in cultured human umbilical vein endothelial cells (HUVEC) following morphine treatment.
Results: Compared with controls, wound closure was reduced in mice treated with morphine (unhealed wound ratios were 8.3±2.4 and 26±7.6, respectively; P= 0.02, n= 6). Higher levels of ROS were generated in wounds treated with high-dose morphine. High-dose morphine significantly reduced numbers of circulating EPC following creation of excisional wound, whereas numbers of EPC were not affected in the absence of excisional wound, suggesting that morphine does not have a significant effect on the bone marrow. Expression of CD31 (a specific cell marker for endothelial cells) was significantly reduced on the Matrigel plug implanted in the abdominal wall of mice treated with morphine. Tube formation of cultured HUVEC on Matrigel assay was also attenuated following treatment with morphine in a concentration-dependent manner.
Discussion: Our study demonstrates that high-dose morphine impairs healing of excisional wound with increased oxidative stress. In addition, we provide the first in vivo and in vitro evidence that high-dose morphine impaired mobilization of EPCs and angiogenesis. These results underscore that high-dose morphine mediates pro-oxidant and antiangionenic responses, including the detrimental effects on the healing of skin-denuded wounds.

S-36.

LIDOCAINE REDUCES MYOCARDIAL INFARCTION SIZE IN MICE BUT DOES NOT INHIBIT RECRUITMENT OF PMNS

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Introduction: The reperfusion syndrome after myocardial ischemia (MI/R) is characterized by a pronounced inflammatory response associated with infiltrates of polymorphnuclear leukocytes (PMN) leading to additional loss of myocardial tissue1. Local anesthetics provide beneficial, anti-inflammatory effects2,3 which could help to modulate this response and therefore reveal new therapeutic strategies in perioperative care. In this study we investigated whether lidocaine could reduce the infarction size after MI/R.
Methods: By authority of the institutional review board (Tierschutzkommission Münster, Germany) the LADs of C57BL/6-mice were ligated for 30min and then reopened allowing reperfusion for 24h. The testing group was administered a bolus of lidocaine i.v. (2µg/g) 10min preceding ligature and continuously during ischemia (0,04µg/g/min). The control group was given PBS instead. The infarction area as part of the area-at-risk (%) was evaluated by TTC/coomassie-blue stain. Paraffin-embedded heart sections were stained immunohistochemically for PMNs with monoclonal antibodies and TUNEL-stained for detection of apoptotic cells. PMNs were isolated from murine bone marrow and used in *in-vitro* adhesion assays to analyze the effects of lidocaine on the adhesiveness of PMNs to endothelial cells (EC, fEND.5). To study dynamic interactions ECs were superfused with peritoneal macrophages in a parallel plate flow-chamber at 100s-1. Data are presented as mean±SD, tested non-parametrically.
Results: The infarction size in the lidocaine group was 32±3% (n=6) compared to 45±8% (n=7; p<0,01) in the control group. Lidocaine did not influence the PMN density of the infarction area (6±9cells/hpf, n=7; control: 10±11cells/hpf, n=9). The TUNEL-staining revealed a slight, even though insignificant antiapoptotic effect of lidocaine by showing a fraction of 8±8% (n=7) apoptotic cells per high-power-field (hpf) in lidocaine-treated mice versus 15±11% in control mice (n=9; p=0,07). The number of firmly adherent PMNs *in-vitro* was 633±194 cells per 15hpfs (=100%, n=12). Activation by TNFα increased adhesion 3-fold (308±143%, n=12). 10-6M-lidocaine had neither any effect on PMN adhesion to untreated (120±62%, n=12) nor to activated ECs (318±132%, n=12). An increase of lidocaine concentrations up to 10-3M had no effect either. Firm adhesion in flow-chamber assays was not influenced by administration of lidocaine (98±29% of control, n=5; control: 57±23 cells/hpf, n=8).
Discussion: Lidocaine reduces the infarction size significantly after MI/R. A reduced recruitment of leukocytes from blood vessels does however not seem to be the determining mechanism for its protective influence. An antiapoptotic potential has still to be further investigated.
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3. Lidocaine reduces ischaemic but not reperfusion injury in isolated rat heart. Ebel et al. Br J Anaesth. 2001 Jun;86(6):846-52.

S-37.

DOSE-DEPENDENT EFFECTS OF APROTININ ON SYSTOLIC PERFORMANCE IN A MOUSE MODEL OF ISCHEMIA-REPERFUSION

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Background: **L**eft ventricular (LV) dysfunction is a common consequence after brief periods of myocardial ischemia with reperfusion (I/R), which occurs in the context of cardiac surgery. Aprotinin (APRO) is commonly utilized in cardiac surgery attendant with I/R, but the effect and mechanisms of action of APRO on LV function remain unclear. Accordingly, this study tested the hypothesis that APRO would have direct effects on LV functional recovery after I/R in a dose-dependent manner.
Methods: An intact mouse model of LV I/R (30 min LAD occlusion, then 60 min reperfusion) was utilized in which LV function was measured by a previously validated high-fidelity microtransducer-volumetry catheter at baseline, 30 min of ischemia, and 30 and 60 min of I/R. Following baseline measurements, including cardiac output (CO) as an index of LV pump function and LV dP/dtmax (LVdP/dt) as a measure of systolic performance, mice were randomized to the following groups: (a) APRO 2mL/kg (n=11); (b) APRO 4mL/kg (n=10); (c) APRO 8mL/kg (n=10) and (d) Vehicle (saline, n=10). APRO doses were reflective of half, full, or 2Xfull Hammersmith doses. APRO (1mL= 10,000 Kallikrein Inhibiting Units) or saline was given by intraperitoneal injection immediately following baseline measurements.
Results: Results are presented in the Table (MeanSEM). CO fell slightly in APRO 2mL/kg at peak ischemia, but was otherwise maintained in all groups at all timepoints, indicating that severe hemodynamic instability did not occur. In Vehicle, LVdP/dt fell sharply at peak ischemia and returned to baseline by 60 min of I/R. While APRO 2 and 4mL/kg facilitated recovery of LVdP/dt by 30 min of I/R, APRO 8mL/kg caused a persistent depression at both 30 and 60 min of I/R. Since CO remained relatively stable despite changes in LVdP/dt, this would suggest that there may be a dose effect of APRO on ventricular-vascular coupling.

Change in Systolic Performance From Composite Baseline Mean					
	Group (n)	Baseline Composite	Ischemia	30 Min Reperfusion	60 Min Reperfusion
LV dP/dt Max (mmHg/s)	Vehicle (10)	10430±830	8098±785+	7582±445+	8774±873
	2mL/kg (11)		7883±754+	8940±901	9207±687
	4mL/kg (10)		8289±820+	9267±660	9784±587+
	8mL/kg (10)		7534±881+	8506±634+	8021±831+
CO (mL/min)	Vehicle (10)	2.23±0.03	2.08±0.22	1.87±0.22	1.9±0.27
	2mL/kg (11)		1.59±0.22+	1.73±0.22	1.99±0.19
	4mL/kg (10)		1.90±0.39	2.26±0.35	2.24±0.44
	8mL/kg (10)		1.84±0.34	2.11±0.21	1.88±0.29

+ p <0.05 v. baseline

Conclusions: The unique findings were 2-fold. First, this study demonstrated a quantifiable effect of APRO in an intact system of I/R as well as selective effects on LV systolic function and ventricular-vascular coupling. Second, APRO administration prior to I/R facilitated recovery of LV systolic function at common clinical doses, but diminished recovery at higher doses. Thus, APRO likely has a narrow pharmacologic window with respect to recovery of LV pump function and systolic performance following I/R.

S-38.

SUPERIORITY OF TEMPERATURE-DEPENDENT LOGISTIC TIME CONSTANT FOR ISOVOLUMIC LEFT VENTRICULAR PRESSURE FALL IN ISOLATED CANINE HEART

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Introductions: The logistic time constant (τ_L) has been proposed as a better index of the rate of left ventricular (LV) pressure fall during cardiac diastole, i.e., lusitropism than the conventional monoexponential time constant (τ_E) (1,2). We have known that τ_E for LV pressure fall is dependent on cardiac temperature (3-5). We assumed that τ_L remains a superior measure of LV pressure fall as temperature varies, although τ_L would be dependent on temperature.
Methods: The isovolumic LV pressure falls from the minimum time derivative of LV pressure (LV dP/dt_{min}) to the LV end-diastolic pressure were analyzed at 5 LV temperatures of 30, 33, 36, 38, and 40oC at constant 2-Hz pacing rate in 27 excised, cross-circulated canine hearts. We evaluated τ_L and τ_E, by curve-fitting using the logistic function: $P(t) = P_A/[1 + \exp(t/\tau_L)] + P_B$ and the monoexponential function: $P(t) = P_0\exp(-t/\tau_E) + P_\infty$. We compared the goodness of the logistic and monoexponential fittings with correlation coefficient (r) and residual mean squares (RMS).
Results: Table 1 showed the τ_L and τ_E values (mean ± SD) of the logistic and monoexponential fittings for the isovolumic LV pressure falls at the five LV temperatures. * showed statistically significant difference compared with 30oC (** $P < 0.001$). # showed statistically significant difference compared with 33oC (# $P < 0.05$, ## $P < 0.001$). Both τ_L and τ_E decreased significantly with increasing LV temperature. However, the r values of the logistic fittings were always significantly larger than those of the monoexponential fittings over the range of LV temperature (P <0.05). The RMS values of the logistic fittings were always significantly smaller than those of the monoexponential fittings (P <0.05).
Discussions: The goodness of the logistic fitting is superior to the monoexponential fitting at any LV temperature, although both τ_L and τ_E are dependent on temperature. The logistic model more reliably characterizes the isovolumic LV pressure fall and τ_L serves as a more reliable lusitropic index regardless of cardiac temperature.

References:
1) Circulation 92: 2318-2326, 1995
2) Anesth & Analg 102: 1032-1039, 2006
3) Circulation 80: III44-48, 1989
4) J Appl Physiol 85: 2135-2139, 1998
5) Am J Physiol Heart Circ Physiol 279: H2855-2864, 2000

Table 1. Logistic and Monoexponential Time Constants at 5 LV Temperatures

	30 °C (n =10)	33 °C (n = 25)	36 °C (n = 27)	38 °C (n = 23)	40 °C (n =18)
τ_L (ms)	55.6 ± 20.1	41.3 ± 6.9**	31.6 ± 5.9**#	27.5 ± 4.9**##	22.7 ± 4.6**##
τ_E (ms)	117.4 ± 76.5	70.7 ± 17.0**	49.1 ± 10.4**	41.9 ± 8.3**#	34.2 ± 7.3**##

S-39.

PROGRESSIVE ACCUMULATION OF THE ACUTE STRESS PROTEIN αB-CRYSTALLIN IN AN OVINE MODEL OF CHRONIC HEART FAILURE

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Introduction: The myocyte chaperone protein αB-crystallin (αBC) translocates from the cytosol to the sarcomeres in response to acute stress. Through the reinforcement of myofibrils at the Z/I-bands, αBC plays a role in preserving myocyte contractility during acute ischemia. The role of αBC in chronic heart failure (CHF) is less clear. αBC may have particular relevance during the remodeling cascade, as increased wall stress imparted on remaining viable myocardium and borderzone myocytes may the necessitate continuous involvement of αBC to maintain cytoskeletal integrity. Using a large animal model of CHF, we test the hypothesis that the acute stress protein αBC progressively accumulates in CHF in association with ventricular remodeling.
Methods: CHF (EF<35%) was induced in sheep via coronary microembolization of the LCx (1). Myocardium (LV posterior, LV anterior, RV free wall) was obtained from control, early CHF (4 months post-embolization) and late CHF sheep (12-24 months post-embolization). Western blots were performed in quadruplicate with αBC antisera. Immunohistochemistry (IHC) was performed on formalin-fixed myocardium to assess gross distribution of αBC protein.
Results: IHC indicated increased sarcomeric αBC content at the Z-discs in CHF myocardium. Western blot revealed LV posterior wall αBC increased 22% in early CHF; however, there was a dramatic increased in αBC in late CHF sheep (167%, p=0.0063) compared to controls, despite no further ischemic insult. LV posterior wall αBC positively correlated to the duration in CHF (r2=0.4282, p<0.0001). While LV anterior wall αBC increased 66%, RV free wall αBC decreased 34% compared to controls.
Discussion: Typically associated with *acute* ischemia, we measured elevations in myocardial αBC protein in *CHF* sheep up to 24 months following the sentinel infarction. αBC accumulation in CHF suggests progressive myocyte injury is taking place which warrants sarcomeric translocation of αBC in concert with the remodeling cascade. Although increased αBC may confer acute survival benefits through the reinforcement of local sarcomere integrity, chronic αBC accumulations may augment myocyte stiffness to further increase the contractile burden on already marginal myocytes. Interventions which target intracellular remodeling at the molecular level may represent novel therapeutic strategies for CHF.
References: (1) *J Card Fail* 2004;10:174-183.

S-40.

EXERCISE INDUCED VENTRICULAR HYPERTROPHY ENLARGES MYOCARDIAL DAMAGE AFTER ISCHEMIA IN MICE

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Introduction: Aerobic endurance training is an accepted measure for primary and secondary prevention of cardiovascular and metabolic diseases 1,2. Previous studies found exercise training to reduce infarct sizes in animal models 3. This effect might be partly mediated by the improvement of endothelial function 4 and increased vasculogenesis by circulating endothelial progenitor cells (EPC) 5. We established a mouse model of ad libitum training using running wheels. Training effects on ventricular size, EPC-mobilization and infarct size were studied.
Methods: Adult wild-type mice (SV129) underwent ad-libitum exercise training of twelve weeks in a running wheel. 2-D-guided M-mode echocardiographic measurements of ventricular dimensions were conducted before and after training. Flow-cytometric analyses of CD117+/VEGFR2+ circulating EPCs using antibodies against CD117 (BD Biosciences) and VEGFR2 (NatuTec) were performed in trained and control mice. Myocardial infarction was induced by ligation of the LAD over PE10 tubing for 30 minutes and reperfusion for 24 hours. Infarct sizes were measured histologically with intravitally injected propidium iodide and area-at-risk (AAR) was estimated with thioflavine injected postmortally after religation of the LAD. Data are presented as mean percent infarcted tissue per area at risk of 4 cross sections 800-1200µm proximally from the apex. Plasma troponin levels were determined using a cardiac reader (Roche).
Results: Exercise training (10 ± 2 km/day) significantly increased LVmass, LVEDD and LVESD in echocardiography (n=4, mean lvmass 73,6 ± 0,9mg vs 94,9 ± 4,9mg, p>0,03; mean LVEDD 2,7 ± 0,14mm vs 3,3 ± 0,1mm, p>0,05; mean LVESD 1,06 ± 0,1mm vs 1,4 ±0,06mm, p=0,057). Trained mice had larger infarctions compared to controls (n=7, mean percentage of AAR 12,86% ± 12,3 vs 3,38% ± 5,6; p>0,05). This resulted in different plasma troponin levels (n=4, mean 0,77ng/ml ± 0,4 vs 2,3ng/ml ± 0,6). The number of EPCs did nor differ between groups. Myocardial infarction mobilized EPCs in both groups.
Discussion:3 months ad-libitum exercise induced ventricular hypertrophy in mice. Surprisingly, infarct sizes were significantly larger in trained mice compared to control animals. We hypothesize that hypertrophy in our training model outweighs the beneficial effects of exercise and unfavorably changes the relation of muscle mass to capillary density. EPC mobilization is neither favourably affected by this form of physical activity. Further research is needed to examine the effects of shorter durations of training and possibly define a threshold of training intensity at which beneficial effects are outweighed by adverse effects.
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S-41.

DEXMEDETOMIDINE PROVIDES ADEQUATE SEDATION AND HEMODYNAMIC CONTROL FOR AWAKE, DIAGNOSTIC TRANSESOPHAGEAL ECHOCARDIOGRAPHY

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BACKGROUND
Transesophageal Echocardiography (TEE) has become firmly established as a sensitive and accurate diagnostic method for the rapid and portable assessment of myocardial contractility, valvular function and pathology, volume status, thoracic aortic injuries, blunt cardiovascular injuries, and suspected aortic dissections. Sedation goals for these procedures include anxiolysis, analgesia, and absolute hemodynamic control without respiratory depression. Dexmedetomidine (DEX) has found a role in many areas of clinical anesthesia for its potent sedative properties and hemodynamic stabilizing effect with no respiratory depression. Although DEX is currently indicated for Intensive Care Unit sedation in mechanically ventilated patients, there are multiple case reports of off-label uses including awake fiberoptic intubation and awake craniotomy.
Dexmedetomidine is a highly potent alpha-2 adrenoreceptor agonist with a distribution half-life of approximately 8 minutes. It provides excellent levels of sedation at therapeutic doses without affecting cardiovascular stability or causing respiratory depression. As with any awake endoscopic procedure, airway management is challenging, and respiratory depression must be avoided. Since many patients who require awake, diagnostic TEEs have significant cardiac disease, cardiovascular instability is always a concern. These goals make DEX an ideal sedative solution for these procedures.
OBJECTIVE
The primary aim of our prospective, double-blinded study was to show that DEX is a safe and effective alternative to the traditional benzodiazepine/opioid regimen used in most echocardiography laboratories. Secondary aims were to assess patient satisfaction by comparing the level of comfort of the patients in the two groups, comparing the collective opinion of patients concerning both the quality of sedation and recall of the procedure, and determining if the DEX group would accept this type of sedation again in the future.
METHODS
20 patients were randomized to received either a placebo or DEX bolus plus continuous infusion, along with supplemental midazolam and fentanyl to achieve a desired sedation level equal to a Ramsey Sedation Score of $\geq$ 4. Levels of sedation, requirements for supplemental medications, ability to tolerate procedure, adequacy of oxygenation, respiration, and hemodynamics were monitored throughout the procedure.
RESULTS
All of the patients achieved adequate sedation with both regimens. There was no respiratory depression in either group, and oxygen saturations were similar. However, hemodynamics were found to be superior in the DEX group. HR and BP remained elevated above normal in the placebo group throughout the procedure, while the DEX group HR and BP approached levels usually associated with adequate beta-blockade. Patient satisfaction levels were superior in all aspects in the DEX group compared to the traditional group.
CONCLUSION
DEX is a safe and effective alternative to traditional benzodiazepine/opiod sedation. It is superior in achieving adequate levels of sedation without causing respiratory depression or decreasing oxygen saturation, and results in improved hemodynamic control over the traditional sedative therapy.

S-42.

ETOMIDATE AND LEFT VENTRICULAR CONTRACTILITY: AN ECHOCARDIOGRAPHIC STUDY

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Introduction: Cardiovascular depression is infrequent following Etomidate (E) compared to other anesthetics since E is responsible for less vasodilation (1) and histamine release (2) and better preserves sympathic tone (3). Animal studies have shown some negative inotropic effect of E, but less than with other agents (4).
Systolic function is usually assessed using the Left Ventricular Ejection fraction (LVEF) or the Fractional Area Change (FAC), but both are known to be load dependant. In this randomized double blind study we measured the Preload Adjusted Maximal Power (PAMP) as a load independent variable of left ventricular contractility (5,6) following a 0.2mg.kg-1 dose of E on mechanically ventilated and anesthetized patients undergoing cardiac surgery.
Methods: 30 patients were, following written informed consent, assigned to group S (Saline) or E. Patients with atrial fibrillation or LVEF < 40% were excluded. Anesthesia was induced using Remifentanil and Propofol and adjusted to keep BIS values between 40 and 60.
Fluid infusion was limited to a maintenance rate during the TEE measurements which were all completed before surgical incision. Cardiac output (CO) was measured at the level of the left ventricular outflow tract (LVOT) and Fractional Area Change (FAC) on a transgastric short axis view at the midpapillary level. PAMP was calculated as SAP.Vmax. (LVOTarea)/EDA2, where SAP is the systolic arterial pressure, Vmax is the peak flow velocity through the LVOT, and EDA the end diastolic area of the LV. BIS was turned off before injection in order to ensure doubleblindness. A full set of triplicate measurements was performed before and 1 min after injection of either E 0.2mg.kg-1or an equivalent volume of S. Data were analyzed using paired and unpaired Student's t-test.
Results: Both groups were comparable regarding age (67.4±14.5 vs. 68.7±9.4), weight (73.3 ± 6.2 vs. 80.75±8.4 kg), height (168±6 vs. 173±8 cm), preoperative LVEF (61±9 vs. 62±12) and preinjection echocardiographic data.
Injection of the trial drug did not significantly change CO, FAC or PAMP in any group.
Discussion: These results suggest that a 0.2mg.kg-1 dose of Etomidate has no negative inotropic effect in anesthetized and mechanically ventilated patients.

Group	Echocardiographic data			
	S (n=15)		E (n=15)	
	Before S	After S	Before E	After E
CO ($l.min^{-1}$)	4.4±1.0	4.6±1.0	3.8±1.1	3.9±1.3
FAC (%)	61±12	60±12	59±11	60±9
PAMP ($Watt.ml^{-1}.10^{-4}$)	2.09±1.11	1.99±1.00	1.64±0.97	1.73±0.82

Means ± SD

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S-43.

NEW ELECTROCARDIOGRAPHY PARAMETERS AMONG CRITICALLY ILL OBSTETRICS PATIENTS

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Introduction: electrocardiography (ECG) parameters dispersion is a new tool to evaluate critically ill patients. P-wave dispersion may be mediated by the alleviation of the fluid overload [1]. QRS dispersion is associated with increased mortality in chronic heart failure patients [2]. A cutoff value > 40 ms had a good sensitivity and specificity in predicting the occurrence of sudden death. Increased QRS dispersion > 50 ms was a strong predictive factor of recurrent malignant arrhythmic events. We examined the incidence of P-wave, QT and QRS dispersion among critically ill obstetric patients.
Methods: 12 lead ECG was recorded from 37 critically ill obstetric patients after delivery. They were compared to 37 obstetric patients who delivered at the term of normal pregnancy. The QRS complex duration was measured from the beginning of the QRS complex to its end. The QT interval was measured from the onset of the QRS complex to the end of the T wave. The P-wave, QT, QRS and dispersions were defined as the difference between the maximum and minimum P-wave, QT and QRS values. We also studied the rate corrected QT duration QTc. The threshold of significance was 0.05.
Results: The average QRS dispersion was significantly lower in critically ill obstetric patients (25.80 ± 12.17 ms vs 37.89 ± 16.18 ms, p=0.013). The average QTc was significantly lower among critically ill obstetric patients (306.42 ± 37.63 ms vs 336.31 ± 26.29 ms, p=0.0012). There was no statistical difference in P-wave and QT dispersion (50.96 ± 21.81 ms vs 49.47 ± 19.28 ms, p=0.40 and 26.25 ± 19.30 ms vs 31.57 ± 15.37 ms, p=0.14).
Discussion: Physiologic changes in cardiovascular status among pregnant patient could explain these parameters. The clinical implications of these results are unknown. This difference could be a poor prognostic factor among obstetric critically ill patients. Further studies are needed in order to elucidate its exact role in this setting.
References:
[1] Ann Non-invasiv Electrocardiol 2005; 10:129.
[2] Am J Cardiol 2000; 85:1212-7.

S-44.

CHRONIC PREOPERATIVE β-BLOCKER USAGE DOES NOT INFLUENCE INTRAOPERATIVE α-BLOCKER ADMINISTRATION IN PATIENTS WITH CAD OR AT RISK FOR CAD

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Introduction: Perioperative use of beta-blockers remains low despite studies that show a benefit in patients at risk for CAD (1,2). While guidelines (3) recommend preoperative β-blockers for some patients, patterns of intraoperative β-blocker administration are not well described. Some have suggested that acute perioperative administration of beta blockers to an otherwise stable patient would be resisted by anesthesiologists. Therefore, we hypothesized that chronic preoperative β-blocker use would influence the anesthesiologist and lead to more frequent administration of beta blockers since it was an accepted preoperative therapy.
Methods: We reviewed the preoperative records of all patients with documented CAD or "at risk for CAD" who had elective non-cardiac surgery between 1/04 and 6/06. CAD and "at risk for CAD" were defined in accordance with a previously published manuscript (2). We collected preoperative and intraoperative β-blocker use on over 4,500 patients.
Results: Of the 21,039 patients who had elective surgical procedures, 1,479 (7%) had documented CAD and 3,075 (14.6%) were at risk for CAD. The relationship between preoperative β-blocker therapy and intraoperative administration of β-blockers was not clinically significant overall or in any of the 4 groups that we considered (e.g. Men at risk for CAD, Women at risk for CAD, Men with CAD, and Women with CAD).

	Received Intraoperative β-blocker		p--value
	Yes	No	
AT RISK			
Men			
On preoperative β-blocker	101	248	0.537
NOT on preoperative β-blocker	350	791	
Women			
On preoperative β-blocker	116	289	0.795
NOT on preoperative β-blocker	346	834	
CAD			
Men			
On preoperative β-blocker	157	301	0.094
NOT on preoperative β-blocker	127	310	
Women			
On preoperative β-blocker	78	155	0.404
NOT on preoperative β-blocker	106	245	

Discussion: For patients with CAD (or at risk for CAD) intraoperative β-blocker administration does not appear to correlate with preoperative usage. Preoperative chronic β-blocker usage did not significantly predict the likelihood of intraoperative administration of β-blockers. We recommend a larger study to rule out a potential influence of preoperative β-blockers use on intraoperative beta blocker use in men with CAD.
Footnotes
1 Rapchuk, S. Rabuka, and M. Tonelli. Can J Anesth, October 1, 2004; 51(8): 761 - 767.
2 Mangano et al., N Engl J Med 335(23): 1713-1721 December 5, 1996.
3 Eagle KA, Berger PB, Calkins H et al. Anesth Analg 2002; 94:1052-1064.

S-45.

INTERCURRENT HYPERTENSION IS ASSOCIATED WITH POSTOPERATIVE TROPONIN INCREASES IN THE NON-CARDIAC SURGICAL PATIENT.

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Introduction: There is an association between hypertension (HT) and cardiac mortality and morbidity [1]. Increased postoperative troponin levels (TnI or TnT) are associated with adverse outcomes [2, 3]. Although some authors find increased troponins in HT patients [4-6], others fail to confirm this in underpowered studies. This meta-analysis examines troponins as markers of myocardial damage in HT patients.
Methods: MEDLINE and PUBMED were searched using the terms: preoperative risk stratification; intraoperative and postoperative cardiac ischemia; troponins; anesthesia. In addition to these searches, there was hand searching of reference lists from identified papers; and examination of abstracts from relevant research societies. The primary endpoint was elevation of troponins above the upper limit of the reference range. HT was defined as patients receiving anti-hypertensive medications or an admission blood pressure >160/95 on two or more occasions. Based on an event rate of 12% in normotensive patients, 2948 patients would be needed to show a 30% increase in troponin levels in HT patients with α=0.05 and β=0.2. Results were calculated as absolute risk increase associated with HT (ARI), number needed to harm (NNH) and relative risk ratio (RRR) [mean $\pm$ 95% CI].
Results: 31 studies were identified. 22 were excluded (in 18 studies, there was no clear division into normotensive and HT sub-groups; three papers reported duplicate data; and one excluded patients suffering any major cardiac event within 30 days of surgery).
The remaining 9 papers include 3516 patients (55% HT; 67% vascular) [2-10]. 569 patients had elevated troponin levels (prevalence 16.2%). Three studies reported increased troponin levels in HT patients. Overall event rates were 18.2% for HT; 12.9% for normotensive patients; ARI 5.36% (NNH: 19 [13-34]). The study size weighted ARI was 7.3%. The RRR for the association of HT and increased postoperative troponins was 1.24 (1.16-1.33).
Discussion: These data show that elevated cardiac troponins (a marker of myocardial damage) occurs more frequently than the 8.5% incidence of major cardiovascular complications and cardiac death in comparable patients following non-cardiac surgery [1], with the incidence of troponin release greater in HT patients. The RRR of 1.24 is similar to the meta-analysis odds ratios for both combined cardiac morbidity and mortality, and cardiac death alone [1]. Because increased cardiac troponin levels may define adverse prognosis [5], monitoring this biomarker may be a useful predictor for post-operative complications in HT patients.
References: 1]. Br J Anaesth 2004; 92: 570; 2]. Anaesthesia 2004; 59: 318; 3]. Circulation 2002; 106: 2366; 4]. Am J Cardiol 1996; 77: 1031; 5]. J Am Coll Cardiol 2004; 44: 569; 6]. Anesthesiology 2005; 102: 885; 7]. J Clin Anesth 2001; 13: 556; 8]. Anesthesiology 2001; 95: 1133; 9]. Acta Anaesthesiol Scand 2004; 48: 1071; 10]. J Vasc Surg 2005; 41: 769

S-46.

COMPARISON OF THREE DIFFERENT EPIDURAL SOLUTIONS IN CARDIAC SURGERY FOR STRESS PROTECTION

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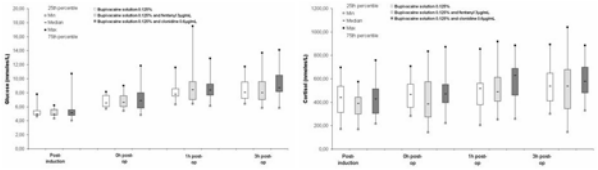
Background. Different solutions are possible for thoracic epidural analgesia in cardiac surgery. So far, local anesthetics alone or in combination with either clonidine or opioids have been used. No study has compared the stress protection provided by different epidural solutions throughout cardiac surgery.
Methods. In this randomized, prospective, double blind study, 42 patients undergoing OPCAB were enrolled. Thoracic epidural analgesia was installed more than 1 h before application of heparin at levels of T2 to T4; analgesia was provided by 8 ml of bupivacaine 0.25% 15 min prior to surgery and extubation, and 10 ml/h during and up to 72 h after surgery using one of the following regimens: bupivacaine 0.125% solely, bupivacaine 0.125% with fentanyl 3 µg/mL or bupivacaine 0.125% with clonidine 0.6 µg/mL. Patients were block-randomized for one of the three treatments. Cortisol and glucose values were determined before surgery, at extubation and 1h and 3h after surgery. Pain scores were assessed up to 48 h after surgery. Hemodynamic stability was also recorded in form of heart rate, systolic and diastolic blood pressure. Multi-comparison ANOVA and Chi-square test were used to compare the data, presented as mean (SD) or median (25th and 75th percentile), $P < 0.05$.
Results. All patient data as well hemodynamic stability were not different between the three groups. All patients were successfully extubated in theatre immediately after surgery. Pain control was very good and not significantly different between the groups. Glucose and cortisol concentrations are presented in the figure; there were no significant differences between the groups.
Conclusions. We conclude that stress protection with TEA is equally effective using solely bupivacaine, bupivacaine with fentanyl or clonidine.



ANESTH ANALG
2007; 104; S-1–S-271

S-47.

GENDER DISPARITIES FOUND IN PREOPERATIVE BETA BLOCKER USE BUT NOT ANESTHESIOLOGISTS' INTRAOPERATIVE USE IN THE MANAGEMENT OF PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING NON-CARDIAC SURGERY

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Introduction: Disparities in treatment based on gender have been shown in treatment of patients with cardiac disease [1]. We hypothesized that such disparities could be seen in the prescription of β-blockers to patients with coronary artery disease (CAD) scheduled for elective non-cardiac surgery. We also hypothesized that anesthesiologists would not be prejudiced by the patient's gender, given their primary focus on physiologic variables. We considered all patients w/CAD undergoing elective non-cardiac surgery seen at our pre-anesthesia clinic (PAC).
Methods: We reviewed preops of all patients with CAD who had elective non-cardiac surgery from 1/04 to 6/06. CAD was defined as s/p CABG, s/p angioplasty, s/p MI, angina or atypical angina with (+) stress test [2]. We examined cardiac status, gender, and β-blocker use on over 1,400 patients. Intraoperative β-blocker use was defined as one or more instances of administration of any β-blocker.
Results: Of 21,039 patients undergoing elective non-cardiac surgery, 1,479 (7%) had CAD, consisting of 895 (60.5%) men, and 584 (39.5%) women. 458 (51.2%) of men vs. 233 (39.9%) of women w/CAD were on preoperative β-blocker therapy ($p < 0.001$) when seen at PAC. Gender had no effect on the likelihood that a patient would receive a β-blocker in the operating room. If a patient w/CAD arrived to the OR without β-blockers , approximately 30% of both men and women received intraoperative β-blockers.
Discussion: There was a significant gender disparity in the preoperative (but not intraoperative) use of β-blockers in patients w/CAD undergoing elective non-cardiac surgery. While the gender disparity in preoperative management requires further investigation, anesthesiologists appear to be gender-blind while caring for patients in the operating room.

[1]Horsfield P, Teasdale S. Generating information from electronic patient records in general practice: a description of clinical care and gender inequalities in coronary heart disease using data from over two million patient records. Inform Prim Care; 11(3): 137-44 2003.
[2] Mangano et al. Effect of Atenolol on Mortality and Cardiovascular Morbidity after Noncardiac Surgery. N Engl J Med 335(23): 1713-1721 1996

S-48.

PILOT STUDY TO DETERMINE SEVOFLURANE DOSING DURING EXTRACORPOREAL CIRCULATION USING BIS MONITORING

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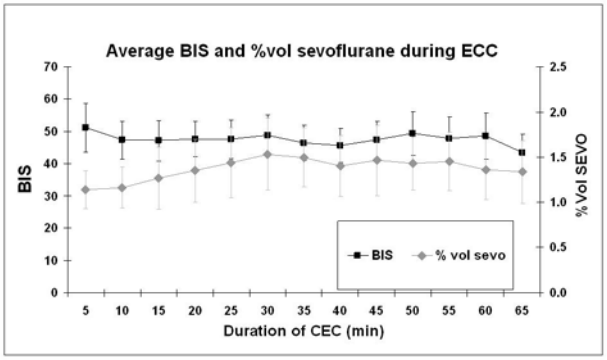
Introduction: Volatile anesthetics provide myocardial protection during cardiac surgery. Sevoflurane has gained popularity in cardiac surgery because of its rapid elimination thus allowing fast tracking anesthesia. Titration of sevoflurane dosing during extracorporal circulation (ECC) is important to avoid awareness and provide hemodynamic stability. In this pilot study, we titrated sevoflurane during cardiac surgery with ECC using bispectral index monitoring (BIS) and measured the volume% of sevoflurane necessary. **Methods**: Cardiac surgery using ECC in normaothermia was performed in 20 patients. Anesthesia was induced using propofol 1 -1.5 mg/kg, fentanyl 3-5 µg/kg, endotracheal intubation was facilitated using rocuronium 0.6 mg/kg. Intraoperative analgesia was achieved using high thoracic epidural analgesia with bupivacaine 0.125% at 10 ml/h. Anesthesia was maintained using sevoflurane throughout surgery; during ECC, sevoflurane was administered into the ECC circuit to maintain a BIS of 40-55. Every min, BIS, the concentration of sevoflurane, systolic, diastolic pressure (SAP, DAP), and bladder temperature were recorded. Data are presented as means (standard deviation). **Results**: Patients (11 men, 9 women, age 69 (12)) underwent different types of cardiac surgery with 70 (24) min of ECC. BIS and the corresponding vol% of sevoflurane are presented in Figure 1. BIS did not exceed 60 in any patient at any time. There was no intraoperative awareness no sweating. SAP ranged between 60 -80 mmHg, DAP between 40-60 mmHg. To maintain BIS between 40-60, the mean vol% of sevoflurane administered into ECC was in the range between 1.2 and 1.5. **Discussion**: This is the first study which uses BIS to titrate sevoflurane administration during ECC in order to obtain reference values of sevoflurane. For cardiac surgery in normothermia, sevoflurane should be administered between 1.2 and 1.5 vol%.



S-49.

RELATIONSHIP BETWEEN INTRAOPERATIVE TRANSCRANIAL MYOGENIC MOTOR EVOKED POTENTIALS MONITORING AND ISCHEMIC SPINAL CORD INJURY AFTER DESCENDING THORACIC OR THORACOABDOMINAL AORTIC SURGERY.

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Spinal cord ischemic injury remains the most devastating complication after descending thoracic (DTA) or thoracoabdominal (TAA) aneurysm repair. In this study, we reviewed retrospectively intraoperative transcranial myogenic motor evoked potentials (tc-MEP) monitoring applied during resection of DTA and TAA aneurysms and investigated the relationship between intraoperative tc-MEP and postoperative ischemic spinal cord injury.
Methods : We reviewed forty patients (DTA, 21 cases ; TAA, 19 cases) monitored intraoperatively with tc-MEP. In all cases, anesthesia was maintained with administration of propofol, ketamine and fentanyl. tc-MEP was recorded from the left anterior tibial muscle. tc-MEPs was recorded at pre-aortic cross clamp (baseline), 30 sec, 1 min, 2 min, 3 min, 5 min, 7 min, and 10 min after aortic cross clamp. An indication of ischemic spinal cord dysfunction was considered by the reductions of tc-MEP amplitude monitored to less than 25 % of the baseline value. Postoperative neurological function was assessed periodically for 3 days of postoperative period.
Results : A total of 15 patients (37.5 %) showed significant reduction of tc-MEP (< 25 % of baseline) as ischemic spinal cord dysfunction. In 14 cases of them, significant reduction of tc-MEP was detected within 2 min after aortic cross clamp. However, in one case, it took about 20 min after aortic crossclamp (between Th4 and Th9) for a significant reduction of tc-MEP. In 12 patients (30.0 %), ischemic changes in tc-MEP were reversed by reimplanting segmental arteries or selective perfusion of intercostals arteries, and none of these 12 patients suffered acute paraplegia. Four patients (10.0 %) who had persistent loss of tc-MEPs awoke paraplegic. MRI in a case with delayed detection of spinal cord ischemia revealed the ischemic injury at the high thoracic level (Th4-6).
Conclusions : Experimental and clinical reports showed that tc-MEP monitoring can provide the rapid detection for the spinal cord dysfunction after spinal cord ischemia (1, 2). According to the present data, however, detection for spinal cord ischemia after aortic clamp can be delayed even in tc-MEP monitoring. This delayed detection may be associated with the ischemia at the high thoracic level (3).
Reference
1) Kakinohana M, et al. J Thorac Cardivasc Surg. 2005 ; 129 : 46 - 52
2) Maylaerts SA, et al. Ann Surg 1999 ; 230 ; 742 - 9
3) Lips J et al. J Thorac Cardiovasc Surg. 2002 ; 123 : 531-8

S-50.

MORPHINE ATTENUATES THE INFLAMMATORY RESPONSE TO CARDIOPULMONARY BYPASS

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Introduction: Experimental data suggests that morphine has potent immunoregulatory properties and may attenuate inflammatory processes related to cardiopulmonary bypass (CPB). In cell culture models and a porcine model of CPB, morphine selectively inhibits activation of granulocytes and macrophages (reductions in phagocytosis, cytokine production, and the expression of adhesion molecules)(1,2). Fentanyl, a commonly used opioid in the perioperative setting, does not appear to downregulate inflammatory cell function (3). The aim of this clinical investigation was to examine the impact of choice of intraoperative opioid (morphine or fentanyl) on the perioperative inflammatory response to cardiac surgery and cardiopulmonary bypass (CPB).
Methods: Thirty patients undergoing elective primary coronary artery bypass surgery were enrolled in this randomized, double-blinded trial. Patients were randomized to receive either morphine (40 mg) or fentanyl (1000 μg) as part of a standardized opioid-isoflurane anesthetic. The study opioid was prepared in identical-appearing 100 mL plastic bags. Surgical and postoperative management was also standardized. Serum concentrations of interleukin (IL)-6 and IL-8 and expression of neutrophil surface adhesion molecules (CD 11a, CD 11b, CD 11c, CD 18) were measured as indicators of the inflammatory response to CPB and surgery. Blood samples were collected immediately following induction of anesthesia (baseline), 15 minutes post-CPB, 3 hours post-CPB, and 24 hours from baseline measurements. Core temperatures were monitored and recorded in the intensive care unit to determine the incidence of postoperative hyperthermia (temperature > 38.0o C).
Results: The two groups were similar in terms of demographic characteristics and intraoperative management. Interleukin-6 and IL-8 concentrations increased in all patients following bypass, peaking 3 hours post-CPB. The rise in serum IL-6 levels was significantly attenuated in the morphine group compared to the fentanyl group 3 hours post-CPB and 24 hours post-induction (P<0.05). Reductions in the expression of all adhesion molecules from baseline values were observed 15- and 180 minutes following CPB, with mean fluorescence intensity returning towards baseline values 24 hours post-induction. In the morphine group, however, the reduction in CD 11b and CD 18 expression was significantly greater than the values observed in the fentanyl group (P<0.05). The incidence of postoperative hyperthermia was more frequent in the fentanyl group (73% of subjects) compared to the morphine group (0% of subjects, P<0.05).
Discussion: Our findings demonstrate that morphine can attenuate the inflammatory response to cardiopulmonary bypass when used as part of a balanced anesthetic technique with isoflurane. When compared to patients receiving fentanyl, subjects in the morphine group exhibited a significant reduction in inflammatory cytokine release, a greater inhibition of adhesion molecule expression, and a lower incidence of postoperative hyperthermia.
References: 1. J Neuroimmunol 2000; 111: 139 2. Int J Cardiol 1996; 53: 39 3. Int J Cardiol 1998; 64: 61

S-51.

A NOVEL APPROACH FOR PAIN RELIEF AFTER CARDIAC SURGERY VIA MEDIAN STERNOTOMY: BILATERAL, SINGLE-SHOT PARAVERTEBRAL BLOCKS

AUTHORS: P. B. Nguyen[1], N. Noiseux[1], D. Bracco[1], J. Olivier[2], N. Le[1], **T. M. Hemmerling**[2];
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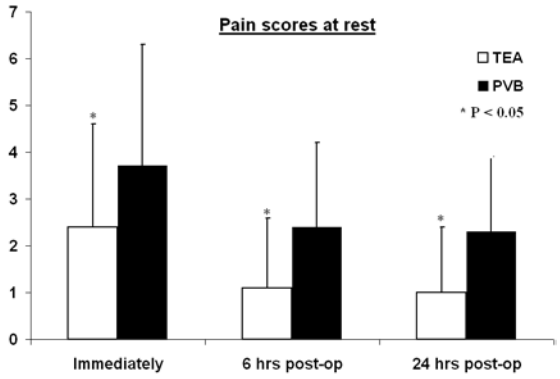
INTRODUCTION: The objective of this study was to evaluate a new technique of paravertebral block (PVB) in conventional cardiac surgery via median sternotomy.
METHODS: This prospective audit compared two groups of patients undergoing an equal number of off-pump CABG, on-pump CABG, or mitral valve replacement. One group (PVB group, n = 27) received a combination of low-dose fentanyl, PVB and general anesthesia. The PVB technique consists of bilateral single shots of 3ml of bupivacaine 0.5% from T2 to T7. The other group (TEA group, n = 27) received a combination of high thoracic epidural (TEA) and general anesthesia. The epidural method consists of continuous infusion of bupivacaine 0.125% (8-10ml/hour at T2-3 level). Immediate extubation in the operating room was aimed for every patient. Patients were audited according to preoperative data, type of surgery and duration of surgery. All patient data were recorded and are shown as mean ± SD. Pain scores taken at rest (on a 1 to 10 scale) immediately, 6 hours, and 24 hours after surgery were compared using standard t-test ($P < 0.05$).
RESULTS: No significant difference was noted in patient data and preoperative co-morbidity between the two groups. Post-operative pain scores were at any point significantly lower with TEA than with PVB (fig 1). All patients were successfully immediately extubated in the operating room, and no complications related to epidural catheter placement were encountered.
DISCUSSION: In our study of 54 patients undergoing cardiac surgery and who were immediately extubated, TEA provided better pain relief than PVB. However, PVB can be seen as a reasonable alternative for ultra-fast-tracking cardiac anesthesia for anesthesiologists who are unwilling to use TEA.



S-52.

CHANGES IN FINGER AND FOREHEAD BLOOD FLOW UPON SQUATTING AND STANDING

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Introduction: It previously has been shown that microvasculature in the distribution of the carotid artery (specifically, the forehead) maintains mean perfusion despite systemic vasoconstrictive challenges which induce a 50% decline in finger blood flow (1,2). The present study was undertaken to determine if this autoregulatory process maintains flow in the context of a challenge which alters perfusion as a consequence of a relative increase or decrease in intravascular volume.
Methods: With IRB approval, 14 healthy volunteers were assessed before, during, and after a three -minute period of squatting with EKG, intermittent brachial artery blood pressure, and laser Doppler flowmetry of the adrenergically rich finger and the relatively cholinergically rich forehead. The changes in each parameter were recorded and expressed as mean (standard deviation). Inter-phase and inter-parameter differences were analyzed with paired t-test.
Results: Systolic blood pressure changed from 117.5 (13) mmHg at base to 131.8 (16) during squatting ($P=0.002$) and 117.9 (15) upon standing ($P<0.001$). Heart rate changed from 86.4 bpm (10) at base to 72.4 (8) upon squatting ($P<0.001$) and to 108.2 (13) upon standing ($P<0.001$). Finger blood flow and forehead blood flow each increased significantly ($P<0.001$) during squatting (Table), and they decreased significantly upon standing ($P<0.001$). The relative changes in finger and forehead flow were not significantly different. Of note, there was a significant "dip" of 69.5±22% in finger blood flow 1-2 min after standing ($P<0.001$). No such decline was noted in the forehead.

Table 1

	% Change Squatting	% Change Standing	Second "Dip"
Finger	+63.3 (64)	-61.0 (20)	-69.5 (22)
Forehead	+104.4 (59)	-56.0 (36)	N/A

Discussion: As previously shown, changes in preload with squatting induce significant changes in blood pressure and compensatory changes in heart rate. Squatting induced significant increases in finger and forehead blood flow, while standing induced decreases in these indices. There were no significant differences between the changes in finger and forehead blood flow. We conclude that, whereas autoregulation of forehead flow can offset vasoconstrictive challenges, it cannot offset the effects of acute changes in intravascular volume (consistent with near-syncope upon standing).

References:
1. Microvasc Res 63:196-208, 2002
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S-53.

CANADIAN SURVEY ON THE PRACTICE OF REGIONAL ANESTHESIA FOR CARDIAC SURGERY

AUTHORS: **P. B. Nguyen**[1], N. Noiseux[1], D. Bracco[1], N. Le[1], T. M. Hemmerling[2];
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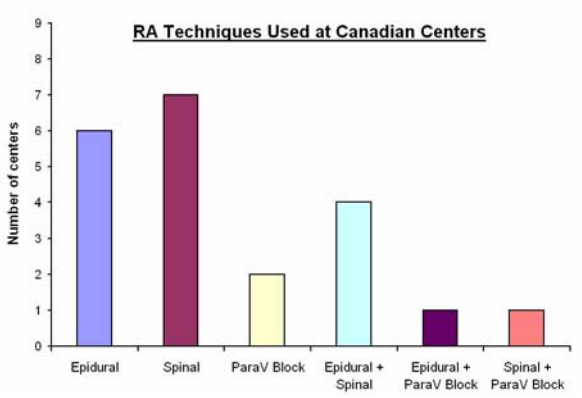
INTRODUCTION: In Canada, the general impression is that regional anesthesia (RA) for cardiac surgery is rarely used. We undertook a survey regarding the use and practice of RA in cardiac surgery throughout Canada.
METHODS: Firstly, a telephone survey was conducted to identify which anesthesiologists use RA in cardiac surgery. Then, a survey was sent via mail or e-mail to these anesthesiologists. Participants were notified that all information was to be kept confidential. The survey contained questions regarding anesthesiologists' practice (used techniques, type of surgery, surgical access, timing of RA vs heparinization, incidence of complications, RA regimens, extubation time), patients' coagulation profile, institutional practice (number of anesthesiologists at site, number of surgeries, number of RA's during previous year), and the anesthesiologists' justification for the use of RA for cardiac surgery (advantages and risk assessments).
RESULTS: Nine out of 41 Canadian cardiac centres use RA. Figure 1 shows the number of centres using different RA techniques. At least 26 Canadian anesthesiologists use RA in cardiac surgery. The majority of centres use RA for off-pump CABG, on-pump CABG, or valve surgery. For anticoagulation management, anesthesiologists mostly followed guidelines given in the 2003 consensus conference paper by Horlocker *et al* [1]. In the event of a bloody tap, anesthesiologists who distinguish blood origin tend to carry on with the procedure if venous blood is encountered, and to postpone surgery if arterial blood is discovered, as proposed by Williams [2]. Anesthesiologists who do not distinguish between venous or arterial blood rely on time to heparinization and needle calibre to determine whether or not to postpone surgery. There was no reported case of epidural or spinal hematoma. All of the respondents considered better stress protection as an advantage of RA, while a little more than 80% selected the risk of spinal or epidural hematoma as a disadvantage to the techniques.



DISCUSSION: About 20% of Canadian institutions where cardiac surgery is practiced have anesthesiologists that use RA for cardiac anesthesia. Therefore, RA in cardiac anesthesia cannot be considered a rarity. Most centres use spinal anesthesia, followed by thoracic epidural anesthesia; only two centres use (different) techniques of paravertebral blocks.
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S-54.

DOES THE ADDITION OF THE ARIZANT HEALTHCARE MODEL 635 FULL-ACCESS UNDER BODY BLANKET TO ROUTINE THERMAL CARE IMPROVE HEAT TRANSFER IN CARDIAC SURGERY PATIENTS?

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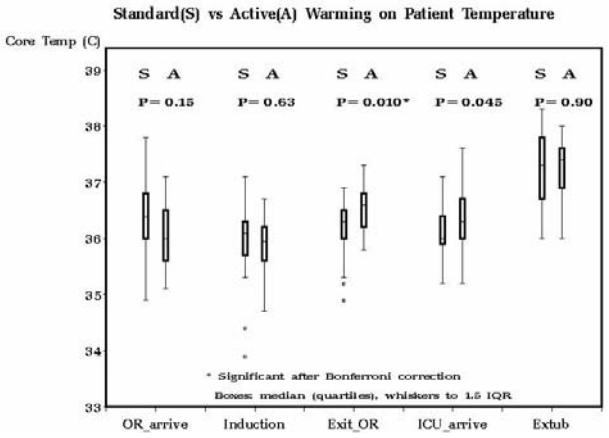
Introduction: Hypothermia during cardiac surgery and in the postoperative period has been associated with adverse outcomes (1, 2). Conventional (over-body) forced-air warming is highly effective. An under-body cover has been developed for use during cardiac surgery where surface access is restricted. We tested the hypothesis that combining under-body forced-air warming with standard thermal management improves core temperature and reduce afterdrop in patients undergoing cardiac surgery.
Methods: With IRB approval and informed consent, patients scheduled for routine, non-emergent cardiac surgery at the Cleveland Clinic between April and July 2006 were enrolled. Patients were assigned to either routine thermal management (n=29) or routine management supplemented by the Arizant under body garment (n=27). Routine heat conservation methods were applied in both groups. Core temperature was measured via bladder foley catheter. Pre-warming and/or pre-cardiopulmonary bypass use of vasodilators was not used. Cardiopulmonary bypass was conducted under normothermic conditions. Groups were compared on the primary outcome of temperature using a mixed effects model in which we assessed the effects of the intervention, time, and intervention-by-time interaction. T-tests were used to compare groups at specific surgical events. Bonferroni correction for multiple comparisons was used. The significance level was 0.05
Results:
Morphometric and demographic characteristics in the two groups were similar, as were anesthetic and surgical management and pre-induction core temperatures. Minimum temperature during bypass was 35.3 ± 1.3 in the standard treatment group and 35.5 ± 1.5 in the active-warming group (P=0.67). The only statistically significant temperature difference between the groups was upon leaving surgery; however, the difference was only 0.2°C (Fig. 1). Afterdrop was similar in the routine management (0.2°C) and forced-air (0.1°C) groups, and did not differ significantly.



Discussion:
Patients undergoing routine thermal management and normothermic bypass did not become hypothermic. There was only trivial afterdrop. Lack of afterdrop indicates that normothermic bypass was effective at warming the core and peripheral tissues. Forced-air warming did not increase core temperature by a clinically important amount in our patients. We note that effective heat transfer would have increased core temperature, even in normothermic patients. Forced-air was minimally effective, presumably, because the under-body cover warms much less surface area than a standard upper- or lower-body forced-air cover.
References:
1) JAMA 1997; 277: 1127-34.
2) Ann Thorac Surg 2000; 70: 175-81.

S-55.

SPONTANEOUS POSTPARTUM CORONARY ARTERY DISSECTION

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Introduction
A 28 year old woman presented on two consecutive days to her local Emergency Department two weeks postpartum complaining of new onset chest pain. On both occasions the patient was reassured by that her symptoms were consistent with anxiety and discharged. The patient then took a four-hour bus ride to a metropolitan city and called for emergency services on arrival to the bus depot.
On arrival to the hospital, review of systems revealed no risk factors for coronary artery disease. An EKG showed a large anterior infarct, creatinine kinase and troponin levels were highly elevated and the diagnosis of an acute myocardial infarction was established. Emergent cardiac catheterization revealed the following stenoses following the administration of 400 micrograms intra-coronary nitroglycerin: 95 % proximal left anterior descending coronary artery (LAD), 100% mid-section LAD, 70% proximal circumflex coronary artery (CX), and 90% obtuse marginal coronary artery (OM). The left ventricular ejection fraction was 25% with an end diastolic pressure of 35 mmHg. An intra-aortic balloon pump was placed and the patient was brought to the OR for emergency coronary artery bypass grafting.
The operative procedure consisted of a 3 vessel off-pump bypass with grafts to the LAD, the OM and to a diagonal coronary artery. At surgery, hematomas of the LAD, CX and OM arteries were found. Trans-esophageal echocardiography revealed hypo-kinesis or akinesis of the apex, the anterior wall, the antero-septal, and antero-lateral walls, as well as mild mitral and tricuspid valve regurgitation.
Except for a second trip to the operating room for post-operative bleeding, the patient's recovery was uneventful: she was extubated post-op day (POD) 1, the balloon pump removed POD 3, and discharged home POD 12.
Discussion
Spontaneous coronary artery dissection is a rare event, more common in women than in men, with the diagnosis usually made post-mortem. While the etiology is unclear, pregnancy is one of the proposed risk factors.[1] It is usually seen in the first few weeks of pregnancy or in the first 3 months postpartum. Most anesthesiologists will never encounter this unusual cardiac disease since the estimated incidence is 1 in 10,000 deliveries.[2] Signs and symptoms of an acute myocardial infarction are often missed since most of the patients are young and otherwise healthy. It has been suggested that elevated level of progesterone alters histological structure of an arterial wall: a loss of corrugation in elastic fibers and fragmentation of reticular fibers have been described.
Most cases reported in the literature describe a single lesion located within 2 cm of the ostium of the LAD. There are few cases of or multi-vessel lesions such as we describe.

[1]Koul AK, et al. Catheter Cardiovasc Interv 2001; 52:88-94.
[2]Engelman DT, et al. Conn Med 1993; 57:135-139.

S-56.

WITHDRAWN

Critical Care Medicine & Trauma

S-57.

PREDICTING FAILURE TO SURVIVE CARDIOPULMONARY RESUSCITATION IN INTENSIVE CARE: EVALUATION OF TWO MORBIDITY SCORES

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Major advances have been made in providing prompt cardiopulmonary resuscitation (CPR) to cardiac arrest patients within the hospital1,2. As patients undergoing cardiac surgery become older and sicker with concomitant co-morbidities, the quality of immediate and long-term postoperative care as well as resuscitation are likely to become increasingly important3**.** Inappropriate and unsuccessful resuscitation of these patients is associated with a large expenditure of health care resources.
The aim of this study is to evaluate the usefulness of two morbidity scores; prognosis after resuscitation score *(*PAR) and modified PAM index (MPI), in predicting failure to survive following cardiopulmonary resuscitation (CPR) in our intensive care unit.

Methods
We reviewed the records of postoperative cardiac adult patients who underwent CPR in our intensive care unit from April 1999 to March 2003 at the Georg-August University Hospital, Göttingen, Germany.

Results
During the study period, 169 patients had cardiac arrest for which CPR was instituted. 80 (53.7%) survived to discharge from the ICU and 71 (47.7%) survived to be discharged from the hospital. PAR score identified 77 patients with a score > 7 and MPI score identified 74 patients with a score > 7 none of whom survived to be discharged from the ICU. The sensitivities of PAR score and MPI for predicting failure to survive following CPR were 86.5% and 83.1% respectively. The PAR and MPI scores did not incorrectly identify a patient as a non-survivor who subsequently survived.

Conclusion
The PAR and MPI scores is useful in identifying patients in whom CPR may be unsuccessful and could additionally provide useful information to physicians and patients involved with decisions about do-not-attempt resuscitation (DNAR) orders.

References
1.JAMA 1986; 255:2905-2989.
2.N Engl J Med 1983; 309:569-576
3.Arch Intern Med 1999; 159:845-50.

S-58.

OUTCOME OF CARDIOPULMONARY RESUSCITATION IN INTENSIVE CARE UNIT IN A UNIVERSITY HOSPITAL.

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Introduction
Over the past two decades several publications have reported the outcome of cardiopulmonary resuscitation (CPR) for in-hospital cardiac arrest[1]. Although the initial successful resuscitation rate in ICU patients may be high, long-term and hospital discharge rates have been reported to be unsatisfactory[2].
The purpose of this study is to identify those factors influencing outcome after resuscitation following cardiac arrest in our ICU.

Methods
We reviewed the records of all patients who underwent CPR in our ICUs at the Georg-August University Hospital Göettingen, Germany from January, 1999 to December, 2003.

Results
During the study period, 169 patients underwent CPR. 80 of the 169 patients survived to hospital discharge giving a survival to hospital discharge rate of 47.3%. The initial monitored rhythm recorded at the time of arrest was asystole in 99 (58.6%) patients. Ventricular tachycardia/fibrillation was recorded in 59 (34.9%) and pulseless electrical activity in 7 (4.1%) patients. 46 (54.8% of the survivors), 31 (36.9%) and 5 (6.0%) patients with initial recorded asystole, VT/VF and PEA rhythms respectively survived to hospital discharge. Of the 80 patients that survived to hospital discharge 75 (93.8%) achieved good cerebral recovery (CPC 1 or 2) and were alert and fully oriented on discharge; 4 patients (5.0%) were severely disabled (CPC 3), while 1 (1.2%) died in local hospital. Illness severity as assessed by SAPS II score on admission was 38.8 ± 16.0. None of our patients with SAPS II score > 40 24 hours after CPR survived to be discharged from the ICU.

Conclusion
Our study showed that nearly half the patients that had cardiac arrest in our hospital ICUs had a favourable outcome despite initial rhythms that are traditionally associated with a poor outcome. Advancing age, coexisting diseases and early initiation of resuscitation protocol had significant effects on the outcome of CPR as observed in our study.

References
1.American Heart Association. Circulation 1997; 95:2213-2239.
2.Arch Intern Med 1994; 154:2426-32.

S-59.

CRITICAL INCIDENTS/NEAR MISSES IN ACUTE INTENSIVE CARE UNIT.

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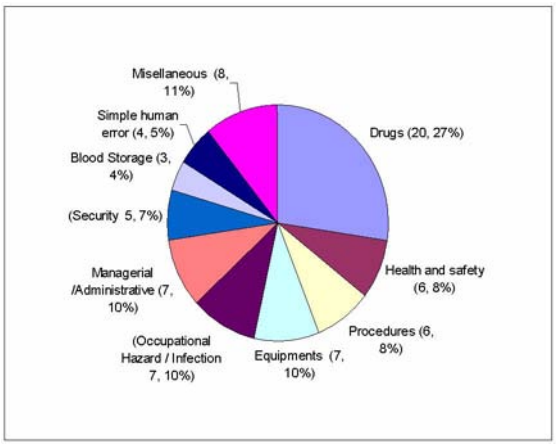
Introduction: We audited causes and consequences of critical incidents or near misses in a 17 bedded multispeciality acute intensive care unit (AICU).
Methods: All reported incidents from AICU between June 2005 and June 2006 were collected. Critical incidents were reported voluntary and anonymously using computerized central hospital incident reporting system (HIRS). Exact location and description, immediate actions taken to prevent harm and remedial actions taken to prevent the incident are required to fill in. Each incident is reviewed in detail and preventive strategies are developed and introduced
Results: 73 incidents were reported from AICU in different categories (figure) of which 83% (60) were preventable. Drug related incidents were the most common (20; 27%). Of these 11 (55%) were related to drug infusions. On five occasions inotropes or vasopressors were not infusing on transfer of patients from other areas to AICU leading to significant hypotension (systolic blood pressure < 70 mm of Hg)on arrival. Factors responsible were low battery, improper monitoring during transfer and empty syringes. Four patients receiving Insulin infusion had significant hypoglycemia (blood sugarl < 3 mmol /L)due to incorrect dosing or failure to monitor blood glucose level and /or stopping the enteral feeding. Five patients (7%) had fall from bed mainly during nursing break time. No harm was reported. Two incidents involved splash of secretions or blood over the face involving eyes or mouth. Failure to check airway and resuscitative equipments, to dispose dirty and sharp equipments and to handover infective status of patient were also reported. Cardiac arrest was reported due to tension pneumothorax during insertion of chest drain. One patient lighted cigarette while in the bed raising serious concerns.
Discussion: ICU is a busy, complex and dynamic environment where various factors contribute to critical incidents which are mostly preventable[1]. Previously our audit has shown procedures and equipments related incidents were common. Now the drug and its infusions related errors are more frequent. Strict protocol for insulin therapy is introduced. Drug infusion transfer form is proposed. Nursing break time is carefully organized. Protective face masks/glasses to protect staff is suggested. Prudent check up procedures for patient properties is done. In conclusion monitoring of incidents has guided us in the continuous improvement in patient safety.

Reference: 1. Crit Care Med. 2005;33:1701



S-60.

IS AN OLD COMPLICATION GETTING WORSE? TRENDS IN POSTOPERATIVE RESPIRATORY FAILURE DETERMINED BY A NATIONAL INPATIENT DATABASE

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Introduction: Postoperative respiratory failure (PORF) is a rare but serious surgical complication (1). Despite recent improvements in surgical and anesthetic practice, we hypothesized that as elderly patients or those with significant comorbidities increasingly undergo anesthesia and surgery, the incidence of PORF would also increase.
Methods: We searched the AHRQ Quality Indicators (QIs) for PORF. QIs measure health care quality using administrative datasets (1994-2002, > 37,000,000 hospital discharges, www.qualityindicators.ahrq.gov). A subset, the Patient Safety Module (PSI), monitors the rate of adverse hospital events considered preventable. PSI #11 concerns postoperative respiratory failure (PORF). PORF was identified as discharges with ICD-9-CM codes for acute respiratory failure within 2d of surgery in any secondary diagnosis field. The numerator used to calculate this value was discharges with ICD-9-CM codes for acute respiratory failure in any secondary diagnosis field, excluding patients with primary diagnoses of preoperative respiratory failure, neuromuscular disease, or tracheostomy. The denominator was all surgical discharges > 18 y defined by specific DRGs and ICD-9-CM codes for an operative procedure. The database includes age, gender, income in patient zip code, patient residence (metropolitan vs non-metropolitan), insurance carrier, hospital location, size, and teaching status. Rates were compared using the t-test adjusted for multiple comparisons, and excluded patients with obstetric, respiratory or circulatory conditions.
Results: The incidence of PORF doubled between 1994-2002 (Table 1). In the most recent yearly databases (2001, 2002), increased PORF was associated with: age > 45y (vs 18-44); patient income < $25K/y (vs >$45K); patient or hospital in non-metropolitan area (vs metropolitan); Medicare or Medicaid (vs privately insured); hospital location in South or West (vs Northeast); public or private for-profit hospital (vs private, non-profit); hospital size < 100 beds.
Discussion: Unlike other reports (2), these data indicate an increasing rate of PORF. This difference may result from the susceptibility of different patients to this complication and to disparities in health care. Our findings suggest that preoperative comorbidies and increased surgical complexity may not be the only factors altering the incidence of PORF. Variability in surgical and anesthetic techniques, and the aggressiveness of postoperative extubation, may also play a role. The healthcare burden of PORF is considerable and studies are needed to understand the mechanisms and develop preventative strategies.

1. Arch Intern Med. 2002;162:2053-7
2. Ann Surg 2000;232:242-53

Post-op Respiratory Failure Rates

YEAR	PORF per thousand patients	P-value vs 1994	P- value vs previous year
1994	1.97 ± 0.1	-	-
1997	2.3 ± 0.1	0.017	0.017
2000	3.4 ± 0.09	<0.001	0.001
2001	3.47 ± 0.09	<0.001	0.61
2002	4.04 ± 0.09	<0.001	0.001

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S-61.

CT SCANS IN CRITICALLY ILL VENTILATED PATIENTS

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Introduction: Critically ill ventilated patients require intra-hospital transport for diagnostic or therapeutic or follow-up computed axial tomography (CT) scans where facilities for portable scanner are unavailable. Transport of critically ill patients has its own potential for complications. ICU physician must weigh risks and benefits of moving these patients. We reviewed CT scans performed in our unit and results are discussed especially with regard to CT head weather there was wasteful use of radiology as per The Royal College of Radiology (UK) guidelines.
Methods: Study was conducted in our 10 bed medical-surgical-trauma ICU from January 2002 to May 2006. All mechanically ventilated patients admitted during this period were included. Data collected included age, gender, date of admission, length of stay, outcome, type of pathology on admission, type of CT scan, reason for request and CT scan result.
Results: We had 436 CT scans performed on 210 patients. Data from16 scans was inadequate. CT head (31%) was the most frequently used technique followed by CT abdomen/pelvis (27%), CT thorax (24%), CT PA (5.7%), CT others (spine, facial bones, sinuses) (12.3%).
CT head: There were 130 CT scans of head of which reports from 3 patients were unavailable. Out of these 25 CTs(19.6%) were not well justified as per guidelines.

Category 1	Repeating investigations which have already been done	2
Category 2	Investigation when results are unlikely to affect patient management	12
Category 3	Investigating too often	6
Category 4	Doing the wrong investigation	0
Category 5	Failing to provide appropriate clinical information	0
Category 6	Over-investigating	0
	Difficult to categorize	5
	Total	25

Discussion: There are mainly 6 chief causes of wasteful use of radiology. Two patients who were transferred from other hospital had repeat scan as films were unavailable. Category 2 scans are those scans in which anticipated positive finding is usually irrelevant or because a positive finding is so unlikely. Out of our 12 scans, 4 showed hypoxic brain injury post cardiac arrest, 3 brain oedema, 2 age-related atrophy, and rest no abnormality. Category 3 repeat scans were mainly on patients who had stroke. Though these CT scans have less positive findings they did make an impact on change of patient management. We suggest there is a need for more specific guidelines to limit wasteful use of radiology and unnecesary transport of critically ill patients.
References
1. Making Best Use of a Department of Clinical Radiology Guidelines for Doctors. Fifth Edition Ref No: BFCR (03)3.
2. Critical Care Medicine 2000 Vol. 28 No 12.
3. Acta neurochirurgica, 1997 vol. 139, no. 11, p. 10427.

S-62.

IS HYPOXIA A RELIABLE INDICATOR OF PULMONARY EMBOLISM?

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Introduction: Regional anesthesia has proven to be beneficial in the total joint arthroplasty (TJA) patient. Intrathecal opioids are widely used for postoperative analgesia in the TJA patient. This has resulted in increased surveillance including monitoring of vital signs and oxygen saturation for at least 24- 48 hours. We have noted an increased diagnosis of pulmonary embolism (PE) at our institute as a result of the increased vigilance and diagnostic testing. The purpose of this study is to evaluate the significance of hypoxia as an indicator for PE in the perioperative period following elective TJA.
Methods: This IRB approved retrospective study identified 90 patients with a confirmed diagnosis of PE by spiral CT scan from January 2000 to December 2004. Of these, 76 patients had complete information available for review. A chart review was performed for sign and symptoms associated with PE: hypoxia with lowest saturations recorded via room air pulse oximetry, history of chest pain, symptom of breathlessness (SOB), and diaphoresis.
Results:

	Single presenting symptom (n = 76)	Greater than one presenting symptom (n = 76)
Chest pain	2 (2.6%)	8 (10.5%)
SOB	4 (5.2%)	25 (32.8%)
Diaphoresis	0 (0%)	6 (7.8%)
Saturation <90%	33 (43.4%)	60 (78.9%)

Number of patients with decrease in oxygen saturation

Sats 50-59%	Sats 70-79%	Sats 80-89%	Sats 90-100%
3	9	48	16

Mean saturation 85.2 [standard deviation 8.48]
95% confidence interval 83.23 - 87.11
Highest saturation 98 %
Lowest saturation 54 %

Discussion: Hypoxia alone is suggestive but not diagnostic of PE. Hypoxia in combination with other signs and symptoms may increase the accuracy of diagnosis. Some patients with normal oxygen saturations but with other symptoms had PE while others with marginal hypoxia also had PE. Normal saturation does not "rule out" the diagnosis of PE. 64 out of 76 patients with a diagnosis of PE (84.21%) had oxygen saturations greater than 80 %.
Conclusion: Each incident of hypoxia requires individual assessment. Normal saturation does not rule-out PE, while transient borderline hypoxia is a poor indicator of PE. Patients with more than one sign/ symptom suggestive of PE should be evaluated closely.

S-63.

HELLP SYNDROME :UTILITY OF SPECIFIC CLASSIFICATIONS AS PROGNOSTIC TOOLS.

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Introduction: HELLP syndrome is a specific complication of pregnancy characterized by Hemolysis, Elevated liver enzymes and Low platelet count. Maternal mortality was reported to be as high as 24%. Two classifications of the HELLP syndrome are widely used (Tennessee [1] and Mississippi [2]). The aim of this study is to determine mortality of HELLP syndrome as defined by each classification and try assessing the most relevant.
Methods: Prospective data collection part of the APRiMO study (Assessment of Prognosis and Risk of Mortality in Obstetrics). Were included all obstetric patients transferred from a referral center for high risk pregnancies maternity in our independent multidisciplinary intensive care unit (ICU). Study period: January 1996 September 2004. Demographic data, obstetric history, morbid events, length of stay (LOS), severity of illness scoring systems and organ dysfunction scores at day 1 of admission were collected.
Exclusion criteria : LOS < 4 hours.
The main outcome of interest was survival status at ICU discharge.
Two groups were compared: Patients with HELLP syndrome as defined alternatively by the two classifications (GroupI) and patients without hepatic dysfunction (GroupII).
Results are expressed as means Standard Deviation (SD). $P < 0.05$ was considered significant. Discrimination of the classifications was assessed by the area under the receiver operator characteristic curve (AuROC). Calibration was assessed by the Hosmer Lemeshow (HL) goodness offit test. Data was computed on SPSS 11.5 Win-XP compatible.
Results: Difference between Group I and Group II was statistically significant concerning obstetric hemorrhagic complication ($P<0.001$), incidence of Acute Renal Failure ($P=0.01$), mortality ($P=0.001$), LOS (6.5 ± 7days vs. 4.4 ± 4 days, $P=0.001$), SAPS-Obst score (24.5 ± 8 vs. 16.8 vs. 7, $P<0.001$). Mississippi classification discriminated well, but calibrated badly. In contrary, Tennessee classification was a poor discriminator but calibrated very well.
Discussion: Both models classified patients according to different criteria but were correlated with mortality. None of the classifications discriminated and calibrated well at the same time. The two models seem to be complimentary. Development of an aggregate classification could to refine the models.

Number of patients, Discrimination and Calibration statistic tests for each classification

Classification	Dead	Alive
Tennessee	n = 45 (20.3 %)	n=177
Missessippi	n = 20 (26.7 %)	n=55
	ROC	HL
Tennessee	0.75	0.001
Missessippi	0.64	0.533

References:
[1] Am J Obstet Gynecol 1993 ;68 :386.
[2] Am J Obstet Gynecol 1996;175:460.

S-64.

EXPERIMENTAL STUDY OF A NEW DEVICE FOR AIRWAY MANAGEMENT DURING PERCUTANEOUS TRACHEOSTOMY

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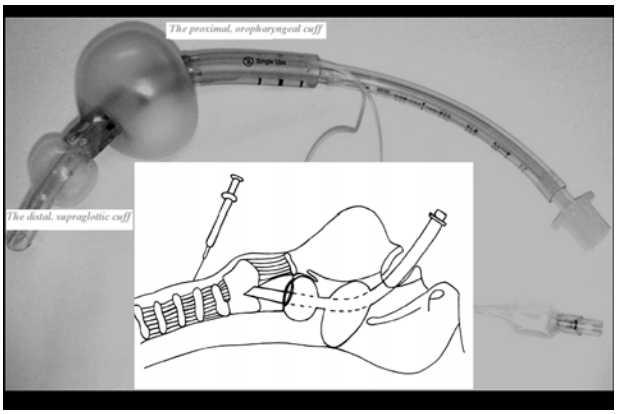
Introduction: During percutaneous tracheotomy, the endotracheal tube is gradually withdrawn to maintain it in a sub-glottal position. This procedure has several risks: 1) Air leaks. 2) The endotracheal tube or its cuff may be punctured if sited too far distally in the trachea. 3) Bronchial inhalation. 4) Accidental extubation estimated at about 7.5% in experienced hands. 5) Damage to the endoscope.
Methodes: We describe a new device for controlling the airways may be an answer to these difficulties. It consists of a tube (Figure) providing ventilatory assistance through intubation limited to one part of the larynx, with a proximal orifice and a distal orifice with two cuffs, the first containing twenty millilitres of air, situated about one centimetre from the distal end and a second of a hundred millilitres of air situated about one centimetre behind the first. The first cuff is placed in a supra-glottal position immediately above the vocal cords. The second cuff once inflated is sited in the oropharynx and thus fixes the device while putting pressure on the first already inflated cuff which in turn exerts pressure around the glottis ensuring a good seal. Clinical use of this concept is possible, while awaiting the arrival of the device on the market, by combining two types of tube, a n°8 endotracheal tube and a disposable n°4 laryngeal tube. A study on cadavers in Strasbourg's Department of Normal Anatomy to check the capacity of this device to control the airways was undertaken before beginning a clinical study.
Results: This device could be introduced in all cases. There are several steps involved in setting up the system, and bag ventilation is effective in all cases. The are no air leaks and the device is quite stable in place.
Discussion: The need to perform the percutaneous tracheotomy as quickly as possible to avoid hypoxia and alleviate the hypercapnia may also be a source of complications. During the learning period or when a patient presents a tendency to rapidly desaturate combined with difficulties in locating his tracheal space, ventilatory safety may be compromised. In reality, in practical terms, neither classic withdrawal of the tube nor the LMA provides good control of the airways during tracheotomy. Preliminary information concerning the use of this new device is encouraging.



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S-65.

ASSOCIATION OF PERIOPERATIVE GLUCOSE LEVELS WITH POSTOPERATIVE INFECTIONS AND COMPLICATIONS FOLLOWING ORTHOPEDIC TRAUMA SURGERY.

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Introduction: Higher intraoperative blood glucose levels are associated with poorer outcomes in diabetics undergoing cardiac surgery (1). Questions exist as to the generalizability to non-diabetics and to other surgeries (2). Orthopedic trauma patients have relatively high rates of postoperative wound infections and other morbidities. We examined the association of glucose levels and postoperative complications.
Methods: A retrospective review of 300 trauma patients requiring primary orthopedic surgery collected data on admitting and POD1 glucose levels, demographics and postoperative complications including wound infection, UTI, pneumonia, thromboembolism and nine other morbidities. We used statistical analyses of Pearson correlations and multinomial regression ANOVA to identify the associations of glucose levels with presence and number of postoperative complications.
Results: Significant correlations existed for presence as well as number of complications and a) admitting glucose, b) POD1 glucose and c) age. Two multiple regression model ANOVA's were performed using age and length of surgery as covariates and independent variables admitting, POD1 and change of glucose levels on dependent variables 1) presence or absence of complications and 2) number of complications. Presence or absence of complications was not associated with any glucose parameter. Number of complications however were significantly related to POD1 glucose ($p=0.014$) and nearly significant for change from admitting to POD1 glucose ($p=0.07$). **Discussion:** The regression equation associated POD1 but not admitting glucose levels with postoperative complications. As with literature supporting intraoperative use of beta blockers, controlling perioperative hyperglycemia in orthopedic trauma patients may warrant a prospective study.
References:
1. Anesthesiology,103:687, 2005
2. Anesthesiology,103:677, 2005

S-66.

IN VIVO TRACKING OF MACROPHAGE RECRUITMENT INTO THE INFLAMED PERITONEUM IN MICE BY FLUORESCENCE MEDIATED TOMOGRAPHY

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AFFILIATION: [1]Department of Anesthesiology and Intensive Care, University Hospital Muenster, Muenster, Germany, [2]Department of Anesthesiology and Intensive Care, Institute for Anatomie, University Hospital Muenster, Muenster, Germany, [3]Institute for Radiology, University Hospital Muenster, Muenster, Germany.

Introduction: Sepsis, often emerging from peritonitis is the leading cause of death in intensive care medicine and goes along with endothelial activation and global recruitment of inflammatory cells. Information on dynamics of leukocyte recruitment in clinical settings would significantly ease diagnosis, therapeutic decision-making and control of therapeutic efficacy. Tools to image homing of macrophages (MQ) to inflamed tissue in vivo are scarcely available. Because of their unique tissue penetration and negligible signal-to-noise-ratio will near infrared fluorescent (NIRF) dyes enable us to visualize fluophor labeled molecular and cellular targets in vivo using 3-D-fluorescence mediated tomography (FMT, Visen)[1)]. We utilized this trailblazing technique to track MQs in a mouse peritonitis model of WT and Urokinse- receptor deficient mice[2)] with a well documented leukocyte adhesion defect.
Methods: Thioglycollate-elicited peritoneal MQs from GFP-transgenic mice were stained with NIRF-dye DiR. The effect of DiR-labeling on in vitro MQ-adhesiveness was tested on TNF-α activated immortalized mouse endothelial cells. To correlate intraperitoneal cell number to fluorescence signal intensity, increasing numbers (10^4 to $5x10^6$) of MQs were injected IP immediately before FMT measurement. For peritonitis studies, 10^7 DiR-tgGFP MQs were injected IV in C57/Bl6 WT or urokinase-receptor deficient mice. Baseline FMT was performed before thioglycollate-peritonitis was induced. Controls received 500µl saline IP. Follow up FMT was conducted every 24h for 3 days. FMT data were quantitated as mean (nM) or over-all (pmol)DiR-fluorescence in the abdominal region-of-interest. Peritoneal fluids were collected by lavage on day 3 and MQs were ex vivo quantified by flow cytometric GFP detection.
Results: Adhesiveness was not affected by DiR-staining (34±8 vs. 34±8 MQ/HPF, ctr. vs. TP, n=6, $P<0.05$). IP injected cell number and fluorescence intensity correlated with $R=0.91$. Fluorescence signal enhancement was significantly stronger in mice suffering from thioglycollate peritonitis (TP) compared to control wt-mice (d1: 3±0.78 vs. 13±0.13; d2: 5±1.28 vs. 19±3.33; d3: 4±0.67 vs. 15±2.67; nM, ctr. vs. TP, n=5/7, $P<0.05$). Flow cytometry revealed significantly more GFP-MQ in peritoneal lavages of wt-peritonitis mice compared to wt-control ($2.62x10^3±8.62x10^2$ vs. $1.17x10^4±2.12x10^3$, ctr. vs. TP, n=5/8, $P<0.05$. Urokinase-receptor KO and WT mice both showed a significant increase in peritoneal MQ-recruitment as evidenced by FMT, which was significantly attenuated in KO mice (d2: 47±20 vs. 78±34, d3: 44±9 vs. 75±27, KO vs. WT, n=6, $P<0.05$)
Discussion: FMT is a powerful tool to track DiR-labeled MQs recruited into the inflamed peritoneum in vivo which was confirmed by flow cytometry. Optical Imaging using NIRF-technology can be used to detect inflammatory processes over time. Our assay demonstrated meaningful detection of MQ-recruitment in WT and adhesion-deficient urokinase receptor-deficient mice. FMT may therefore allow to estimate the extent of inflammation and guide diagnosis and therapy of peritonitis and other inflammatory diseases.
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S-67.

DEVELOPMENT OF LATERAL FLOW DIAGNOSTIC DEVICE FOR RAPID DETECTION OF CEREBROSPINAL FLUID LEAKS*

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Introduction: Cerebrospinal fluid (CSF) leaks occur in conditions like placement of needle/catheter for epidural anesthesia and analgesia, trauma, skull fractures, intracranial surgical procedures, infection, hydrocephalus, congenital malformations, neoplasms, rhinnorhea and otorrhea. A technique to rapidly identify CSF in biological fluids was developed, which would help the physicians and support personnel to detect CSF leaks in a rapid, simple manner. The technique is based on identifying lipocalin type brain specific Prostaglandin D2 synthase (PGDS), a CSF specific protein marker, by highly specific antibodies adsorbed to latex beads on a lateral flow device.
Methods: Two positive hybridoma clones (for their ability to identify both native and denatured PGDS by methods of ELISA, dot blot and immuno blotting) were selected for large scale production on *in vitro* ascites. Purification of monoclonal antibodies was accomplished by affinity chromatography. The test antigen (rPGDS) that is to be used in the diagnostic strip was cloned and expressed in a bacterial expression vector with an N-terminal His tag and purified using affinity chromatography. A lateral flow device using NT membranes was designed and the different reagents that were made were used to test for their ability to identify CSF in a rapid format. Tests were assembled into dipstick format and cut at 4.2 mm. Latex conjugate dilutions were placed in a plastic well along with varying amount (0-10µl) of antigen. Latex conjugation was performed by mixing the antibodies with latex beads. rPGDS and peptide antigens were printed, and all latex conjugations were tested. Sandwich lateral flow experiments were also performed by coating different monoclonal and polyclonal antibodies on the membranes. Multiple experiments using different amounts and different concentrations of each antigen were performed.
Results: rPGDS and highly immunogenic peptide antigens of PGDS showed strong interaction with latex conjugated PGDS antibodies on the lateral flow device. CSF samples were also analyzed and were shown to positively react with the antibodies. rPGDS, PGDS peptide, CSF and ammonium sulfate precipitated antigens were coated on to the membrane and inhibition assays were performed. Both systems (capture and inhibition) worked efficiently on the lateral flow device detecting CSF marker.
Discussion: This technique to rapidly identify CSF in body fluids would help the health care provider to diagnose the disease, avoid associated complications in invasive procedures, and serves as a tool to rapidly decide on optimal patient management as well as help assess the efficacy of treatment. It is expected that such a test will be used as a routine safety/diagnostic test for anyone undergoing epidural anesthesia, suffering base of skull fracture, skull based surgery and in any conditions where it is important to detect the presence of CSF.

S-68.

STROKE AND PREGNANCY: ETIOLOGY, TIMING AND OUTCOME

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Introduction: Most previous studies on stroke during pregnancy have been mainly focused on incidence and risk factors. These studies have not reported details of etiology and stroke outcome. In our study, we tried to evaluate the etiology, timing and outcome of stroke occurring during pregnancy.
Methods: We conducted a retrospective analysis on all obstetric patients who have been diagnosed with stroke during pregnancy or were within 8 weeks postpartum. These patients were transferred to our multidisciplinary intensive care unit between January 1996 and December 2004. All patients were investigated with a CT scan of the brain, and MRI and/or cerebral angiography.
Results: eighty eight patients were included, 34 patients of them were excluded (incomplete investigations or non-stroke diagnosis: reversible leucoencephalopathy, cerebral abscess…). Fifty four patients with a diagnosis of stroke were identified 30 patients with ischemic stroke (IS) and 24 patients with hemorrhagic stroke (HS). The majority of events (45 patients, 83%) occurred in the third trimester and postpartum period (p=0.02). A specific cause was identified in 24 patients (80%) of IS and in 21 patients (87%) of HS. Causes of IS include pre-eclampsia/eclampsia in 11 patients, venous thrombosis and coagulopathies (deficiencies of protein C, protein S, and activated protein C resistance) in 9 patients, valvular heart disease with history of prior stroke in 4 patients and 6 patients had no definable cause. The major causes of HS were pre-eclampsia/ eclampsia in 8 patients, 4 patients presented with hemorrhage secondary to aneurysmal rupture, 3 patients presented with bleeding from arterio-venous malformations (AVM), bleeding as a consequence of disseminated intravascular coagulation (DIC) occurred in 2 patients and 7 patient had hemorrhagic events of unknown origin. Hypertensive disorders of pregnancy were the most common comorbid conditions (32%).
Nineteen deaths (35%) occurred in our study, 8 patients with infarction and 11 patients with hemorrhage. Thirty one patients left the hospital with neurologic deficits, requiring chronic care or rehabilitation.
Discussion: The results of our study complement the results of previous studies on timing of stroke in pregnancy [1,2]. We found that pre-eclampsia/eclampsia and intracranial vascular malformations were the major causes of stroke in pregnancy, which agrees with other findings [2,3]. Our study shows a high mortality rate of 35%, this can be explained by the fact that our population does not have the same access to medical attention as western populations.
References:
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S-69.

PHYSIOLOGICAL CONCENTRATION OF 17-β-ESTRADIOL SUPPRESSES NF-κB ACTIVATION MEDIATED BY BACTERIAL INFECTION

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Objective: Among the patients (patients' ages; 20-45 years of ages) who admitted to our hospital from 2002 to 2004, the number of those who required mechanical ventilation for respiratory complications and for the subsequent development of acute respiratory distress syndrome was significantly lower in females than in males (Number of the patients admitted to our hospital: male 74474, female 75518; Number of the patients required the mechanichal ventilation: male 583, female 340; $p<0.01$). In order to elucidate the molecular basis of the gender-related differences in the incidence of development of respiratory complications, we sought to clarify the roles of 17-β-estradiol on inflammatory responses induced by bacterial infection.
Methods: RAW264.7 cells were transiently transfected with *cis*-reporing NF-κB reporter plasmid and the cells were then stimulated with 1μM of CpG oligodeoxynucleotide (ODN), a constitution of bacterial DNA which has been shown to induce strong immune responses on mammalian immune systems (1, 2), in the presence or absence of 17-β-estradiol. Relative luciferase activities were measured following the stimulation with CpG ODN.
Results: Treatment with CpG ODN alone was sufficient to induce NF-κB activation as assessed by 5-10 fold induction of relative luciferase activities. In the presense of physiological concentration of 17-β-estradiol (10^{-8}M), the relative luciferase activities induced by CpG ODN were significantly suppressed than those stimulated in the absence of 17-β-estradiol.
Discussion: In addition to the classic effects of estrogen on the female reproductive systems, it has been shown to exert a diverse array of biological effects on, such as, bone density, plasma lipid profiles, and on cardiovascular systems. Here we show that estrogen also exerts anti-inflammatory properties by preventing inflammatory gene transcription by inhibiting NF-κB activation. Cellular events associated with inflammation are mediated through NF-κB, a redox-sensitive transcription factor that regulates a multitude of inflammatory genes, including cytokines, adhesion molecules, and acute phase proteins. Although the precise mechanisms by which estrogen interferes with the activation of NF-κB and the subsequent degradation of IKK remain to be elucidated, the results presented herein provide a novel therapeutic approach to the potentially life-threatening complications such as acute respiratory distress syndrome.
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2. Hemmi H *et al.* Nature 2000;408:740-745

S-70.

HYPONATREMIA ABSORPTION SYNDROME IS NOT OBSERVED WITH PHOTO SELECTIVE VAPORIZATION OF THE PROSTATE.

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INTRODUCTION: Routine treatment for benign prostatic hypertrophy (BPH) is transurethral resection of the prostate (TURP) utilizing loop wire electrocautery. Hyponatremic absorption syndrome ("TURP syndrome") can occur with this procedure and result in significant morbidity and mortality.[1] Consequently, alternative treatments are being developed. Lasers for photoselective vaporization of the prostate (PVP) is a newer therapy. The true extent of PVP with absorption hyponatremia remains unknown. We therefore tested the hypothesis that PVP does not cause absorption hyponatremia.
METHODS: As an alternative treatment to traditional loop wire electrocautery TURP, 20 of 66 select patients presenting with BPH over an 18-month period accepted outpatient PVP as part of an IRB approved study. Preoperative gland size, pre- and post-operative serum sodium, and resection time were measured. All patients received a balanced general anesthetic which included a propofol induction, laryngeal mask airway (if not contraindicated), N_2O/O_2, and a volatile anesthetic. The bladder was irrigated with sterile water. Serum sodium concentrations before and after the procedure were compared using paired *t* tests. Results are presented as means ± SDs; $P < 0.05$ was considered statistically significant.
RESULTS: Preoperative gland size was 54 ± 32 g and resection time was 104 ± 43 minutes. No clinical signs of hyponatremia absorption syndrome were observed. There was no statistically significant difference between the pre- and post-operative serum sodium concentrations (Fig). The pre-to-post-operative sodium difference averaged 0 ± 3 mEq/L. One patient was excluded from the analysis after intraoperative bladder perforation resulted in ICU admission, invasive monitoring, and dialysis. This patient experienced considerable hyponatremia, with serum sodium decreasing by 26 mEq/L.
CONCLUSIONS: Despite an average resection time exceeding an hour-and-a-half and bladder irrigation with sterile water, no significant changes in pre- to post-operative serum sodium were observed. The absence of hyponatremia absorption syndrome is likely due to the instantaneous coagulation of absorptive venous channels during resection caused by the laser's specificity for oxyhemoglobin.[2] PVP appears to offer an increased safety advantage over standard loop wire electrocautery TURP in terms of hyponatremia. Our experience indicates that bladder perforation is possible, and predictably has serious consequences. We currently use and recommend irrigating the bladder with normal saline to reduce the morbidity associated with possible bladder perforation.
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S-71.

IMPACT OF MEDICAL COMPLICATION ON NEUROLOGICAL OUTCOME AND MICROALBUMINURIA AFTER ANEURYSMAL SUBARACHNOID HEMORRHAGE

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Introduction: The prevalence of microalbuminuria is several-fold higher in the patients with aneurysmal subarachnoid hemorrhage (SAH) patients, and it has been suggested that an albumin-creatinin ratio > 200 mg/g during the first 8 days is the best independent neurological prognostic predictor among some established predictors1). Among medical complications after SAH, fever, anemia, and hyperglycemia were significantly associated with unfavorable neurological outcome2). Microalbuminuira is an established risk factor for several diseases including diabetes mellitus, essential hypertension, and heart failure. The present study was carried out to determine the pathophysiological conditions which influence the development of microalbuminuria and the unfavorable neurological outcome after SAH.
Methods: After approval of Institutional Research Committee, informed consent was obtained from each patient's relatives. We studied consecutive 51 patients who underwent surgical aneurysm clipping and endovascular surgery within 3 days after SAH from October 2003 to September 2005. After the operation, all patients received conventional brain-oriented intensive care therapy according to clinical requirement. Urine was collected before surgery and every day for 7 days for measurements of urinary microalbumin. To exclude the influence of urinary flow, we calculated urinary microalbumin / urinary creatinine ratio (MACR). Neurological outcome was assessed with the Glasgow Outcome Scale (GOS) three months after the ictus and stratified into two states - unfavorable outcome (death, vegetative state and severe disability) and good outcome (moderate disability and good recovery). We reviewed medical chart before surgery and every day for 7 days and calculated the frequency of medical complications according to prespecified criteria, and evaluated their impact on outcome using univariate logistic regression, and their associations to the MACR using the Spearman rank correlation test. $P < 0.05$ was considered to be statistically significant.
Results: Among 51 patients, 25 (49%) had unfavorable outcome. The prevalence rates of microalbuminuria (MACR > 30 mg/g) were 74.5% during the first 8 days. The most frequent complications were hypertension (>160 mmHg systolic; 75%) followed by anemia which required transfusion (69%), temperature > 38.3°C (55%), seizure (20%), myocardial ischemia (18%), and hyperglycemia > 200mg/dL (16%). Fever (odds ratio [OR], 6.0; 95% confidence interval [CI], 1.8-20.3; $p < 0.01$), hypertension (OR, 4.6; 95% CI, 1.1-19.4; $p = 0.04$) and seizure (OR, 5.7; 95% CI, 1.1-30.0; $p = 0.04$) significantly predicted unfavorable neurological outcome. The highest MACR during the first 8 days significantly correlates with hypertension ($r = 0.37$; $p < 0.01$) and seizure ($r = 0.36$; $p < 0.01$).
Discussion: Fever, hypertension and seizure are significantly associated with unfavorable neurological outcome. Hypertension and seizure contribute to the development of microalbuminuria. Control of hypertension and seizure may improve both the development of microalbuminuria and neurological outcome after SAH.
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S-72.

KETAMINE HAS A FAVORABLE EFFECT ON AUTONOMIC CARDIOVASCULAR REGULATION DURING DECOMPENSATED HEMORRHAGIC SHOCK IN PIGS.

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Introduction: Ketamine is often the anesthetic of choice in patients suffering from hemorrhagic shock (HS) secondary to its pressor effect from central sympathetic stimulation. However, there is concern about its direct myocardial depressant effect and its ability to cause hypotension in catecholamine deficient patients. Our objective was to examine the autonomic regulation after ketamine administration during decompensated HS.
Methods: Six pigs (mean weight 33.56 kg) were anesthetized with isoflurane, mechanically ventilated and bled to a mean arterial pressure (MAP) of 40 mmHg. After an inability to compensate, based on a lactate greater than 3 or needing its shed blood re-infused for greater than 30 seconds to maintain its MAP of 40 mmHg, ketamine (500 mcg/kg/min) was infused for 10 minutes. Ectopy-free 800-beat segments of RRI and systolic arterial pressure (SAP) waveforms were acquired at 500 Hz at baseline (BL), during HS and at peak plasma ketamine concentration (Ketamine). RRI and SAP variability was investigated by frequency domain (fast Fourier transform), non-linear and complex demodulation analyses using a commercially available software.

Results:

	Baseline	HS	Ketamine
R-to-R Interval	483	293***	328
Mean Arterial Pressure	72	44***	42
RRI Approximate Entropy	0.92	0.74*	0.7
RRI Sample Entropy	0.89	0.66*	0.63
RRI Low frequency power, normalized	0.04	0.17*	0.24
RRI High frequency power, normalized	0.73	0.72	0.55*
RRI LFP/HFP ratio, normalized	0.06	0.42*	0.6
Baroreflex slope	0.54	0.15***	0.13
RRI High frequency power, nonnormalized	1.8	0.17	0.17
RRI LFP/HFP ratio, nonnormalized	6	42	60
Amplitude of HFP of RRI, by complex demodulation	1.4	0.5	0.33
SAP Approximate Entropy	1.17	0.82	0.72
SAP Sample Entropy	1.31	0.8*	0.63
SAP Total power	6	23**	18
SAP Detrended Fluctuations	1.12	1.61***	1.72
SAP Low frequency power, normalized	0.03	0.01	0.03
SAP High Frequency Power, nonnormalized	0.87	0.93***	0.94
Amplitude of HFP of SAP, by complex demodulation	2.9	5.8**	4.67

*, $p<0.05$, **, $p<0.01$, ***, $p<0.001$, mixed model ANOVA.
Discussion: Ketamine preserved RRI and MAP in decompensating animals; decreased the vagal modulation of the RRI and showed a trend toward increased sympatho-vagal balance as evidenced by an increase in the RRI LFP/HFP ratio. Ketamine may benefit physiologic compensation during HS and does not interfere with the linear and nonlinear metrics explored in this study.

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S-73.

TURNOVER TIMES BETWEEN SURGERIES VARY WITH TIME OF DAY

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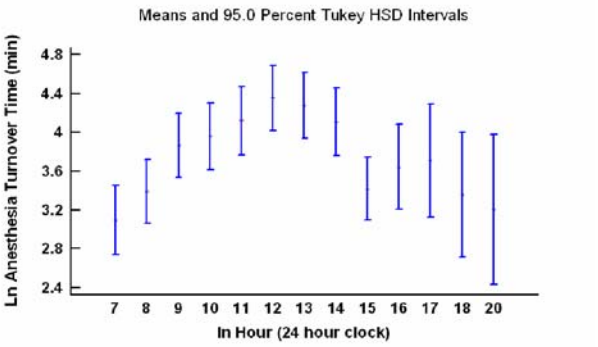
INTRODUCTION: We investigated anesthesia turnover times (ATT) and the variability in ATT between surgeries. Our ultimate goal was to describe variability in ATT and the associated factors that might be predicted, controlled, or altered to improve surgical scheduling.
METHODS: With institutional approval, we studied 47,019 surgical procedures undertaken at a large teaching hospital (1) each with exactly one surgical procedure classified by common procedural terminology (CPT) code. We modeled only ATT occurring on regular scheduled workdays. To ensure the analyses were technically feasible, we divided the data into 20 categories based on main headers of the CPT classification and surveyed ATT for the 3 most numerous CPTs in each category so our conclusions would be applicable over a broad range of surgical experience. To ensure we were able to estimate surgeon effect, we retained only those CPTs with 2 or more surgeons each with a minimum of 10 surgeries. The resultant representative database consisted of 12,533 surgical turnovers, 41 CPTs, and 98 surgeons. A main effects general linear model was used to investigate the association between ATT and 10 independent variables: in_hour, same_surgeon, first_of_day, ASA risk class, surgeon, demand, gender, age, turnover_vs_startup, and type of anesthesia. The natural logarithm (ln) of ATT was analyzed because of prior indications of lognormality of the response variable (2).
RESULTS: In order of importance among 41 CPTs, the main effects for ATT were found to be statistically significant at the 0.05 level for in_hour (37 codes, 95%), foday (80%), to_su (61%), same_sur (58%), anes (37%), ASA (24%), surgeon (22%), demand (10%), age (7%), and gender (3%). Our results indicated ATT varied with time of the day for 95% of the 41 surgical procedures surveyed (see figure). As a guide to significance, 5% or less of main effects surveyed would be expected to be significant by chance alone.

FIGURE: Natural logarithm of the adjusted mean ATT by hour of the day, CPT 19120 = Excision of breast lesion, n = 689 turnovers, r2 = 60%.



CONCLUSIONS: Our analyses suggest that TT is specific to time of day and knowledge of the sources of variability in ATT are needed to improve modeling and thus surgical scheduling. Poor scheduling may lead to sub-optimal utilization of costly operating rooms.

S-74.

ROLE OF ANESTHESIA IN THE DELAYS TO THE ON-TIME TRANSFER TO THE OPERATING ROOMS

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Introduction: The preoperative preparation of patients is a complex process. On-time transfer to the operating room (OR) represents a critical step to OR efficiency. This time study was designed to assess the role of anesthesia to an on time transfer to the operating room.
Methods: All patients scheduled as a first case in a same day admission unit were included in a 29 consecutive weekday on time study. On time transfer to the OR was defined as no later than 07:10 min. An independent observer followed each patients and recorded the times of (1) arrival in the pre-operative unit, (2) patient's readiness following the nurse evaluation and IV placement, (3) History and Physical (H&P) completion or update by physician's assistant; (4) completion of the pre anesthesia evaluation, (5) readiness for transfer and (6) actual transfer to the operating room. Data are presented as mean ± SD. Alpha was set up at 0.05. Comparison between groups was analyzed using an analysis of variance.
Results: 151 patients were included in this time motion study. Among them 6 patients were excluded, because they were either cancelled or rescheduled. 41% of patients left on time for the OR. The patients entered the pre-operative location at 5:26 AM ± 17 min and left for the OR at 7:04 AM ± 4 min.
Speak w/surgeon = Pt wanted to speak w/surgeon ; Bathroom=Patient going to the bathroom prior to transfer; IV/Evaluation=nursing evaluation and IV placement.
Discussion. Our study demonstrates that the most frequent causes of delays were related to the surgical consent and lab and X-ray performed on the day of surgery. Delays caused by anesthesiologists were less frequent.
Conclusion: This study demonstrates that anesthesiologists do not represent the most frequent cause of delays to the OR transfer.

Causes and magnitude of delays

Cause of Delays	N	magnitude of delays
Patient Late	5	64 ± 41min
Surgical Consent	17	31 ± 18 min
H&P	10	49 ± 24 min
IV/Evaluation	4	38 ± 4 min
Speak w/surgeon	3	20 ± 4 min
Anes pre-op evaluation	5	12 ± 11 min
Lab and X-ray	17	25 ± 8 min
Bathroom	2	21 ± 9 min
Late leaving for the OR	6	28 ± 23 min

S-75.

ECONOMIC BENEFITS OF AN ACUTE INTERVENTIONAL POSTOPERATIVE PAIN SERVICE

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Introduction: Anesthesiologists are been increasingly requested to participate in postoperative pain management. [1] Although, it is established that such an involvement requires resources, it is often difficult to obtain them, because it is claimed that postoperative pain management does not produce any tangible benefits for the health care system. Thus, previous studies [2,3] have established that improved postoperative pain management results in an increase patient satisfaction, but the economic benefit of such an end point is unclear. This study was designed to assess the effects of an acute interventional postoperative pain service on the length of stay in the hospital in a community hospital.
Method: Length of hospital stay (LOS) were established for 1 year period before (July 1, 2001 through August 30, 2002) and after (July 1, 2004 through August 30, 2005) the implementation of an acute interventional postoperative pain service (AIPPS). For this analysis, the following procedures were selected: primary total hip and total knee replacement surgery, thoracotomy and prostatectomy. These procedures were chosen because (1) the same surgeon performing the surgery before and after the implementation of the acute interventional postoperative pain service and (2) they represented the types of surgery requiring most frequently the involvement of the acute intentional postoperative pain service. Data are presented as mean SD.
Result: A total of 1,492 patients were included in this analysis (479 before and 1023 after the implementation of the acute interventional postoperative pain management). The length of hospital stay prior to the implementation of the acute interventional postoperative pain service was 3.68± 1.5 day per patient. The use of AIPPS was associated with a reduction of LOS by 0.69 day per patient for a total of 702 day per year.
Discussion: Our data demonstrates that AIPPS can help reduce LOS. This represents a direct and indirect economic benefit. It reduces the overall patient cost (direct effect) and provides opportunity to increase the number of patients being admitted (indirect effect). This is especially interesting in hospitals within a very high occupancy ration. In the present model, the described reduction represents an opportunity for admitting an additional 234 patients per year

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S-76.

OUTCOMES PATIENTS WISH TO AVOID AS A FUNCTION OF PREOPERATIVE ANXIETY

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Introduction: Tailoring anesthesia services to match patient preferences may result in higher rates of satisfaction. A novel study asked patients to allocate $100 among 10 categories of anesthesia side effects such as nausea, pain, shivering, recall, etc. in importance of avoiding that outcome (1). We attempted to replicate that study while measuring preoperative anxiety to investigate if patients' concerns are mediated by anxiety levels.
Methods: Patients scheduled for elective surgery were approached at our preadmission testing facility, consented with IRB-approved forms and asked to complete a questionnaire listing ten potential side effects of anesthesia. Subjects were asked to order these outcomes from 1 (most undesirable) to 10 (most desirable) and assign a relative value to each outcome represented by spending a hypothetical $100 (the more they spent on any one outcome, the less likely it would be to occur). Finally, subjects were asked to complete the State Trait Anxiety Inventory [STAI] (2).
Results: 79 patients were recruited with valid data for 76. A quartile split of highest and lowest STAI patients were compared. The median absolute ranks as a determination of patient preferences were not different between groups. The relative values of mean dollars spent showed higher anxiety patients spending a mean of $43.25 of $100 on avoidance of pain whereas low anxiety patients spent $19.85 (ind sample t test, p=0.03) (see Fig 1). For all patients, the linear regression of anxiety versus spending to avoid pain shows r= 0.29 (p=0.01)

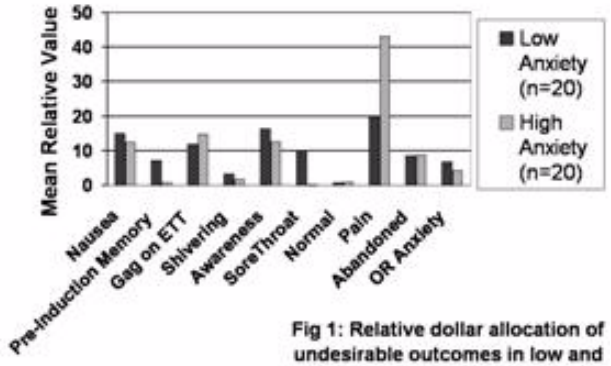

Fig 1: Relative dollar allocation of undesirable outcomes in low and high anxiety groups

Discussion: As expected, a normal outcome had a median rank of 10 and relative value mean near zero dollars. Non-parametric ANOVA revealed no significant differences in the absolute rankings between high and low anxiety patients; however significant differences were found in relative values. High anxiety patients allocated a greater proportion of total resources ($100) to avoid pain than low anxiety patients. Avoidance of pain is of far greater value to high anxiety patients when performing relative rankings of peri-anesthetic outcomes. We conclude that relative rankings ("spend a total of $100") allow better discrimination of patient preferences than do absolute rankings ("rank 1-10").
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S-77.

CHANGES AND CONSEQUENCES - A CLINICAL PRODUCTIVITY PLAN IN A LARGE MULTI-SITE ACADEMIC ANESTHESIOLOGY DEPARTMENT

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Introduction: A large multi-site academic department developed two faculty tracts within its overall organization, one purely clinical, the other clinical academicians. Both groups had a portion of their financial package based on a clinical incentive compensation plan. The changes in clinical work performed and staffing needs were studied via outcome measures.
Methods: Clinical site specific benchmark means were developed two years prior to implementation of the plan with Actual Billable Hours with Overlap(overlapping hours due to concurrencies). Incentive tiers were developed based on variation from the mean site specific data. Of the nine hospitals covered by the anesthesiology department, four were chosen to evaluate. The clinical productivity data was analyzed to determine the overall impact for the department, for each site and for individual faculty members.
Results: For Fiscal Year 2005, the Department increased the total Billable Hours with Overlap by 14% while reducing overall FTE count by 2.4 (2%). The number of additional FTEs that would have been required to provide service to cover the increased hours and FTE loss based on benchmark means totaled 13.71(14%). All sites showed increases in total anesthetizing hours both overall, and on a per FTE basis.

Hospital	A	B	C	D
Specialty	OB	Cardiac, Transplant, General Surgery	Cardiac, General Surgery	Orthopedic, General
# of Operating Rooms	12	41	29	13
# of cases	13,408	22,485	18,483	10,987
Faculty (Total Clinical+ Academic)	19	39	22	7
Medical Direction	Yes	Yes	Yes	Yes
CA-1 Anesthesia Residents	Yes	Yes	Yes	No
Student Nurse Anesthetists	Yes	Yes	Yes	Yes

Hospital	A	B	C	D
Concurrency	2	2	2	3
Clinical Hours AFTER Plan	30,212	74,964	45,385	20,583
Clinical Hours Before Plan	26,480	67,141	35,304	20,125
% Change	14.09	11.65	28.56	2.27
Average Clinical Hours per FTE	1741	1861	2012	3430
% Change per FTE	13%	18%	22%	2%
Potential additional Clinical FTEs to cover workload increases	2.1	4.2	5	0.1

Discussion: One measure of success for a clinical incentive plan is generating more unit hours with either the same or less number of faculty, through either longer work days or increasing concurrencies. Of the clinical sites analyzed, the smaller community hospitals which were already highly productive sites showed the least change. The sites with the greatest number of clinical faculty were able to institute the behavioral changes expected when monitoring clinical productivity showing substantial increases in individual productivity. This was accomplished through budgetary planning based on the compensation goals of the faculty members at each site.

S-78.

THE PHARMICOECONOMICS OF LOW-FLOW ANESTHESIA AT A UNIVERSITY HOSPITAL

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Introduction: Choosing newer inhalational anesthetics with lower blood solubility instead of older agents leads to a significant increase in anesthetic cost. Despite this fact, newer agents are often selected for specific clinical reasons, such as the need for inhalational induction, or rapid emergence. This cost increase can be minimized by using lower fresh gas flow (FGF) rates[1]. With the use of non-hydroxide containing CO_2 absorbents, anesthesia may be safely administered with low or minimal flow anesthesia[2]. We designed a study to estimate the theoretical cost savings had by lowering our FGF rates during the maintenance of anesthesia.
Methods: We performed a retrospective review of hand-recorded anesthesia records to obtain the total FGFs used, by individual rates, during 1364 hours of anesthesia. The smallest time increments recorded for each FGF rate was 5 minutes. We then calculated both a total time and percent usage for each total FGF rate. Using annual anesthetic costs, we estimated the cost savings that would be obtained by decreasing FGF from 2 l/min to 1 l/min.
Results: At our academic institution, a FGF of 2 l/min was used 52.2% of the time. Our total annual cost of inhalation anesthetics is $477,338. Thus, a savings of approximately 26.1% or $124,107 per year could be realized by using 1 l/min instead of 2 l/min.
Discussion: Decreasing FGF from 2 to 1 l/min has been purported to lead to a 50% decrease in the cost of inhalational anesthetics. However, this holds true only if 2 l/min are used 100% of the time, which is not the case. Still, a marked reduction in cost may be obtainable by instituting a change in practice from using a FGF rate of 2 l/min for the maintenance of anesthesia to 1 l/min. With the recent clinical availability of non-hydroxide containing carbon dioxide absorbents, we can incorporate this economical practice without compromising patient safety. Our figures may over-estimate the cost savings because of higher FGF used during induction, and the brief, unrecorded use of higher flows during rapid titration of anesthetic delivery during the maintenance phase of anesthesia. Each institution must also adjust the cost savings of lower FGF with the increased cost of these newer absorbents. Limitations of our study include the analysis of hand-recorded anesthetic records and approximation of time to five minute intervals, analysis of only a portion of the total anesthetics performed, and extrapolating the data from 1364 hours to estimate the expected annual savings.
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S-79.

FACTORS AFFECTING SURGICAL TIME IN OUTPATIENT LAPAROSCOPIC CHOLECYSTECTOMY

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INTRODUCTION
Obesity is a worldwide epidemic with multiple adverse health effects which ultimately have a negative impact upon health care delivery (1). Early identification of patients who may require an increased surgical time (ST) is important for health care resource planning. We use a novel modeling method, Classification and Regression Trees (CART) (2) to develop a predictive model of peri-operative morbidity following outpatient larparoscopic cholecystectomy.
METHODS
After obtaining approval from the Research Ethics Board, a retrospective chart review of all inpatients having laparoscopic cholecystectomy over a 20 month period was carried out. Data were collected on multiple co-morbid conditions. Classification and Regression Trees[1] were created using S-Plus 6.1 using median ST as an outcome. Ten fold internal cross-validation was performed on the results. Logistic regression analyses were carried out on the same data set for comparison.
RESULTS
Using a classification tree with median ST as a response, ST was more likely to be greater than the median for the following predictive patterns i) age < 65 plus BMI < 26 plus hypertension (probability = 0.75); ii) age > 65 plus BMI < 26 (probability = 0.74); iii) BMI > 30 plus diabetes mellitus (probability = 0.85). Logistic regression analysis indicates that the probability of ST greater than the median is increased in patients older than 65 years (OR=1.909). Logistic regression analysis demonstrates that the OR of ST greater than the median was increased in a linear fashion as follows: BMI 26-30.99 (OR=1.363); BMI 31-35.99 (OR=1.957); BMI 36-40 (OR=2.938).
DISCUSSION
CART analysis is a useful method for predictive modeling of resource allocation. CART analysis of multiple co-morbid conditions demonstrated that there is an increase in ST associated with both low and high BMI. This is consistent with the J-curve described by Calle *et al* (3). Age, hypertension and diabetes were also identified as contributing factors to increased ST. Logistic regression analysis indicates that the OR of increased ST was increased in a linear fashion with increasing BMI. Age > 65 increased the OR of ST greater than the median. Pre-operative identification of these factors may optimize health care planning for ST.
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2) *Classification and Regression Trees*. Wadsworth, Belmont Ca. 1984
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S-80.

INFLUENCE OF ASA PHYSICAL STATUS ON DURATION OF PRE-ANESTHETIC ASSESSMENT

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Introduction: Widespread acceptance of the ASA physical status as an indicator of systemic disturbance has led to its application -- alone or as a component of multifactorial indices -- to predict perioperative morbidity, length of hospital stay, and hospital costs (1,2). It also serves as a modifier for anesthesia-based value units. The present study was undertaken to determine if ASA physical status would serve as a reliable means for predicting the amount of time that should be allocated to the pre-anesthetic history and physical in the Pre-Admission Center of a tertiary care hospital.
Methods: With IRB approval for data collection without patient identifiers, the time required for the preoperative history and physical by two nurse practitioners under the supervision of an anesthesiology attending was recorded in 500 consecutive patients evaluated in our Pre-Admission Center. This typically was performed after vital signs, allergies and medications were recorded by Nursing personnel. If consultation with other caregivers (e.g., surgeon, primary care provider or cardiologist) was required after completion of the interview, then this time was not recorded. The recorded interview time was compared to the ASA physical status with ANOVA and t-test.
Results: As shown in the table, there was a progressive increase in interview time with increasing ASA physical status. The time ranged from a mean of 35:54 (minutes:seconds) for ASA 1 patients to 57:48 min:sec for ASA 4 patients ($p<0.0001$ for intergroup differences by ANOVA; $p<0.001$ for differences between status 1 and 2 vs status 3 and 4)).
Discussion: The data suggest that, to optimize efficiency, more time should be allocated for preoperative assessment of ASA 3 and 4 patients. For billing purposes, ASA 3 and 4 are assigned 1 and 2 additional base units, respectively. The findings indicate that the additional remuneration is consumed in large part during pre-anesthetic assessment and planning.
References:
1. Anesthesiology 2:281-4, 19412. ASA annual abstracts 2006;A195

	VISIT LENGTH (Minutes:Seconds)							
					95% Confidence Interval			
	N	Mean	Std. Deviation	Std. Error	Lower	Upper	Min	Max
1	32	35:54	14:07	02:29	30:48	40:59	14:59	15:00
2	447	48:03	18:18	00:51	46:21	49:45	14:59	129:00
3	272	57:28	20:13	01:13	55:03	59:52	19:59	120:00
4	27	57:48	21:18	04:06	49:23	66:14	33:59	101:59

S-81.

CAN ANESTHESIA ADVERSE EVENTS BE ELECTRONICALLY EXTRACTED?

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INTRODUCTION: Anesthesia departments traditionally use voluntary disclosure of adverse events (AE) to detect quality assurance (QA) issues. This method has obtained improvements in anesthesia safety [1,2]. Underreporting the incidence and severity of AE is an accepted limitation of voluntary systems [1,3,4]. Queries of anesthesia information management systems (AIMS) can capture certain AE better than voluntary reporting [4]. The optimal role of man and machine in medical AE detection is yet to be understood. We analyzed our QA indicators and AIMS database to describe the role of man and machine in anesthesia QA reporting.
METHODS: We identified the AE currently specified in our AIMS QA module. We defined the clinical criteria necessary for confirmation of each AE (assuming voluntary reporting was unavailable). We then assessed the availability of the necessary clinical data collection in our AIMS database.
RESULTS: We found that 28.9% of our AE could be confirmed solely by queries of the AIMS database, 28.9% of our AE could only be confirmed by voluntary reporting, and 42.2% of the AE could be confirmed by some combination of AIMS database queries followed by human clarification. Each AE was classified into one of three distinct categories (Table 1).
CONCLUSIONS: Voluntarily identifying AE is the best method to confirm most QA issues, but is limited by low compliance and underreporting. Queries of AIMS records can confirm the presence of certain AE and can be used to guide the investigation of others. The combination of man and machine may offer a superior model to current QA practices.
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Table 1 Anesthesia AE Classification

AE Types	Category-Frequency (%)	Definition	Example
Type I AE (Data Evidence)	28.9%	The AE can be detected by database query alone.	Hypoxemia (SaO2 < 90% for > 1 min) Hyperthermia (Temp > 38C)
Type II AE (Circumstantial Evidence)	42.2%	An AE is suggested by database query, but confirmation by chart review or voluntary disclosure is required.	Drug Allergy (Administered drug and documented drug allergy match) Pneumothorax (pulmonary/vital sign changes exist)
Type III AE (Human-evidence)	28.9%	Without voluntary disclosure, no database evidence of AE would exist.	Dental Injury Accidental Dural Puncture

Classification of AE based upon the clinical criteria necessary to confirm them the and information discoverable in the AIMS record. The category definition, frequency, and an example are provided.

S-82.

PATIENT SAFEY; INSTANT VOICE OVER INTERNET COMMUNICATIONS.

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Introduction; Anesthesiology emergencies are time sensative. This is particularly true with trainees. Our institution supports the training of both an anesthesiology residency and CRNA program with an excess of 45 anesthesia locations. Conventional paging has been the stalwart of notification but there have been incidents of unacceptable delay.
We looked to other technologies to accomplish our needs of instant directed, verifiable communication.
Cellular and push-to-talk technologies were cumbersome, of poor quality and took precious moments away from key personnel.
We subsequently looked at wifi LAN based hands free communications (Vocera Inc., Cuperton, California)
Methods; We timed from initial anesthetist call for assistance to attending physician call back by conventional digital paging system and by Vocera. Digital page was issued by the circulating nurse at the request of the resident/ nurse anesthetist.
Results; Digital paging systems time to call back varied from 1 minute 5 seconds to 4 minutes and 25 seconds with an average of 2 minutes and 41 seconds. The Vocera system had a range of 10-17 seconds with an average of 15 seconds.
Conclusion; Digital paging system has been a traditional method of contacting key personnel in spread out areas. The pitfalls however are numerous, it has been estimated that delay can be up to as much as 30 minutes[1]. Furthermore there is no way to ascertain whether the page had been received with an estimated beeper failure rate of 15%[1]. For the person being paged, there is the matter of finding a phone, being fixed in location while waiting for the call back to answer, ascertaining the needs and then heading for the locale. Clearly when minutes may mean life and death this system is not ideal.
The wifi LAN based hands free system allowed near instant communications directly with the resident/ Nurse Anesthetist. Furthermore, the portability of the devices allowed communication while in transit. In one instance, when a additional faculty anesthesiologist was needed, the wifi LAN based hands free communication system provided a nearby attending with verifiable real time confirmation.
Practices where in immediate face to face communications are not available, wifi LAN based hands free devices or similar are essential and could be deemed an essential life saving tool.
[1]Previte. Int'l Anes. Clinics 44(1):179-97, 2006

S-83.

A MODEL FOR BUILDING A STANDARDIZED HAND-OFF PROTOCOL FOR ANETHESIA CARE

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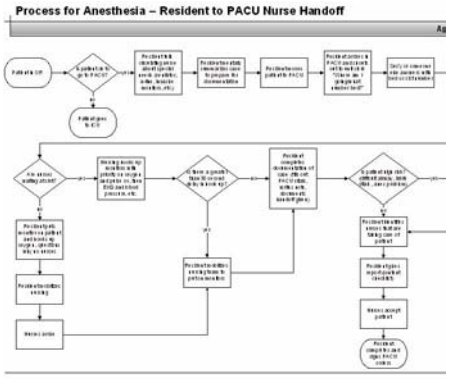
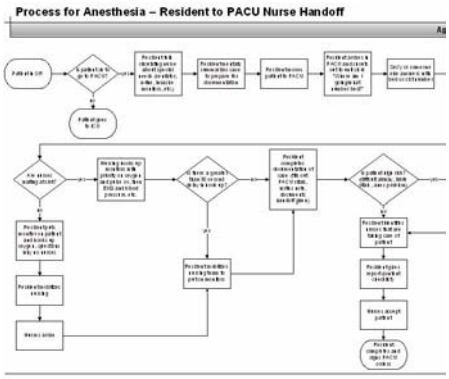
INTRODUCTION:
In 2006, the JCAHO made a standardized approach to hand-off communications a National Patient Safety Goal. The discontinuity of care that results from increasing hand-offs poses danger to patients. The safety of the hand-off process has been called into question by a number of different studies which suggest that hand-offs are often characterized by communication failures, environmental barriers and adverse care. We viewed the hand-off as communication of information that was occuring in both written and verbal formats. The goal of this study was to create a standard protocol, including process and content, for hand-offs between anesthesia providers.
METHODS:
We engaged anesthesia residents in a process mapping exercise designed to elicit the hand-off process. Process mapping is a method that can be used to describe and analyze how an individual clinician interacts with the system itself and with others within that system. Next we determined the standard content that needed to be included in each hand-off. Process and content were then vetted with other anesthesia residents for input and buy-in with the result reflecting the model of care.
RESULTS: We found great variation in practice. Figure 1 includes the process map. An Anesthesia hand-off chekclist tool was developed, "PACU To-Do" (see Figure 2).
CONCLUSIONS:
We found great variation in practice and a lack of systems appreciation. Understanding patient hand-offs as a process is important because a high degree of process awareness often drives the design of the work. By mapping the PACU hand-off process, the members of the anesthesia team gained insight into how their colleagues perceive the same tasks. This helped create a standardized checklist which is now being implemented. We have designed and implemented a model for Anesthesia departments striving to meet the JCAHO National Patient Safety Goal, to implement a standardized hand-off protocol in the perioperative environment.





S-84.

THE EFFECT OF PROLONGED STEEP TRENDELENBURG POSITION ON INTRAOCULAR PRESSURE DURING ROBOTIC-ASSISTED PROSTATECTOMY: *DOES IT CHANGE OVER TIME?*

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Introduction: As part of the Vatikutti Urology Institute, we have performed over 2600 robotic-assisted prostatectomies. The Vattikutti Institute Prostatectomy (VIP)[1], requires patients be placed in a 25º head-down position for at least 2.5 hours, which is known to increase intraocular pressure (IOP).[2] In addition, abdominal CO_2 insufflation, increases in blood pressure, end-tidal carbon dioxide and central venous pressure result in increases in IOP.[3-6] The effects of steep Trendelenburg position with pneumoperitoneum have not been studied for the duration and severity of head-down tilt that is required for the VIP. Our objective is to measure changes in IOP at several time intervals throughout VIP surgery to determine IOP over time.
Methods: After obtaining IRB approval and informed consent, IOP was measured in 40 patients undergoing VIP for prostate cancer. Patients with glaucoma, visual defects, blindness, and prior corneal abrasions were excluded. Using a Medtronic Tono-Pen XL®, IOP measurements were taken at six time intervals; pre-op (baseline), immediately post-induction (induction), placement in trendelenburg (trend 0), one hour in trendelenburg (trend 1), two hours in trendelenburg (trend 2), and then supine under anesthesia (supine). Induction medications were standardized. Maintenance of anesthesia was with isoflurane in oxygen. End-tidal CO_2, intraabdominal pressure, mean arterial pressure (MAP), and end-tidal isoflurane levels were recorded. Each of the five time points were compared to baseline value using paired two-sided t-tests. Statistical significance was measured at the 0.05 type-I error rate.
Results: Forty patients, mean age 59 (range 46-76) had a mean baseline IOP of 16.3 (±5.8). IOP changes from baseline were statistically significant when compared to baseline ($p < 0.001$) at Induction (mean EIOP=-5.7±5.5), Trend 1 Hour (mean ΔIOP=8.9±6) and Trend 2 Hour (mean ΔIOP=9.8±6.3). There was no significant difference in IOP compared to baseline at the Trend 0 ($p=0.39$) and supine ($p=0.11$) time points.
Discussion: Initiation of the head-down tilt position and pneumoperitoneum resulted in a significant increase in IOP which persisted, but did not increase with time. Our data suggests the elevation in IOP that results from Trendelenburg position and increased intraabdominal pressure occurs early and may not increase with an increased duration of surgery. Further studies are needed to determine if there is a time dependent increase in IOP. The clinical significance of persistant elevation of IOP during robotic-assisted prostatectomy requires further study.
References:
1) J. Urology 2003, June; 169(6): 2289-92
2) Acta Opthalmology 1981 Aug; 59(4):465-75
3) J. American Association of Gynecologic Laparoscopists 5(2):125-128 May 1998
4) Gynaecological Endoscopy 2002, 11, 383-387
5) Anaesthesia 1996 Dec;5112):1106-8

S-85.

CHANGES IN INTRAOCULAR PRESSURE IN PATIENTS UNDERGOING ROBOTIC-ASSISTED PROSTATECTOMY: *DOES MEAN ARTERIAL PRESSURE HAVE A ROLE?*

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AFFILIATION: [1]Department of Anesthesiology, Henry Ford Hospital, Detroit, MI, [2]Department of Opthalmology, Henry Ford Hospital, Detroit, MI, [3]Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI.

Introduction: As part of the Vatikutti Urology Institute, we have performed over 2600 robotic-assisted prostatectomies. The Vattikutti Institute Prostatectomy (VIP)[1] requires patients be placed in a 25º head-down tilt position for at least 2.5 hours, which is known to increase intraocular pressure.[2] In addition, abdominal CO_2 insufflation, increases in blood pressure, end-tidal carbon dioxide and central venous pressure result in increases in IOP.[3-5] Our objective is to determine whether changes in mean arterial pressure (MAP) correlate with changes in IOP at several time intervals during the VIP.
Methods: After obtaining IRB approval and informed consent, IOP was measured in 40 patients undergoing VIP for prostate cancer. Patients with glaucoma, visual defects, blindness, and prior corneal abrasions were excluded. Using a Medtronic Tono-Pen XL®, IOP measurements were taken at six time intervals; pre-op (baseline), immediately post-induction (induction), placement in trendelenburg (trend 0), one hour in Trendelenburg (trend 1), two hours in Trendelenburg (trend 2), and then supine under anesthesia (supine). Induction medications were standardized to lidocaine, fentanyl, propofol, cisatracurium or succinylcholine. Maintenance of anesthesia was with isoflurane and cisatracurium. MAP, end-tidal CO_2, intraabdominal pressure, and end-tidal isoflurane levels were recorded. Each of the five time points were compared to baseline values using paired two-sided t-tests. Pearson correlation coefficients were reported for changes in MAP versus changes in IOP from baseline.
Results: Forty patients, mean age 59 (range 46-76) had a mean baseline IOP of 16.3(±5.8). At induction, IOP decreased significantly (p=.0001). The change in MAP vs. the change in IOP at induction and the supine time interval were not significant. Significant correlations were observed between changes in MAP vs. changes in IOP from baseline at trend 0 (r=-0.46;p=<0.01), trend 1 (r = -0.38; p = 0.03), and trend 2 (r = -0.40; p = 0.02).
Discussion: At induction, the significant reduction in IOP did not correlate with MAP, confirming prior studies. MAP had a significant correlation with a persistent increase in IOP in the head-down tilt position in the VIP. Tight regulation of MAP may be helpful during robotic-assisted prostatectomy to control IOP. Further studies are needed to determine the clinical significance of the persistent increase in IOP.

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1) J. Urology 2003, June; 169(6): 2289-92
2) Acta Opthalmology 1981 Aug; 59(4):465-75
3) J. American Association of Gynecologic Laparoscopists 5(2):125-128 May 1998
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5) Anaesthesia 1996 Dec;5112):1106-8

S-86.

THE IMPACT OF ADVERSE EVENT NARRATIVES IN ELECTRONIC MEDICAL RECORDS FOR TRACKING ADVERSE EVENTS

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INTRODUCTION: Reducing mishaps from medical management is central to efforts to improve anesthesia care. The IOM declared adverse events a major source of morbidity and mortality, and cited the improvements in anesthesia safety [1]. Although the safety profile is in debate [2], most agree that anesthesia care has room to improve. Anesthesia departments have used voluntary disclosure of adverse events (AE) as the primary mechanism for detecting and addressing safety issues. Poor clinician compliance with voluntary disclosure has hampered QA efforts [3,4]. Interestingly, even QA programs with 100% clinician participation significantly under report both the incidence and severity of AE [5]. Failure to voluntarily disclose is felt to be due to perceived fear of consequences [6]. We conducted a study to assess the QA narrative documentation compliance and the effect of detectable adverse events on compliance.
METHODS: We conducted a retrospective analysis of all QA de-identified data in our anesthesia information management system (AIMS) for a one-year period. The clinical database was queried for the presence of three AE with defined clinical and database criteria. Based on the presence/absence of these AE, we divided the QA data into an AE-present and AE-absent group. We analyzed each sample for documentation compliance, identification of AE, and data content. Chi-square testing was used for statistical analysis.
RESULTS: We analyzed 21,924 cases, 11,954 (54.5%) in the AE-present group and 9,970 (45.5%) in the AE-absent group. We found 67.9% of the AE-present and 65.5% of the AE-absent group to be compliant with QA documentation (chi2=14.0, p<.001). We found that 64.7% of the AE-present and 62.8% of the AE-absent documentation denied the existence of an AE (chi2=8.5, p<.01). We found that 3.2% of the AE-present and 2.7% of the AE-absent documentation documented the presence of at least one AE (chi2=4.6, p<.05). We found that 59% of reported AE addressed an occurrence that posed a clear identifiable risk to the patient, 41% reported system failures without clear patient consequences, and 69% contained narrative that further clarified the event.
CONCLUSIONS: Clinician participation in QA documentation remains low. Voluntary documentation was missing approximately 1/3 of cases. When voluntary documentation exists, it contains valuable narrative and addresses events that pose a clear threat to patients. Automated extraction captured significantly higher occurrences of some AE than were reported voluntarily. Fear of consequences does not appear to be the cause of failed voluntary reporting as the number of AE reported and compliance actually increased when AE were detectable by electronic methods. Narrative reporting of clinician experiences is a key AIMS tool to help us better understand the systems barriers and safety enablers.

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S-87.

ARE WE AS GOOD AS WE THINK? TRENDS IN ANESTHETIC COMPLICATION RATES DETERMINED BY A NATIONAL INPATIENT DISCHARGE DATABASE

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Introduction: Arguments that anesthesia has become increasingly safe are controversial (1, 2). AHRQ Quality Indicators (QIs) measure health care quality using hospital administrative datasets (1994-2002, > 37,000,000 hospital discharges). A subset of these data, the Patient Safety Module (PSI), includes anesthesia complications. We reviewed PSI data for trends in anesthesia complications between 1994 and 2002, and characteristics of the involved patients.
Methods: Our IRB deemed this study "exempt." Data collection and statistical analysis procedures are available at: www.qualityindicators.ahrq.gov/psi_overview.htm. The anesthesia PSI captures cases of anesthetic overdose, reaction, or endotracheal tube misplacement per 1,000 surgery discharges with an operating room procedure, and hospital discharges with ICD-9-CM diagnosis codes for anesthesia complications in any secondary diagnosis field. The denominator consists of all surgical discharges 18 y or older defined by specific DRGs and and ICD-9-M codes for an operative procedure. Data include age, gender, median income in patient's zip code, patient residence (metropolitan vs non-metropolitan), insurance carrier, hospital location, size, and teaching status. Complication rates were adjusted for age, gender, age-gender interactions, comorbidities, and DRG clusters. Rates were calculated as described at: http://hcup.ahrq.gov/psi_guide_rev2.pdf?, and compared using the t-test statistic.
Results: Anesthetic complications have increased significantly at every successive sampling year since 1994 (Table, $P < 0.036$). In the most recent databases (2001, 2002) factors associated with higher risk for anesthesia complications were: age > 45 y; Medicare, Medicaid, or uninsured patients (vs privately insured); hospital location in the Midwest (vs Northeast); public (vs private hospital); hospital size > 500 beds; and teaching hospital (vs non-teaching hospital). The incidence of postoperative respiratory failure increased significantly between 1994 and 2002 (1.97 to 4.04 per thousand, $P < 0.05$). In contrast, other PSIs, including retained foreign body, and abdominal wound dehiscence have decreased.

Complication Rates in Database

Year	Risk per 1000 patients	P- value vs 1994	P value vs previous year
1994	0.673 ± 0.039	-	-
1997	0.785 ± 0.037	0.04	0.04
2000	0.781 ± 0.035	0.04	0.94
2001	0.889 ±0.035	<0.001	0.03
2002	0.922 ± 0.036	<0.001	0.51

Discussion: Despite well recognized improvements in anesthetic care, these data indicate that several anesthetic complications have increased over time. These complications were more common in the elderly, in specific geographic regions, and in larger busier teaching hospitals. This increase may reflect an increasing number of elderly and sicker patients presenting for anesthesia and surgery, and/or changes in detection/definition.
1. To Err is Human, National Academy Press, 1999; p 241
2. Anesthesiology 2002;97:1609-17

S-88.

APPLYING PROBABLISTIC FAULT TREE ANALYSIS IN HEALTH CARE: MODELING MEDICAL ERRORS

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In attempting to explain and predict preventable adverse events in medicine, we begin with the assumption that such events are caused by healthcare as a system. This contradicts the view that adverse events are caused by individual malfeasance. The nuclear power and aviation industries long ago assumed a systems' view and have used it to develop methods for analyzing the risk in these settings. We adapt and deploy these methods to understand errors in medicine.
METHODS:
It is often hard to estimate the probability of preventable adverse events. We may lack either the data or the infrastructure. Fault tree analysis (FTA) is a kind of probabilistic risk assessment. Fault trees reduce events whose probabilities we cannot measure directly to other, "basic," events whose probabilities we can estimate. The question is whether we can use FTA in hospital settings.
We used fault trees to model (preventable) adverse events associated with hospital transitions of care (handoffs). Transitions occur when responsibility for patient care passes from one set of agents in a hospital to another e.g., from the Emergency Department to the Intensive Care unit. Transitions add organizaitonal complexity and may increase the likelihood of adverse events.
We interviewed 30 physicians, nurses and other staff in Trauma, ICU and Emergency Divisions in major trauma center. We used findings from the interviews to develop a fault tree model. To estimate parameters in the model, we used data from two sources: i) an electronic patient care management system, and ii) expert opinion sampled in a second round of 30 interviews.
RESULTS:
We tested the feasibility of applying fault trees to explain and predict preventable adverse events associated with transitions of care. The model captured the intuitive behavior of actual hospital systems. It also identified more than 25,000 possible sequences of events that can generate an adverse outcome. Absent a fault tree model, it is very unlikely that we could identify all of these sequences. Finally, model estimates approximate benchmarks in the literature.
Fault trees, however, assume that the "basic" events are independent of one another. The independence assumption is likely to be false in our application, and this could vitiate the probability estimates that we derive. Moreoer, the task of finding data to estimate model parameters remains a serious challenge.
CONCLUSIONS: FTA is a rigirous risk assessment tool that might have usefulness in healthcare. Our model behaved intuitively and the method rigourously identified ways in which a system can generate errors. We cannot easily dispense with the independence assumption, however, and this may restrict the range of cases where we can apply FTA. More work is needed to assess the external generalizability of using FTA probabilistic risk assessment tools.

S-89.

SURVEY OF PROPOFOL ABUSE IN ACADEMIC ANESTHESIA PROGRAMS: A FINAL REPORT

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Background: Although propofol has not traditionally been considered a drug of abuse, sub-anesthetic doses have been described as possibly having an abuse potential. This survey was conducted to assess the prevalence and outcome of propofol abuse in academic anesthesiology programs and assess the pharmacy control of propofol in these centers.
Methods: Email surveys were sent to the 126 academic anesthesiology training programs in the United States. Follow-up surveys were sent to non-responders.
Results-:The response rate was 100%. All data is summarized in table 1. We found that 20% of the departments had one or more incidents of propofol abuse or diversion in the past 10 years. The mortality rate of propofol abuse in anesthesia providers was 33%. The rate of successful return to anesthesiology practice was low at 16.7%. Our data also revealed 71% of programs had no established system to control or monitor propofol as is done with opiates. Chi-square analysis reveals a very statistically significantly association between lack of pharmacy control of propofol and positive diversion/abuse ($p < 0.001$).
Conclusions: Our data reveal that propofol abuse in academic anesthesiology appears to have increased over the last 10 years. This problem is particularly concerning in resident physicians, who were found to have a significant risk of mortality when abusing propofol. A significant majority of academic anesthesia programs have no pharmacy accounting or control of propofol stocks. This is particularly concerning given that almost all academic programs reporting deaths following propofol abuse were centers in which there was no pharmacy accounting for the drug. It is possible that increased pharmacy accounting and more rigorous drug testing in at risk individuals may assist in reducing this lethal problem.

Table 1: Individuals Abusing Propofol
Data based on 126 of 126 academic anesthesiology departments with residency programs in the United States.

	Attendings	Residents	CRNA's	OR/Anes Techs	Other	Totals
Number found	6	16	3	2	2	29
Deaths from abuse	1	6	0	2	0	9
Completed Rehab.	4	7	2	0	2	15
Relapse of use	1	1	1	0	1	4
Still in Anesthesia	1	2	0	0	0	3
Changed Specialty	0	5	0	0	0	5
Left Medicine	4	3	3	0	0	10

S-90.

ASSESSMENT OF CLINICAL PERFORMANCE OF FIRST RESPONDERS DURING A SIMULATED RESPIRATORY ARREST: A COMPARISON OF INTERNS TO SENIOR RESIDENTS

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Introduction: Medical interns and residents, often the first responders to in-hospital emergencies, may not possess the basic skills to attend to these emergencies, such as an unresponsive patient, thereby jeopardizing patient care. Previous studies have identified emergency/crisis management skills in anesthesia as technical and non-technical[1,2], with more recent studies questioning how best to identify and teach gaps in non-technical deficiencies[3]. This study investigated performance among first responders comparing skills of PGY-1 interns to those of senior residents (PGYSr) using the SimMan patient simulator. Recognition of Loss Of Consciousness (LOC) and evaluation of resuscitation skills were main objectives of this testing.
Materials and Methods: 52 PGY-1 and 28 PGYSr house officers, all having received standard training and certification (BLS/ACLS) prior to this program, gave written informed consent for this IRB approved study. All participants also attended an emergency response lecture and were individually introduced to the functions and limitations of the simulator before testing. Testing was standardized and the subject read a description of the patient prior to entering the room. Subjects were required to recognize that the patient was now unconscious and begin resuscitation. The skills in the scenario were timed and scored as successfully completed, missed, or out of sequence. Videotaping was used to review performance.
Results: One PGY-1 successfully completed the scenario (3:54 min) and one PGYSr was able to successfully complete 7 of the 8 skills in 2:10 min omitting the final step (pulse check). On average PGY-1 required 44±54 sec to recognize LOC compared to 23±32 sec in PGYSr ($p=0.01$). 15% of PGY-1 never attempted ventilation while all PGYSr did. Mean time to first attempt at ventilation was 158±80 sec in the PGY-1 compared to 97±36 sec ($p<0.001$) in PGYSr with corresponding SpO_2 of 70.2±7.7 and 76±4.0 percent ($p=0.001$), respectively. A main objective of the exercise, achievement of successful ventilation, was evaluated regardless of whether or not the skill was performed out of sequence. 56% of the PGY-1 did not ventilate compared to 35% of the PGYSr ($p=0.08$).
Discussion: Some critical deficiencies were noted using simulation testing to evaluate new interns and residents faced with an unexpectedly unconscious patient using a simple scenario. First attempt at ventilation was delayed in both groups resulting in significant hypoxia regardless of level of training. Videotaping showed the unnecessary tasks performed while delaying ventilation. Important steps were omitted, or carried out of sequence from accepted resuscitation algorithms. More effective training of first responders could be provided based on identified deficiencies with focus on recognition of unexpected patient events. Simulation can be useful to identify and teach technical and non-technical life saving skills to first responders.
1. Anesthesiology 1998; 89(1):8-18.
2. Br. J Anaesth 2002;88:418-429.
3. Anesthesiology 2005;103:241-8

S-91.

PERIOPERATIVE REMOVEABLE DENTAL APPLIANCES-ANESTHESIA RESIDENCIES DO NOT PRACTICE WHAT THE JOINT COMMISSION PREACHES

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Introduction: Joint Commission on Accreditation of Healthcare Organizations (JCAHO) guidelines state that "Before going to the pre-operative area, you (patients) must remove...dentures" (1). Dental appliances are well known causes of oral soft tissue trauma and foreign body aspiration, which often result in the need for surgery or possibly even death (2,3). Despite the above, perioperative removal of dental appliances is not consistently performed in our institution. Therefore, we wished to determine to what extent (if any), other anesthesia residency training programs tolerate the presence of removal dental appliances (RDAs) during the perioperative period.
Methods: After IRB approval, the 145 ACGME-approved anesthesia residency training programs were queried regarding RDAs in the perioperative period. Surveys were mailed once and followup emails were sent twice to non-responding programs. Survey questions included: presence of RDAs during various anesthetic techniques, timing of RDA removal/reinsertion, procedures/protocols for RDAs, and known complications related to these devices.
Results: 145 programs were queried; 46 responded (32%), which is typical for physician surveys (4). We found significant variation in practice patterns regarding removal of RDAs in the perioperative period (SEE TABLE). In addition, 45% of programs allowed exceptions to RDA removal based upon patient preference. Also, 25% of programs made exceptions based upon surgeon preference. Finally, 22% of programs admitted knowledge of adverse outcomes as a result of RDAs.

	Removal of RDAs Prior to OR					
	Always	Usually	Sometimes	Occasionally	Rarely	Never
Local Anesthesia W/O Sedation	20%	0	13%	37%	15%	15%
Mac	39%	20%	15%	20%	6%	0
Regional Anesthesia	39%	20%	13%	24%	4%	0
Oral/nasal Intubation	82%	10%	4%	2%	0	0
Mask Ventilation	54%	28%	15%	4%	0	0
Lma	72%	15%	9%	2%	0	2%
Other Airway	61%	16%	9%	2%	0	11%
Awake Intubation	80%	15%	2%	2%	0	0

Discussion: This project was conceived after an incident in our institution during which orotracheal intubation proceeded with dentures in place because of surgeon and patient insistence. Our survey responses demonstrate that over 17% of institutions surveyed tolerate the presence of RDAs for oral intubation, over 60% during regional anesthesia and over 80% for local cases in more than truly exceptional circumstances. Reasons for this were not assessed; however, we postulate that political/economic realities may play a significant role as with the incident in our hospital. Regardless, a Google internet search revealed that all of the responding institutions are JCAHO-participating facilities. Since these hospitals are training future anesthesiologists, consideration should be given to either modifying practice patterns or loosening JCAHO standards with regard to RDAs in the perioperative period.
References:
1. JCAHO Wrong Site Brochure.
2. Surg Laparosc Endosc Percutan Tech 2004; 14:234-7.
3. Niger Postgrad Med J 2005 12:65-6.
4. Health Serv Res 2001; 35:1347-55.

S-92.

SURVEY OF INHALED ANESTHETIC ABUSE IN ACADEMIC ANESTHESIA PROGRAMS

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Introduction: Substance abuse in anesthesia is well established. Opiates are the most commonly abused substances; however, little data exist regarding the abuse of inhaled anesthetics among anesthesia personnel. We aimed to determine the current dimensions of this problem among academic centers in the United States.
Methods: We conducted an online survey of anesthesiology department chairpersons in the United States about their experience with inhaled anesthetic abuse in their departments.
Results: Ninety (90) surveys were completed of the 126 departmental chairpersons surveyed (71% response rate). Of these 90 anesthesiology departments, 21 (23%) had at least one instance of inhaled anesthetic abuse in the past 25 years. The number of cases may be increasing with time, with 61% occurring in the past 6 years. The most commonly abused inhaled anesthetics were nitrous oxide (56%), isoflurane (28%), sevoflurane and halothane (both 17%). Of anesthesia personnel, resident physicians were most likely to be involved in inhaled anesthetic abuse (43% of cases), followed by CRNAs (21%). There were 4 reported cases (14%) of attending physicians as well as one case of a part-time faculty member abusing inhaled anesthetics. Anesthesia technicians were involved in 2/28 cases (7%). In addition there were single reports of an operating room nurse, an operating room technician and a member of the housekeeping staff abusing inhaled anesthetics. Fifteen persons (54%) were sent for rehabilitation. Of these 15, seven (47%) successfully returned to anesthesia practice in the OR, two (13%) returned to anesthesia and then had a relapse of abuse, and five (33%) changed specialties. Death was not an uncommon outcome resulting from abuse of inhaled anesthetics, with 6/28 (21%) cases resulting in death. Often, death was the presenting sign of the abuse. Of the academic centers returning information 81/88 (92%) do not secure and account for their inhaled anesthetics like other controlled substances (e.g. opiates).
Discussion: This data indicates that nearly one-quarter of academic anesthesia centers that answered our survey have had an individual abusing inhaled anesthetics in the past 20 years. This is a significant number because it does not take into account the many larger private practice groups throughout the country. In addition, the number of cases of inhaled anesthetic abuse appears to be increasing with time, although recall bias could effect this number. Unlike other substances of abuse, inhaled anesthetic abuse does not seem to be prevalent among personnel in other specialties. However, much like that seen with the increase of propofol abuse, abuse of inhaled anesthetics commonly has death as an initial sign of abuse and unfortunate concomitant endpoint. Our data also indicate that despite its abuse potential, few (8%) of academic centers secure inhaled anesthetics as they do other controlled substances.

S-93.

INTRAVENOUS CANNULATION SIMULATOR LIMB EXPERIENCE IMPROVES MEDICAL STUDENT SUCCESS RATE

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Introduction: The authors evaluated the effect of practice with a Laerdal Medical Intravenous Simulator Limb on the success of Intravenous (IV) cannulation of anesthetized patients by junior medical students.
Method: Eighteen junior medical students (MS3), without prior IV cannulation experience, were randomly assigned to two groups. Both groups received thirty minutes of one-to-one instruction in IV cannulation by the same senior anesthesiologist. After instruction, group A (n=9) proceded directly to IV cannulation on anesthetized patients requiring additional IV access. Supervisors offered all students verbal prompts but no physical assistance. Group B (n=9) practiced IV cannulation with a Laerdal Simulator Limb, and only attempted on anesthetized patients after completing 3 successful IV cannulations on the simulated limb. Group B, as Group A, were offered verbal prompts only when attempting IV cannulation on anesthetized patients.
Results: Group A achieved success in 14 of 30 total attempts, or 47%. Group B achieved success in 26 of 30 total attempts, or 87%. This is a significant increase of 46%.

IV Cannulation Group A - Success v. Attempts	
1	3
2	4
1	3
2	3
2	4
2	4
1	3
2	3
1	3
Total Success: 14	Total Attempts: 30

IV Cannulation Group B - Success v. Attempts	
2	3
3	3
3	3
3	4
3	3
3	3
4	4
3	4
2	3
Total Success: 26	Total Attempts: 30

Discussion: Prior studies have shown that simulator limbs improved skill in phlebotomy (1), but this is the first attempt to study if the simulator limb improved success rates in IV cannulation. This early, on-going, study has shown a significant improvement in inexperienced MS3 IV cannulation success with the use of a simulator limb.
References: Scerbo, Human Factor, 48(1) 72-84, 2006

S-94.

USE OF AN AUDIENCE RESPONSE SYSTEM TO FACILITATE RESIDENT AND FACULTY INVOLVEMENT IN THE DEVELOPMENT OF ASSESSMENT TOOLS FOR THE ACGME GENERAL COMPETENCIES

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Introduction: The Accreditation Council for Graduate Medical Education (ACGME) requires residency programs to teach and evaluate six general competencies. Residency programs are encouraged to implement evaluation methods that best meet the needs of their educational programs. We utilized an audience response system (ARS) to determine departmental opinions concerning the best methods for assessment of the competencies.
Methods: During our weekly General Competencies Conference, resident and faculty attendees (n = 30) were given an explanation of suggested ACGME assessment methods (1) and were asked to recommend evaluation methods for each competency. Eight to ten methods were recommended for each competency. An ARS utilizing TurningPoint software integrated into a PowerPoint presentation was used to anonymously survey all conference participants on whether a proposed assessment method would be a good tool for evaluating that competency.
Results: At least 65% of participants believed the following assessment tools were good methods for evaluating each of the competencies. Patient Care - monthly global evaluation, performance during simulation sessions; Medical Knowledge - written examination of didactic curriculum, in-training examination (ITE), performance during simulation sessions, oral examination, Anesthesia Knowledge Test; Interpersonal & Communication Skills - 360º evaluation, monthly global evaluation, peer evaluation by fellow residents; Professionalism - peer evaluation, 360º evaluation, monthly global evaluation; Practice-Based Learning & Improvement - case-stimulated recall oral examination. No assessment method suggested for Systems-Based Practice was believed to be effective by a majority of participants. The evaluation method felt by the greatest number of participants to be the best assessment tool for each competency and the percentage of attendees who chose that as the best method are shown in the table.

Competency	Assessment Method	Percentage of participants (95% CI)
Patient Care	Global Evaluation	63% (45-78%)
Medical Knowledge	ITE	79% (62-91%)
Interpersonal/Communication Skills	360º Evaluation	53% (36-69%)
Professionalism	360º Evaluation	42% (27-60%)
Practice-Based Learning/ Improvement	Chart-stimulated recall oral exam	48% (30-64%)
Systems-Based Practice	Written exam/ Resource Utilization Project (tie)	17% (7-34%)

Discussion: The results of our survey confirm the difficulty in implementing assessment tools for the competencies, especially those competencies that weren't previously part of the traditional residency curriculum. Multiple evaluation tools rather than individual methods are most likely needed for accurate assessment. Our departmental General Competencies Committee plans to use the information obtained from department members via the ARS to further revise and improve our assessment methods.
References: www.acgme.org/Outcome/assess/Toolbox.pdf

S-95.

DIAGNOSTIC ACCURACY OF ADVANCED COMPETENCIES IN PERIOPERATIVE ECHOCARDIOGRAPHY: PRELIMINARY DATA FROM EXECUTIVE MEDICAL FELLOWSHIP STUDENTS

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Introduction: The Executive Medical Fellowship (EMF) and remote supervision concepts were first implemented in September 2005. The purpose of this study was to evaluate advanced competencies of a select group of EMF anesthesiology students to identify areas where more focused training is warranted. **Methods:** The EMF program is based on 3 components: 1) in-person lectures and case presentations, 2) hands-on training with direct supervision, and 3) remote supervision of procedures performed on real patients. The perioperative echo EMF program is divided into 4, three-month sessions: freshman, sophomore, junior and senior. During one of the freshman sessions, four EMF anesthesiology students were asked to interpret echocardiography images of five different cases each. These cases were chosen based on their high clinical relevance. Each student evaluated each case at two different times during the freshman session. The students' diagnostic accuracy was graded on a 100 point scale and their score was reduced 15 to 20 points (based on the instructor's discretion) for mild discrepancies in diagnoses between the student and instructor, 40 points for moderate discrepancies, and 60 points for severe discrepancies. The scores from each student for each relevant, advanced competency were averaged for each of the five cases. The following comparisons between average scores were made: 1) mitral valve disease vs. aortic and tricuspid valve disease, 2) valvular regurgitant lesions vs. valvular stenotic lesions, and 3) mitral regurgitation vs. aortic stenosis. **Results:** Scores related to discrepancies in diagnoses ranged from 0 to 100 points. Diagnostic accuracy was greater for mitral valve disease vs. aortic valve disease and tricuspid valve disease (65% vs. 39% vs. 36%, respectively), valvular regurgitant lesions vs. valvular stenotic lesions (43% vs. 38%), and more specifically, for mitral regurgitation vs. aortic stenosis (57% vs. 38%). **Discussion:** This study provides quantitative information regarding advanced diagnostic accuracy of anesthesiologists beginning a comprehensive perioperative echocardiography training program. The relatively higher diagnostic accuracy for mitral valve disease compared to tricuspid and aortic valve disease may be explained by the increased prevalence and familiarity with assessment of the mitral valve. Nonetheless, the diagnostic accuracy of valvular disease as a whole is relatively low. The results of this study suggest that the ideal curriculum for anesthesiologists learning perioperative echo should focus more attention on valvular disease, with special attention to the tricuspid and aortic valves.

S-96.

THE EFFECTIVENESS OF A NOVEL APPROACH ON EEG INSTRUCTION FOR ANESTHESIOLOGY RESIDENTS

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Introduction:
One of the ACGME requirements for the completion of an anesthesiology residency is the possession of "significant EEG experience". Traditionally in our institution EEG didactics have been largely lecture based interspersed with operating room EEG exposure. In 2004, a new method of EEG instruction was implemented during a resident's rotation in the Neurosurgical ICU in collaboration with one faculty from the Department of Neurology. In addition to the traditional learning approach, the resident learns from the neurology attending during their EEG reading sessions twice a week and from clinical correlations during live EEG monitorings thoroughout the hospital. No precedent of similar models were found in the literature.
Method:
After obtaining approval for IRB exemption, residents within the University of Kentucky anesthesiology training program were voluntarily evaluated. The evaluation tool was made of 25 questions composed by the investigators which included 12 clinically relevant EEG tracings for interpretation. Residents who had the additional EEG training during the Neurosurgical ICU rotation (the novel group) were compared to those who did not receive this educational opportunity (traditional group). An independent third party graded the answers and made the results available to the investigators thus blinding them to the identity of the exam takers. The results were then analyzed using the unpaired Student's t-test.
Results:
A total of 35 residents were evaluated. Thirteen of them had the novel EEG learning opportunity and the rest had the traditional learning experience. The means were 10 and 19, for the traditional and novel group respectively. The standard deviations were 3.2 and 3.6 respectively. These results were statistically significant ($p < 0.001$).
Discussion:
The results of this study strongly suggests that the joint collaboration by the Anesthesia and Neurology departments on the EEG instruction to the anesthesiology residents has been beneficial and has had a great impact on the possession of "significant EEG experience" as required by the ACGME. In our institution and likely also in other centers, most EEG learning mainly come from lectures as the opportunities for the clinical learning of EEGs in the operating room can be sporadic. Thus, our institution took EEG instruction to a different level by seeking the collaboration of a Neurology faculty with EEG expertise during an ICU rotation with a focus in brain related issues. This concentrated experience with clinical applicability will hopefully result in better retention of this material and is potentially an area of future investigation.

S-97.

TEACHING NEW ROBOTS OLD TRICKS FOR EPIDURAL PLACEMENT USING A VIRTUAL REALITY SIMULATOR

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Introduction: Is it possible for robots to perform epidurals? With the widespread use of regional anesthesia in obstetrics, there are concerns whether enough anesthesiologists will be available to relieve labor pain: 1) fewer residents are entering the specialty. 2) aging populations use most of the resources devoted to medical care. If mannequins are being used to train resident to perform general anesthesia, now a rare event in obstetrics, is it possible to train robots on simulators to perform a common procedure?
Methods: 10 experts were asked to rank a list of 20 skills needed for epidural replacement. The top 5 were: 1) identification of the correct interspace. 2) proper needle angle. 3) needle redirection. 4) recognition of ligamentum flavum. 5) detection of loss -of- resistance. A computer-generated simulation was programmed with a 3-D model of the lumbar spine consisting of skin, ligaments, muscle, bone, and spinal cord. Force required to penetrate the tissue ranges from 3.6 N for the skin to 6.0 for the ligamentum flavum. Skin to epidural space ranges from 4 to 10 cm. A robot was then trained to interact with the virtual reality simulator by means of a microphone and an electro-mechanical force feedback linkage. Similar to a resident, the robot has the bad habit of uttering “oops” when it accidentally drops the needle-syringe assembly. The computer responds by changing the virtual spine from the flex to the extended position, making epidural placement more difficult, thereby teaching the robot to behave more appropriately. After 5 failed attempts, the computer responds with “are you sure you know what you’re doing?”
Results: A plot of time required for correct placement vs. number of trials follows a typical negative exponential curve as the robot learns to correct for mistakes by means of an artificial intelligence feedback loop.
Discussion: Industrial robots currently perform dangerous assembly line jobs such as welding and painting, which require repetitive motions. These machines are poorly suited to perform complicated variable tasks. Smaller robots handle instruments that have appropriately scaled moments of inertia such as needles and syringes and can be trained to adjust to the great variability in human anatomy.

S-98.

APPLICATION OF GAME THEORY IMPROVED POSTANESTHETIC OUTCOMES IN PERIOPERATIVE ANESTHETIC MANAGEMENT MODELS - SIMULATION STUDY

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INTRODUCTION: The goal of the perioperative medicine should be focused at the optimized patients outcomes and hereby their satisfaction. We reported the perioperative anesthetic management models (1) to show the relationship between pre- and intra-anesthetic problems or incidents and the anesthetic outcomes. Using these models may enable us to obtain better postanesthetic outcomes with least incidents of adverse events. In this study, we analyzed how the control or modification of preoperative patients or anesthetic techniques parameters might affect postanesthetic outcomes and intra- and post-anesthetic adverse events by applying game theory to the perioperative anesthetic management models.
METHODS: After obtaining the approval of the study protocol by the local ethical committee, this study was carried out retrospectively. Using the perioperative anesthetic management models (quality of recovery status (QORS)(range:0 - 18), postoperative pain (POP) (range:1 - 5), postoperative nausea and vomiting (PONV)(range:1 - 5), the number of unsatisfied items (UNSAT)(range:0 - 13), postanesthetic satisfaction score (PAS) (range:1 - 5)), the independent variables in all the models were divided into two categories; controllable variables and uncontrollable variables. The coefficient of dependent variable in the controllable variables were calculated for each model, and their values were modified in order for the dependent variable to be an optimal value by applying the game theory to modify anesthetic techniques and to improve preoperative patient’s condition so far as to meet logically patient’s and surgical procedure's capabilities. The perioperative anesthetic database (n=2,155) obtained in Iwaki Kyoritsu General Hospital was used in this study. The original group consisted of the calculated postanesthetic outcomes values using the perioperative anesthetic management models and the modified group consisted of the calculated postanesthetic outcomes values after the game theory application to the models. Statistical analysis was carried out to evaluate the effect of the game theory application on the postanesthetic outcomes using Student’s t-test between the original and the modified groups.

RESULTS: The optimization of independent variables by applying the game theory significantly improved QORS, PONV, UNSAT, and PAS values, but not POP values (Table 1).

Percent changes in postanesthetic outcome values after game theory application

	QORS	POP	PONV	UNSAT	PAS
Mean	102.5	99.8	107.6	85.0	101.2
SD	2.9	3.7	5.5	17.3	1.1
Maximum	107.6	104.5	127.2	100.0	103.2
Minimum	100.0	91.4	98.0	56.5	99.9
p-value	<0.001	0.102	<0.001	<0.001	<0.001

CONCLUSIONS: It may be possible to improve postanesthetic outcomes by applying the game theory to optimize their independent variables based on the perioperative anesthetic outcome models.
REFERENCE: 1. Yamaguchi H. 2005.

S-99.

META-ANALYSIS OF DIAGNOSTIC TESTS: TWO-STAGE HIERARCHIC MODEL FOR COMBINING LIKELIHOOD RATIOS FOR POSITIVE AND NEGATIVE TEST RESULTS

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Introduction: Traditionally, diagnostic tests are employed to "rule-out" or "rule-in" the underlying disease states. Alternatively, in the context of perioperative care, diagnostic tests are also used to predict adverse postoperative outcomes resulting from the underlying disease states. For diagnostic tests summarized in 2 x 2 tables, sophisticated methods of meta-analysis that use relative diagnostic odds ratios, summary receiver operating characteristic curve and likehood ratio scatter plots have been employed (1-3) for better evaluation of the discriminative value of diagnostic tests. A combined point estimate and 95% confidence intervals (CIs) for the likehood ratio (LR) for a positive test (LR-pos) and LR for a negative test (LR-neg) would also be useful.
Methods: We propose a two-stage hierarchic model (4) to combine information about LR separately for positive and negative test. An empirical Bayes procedure with a normal-normal heirarchic model was used get a meta-analytic confidence interval for overall median for LR-pos and LR-neg. For a single study, 95%CIs for LR-pos and LR-neg were computed using standard formulas (5). The variance between the studies was estimated using method of moments approach described by DerSimonian and Laird (6). The methodology was applied to the data summarized in a recent meta-analysis that evaluated accuracy of six diagnostic tests for predicting perioperative cardiac risk in patients undergoing major vascular surgery (2)
Results: The combined summary measure point estimate and 95% CIs for each of LR-pos and LR-neg are given in table 1.

Table 1

Test	LR-pos (95% CI	LR-neg (95% CI)
Ambulatory ECG	1.81 (1.30 to 2.51)	0.99 (0.86 to 1.13)
Exercise ECG	2.72 (1.85 to 4.00)	0.51 (0.30 to 0.86)
Radionuclide ventriculography	6.52 (2.43 to 17.51)	0.72 (0.54 to 0.97)
Myocardial perfusion scintiggraphy	1.65 (1.43 to 1.89)	0.49 (0.34 to 0.71)
Dipyridamole stress echocardiography	4.96 (2.31 to 10.62)	0.40 (0.17 to 0.90)
Dobutamine stress echocardiography	3.03 (2.06 to 4.46)	0.35 (0.23 to 0.51)

Discussion: For periperative risk stratification, LR-pos and LR-neg should be greater than 10 or less than 0.2 respectively, because these values indicate a substantial change in risk from the pretest level (7). Using such interpretation, even the dobutamine stress echocardiography, which was concluded as the best among the 6 tests for prediction of adverse cardiac outcome after vascular surgery (2), cannot be regarded as the ideal test.
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S-100.

THE CLINICAL EFFICIENCY OF NEW GENERATION CO2 ABSORBENTS: AMSORB PLUS AND SODASORB LF

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Introduction: Given the cost advantages of low flow anesthesia, and the potential risks of using older absorbents which contain strong bases, new generation CO_2 absorbents have been developed that do not significantly react with inhalational anesthetics. These new absorbents are more expensive and competing products need to be evaluated under clinical conditions to measure efficiency and confirm in vitro performance[1]. We designed a retrospective, single-blinded study to compare the duration of clinical usefulness of the CO_2 absorbents Sodasorb LF and Amsorb Plus.
Methods: Without the knowledge of any participating anesthesia providers, canisters of both absorbents were tested in anesthesia machines throughout our academic institution. Times and dates were recorded when these absorbents were changed. Changes were made when CO_2 rebreathing signaled the exhaustion of absorbent ($EtCO_2$ = 5 cm H2O). Then, the total time and fresh gas flow (FGF) rates used during general endotracheal anesthesia for each canister of absorbent were obtained through retrospective chart review. Because the rate at which CO_2 absorbent is exhausted is greater with lower FGFs, the total time spent at a given FGF rate was divided by the FGF rate to give a weighted time value. Thus in our calculations, the time the absorbent was utilized at 4 l/min. contributed only half as much to the time measured until absorbent exhaustion when compared to the time spent at 2 l/min. The average of these time weighted values for each brand was calculated, their coefficients of variance, the 95% confidence interval for those means, and p-value for the likelihood that the means of the brands differ using the student's 2-sample t-test.
Results: The mean flow corrected times for Sodasorb LF and Amsorb Plus were 1811.8 and 1088.7 respectively. The coefficients of variance for their means were 1624 and 209 respectively. Under clinical conditions, no statistically significant difference in performance was measured between Sodasorb LF and Amsorb Plus (p=0.132).
Discussion: While in vitro differences between various absorbents can be measured, the clinical performance is more important when making decisions regarding which absorbents to use. Only when clinical performances are known can sound decisions be made when evaluating which products are most efficient, and most economical. Difficulty in comparing two samples of absorbent arises from uncertainty in exactly how much CO_2 a sample of absorbent has been exposed to. Wide variations in CO_2 production occur between patients, and we have not attempted to correct for them in the present study. By blinding those using the absorbents, we were unable to perform the study under uniform FGFs, as has been done in previous in vitro studies[1]. These factors may explain the large coefficient of variance seen in this study.
References: 1. Woehlck, HJ et al. Anesthesiology 2005; 103: A1164

S-101.

UNINTENTIONAL REDUCTIONS OF FLOW RATES IN CENTRAL AND PERIPHERAL IV CATHETERS

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Introduction: There are several valid reasons to modify fluid administration sets during the perioperative period. For example, Hotline® tubing is often used to decrease the risk of hypothermia during administration of cold IV fluids. Needleless injection adapters decrease the risk of accidental injuries and are promoted by JCAHO to prevent infection. These adapters also allow for quick, repeated IV access during multiple drug injections and facilitate two infusions into a single lumen catheter. However, these conveniences employed at our institution are not without detrimental effects on catheter performance. Although subjective clinical observations suggested a decrease in flow, the actual reduction following all but one of these modifications[1] had not been quantitated. We designed in vitro experiments to measure these reductions in flow rates.

Methods: We tested peripheral IV catheters ranging in size from 24- to 14-gauge, an 8.5 Fr. rapid infusion catheter, and central catheters size 7 through 9 Fr.

The flow rates of 1 L of 0.9% saline were measured with a stop watch as it flowed into a 1 L graduated cylinder. For each experiment, the top of the fluid level in the bag was positioned 100 cm above each catheter. Times were recorded to the nearest second for both the first and second 500 mL of flow as the fluid drained from the bag. These times were averaged and recorded as a rate in ml/min for each 1 L experiment. The IV fluid administration set was then sequentially modified by the addition of Hotline® extension tubing, Interlink® and Y-adapters. The experiment was repeated a total of 3 times after each modification, and an average recorded.

Flow rates were also measured after pressurization to 300 mm Hg. Pressurization was achieved and maintained using a hand inflated pressure infuser bag, and measured with a manometer. Similar modifications were made following pressurization.

Results: Flow through Hotline® tubing, Interlink® connectors and Y-adapters was lower for all catheters. The limitation to flow was proportional to catheter radius, increasing in severity with an increase in catheter size. The most severe restrictions were associated with Y-adapters, ranging from 63.5% to 72.8% under gravity flow.

Discussion: Following certain commonly-used modifications, marked restrictions to flow occur that can only partially be overcome by pressurization. When rapid fluid administration is needed, this may create unnecessary challenges. Awareness of the magnitude these effects, and knowledge of central and peripheral IV catheter flow rates in general, will allow healthcare providers to make rational decisions when choosing IV catheters. Intelligent catheter selection and avoidance of detrimental modifications will insure the availability of adequate IV access.

References: 1. Shaw, S., Arendts, G. The Effect of the InterLink Cannula on Fluid Flow Rates and Haemolysis. Emergency Medicine (2001) 13, 456-459.

S-102.

DOES A "DIFFICULT AIRWAY" TRANSLATE TO LONGER INDUCTION?

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Introduction: A recent survey indicated that "difficult ETT" contributed more to anesthetic complexity than did severity of patient illness (1). The present study sought to determine if airway factors recorded during pre-anesthetic assessment with a two-part airway score for mask ventilation (MV) and intubation (Int) (2) accurately reflected: anticipated time from start of induction until "release" of patient to the surgeon, actual "release" time, and post-induction assessment of induction complexity.

Methods: For 453 patients seen in our institution's pre-anesthesia clinic prior to the day of surgery, scores were determined for anticipated difficulty with MV and Int. The former category was based on five factors: age; BMI; snoring and/or sleep apnea; airway pathology; and miscellaneous factors including beard, dentition and distorted facial anatomy. The latter category was based on: Mallampati classification; mouth opening; thyromental distance; ability to prognath; and neck mobility/instability (2). Each factor was rated 0-5, with an appreciation that there could be overlap among categories as well as factors. Outcome variables on the day of surgery included: anticipated "release" time by the attending anesthesiologist; actual "release time" as recorded by an independent observer; report of induction difficulty on a 1-5 scale (1=very easy; 5=difficult) by the anesthesiologist (3); and incidence of fiberoptic intubation.

Results: There was no statistically significant correlation between the MV, Int, or MV+Int scores and time or complexity outcome measures. The Pearson Correlations for MV+Int vs. outcomes were 0.091 ($p = 0.054$) for anticipated "release" time, 0.056 ($p = 0.233$) for actual "release" time, and 0.089 ($p = 0.058$) for assessed complexity. However, 7 of 23 patients with a high intubation score (≥4.5) underwent fiberoptic intubation, while only 20 of 194 patients with an Int score ≤2 underwent a fiberoptic ($p = 0.006$ by Chi-squared analysis). Moreover, 8 of the 20 patients with a low Int score had a MV score ≥2 as a result of airway pathology (n=6) or morbid obesity (n=2).

Discussion: The data indicate that scoring Int factors according to the aforementioned criteria does not predict the time required for induction; for most cases, it thus should not influence predictions affecting operating room time. While the score did not predict actual difficulty, the findings indicate that an appreciation of potential MV or Int difficulties is associated with a higher incidence of altered airway management (e.g., fiberoptic intubation). This suggests the importance of preoperative assessment and planning so as to minimize day-of-surgery delays and avoid potential day-of-surgery disasters.

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S-103.

ON-LINE PATIENT EDUCATION AND INFORMED CONSENT FOR OBSTETRICAL PATIENTS

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Introduction:
Consenting of obstetrical patients for epidural placement is difficult. Generally, the patient presents to labor and delivery (L&D) in labor and in pain. Since the patient is in pain, the question arises as whether a consent at this time is coercive and whether the patient can make an informed decision about their health care. Here, we propose a unique method of solving these issues.
Methods:
To address communicating to patients regarding scheduled surgeries, several companies have developed web based products to provide education to patients. The University of Pittsburgh Medical Center (UPMC) decided to implement the EMMI (EMMI Solutions, Chicago, IL). EMMI is an internet based, interactive patient education series that manages the expectations of people who are scheduled for surgery. Using easy-to-understand language, EMMI walks patients through the entire experience from pre-op to post-op, including risks and alternatives. Enhancing traditional informed consent, EMMI captures and documents the entire information exchange, making it a powerful risk management tool. At UPMC, a new EMMI was created to address the labor epidural. A website address and login process was conveyed to all of the offices of UPMC obstetricians so that their patients could be instructed to take the OB EMMI.
Results: Survey results for patients were accumulated for patients that viewed the program (335 patients).
1. 92% said EMMI improved understanding of what to expect.
2. 80% of patients said EMMI gave them a better understanding of how to take care of themselves before or after the procedure.
3. 84% said EMMI covered risks that they didn't know about previously.
4. 67% said EMMI answered questions they had planned to call their doctor to discuss.
5. 74% are planning to share EMMI with friends and family.
6. 89% received new information about their procedure through EMMI
7. 83% are more comfortable about their upcoming procedure after viewing EMMI
8. 82% of patients experienced increased confidence in their doctor due to EMMI
Discussion: The EMMI program allows a patient to review and learn about the labor analgesia process prior to the onset of labor. The EMMI contains an educational component, which from the survey results above, reflects a high quality educational process. In addition, the program documents the information that the patient has reviewed as well as providing a mechanism by which the patient may collect questions that are answered on the day of the procedure. Though not demonstrated by this work, it is felt that this program provides a higher level of protection from legal suites based on an inadequate consent.

S-104.

THE ROLE OF HAND-OFFS: ASSESSING THE ISSUES OF COMMUNICATING PATIENT CARE INFORMATOIN IN CRITICAL CARE SETTINGS

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Introduction
For industries that must be operative 24 hours a day, reliable exchanges of information during and between shift changes is critical for maintaining the continuity of safe and effective work operations. In hospitals, the sign-out report serves as the basis for transitioning patient care responsibility between incoming and outgoing medical providers in/across shifts and directly impacts patient outcomes. Many variables associated with handoffs can create opportunities for incidents and adverse patient outcomes.
Methods
We conducted observations and interviews at a large metropolitan hospital Intensive Care Unit. The goal of the study was to obtain a detailed understanding of the factors that underlie shift change reporting in critical environments. Eight nurses and four physicians participated in the observational component of the study, and each participant giving the sign-out report was observed on at least two different occasions. Prior to consenting to participate in the study, providers were informed about the objectives of the study.
Results
In 24 observations: face-to-face communication was used in all cases (24/24); Charts/handwritten materials were used in 23 cases (23/24); Monitors/equipment were referred to in 13 cases (13/24); Electronic records, computer aids were never used (0/24); Pointing to the patient occurred in 21 cases (21/24); Touching the patient occurred in 5 cases (5/24) ;Verbal communication with the patient or family never occurred (0/24) despite open visiting hours.
There are many factors that adversely affect sign-out reports during shift changes in critical care settings, and these factors can interact in complex ways. Interventions that can attentuate the negative consequences of these factors need to be carefully designed. The challenge is to identify interventions which are most likely to result in the greatest benefits, and which will cause the least disruption of the provider's workflow in an already protocol-saturated environment. It is necessary to be able to measure the effects of these interventions, and to demonstrate that these interventions do not alter existing contexts in ways that could produce new errors or other unwanted consequences.
Conclusions
This study addresses issues associated with sign-out reports occurring during shift changes. The issues include the need for organizing our knowledge concerning the types of errors that providers are susceptible to during the sign-out process, the roles of personality, experience, and cultural factors, particularly as they may affect the incoming providers inquisitiveness, and the potential impact on patient care of various different methods of performing sign-outs.
Overall, our data on shift change sign-outs in acute care settings confirmed the resiliency of health care providers and their capability for managing patient care under extremely demanding conditions. More work is needed to help develop explicit, reliable and provider-tested tools to help clinicians cope with the degradation of data in acute care patient hand-offs.

S-105.

FLOW RESTRICTIONS ASSOCIATED WITH SWAN-GANZ AND SINGLE-LUMEN INFUSION CATHETERS IN PERCUTANEOUS SHEATH INTRODUCERS

AUTHORS: F. V. Cobos II, **M. Christo**;
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Introduction: Central IV access is often secured via percutaneous sheath introducers in order to measure CVP, insert Swan-Ganz catheters, and allow rapid administration of fluids. The expected reduction in flow rate following insertion of Swan-Ganz catheters is reported by the manufacturer[1], but is not reported when CVP is measured through single lumen infusion catheters (SLICs). We designed in vitro experiments to measure the effects of these modifications and test whether or not pressurization could be used to compensate for the restriction to flow. We also compared the reduced flow rates to those rates achieved with peripheral IV catheters.
Methods: We tested 3 Arrow® catheters ranging in size from 8.5 Fr. to 9 Fr.
The flow rates of 1 L of 0.9% saline were measured with a stop watch as it flowed into a 1 L graduated cylinder. At the start of each experiment, the top of the IV fluid level in the bag was always positioned 100 cm above each catheter. Times were recorded to the nearest second for both the first and second 500 mL of flow as the fluid drained from the bag. Then, 7.5 Fr. and 8.0 Fr. Swan-Ganz catheters were placed into each introducer (8.5 and 9 Fr. respectively) and the experiments repeated. After removing the Swan-Ganz catheter, a SLIC was inserted and the experiments repeated. Each flow rate was measured 3 times, and an average recorded. Finally, flow rates for each modification were also measured while pressurizing the IV fluid to 300 mm Hg, using a hand inflated pressure infuser bag and manometer. Peripheral IVs were tested in under identical conditions for comparison.
Results: Without modification, each sheath performed similarly. With Swan-Ganz catheters, the 8.5 Fr. introducer outperformed the 9 Fr. introducer. Overall, reductions in flow ranged from 66.8 to 371.4 ml/min. Under gravity flow, insertion of Swan-Ganz catheters reduced flow rates to 28.1-58.3 ml/min, approximately equal or less than the equivalent of one 20-g peripheral catheter. Flow rates of 60.2-92.3 ml/min were measured after inserting SLICs, the equivalent of less than two 20-g peripheral catheters. Pressurization did not compensate for the reduction in flow when Swan-Ganz catheters were inserted into single-lumen 8.5 and 9 Fr. introducers, but can more than compensate if a 9 Fr. two-lumen catheter is used.
Discussion: Insertion of Swan-Ganz or SLICs reduces flow to a surprising extent, and pressurization may not overcome these limitations under clinical conditions. Careful consideration should be given as to whether or not to obtain additional IV access when using Swan-Ganz or SLICs within central venous introducers. Failure to compensate for these anticipated decreases in IV flow rates may lead to unnecessary challenges when rapid fluid administration is needed.
References: 1. Arrow International, Reading, PA, USA.

S-106.

CLEANER, DIRTIER, OR SICKER? TRENDS IN POSTOPERATIVE SEPSIS DETERMINED BY A NATIONAL INPATIENT DATABASE

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Introduction:
Postoperative septic shock (POSS) is a serious complication of anesthesia and surgery. Although improvements in perioperative care have targeted postoperative sepsis (1), resistant organisms (2), increasing surgical complexity , and a greater number of surgical patients with significant comorbidities may also play a role. We hypothesized that because of increasing patient, anesthesia, and surgical complexity, the incidence of POSS in the United States has increased.
Methods: We examined the incidence of POSS using AHRQ Quality Indicators (QIs). QIs measure health care quality using administrative datasets (1994-2002, > 37,000,000 hospital discharges, www.qualityindicators.ahrq.gov). A subset, the Patient Safety Module (PSI), monitors the rate of adverse hospital events considered preventable. PSI #13 examines POSS. PSI #13 is defined as sepsis of at least 3 days duration/1000 elective surgical discharges. Immunocompromised or obstetric patients, those hospitalized for <4 days, or admitted for infection, were excluded. POSS was detected as discharges with ICD-9-CM codes for septic shock in any secondary diagnosis field. The denominator was all surgical discharges >18 y defined by specific DRGs and ICD-9-CM codes for an operative procedure. Discharges with sepsis in the primary diagnosis code were excluded. The database includes age, gender, income in patient zip code, patient residence (metropolitan vs non-metropolitan), insurance carrier, hospital location, size, and teaching status. Rates were compared using the t test statistic with $p<0.05$ as significant.
Results: POSS nearly doubled between 1994 and 2002 (Table 1). In the most recent yearly databases (2001, 2002), POSS was associated with: age > 65 y (vs 18-44); female (vs male) gender; patient income < $25K/y (vs $45K or more); patient or hospital location in non-metropolitan area (vs metropolitan); Medicare or Medicaid (vs privately insured); hospital location in South or West (vs Northeast); and hospital size < 100 beds.

Rates of postoperative septic shock

Year	POSS (per thousand patients)	P value vs 1994	P value vs previous year
1994	6.24 ± 0.31	-	-
1997	8.53 ± 0.33	<0.001	<0.001
2000	10.53 ± 0.31	<0.001	<0.001
2001	10.11 ± 0.31	<0.001	0.338
2002	11.55 ± 0.31	<0.001	0.001

Discussion: Despite advances in anesthetic and surgical care, these data indicate an increasing rate of post-operative sepsis in elective surgical patients. The risk was greater in the elderly, in the poor, and in smaller hospitals, as well as in specific geographic regions. Our findings suggest that factors other than patient age, comorbid status, or surgical complexity may play a role. The costs and healthcare burden of POSS are considerable, and studies are needed to examine mechanisms and develop strategies for its prevention.

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S-107.

PROSPECTIVE ANALYSIS ON ALLERGIC REACTIONS TO APROTININ AS A BLOOD CONSERVATION MEASURE IN MAJOR ORTHOPEDIC SURGERY PATIENTS.

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Introduction: Aprotinin (APRO) reduces blood-loss and, thus, the need for allogeneic blood-transfusion in various kinds of major surgery. However, as it is made of bovine lung-tissue, it is associated with the potential risk of allergic reactions (AR) after intravenous application. Prospective data on analyzing frequency and severity of these AR are sparse; appropriate data in patients with otherwise known pre-existing allergic diseases are even lacking.
Methods: After IRB-approval, this prospective cohort study was performed in 1,307 major orthopedic surgery patients with an assumed blood-loss necessitating blood- transfusion, operated on either under general (GA), regional (RA) or combined anesthesia (GA + RA). After application of histamine blocking drugs (H1/H2), a test-dose of APRO was infused, followed by a bolus-infusion of 2 millions KIU (kallikrein inhibiting units) of APRO, followed by continuous infusion of 0.5 millions KIU p. hour at least until end of surgery. AR were assessed to Ring and Messmer (1) with respect to age, gender, first-time/repeat APRO, time-interval between actual H1/H2 and actual APRO, time-interval between actual and previous APRO, kind of anesthesia applied, and otherwise already known pre-existing allergic diseases. Statistical analysis concerning frequency and severity of AR was performed by logistic regression analysis and Chi²-test (likelihood-quotient); statistical significance was adopted with $p<0.05$.
Results: AR happened in first-time APRO in 0.74% (9/1,209 pts.), and in repeat APRO in 8.2% (8/98 pts.). When repeat APRO was given within 3 months after a previous application, AR occurred more often than when given later than 3 months (6/27 [22.2%] vs. 2/71 [2.9%]; $p = 0.0034$). Other pre-existing allergic reactions were not demonstrated of impact on AR to APRO. No fatal AR to APRO happened.

Tab. 1 gives an overview of the statistical analysis.

Tab. 1	frequency of AR			severity of AR		
variables	Chi²	df	p	Chi²	df	p
age	0.004	1	0.9527	2.32	4	0.6780
gender	0.02	1	0.8815	5.71	4	0.2219
known pre-existing allergic diseases	1.86	1	0.1724	3.73	4	0.4437
time H1-/H2-blockers to APRO-administration	2.35	2	0.3082	10.98	8	0.2026
pre- / intra- / postop. APRO-administration	2.35	2	0.3094	12.07	8	0.1480
type of anesthesia applied	4.26	2	0.1187	19.45	8	0.0126
time previous to actual APRO-administration	8.59	1	0.0034	9.21	2	0.0100
first-time vs. repeat APRO-administration	19.86	1	0.0001	32.34	4	0.0001

Discussion: When considering APRO-application in major surgery patients, one has to individually outweigh the potential risk of AR to APRO itself vs. potential non-/life-threatening adverse events of allogeneic blood-transfusion vs. potential complications associated with the extent of blood-loss itself in patients with probably pre-existing limited compensatory mechanisms concerning massive blood-loss/fluid shift.
References: 1. Anaesthesist 1977;26:279

S-108.

THE INCIDENCE OF POSTOPERATIVE NAUSEA AND VOMITING IN RECOVERY ROOM IS SIGNIFICANTLY LOWER THAN PREVIOUSLY REPORTED

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Introduction: Incidence of postoperative nausea and vomiting (PONV) has been reported to be as high as 70% in high-risk patients (1), with most reporting an overall incidence of 25-30% (1, 2). However, the incidence of PONV after inpatient surgery remains controversial (2). This retrospective study was designed to evaluate the incidence of PONV and the duration of stay in postanesthetic care unit (PACU) stay at our tertiary care hospital.
Methods: With IRB approval, prospectively collected data were retrieved retrospectively from our PACU quality assurance database. All adult patients admitted to the PACU were included in the analysis. Data collected included the number of patients that had to stay in the PACU for more than one hour due to PONV. To further evaluate the need for rescue antiemetic in the recovery room, data were collected with respect to need for rescue medication with one or two antiemetics as well as incidence of nausea and emesis in the PACU. During this period, practice guidelines for use of prophylactic antiemetics at our hospital recommended that ondansetron should be used only in patients at high risk of PONV and only in combination with at least one other antiemetic (i.e., droperidol, dexamethasone, or metoclopramide).
Results: The data between July 2005 and June 2006 contained a total of 11738 patients that were included in the analysis. Of these 0.3% had delayed discharge from the PACU due to PONV, defined as a longer than one hour PACU stay due to PONV. Prophylactic antiemetics were administered in 49%of all patients. Upon further review, 3% of all patients experienced the PONV in the PACU and among them, 81% required one rescue antiemetic, 16% required two and 3% did not require treatment.
Discussion: Our finding suggests that the incidence of delayed discharge from the PACU due to PONV is significantly lower than that reported previously (1, 2). The incidence of PONV was lower in the PACU despite a lower use of prophylactic antiemetics.
References: 1. Apfel CC, et al: N Engl J Med 2004; 350: 2441-51.
2. Habib AS, et al, Current Medical Research and Opinions 2006; 22: 1093-99.

S-109.

DIAGNOSTIC ACCURACY OF CORE COMPETENCIES IN PERIOPERATIVE ECHOCARDIOGRAPHY: PRELIMINARY DATA FROM EXECUTIVE MEDICAL FELLOWSHIP STUDENTS

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Introduction: The Executive Medical Fellowship (EMF) and remote supervision concepts were first implemented in September 2005. The purpose of this study was to evaluate baseline core competencies of a select group of EMF anesthesiology students to identify areas where more focused training is warranted. **Methods:** The EMF program is based on 3 components: 1) in-person lectures and case presentations, 2) hands-on training with direct supervision, and 3) remote supervision of procedures performed on real patients. The perioperative echo EMF program is divided into 4, three-month sessions: freshman, sophomore, junior and senior. During one of the freshman sessions, four EMF anesthesiology students were asked to interpret echocardiography images of five different cases each. The cases were chosen based on their high clinical relevance. Each student evaluated each case at two different times during the freshman session. Diagnostic accuracy was graded on a 100 point scale and students' scores were reduced 15 to 20 points (based on the instructor's discretion) for mild discrepancies in diagnoses between the student and instructor, 40 points for moderate discrepancies, and 60 points for severe discrepancies. The two scores from each student for each, relevant core competency were averaged for each of the five cases. The following comparisons between average scores were made: 1) chamber size and contractile function vs. valvular structure and function, 2) chamber size vs. chamber contractile function, and 3) overall right heart structure and function vs. overall left heart structure and function. **Results:** Scores related to discrepancies in diagnoses ranged from 0 to 100 points. Diagnostic accuracy was greater for chamber size and contractile function compared to valvular structure and function (75% vs. 45%, respectively), for chamber size compared to chamber contractile function (80% vs. 65%), and for overall left heart structure and function vs. overall right heart structure and function (82% vs. 57%). **Discussion:** This study provides quantitative information regarding baseline diagnostic accuracy of anesthesiologists beginning a comprehensive perioperative echocardiography training program. Evaluation of chamber size and contractile function rely on 2-D imaging, which appears to be an easier skill to acquire based on the relatively high diagnostic accuracy of these competencies in the present study. In comparison, valvular structure and function rely on a combination of 2-D imaging and color and spectral Doppler, which may explain the lower diagnostic accuracy of valvular structure and function. In addition, the greater complexity of the right heart structures compared to the left heart may explain the lower diagnostic accuracy of conditions involving the right heart. The results of this study suggest that the ideal curriculum for anesthesiologists learning perioperative echo should focus more attention on valvular and overall right heart structure and function.

S-110.

THE PERCEPTION OF THE PERIOPERATIVE EXPERIENCE IN RELATION TO RACE, SOCIOECONOMIC STATUS, AGE, AND GENDER.

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Introduction: It is well known that patient perceptions of care vary widely with race and other demographic factors (1). A large body of literature also asserts that care may be sometimes offered according to such demographics rather than medical indication (2). In short, the specter of discrimination indeed plagues parts of the medical enterprise.
The perioperative experience is a particularly refined component of medicine. Extensive research has been dedicated to optimizing the perioperative care a patient receives (3). With over 35,000 anesthetics administered per year, this is particularly true at Mt. Sinai. But given these disparate patient perceptions of care, has the effort to provide streamlined and uniform perioperative care been perceived by patients as such? Our investigative team explored how effectively such efforts resulted in the perception of uniformly excellent perioperative care, with regard to race, socioeconomic status, gender, and age.
Methods: A 15-item survey was distributed to patients in the Mt. Sinai PACU. Patients provided demographic data, and were then asked to rate statements pertaining to their perioperative experience from 1 (strongly disagree) to 7 (strongly agree). This included an item that asked patients to attribute the degree to which their own racial and socioeconomic characteristics influenced their experience.
Results: A total of 185 surveys were completed. Reported ethnicity was 70% Caucasian, 14% African-American, 11% Hispanic, and 5% Asian. Satisfaction with the perioperative experience was found to be extremely high. Items evaluating the courtesy, concern, thoroughness, and overall performance of the anesthesiologist were rated 6.10 or higher, regardless of ethnicity. There was no significant difference between ethnic groups. Patients strongly felt that race did not have an impact on their treatment (no significant difference between racial groups). Socioeconomic status, gender, and age also didn't have a significant effect on the perception of care.
Discussion: At study onset, the perioperative experience appeared to be one of conflict -- the desire to standardize and streamline the patient experience apparently differed with the tendency for patients to perceive their experience differently according to demographics such as race and socioeconomic status. According to our results it appears that when care is optimized as in the perioperative setting, variability in patient perceptions of their experience is minimized, if not eliminated. These findings essentially validate efforts to make the perioperative experience uniform and efficient. They also suggest that for other hospital experiences in which disparate patient perceptions of care exist, efforts to standardize the experience may indeed result in less inconsistent and improved perceptions of care. For the anesthesiologist, such validation should serve as both a reaffirmation in methodology and a reminder for future vigilance.
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S-111.

UTILIZING RECORDED COMMANDS FOR A BILINGUAL PATIENT DURING EMERGENCE FROM ANESTHESIA

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Introduction: More than 11% of the US population is foreign born and nearly 18% of the US speaks a language other than English at home. (1) Emergence from anesthesia is an important example of where the lack of English proficiency may challenge the safety of this population because anesthesiologists need to communicate to patients in the form of verbal commands. From these commands, the anesthesiologist can safely extubate, determine neurologic functioning, and level of pain in the patient. (2) Also, studies show that bilingual speakers preferentially revert back to their native language in times of pain, when dreaming, and when feeling tired. (3) These characteristics are comparable to emergence from anesthesia following surgery. Our goal was to determine if bilingual speaking patients respond faster and more effectively to their native language over English during emergence. We used recorded commands in the native language of the patient to compare the response times and evaluate which language provides a safer and more communicative environment for bilingual patients.
Methods: We used a normal laptop computer with built-in sound recorder to record and play back the commands. During emergence, the English and native language commands were given together with a brief pause in between to allow for a response. The order would alternate for each successive command.
Results: Four commands were used on a bilingual patient during emergence from anesthesia. For the first command of "open your eyes," the patient responded to his native language one minute prior to a response to the command in English. The next command, "squeeze my hand," did not show any separation in responsiveness. For the command "take a deep breath," the patient responded immediately to his native language but needed to be asked twice in English. There was no difference in time in the patient's response to the fourth command, "wiggle your toes."
Discussion: These results reveal a separation in response time to verbal commands in a bilingual patient. The data may show a tendency for bilingual patients to recognize their primary language faster during emergence. The patient did not respond faster to any of the English commands. The proficiency in English of the bilingual speaker may cause some differences in response time. However, by alternating the commands in English and the native language there does appear to be some reversion to the native language of the patient. By accepting and accommodating this reversion, a safer and more effective emergence may result.
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S-112.

MANAGEMENT OF LUMBAR DRAINS AFTER THORACIC AORTA ANEURYSM SURGERY

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Introduction:
Lumbar drain (LD) placement for CSF drainage is commonly performed for thoracic aorta aneurysm (TAA) repair. In our institution, the pain service has been routinely tasked to remove LDs, without knowledge of LD placement, medical history, postoperative sedation, anticoagulation status, etc. A literature search revealed no published LD management/practice guidelines. Therefore, this survey was designed to gather information regarding the postoperative management of LDs at institutions performing TAA repair in the U.S.
Methods:
Following IRB approval, we surveyed the use of LDs for TAA repair in the 181 ACGME- accredited thoracic and vascular surgery training programs in the U.S. Mailing addresses were obtained from the AMA-ACGME website. Topics in the survey included frequency of LD placement, parameters for LD removal (i.e. platelet count, INR), postoperative anticoagulation, presence of neurological exam following LD removal, and sedation status pre- and post-LD removal.
Results:
(See Table). 181 surveys were mailed and 58 surveys were returned (32%), which is typical for physician surveys (1). 86% of responding programs use LDs for TAA surgery and all use standard 4 Fr. drains. 35/51 centers (69%) that place LDs utilize them in >50% of TAA repair cases. Anesthesiologists place LDs in 92% of institutions and remove them 74% of the time. Prior to LD removal , 86% of centers ensure that the platelet count is >75 K and the INR is < 1.5. 50% of centers administer aspirin postoperatively while only 16% use low molecular weight heparin. 24% of centers use no anticoagulation.

Lumbar Drain (LD) Management for TAA Repair

	n	%
Frequency of Centers Utilizing LD for TAA Repair	50/58	86%
Frequency of Centers Utilizing LD for TAA Repair >50% of cases	35/51	69%
Placement of LD by Anesthesiology	46/50	92%
Removal of LD by Anesthesiology	37/50	74%
Platelet requirement >75k prior to LD removal	43/50	86%
INR requirement <1.5 prior to LD removal	43/50	86%
Post-Op sedation with LD	41/50	82%
Discontinuation of sedation prior to LD removal	26/47	55%
Neuro exam prior to LD removal	47/50	94%
Radiologic studies prior to/after LD removal	4/50	8%

Discussion :
This survey was undertaken due to lack of published information/standards concerning postoperative management of LDs after TAA repair in U.S. hospitals. While variations exist with regard to criteria prior to LD removal, there is significant concensus regarding involved teams, appropriate laboratory values, post-op anticoagulation, and neurological exams. This survey demonstrates that LD practice standards parallel guidelines previously set forth in the 2003 ASRA Consensus Conference regarding Regional Anesthesia in the Anticoagulated Patient: Defining the Risks, as well as other published surveys (2,3). In conclusion, it appears that removal of LDs by anesthesia providers is in accordance with previously established standards for removal of neuraxial catheters.
References:
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2. Reg Anes Pain Med 2003; 28:172-97.
3. Int J Obstet Anesth 2002; 11:170-5.

Equipment/Monitoring

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S-113.

A PROSPECTIVE STUDY TO EVALUATE THE DEPTH OF SEDATION IN PATIENTS UNDERGOING PROCEDURAL SEDATION

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Introduction: Sedation for procedures by non-anesthesia personnel is a routine practice that occurs daily in multiple areas of the hospital outside the operating room and is gaining wide acceptance as a means to expedite the performance of minor procedures on children and adults. One model utilizes trained nursing staff to administer sedative medications for practitioners with minimal anesthesia training. There is evidence that with increasing depth of sedation the likelihood of adverse events increases[1,2]. A small study revealed that sedation scores and EEG monitoring were consistent with general anesthesia during these procedures[3]. Adverse events that occur include respiratory depression, apnea, aspiration, hemodynamic instability, and death. We performed a prospective blinded study utilizing a processed EEG monitor to evaluate depth of sedation in patients sedated by non-anesthesia personnel for procedures. We evaluated how often monitoring indicated general anesthesia and complications requiring clinical intervention.
Methods: After IRB approval 100 patients scheduled to undergo procedural sedation were enrolled in a prospective study to evaluate depth of sedation using a SEDLine monitor(Hospira). The medical staff involved with sedation were blinded to the monitor. After enrollment and prior to sedation all subjects were connected to standard monitors (NIBP, ECG, SPO2) and supplemental oxygen by nasal cannula. In addition, a SEDLine EEG sensor was placed on each subject prior to administration of the sedation. Throughout the procedure a Ramsay sedation score was documented every 5 minutes along with SEDLine data (PSI values) and vital signs. All medication administrations were documented. All sedation related complications were also documented.
Results: Of the 100 patients enrolled (ages 12-93 mean 55.6±18.8), 32 experienced episodes of general anesthesia (PSI <50). Five patients experienced episodes of deep general anesthesia (PSI <30). All the patients who received propofol experienced episodes of deep general anesthesia. Seven patients had desaturation events and required increasing supplemental oxygen. Two patients required airway intervention to alleviate respiratory obstruction and improve respiration.
Discussion: Procedural sedation provided by non-anesthesia trained practitioners is a common medical practice. Monitoring with a sedation scale is the current standard of care. In this study, 32% of the patients receiving procedural sedation had episodes of general anesthesia as evidenced by the SEDline monitor. A previous study demonstrated a strong correlation between the SEDLine PSI values and the Ramsay Sedation Scale[4]. Several complications occurred in this including desaturation(7%) and need for airway intervention(2%). This contrasts with a gastroenterology study indicating an incidence of oxygen desaturation of 0.2%[5]. The present study shows that a significant number of patients receiving procedural sedation are suppressed to general anesthesia patterns on processed EEG.
References:
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3. Annals of Emergency Medicine. 2003;41:2;234-241
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S-114.

A SURVEY OF ANESTHESIA ALARM USAGE IN A TERTIARY CARE FACILITY

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Introduction: The use of audible alarms in anesthesia has been strongly advocated by the Anesthesia Patient Safety Foundation (APSF) and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO).1,2 Alarm use has been credited for minimizing the morbidity associated with anesthetic incidents. Unfortunately, anesthesia providers frequently silence alarms because of various reasons. We determine in this study the frequency of alarm deactivation and pulse oximeter tone deactivation or inaudibility in a major trauma center located in a major U.S. city.
Methods: At 0600, the anesthesia machines in twenty-five operating rooms were turned on and the alarms were activated. The same observer returned to each operating room thirty minutes after start time and determined if any alarms had been deactivated. In addition, it was noted if the pulse oximeter tone was deactivated, or if its volume at 6 feet from the anesthesia machine was inaudible. The training level of the most senior anesthetist in the room was noted as was the type of case.
Results: 200 first cases were observed over a four weeks on non-consecutive days. The average number of cases observed per day was 18 (range 13-23) and the number of rooms with alarms silenced was 6 (range 2-9). The total percentage of alarms that were completely deactivated was 31%. The range was from a low of 12% to greater than 50%, which occurred on four of eleven days. A pulse oximeter tone, whose volume was imperceptible within 6 feet of the anesthesia machine was noted in approximately 36% of the rooms. Stratifying the alarm deactivation occurrences by level of training, CRNAs accounted for a majority of the rooms with deactivated alarms and inaudible pulse oximeter tones. CA-1 level residents were close behind.
Discussion: The most common reason given by the providers for disabling the alarms was because of the high incidence of false alarms. Other causes cited include that false alarms caused a “panic” reaction amongst operating room staff, and what can be interpreted as the hubris of several providers. These providers felt that keeping an active eye on the patient was more valuable than anesthesia alarms. Alarms are not meant to supplant the vigilance of the provider, but to augment it. Several well-publicized bad outcomes prove that relying on one’s own vigilance is not enough.
The disparity between the number of residents and the number of CRNAs who deactivate alarms is not easily explained, and is likely multifactorial. It may be that practitioners in their training are less comfortable and more vigilant than those practitioners who have graduated and have practiced for several years or it may represent fundamental differences in training and clinical perspective.
References:
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S-115.

IS PERIOPERATIVE BLOOD SALVAGE A REASONABLE, EFFICACIOUS AND EFFECTIVE ALTERNATIVE TO PREOPERATIVE AUTOLOGOUS DEPOSIT? CONFIRMATION OR REJECTION BY MEANS OF AN INTRA-INDIVIDUAL MATHEMATICAL ANALYSIS OF ORIGINAL PREOPERATIVE AUTOLOGOUS DEPOSIT DATA FROM THE LITERATURE.

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Introduction: Clinical data comparing effectiveness of preoperative autologous deposit (PAD) to perioperative blood salvage (PBS) are very sparse (1) and lack of an appropriate study design. Intra-individual mathematical comparison of original PAD-data to PBS (if no additional PAD had been performed) has demonstrated PBS at least as efficacious (i.e. increase in RBC-mass [+RBC]) and effective as PAD [i.e. substitution of maximal allowable blood-loss w/ +RBC but w/o allogeneic blood (MABL)]. This might have been due to an inappropriate PAD-concept applied. Therefore, we decided to mathematically analyze and intra-individually compare original PAD-data from the literature to PBS if no additonal PAD had been performed in these patients.
Methods: Search for complete data sets in the 'autologous literature' allowing appropriate mathematical comparison of PAD to PBS w/o preceding PAD. Comparison was based on reported mean-/median values. RBC-recovery to PBS (+RBC) was considered 30 percent, only (PBS30) (2, 3), and minimal hct-level was set with 24 and 21 percent (0.24/0.21), respectively when starting re-transfusion of pre-deposited/salvaged RBC; only then was total +RBC/+RBC30 re-transfused. Re-transfusion was applied to keep hct min constant despite ongoing blood-loss together w/ infusion of an artificial colloid (volume-effect 1.0) in order to maintain normovolemia. Appropriate formulae were published elsewhere (4). No statistical analysis had to be applied for this intra-individual mathematical comparison of mean-/median-values from various studies from the literature.
Results: Complete data-sets in the literature allowing this kind of analysis are sparse (ref. 5 - 8). Tab. 1 gives appropriate data of PAD and the results of this intra-individual mathematical comparison to PBS30.

author / year	hct min	PAD		PBS30	
(type of surgery/pts.)	(%)	+RBC (ml)	MABL (L)	+RBC (ml)	MABL (L)
reference [5]	24	386	4.0	298	4.2
(orthopedic surgery)	21		4.9	342	5.3
reference [5]	24	239	2.8	214	3.2
(orthopedic surgery)	21		3.5	254	4.1
reference [6]	24	220	2.6	290	4.1
(orthopedic surgery)	21		3.6	334	5.2
reference [7]	24	105	2.3	294	4.3
(urology surgery)	21		3.1	343	5.4
reference [8]	24	51	1.3	124	2.0
(rheumatoid arthritis)	21		1.9	163	2.8

Discussion: Intra-individual mathematical analysis/comparison of PAD-data from the literature to PBS if preceding PAD had not been performed demonstrates PBS the superior routine autologous blood conservation measure. Thus, only when applying strong indications, and rationally following a physiologically-based PAD-concept, PAD can be a reasonable, efficacious and effective blood conservation measure; otherwise, PBS is the autologous measure of choice.
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S-116.

PRELIMINARY EVALUATION OF AN IN-HOSPITAL AUTOMATED BLOOD GLUCOSE MONITOR (OPTIMUS®) IN HEALTHY VOLUNTEERS

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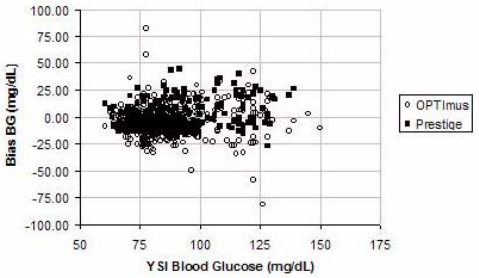
Introduction: In critically ill and cardiac surgery patients, normalization of blood glucose (BG) with intensive insulin therapy (IIT) can improve patient outcomes but requires multiple BG tests. There is currently no in-hospital automated BG monitor to provide frequent BG measurements in hospitalized patients. The Glucon OPTImus™ enables frequent automated glucose monitoring for the purpose of implementing IIT. This study evaluated the operational aspects of the OPTImus™ system in healthy volunteer subjects.
Methods: 15 healthy volunteers were recruited for this IRB approved study. One anesthesiologist placed an IV catheter in an arm or hand vein. OPTImus™ was connected to the subject's IV and normal saline was infused for line flushing. Blood draws were performed at ~15 min intervals for 8 hrs and referenced against a YSI 2300 BG analyzer and a Prestige BG meter that uses the same analytical technology as OPTImus™. Recorded variables included vein size, BG concentrations, BG meter errors, blood draw failures, and auto sampler failures. BG data were analyzed using the Bland and Altman technique, MARD, and correlation analysis. ANOVA was used to examine bias between instruments. Data are reported as means ±SD.
Results: 14 subjects (1/13 M/F), ages 20-56 (mean 41.1±9.2), BMI 22-36 (mean 30.9±7.4) completed the 8 hr protocol. One subject was withdrawn from the study due to difficult IV access. Subjects' peripheral vein OD were ≤3 mm in 9/14 (64%), and >3 mm in 5/14 (36%) subjects. BG ranged from 60-150 mg/dL based on YSI reference. Of the 379 blood draws evaluated, 23 (~6%) were attributable to BG meter errors, 19 (~5%) to auto sampler technical problems, and 32 (~8%) to blood draw difficulties. OPTImus™ mean bias versus YSI was 0.7±13.6 mg/dL (Figure), MRAD 10.88%, and R=0.80 while Prestige mean bias was -3.5±12.2 mg/dL, MRAD 12.0%, and R=0.85. Prestige bias was significantly ($p<0.001$) more negative than OPTImus™.
Discussion: OPTImus™ was able to safely draw and reinfuse blood from average weight and obese adults using various size IV catheters. Difficult draws requiring operator intervention were encountered approximately 8% of the time. OPTImus™ BG measurement accuracy was slightly better than the Prestige point of care device as determined by YSI reference. Other studies are being conducted to optimize BG calibration, along with a new software release with advanced pump control features.



S-117.

AN IMPROVED SENSOR FOR MONITORING RESPIRATION IN PEDIATRIC PATIENTS.

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Introduction: Monitoring respiration of spontaneously breathing patients is a concern in the operating room, post anesthesia care unit (PACU), and on general care wards. Present technology has focused on capnometry attached to the patient's airway via a nasal cannula as the best method of providing this monitoring. [1] There are multiple problems with this method of monitoring respiration. The cannula is frequently dislodged, partially dislodged, or occluded with nasal secretions leading to inaccurate data or complete loss of monitoring.[2] A novel bioacoustic sensor for monitoring respiration has been developed. We evaluated patients' tolerance for the capnometer cannula system and the new bioacoustic sensor.
Methods: Following institutional IRB approval, informed consent was obtained prior to enrollment. Pediatric patients, upon arrival to the PACU, were monitored in the standard fashion. In addition, a nasal cannula was placed, secured with tape, and connected to a BCI capnometer. An adhesive bioacoustic sensor connected to a breathing frequency monitor prototype (Masimo Corp, Irvine CA) was applied to the patient's neck just lateral to the cricoid cartilage. Both the capnometer and the bioacoustic monitor were connected to a computer for continuous data recording. When either signal was lost, the appropriate sensor was checked for proper positioning and attachment. Time was noted when either sensor was dislodged resulting in loss of data. Data was compared using paired t-test or Chi square where appropriate, with $p<0.05$ considered significant. No restraints were applied to the patients to prevent dislodgment of the sensors.
Results: All data is expressed as mean $\pm$ SD. Fifteen pediatric patients (age = 6.6 $\pm$ 3.6 years, weight = 36.6 $\pm$ 26.2 kg) were enrolled. Duration of monitoring time in PACU was 58.7 $\pm$ 39.6 minutes. Premature cannula dislodgement occurred in 14 patients. Loss of signal due to dislodgement of the capnometer occurred after 15.2 $\pm$ 19.4 minutes. In no patient was the bioacoustic sensor dislodged before the end of stay in PACU ($p< 0.001$).
Discussion: This data shows the relative ease and high incidence of capnometer cannula dislodgement compared to the new bioacoustic sensor. In clinical settings where continuous and reliable monitoring of spontaneous respiration is important the new bioacoustic sensor provides significantly greater patient connection time, which should lead to significantly more reliable monitoring of respiration rate.
References:
1) *Pediatrics* 2006;117;1170-1178
2) *Medical and Biological Engineering and Computing* 2003;41;377-383

S-118.

EVALUATION OF THE AIRWAY SCOPE IN SIMULATED DIFFICULT TRACHEAL INTUBATION: A MANIKIN STUDY

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Introduction:
The Airway Scope AWS-S100 (AWS, Pentax Corp., Tokyo, Japan) is a single-use optical laryngoscope, designed to provide a view of the glottic opening without aligning the oral, pharyngeal, and laryngeal axes. The AWS has an imaging CCD with a specialized laryngoscope blade and a 2.4-inch color LCD monitor to allow the operator to verify conditions in the oral cavity and the intubation status during tracheal intubation. Therefore, the AWS is likely to be a good option for scenarios where conventional direct laryngoscopy might prove to be difficult or dangerous. We designed a study to assess the utility of the AWS for the simulated difficult intubation with respect to rapidity of glottic visualization and orotracheal tube insertion.
Methods:
To simulate difficult intubation, a rigid neck collar was attached to a Laerdal Airway management Trainer Manikin. Under this setting, a Grade 3 Cormack laryngoscopic view was simulated. Following brief instruction, eight experienced anesthetists were allowed up to three attempts to intubate the trachea by AWS. Before all the AWS attempts, the investigator confirmed difficult laryngoscopic view by using Macintosh direct laryngoscope. The investigator recorded the time taken to get a full view of glottis (T1) and the time taken to complete orotracheal tube insertion after setting the glottic opening at the target mark on the LCD monitor of the AWS (T2). All statistical analysis was conducted using SPSS 11.0 for windows (SPSS Inc., Chicago, Ill.).
Results:
All anesthetists could rapidly achieve a full view of manikin's glottis by using AWS and then they could complete orotracheal intubation in all attempts. The median (range) of T1 and T2 were 7.08 sec. (2.57 to 14.16) and 9.31 (1.16 to 49.25), respectively. There were wide inter- and intra- individual variations in T2, although T1 was not scattered.
Discussion:
Our preliminary study indicated that the AWS could easily provide a full view of the glottis even under the Cormack grade 3 condition by using direct laryngoscope for every medical practitioner but smooth orotracheal tube insertion by using the AWS depended on the skill of them.
References:
J Emerg Med. 2005; 29: 253-7.

S-119.

TRUVIEW EVO-2 LARYNGOSCOPY IS SUPERIOR TO MACINTOSH LARYNGOSCOPY IN TERMS OF FORCE USED, GLOTTIC VIEW & HEMODYNAMIC CHANGES

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Introduction: Laryngoscopy is one of the most invasive stimuli during orotracheal intubation [1, 2]. Most anesthesiologists agree that a considerable force is applied to the patient's larynx using a conventional rigid laryngoscope leading to undesirable hemodynamic responses[3, 4]. In addition, the apneic conventional laryngoscopy often leads to oxygen desaturation. Lastly, a complete glottic view is not assured. Truview Evo-2 [TE] laryngoscope [Truphatek, Israel] is a recently introduced modified laryngoscope which has been found to be associated with a decreased use of force. It incorporates an unmagnified optic side port to its special blade which provides a better glottic view and has provision for O2 insufflation. We aimed to compare TE with a conventional Macintosh blade [MB] laryngoscope in terms of: 1. Axial Force used during laryngoscopy & intubation [LI] as recorded on a Force Meter attached to laryngoscope blade, 2. Duration of LI, 3. Hemodynamic changes, 4. Oxygen desaturation and 5. POGO scoring.
Methods: Following approval by Board-of-Studies, 30 ASA I & II patients of either sex [age range 20-50 years] undergoing general anesthesia for elective surgery [non-malignant, non-head & neck surgery] were included. Patients with predicted difficult intubation were not included. After informed consent, patients were randomly divided into 2 groups on a random basis using Chit-in-a-box technique. Patients of Group - I [Control, n=12] were intubated using conventional MB laryngoscope, while patients of Group - II [Study, n=18] were intubated using TE laryngoscope. All intubations were carried out by experienced laryngoscopist [with both type of laryngoscope] after a uniform premedication, standard induction and relaxation technique. Laryngoscopy time was calculated from the time of picking up of laryngoscope from the table to its re-placement on the table. Surgery was allowed to commence only after the collection of the last hemodynamic data at 5 minutes post-intubation interval. Unpaired't' test was used to compare inter-group data.* $p<0.05$ was taken as significant.
Results & Conclusions: Our result shows that the maximum force used *3.2 vs1.8 & maximum rise in systolic BP *41.3 vs 28.8 following LI was significantly lesser [$p<0.05$] in patients intubated using TE as compared to MB laryngoscopy. Other advantages observed with TE laryngoscopy was no reduction in SpO2 and a complete laryngeal view [POGO Score=100% compared to 75%]. Thus, a better attenuation in hemodynamics, better maintained SpO2 and a full glottic view with TE device would not only make it a better intubating aid in elective OR situations as well as in ICU patients needing intubation who are often desaturated & are hemodynamically unstable.
References: 1. J Clin Anesth 1996; 8: 63-79, 2. Br J Anaesth 1987; 59: 295-9, 3. Anesth Analg 1996; 82: 456-61, 4. Anaesthesia 1994; 49: 1064-70.

S-120.

PATHWAYS OF NASOTRACHEAL INTUBATION: A COMPARISON OF THERMOSOFTENED PREFORMED AND REINFORCED TUBES.

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Introduction: In nasotracheal intubation, there are two pathways in the nostril through which the endotracheal tube may pass[1]. The lower pathway lies along the floor of the nose underneath the inferior turbinate. The upper pathway lies alongside the inferior turbinate, just below the middle turbinate. The lower pathway is considered to be the safer route as it is located away from the middle turbinate and cribiform plate. The middle turbinate is a vascular structure with a thin stalk which makes it prone to traumatic avulsion. This may lead to severe epistaxis, tracheobronchial obstruction, CSF leak and olfactory nerve injury[2, 3]. The aim of this study was to compare the frequency with which reinforced and thermosoftened preformed polyvinyl chloride tubes pass through the upper and lower pathways.
Methods: Following Local Research Ethics Committee approval and informed patient consent, 40 patients undergoing elective maxillofacial surgery requiring nasotracheal intubation were recruited. Xylometazoline was applied to the nasal mucosa. Anaesthesia was induced with propofol, fentanyl and atracurium, and the patients were randomly allocated to receive either a reinforced or a thermosoftened preformed tube. Anterior rhinoscopy was performed and the fibrescope was passed along the upper and lower pathways in each nostril to identify the most patent nostril. Standardized traditional nasotracheal intubation was then performed using the Macintosh laryngoscope, initially attempting to direct the tube along the floor of the nose. If obstruction was encountered, the direction of the tube was adjusted slightly lower and then slightly higher, as necessary. Tracheal intubation was completed and ventilation re-established. The fibrescope was then passed above and below the tube in the nostril, to a distance of 1.5cm, and the pathway taken by the tube established. Videotape recordings of the endoscopic procedures were made for later review.
Results: Data were analyzed using Fischer's Exact test. Significantly more thermosoftened preformed tubes passed along the upper nasal pathway compared with reinforced tubes ($P<0.05$).

	Lower pathway	Upper pathway
Thermosoftened preformed tubes	4	16
Reinforced tubes	11	9

Discussion: Although both types of tube frequently took the unfavourable upper pathway, it is possible that reinforced tubes are less likely to traumatize the middle turbinate.
References:
1. Anaesthesia1999; 83: 882-862.
2. Anaesthesiology 1999; 90:1782-84.
3. ENT Journal 2006; 85: 380-83.

S-121.

FEMORAL AND RADIAL ARTERIAL PRESSURE WAVEFORM ANALYSIS FOR CONTINUOUS CARDIAC OUTPUT MEASUREMENT IN CARDIAC SURGERY PATIENTS: *A COMPARISON OF FLOTRAC/VIGILEO AND PICCOPLUS WITH INTERMITTENT THERMODILUTION*

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Introduction: Pulse contour analysis calibrated by transpulmonary thermodilution (PiCCOplus, Pulsion Medical Systems, Munich, Germany) has shown in the last years to be a reliable alternative to the pulmonary artery catheter for cardiac output (CO) assessment in different clinical settings[1]. A new arterial pressure waveform analysis device, which does not need external calibration (FloTrac/Vigileo system, Edwards Lifesciences, Irvine CA, USA), became recently available for CO measurement from a femoral or radial arterial line. However, only limited validation data for this technique are available so far. The aim of this study was to assess CO determined by the Flotrac/Vigileo system using a femoral (FCOf) and a radial line (FCOr) and the PiCCOplus system using a femoral line (PCO) compared with CO assessed by intermittent pulmonary artery thermodilution (ICO).
Methods: With local ethic committee approval and written patient informed consent patients undergoing elective cardiac surgery were studied in the perioperative period. CCO, FCO and PCO were recorded after induction of anaesthesia (= study initiation) and 1,2,4,8 and 12h post initiation and thereafter every 12h to a total observation time of 48h. At each measurement point ICO was assessed as mean of 3 repeated bolus injections. Statistical analysis was done using Bland-Altman analysis of absolute values and of %changes (Δ) between consecutive measurements (= trend analysis).
Results: 172 matched sets of data were obtained from 22 patients (ASA III, M/F ratio = 21/1, mean age±SD = 66.7±10.6y [range: 46-81y], mean body mass index±SD = 29.0±5.4 kg m^{-2} [range: 23.5-48.0 kg m^{-2}]). CO values recorded during the study period ranged from 2.40 to 9.10 l min^{-1}. Bland-Altman analysis revealed a mean bias±2SD (limits of agreement) of 0.29±2.02 l min^{-1} for FCOf-ICO, 0.2±2.25 l min^{-1} for FCOr-ICO and 0.43±2.45 l min^{-1} for PCO-ICO. CO changes (Δ) ranged from -39% to + 70%. For ΔFCOf-ΔICO a mean bias±2SD of -2.9±46.0% was observed, for ΔFCOr-ΔICO mean bias±2SD was -2.4±43.3%, whereas for ΔPCO-ICO mean bias±2SD was -0.3±55.3%.
Discussion: These results show that the FloTrac/Vigileo system using either a femoral or a radial arterial line for signal detection is a reliable alternative to the $PiCCO_{plus}$ system for CO measurement in patient undergoing cardiac surgery as compared to intermittent pulmonary artery thermodilution.
References:
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S-122.

DOES THE USE OF A LARYNGOSCOPE FACILITATE OROTRACHEAL INTUBATION WITH A SHIKANI OPTICAL STYLET WITH THE HEAD IN AN EXTENDED POSITION?

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Introduction
The Shikani Optical Stylet (Clarus Medical, LLC, Minneapolis, MN) is an optical stylet with a malleable shaft and a lightweight (8cm x 2.5cm x 2cm, 2.6oz) battery powered LED light source that was originally designed as an aid for difficult intubations. Recently, the Shikani Optical Stylet (SOS) has also been shown to be useful for routine intubations[1]. The purpose of this investigation was to determine if extending the head while using a laryngoscope facilitates simulated difficult intubations with the SOS.
Methods
Thirty consecutive patients (ASA I-III) who presented to for elective surgery requiring general orotracheal anesthesia were studied. Standard airway indices, height, and weight were recorded. After induction of anesthesia, a Macintosh 3 or 4 blade was inserted only to expose the epiglottis, the tip of the SOS was placed beneath the epiglottis under direct vision, and then the vocal cords were visualized through the eyepiece to intubate the trachea. The first 15 patients were intubated with the head in a neutral position. The next 15 patients were intubated with the head fully extended. Intubations were timed with a stopwatch (time from laryngoscope insertion to SOS removal). A senior resident with extensive SOS experience performed all intubations.
Results
SOS + Laryngoscope, Neutral Group (n=15): The mean time to intubate was 43.1s (range 22-133s)
SOS + Laryngoscope, Extended Group (n=15): The mean time to intubate was 27.7s (range 16-61s)
Statistical Analysis: The groups did not differ to a statistically significant degree in age, airway indices, BMI or mean time to intubate.
The p=0.0517 for SOS +Laryngoscope in head neutral position vs SOS+ Laryngoscope in head extension position
Discussion
Since the SOS is a relatively new advanced airway management tool, literature regarding the most efficacious technique for its use is lacking. Previous data[1] with an experienced user suggest that the SOS can be used effectively and efficiently by itself. Our recent study suggested that the SOS can be used efficaciously with a laryngoscope to facilitate intubation in a simulated difficult direct laryngoscopy (2) However, the use of an optimal patient positioning have not been evaluated.
We found that extending the head was clinically more efficient than using a neutral head position when using a SOS with a laryngoscope for simulated difficult intubations. Generalization of these results to actual difficult direct laryngoscopy should be made with some caution.We feel nonetheless that statististical significance may be demonstrated in future if greater number of patients are studied.
References
1. Comparison of the Shikani Optical Stylet to direct laryngoscopy for orotracheal intubation by a first year anesthesiology resident. (Abstract). Anesthesiology, 2004
2. Can the Shikani Optical Stylet facilitate intubation in simulated difficult direct laryngoscopy? Abstract accepted for presentation at ASA 2006

S-123.

MONITORING CARBON DIOXIDE TENSION IN LAPAROSCOPIC SURGERY

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Introductions: Intra-abdominal insufflation of carbon dioxide in laparoscopic surgery may produce peritoneal irritation, hypercarbia, acidosis and severe hemodynamic changes. Monitoring carbon dioxide during laparoscopic surgery is quite important for detection and reduction of complications. In order to evaluate the feasibility of pressure of cutaneous carbon (PcCO2) monitoring in laparoscopic surgery, we measured PcCO2 in patients under general anesthesia by means of a new sensor probe attached to the ear lobe, and compared the data with PaCO2 and end tidal carbon dioxide (PetCO2).
Methods: The study was undertaken following approval from the Ethics Committee of our hospital and the written informed consent from patients were obtained. Patients classified ASA physical status I - II and undergoing laparoscopic surgery were enrolled. Total intravenous anesthesia was used. PcCO2 was measured using a combined digital earlobe sensor (Sentec, Switzerland) as recommended by the manufacturer. Arterial blood samples were taken and carbon dioxide tension was determined with an i-STAT G7 + Cartridge (Abbott Laboratories SA .USA). PetCO2 was monitored continuously by Datex Cardiocap II® (Datex Instrumentarium, Finland). The simultaneously obtained cutaneous, end-tidal and arterial carbon dioxide tension values were compared with the Bland and Altman method. Significance was assumed at the $P < 0.05$ level.
Results: Twenty-five patients were enrolled in this study. 63 data triplets (PaCO2, PcCO2 and PetCO2) were obtained. The PcCO2 value showed a significant positive correlation to PaCO2 (r^2=0.15, P<0.01). Bland and Altman's analysis revealed a mean difference of d = 6.85 mmHg with a precision of 6.54mmHg and limits of agreement ranged from -5.96 mmHg to + 19.66 mmHg. The mean difference was significantly different from zero. So paired student *t* test was used and indicated that PaCO2 was greater than PcCO2 significantly (P<0.01). For the PetCO2 and PaCO2, the coefficient of determination was 0.55 (P<0.01). The bias and precision was 9.20mmHg and 2.80mmHg respectively. The Bland and Altman limit of agreement of the PaCO2-PetCO2 was 8.50 to 9.90. Subsequent *t* test showed that PetCO2 was significantly different from PaCO2 (P<0.01). All the PetCO2 values were lower than PaCO2.
Discussion: PcCO2 and PetCO2 are both noninvasive methods of estimating PaCO2. Our results demonstrate that: (1) the PcCO2 and PetCO2 value show a significant positive correlation to PaCO2; (2) the gap between PcCO2 and PaCO2 is 6.85 mmHg, and 9.20mmHg for PetCO2 from PaCO2; (3) paired student *t* tests show that both PcCO2 and PetCO2 are significantly different from PaCO2. Thus we hypothesize that PcCO2 and PetCO2 may predict the trends in changes of PaCO2 in laparoscopic surgery, but difference to PaCO2 is too large to estimate the actual values of PaCO2. Direct measuring PaCO2 by arterial blood gas analysis may be necessary to detect hypercarbia.

S-124.

ECHOCARDIOGRAPHIC DETECTION OF VENOUS EMBOLIZATION DURING TOTAL SHOULDER ARTHROPLASTY (TSA)

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Introduction: Total joint (knee and hip) arthroplasty involve bone reaming and the use of methyl methacrylate cement. Venous embolization of bone marrow, fat, and cement may produce physiological sequelae including hypoxia, hypotension, pulmonary hypertension, and acute respiratory distress syndrome.[1] We have observed the occurrence of these physiological events during total shoulder arthroplasty (TSA) however, venous embolization has yet to be demonstrated in this population. The purpose of this study was to determine the incidence, magnitude and timing of venous embolization occurring in patients undergoing TSA utilizing intraoperative echocardiography.
Methods: 26 patients undergoing primary TSA, presenting for cemented vs. non-cemented TSA were prospectively studied. All patients received an intra arterial catheter and either an interscalene block with sedation or general anesthesia. Transthoracic or transesophageal echocardiography was utilized for cardiac imaging. The heart was observed for emboli during 5 intraopertive epochs: Baseline, Glenoid prep, Humeral reaming, Humeral cementing and Shoulder reduction. Hemodynamic data was similiarly obtained during these epochs. Intraoperative images were graded by the investigators and scored using a modified Mayo Clinic System for Echogenic Emboli [2]. All data expressed as mean $\pm$ S.D. $p < 0.05$ statistically significant.
Results: Mean age 68 $\pm$ 11yrs, BMI 27 $\pm$ 4. There were 6 female pts. Six patients were excluded due to inadequate visualization. Final n = 20 patients, 13 cemented and 7 noncemented TSA. During Humeral insertion, 12/13 cemented TSA exhibited echogenic emboli vs. 2/7 non-cemented TSA. Grade 2 or 3 echogenic emboli were detected in 8/13 cemented TSA vs. 0/7 non-cemented TSA during the same epoch. 3/13 cemented TSA had $\geq$ 20 % decrease in systolic blood pressure during Humeral insertion vs 0/7 non-cemented TSA. The cemented TSA group continued to shower echogenic emboli during Shoulder reduction, 5/13 pts vs. 0/7 non-cemented TSA

	Grade	Cemented n=13 patients	UnCemented n=7 patients
Humeral Reaming	0	11	4
	1	2	3
	2	0	0
	3	0	0
Glenoid Prep	0	9	6
	1	3	1
	2	1	0
	3	0	0
Humeral Insertion	0	1	5
	1	4	2
	2	6	0
	3	2	0
Shoulder Reduction	0	8	7
	1	4	0
	2	1	0
	3	0	0

Discussion: Patients undergoing cemented TSA vs. non-cemented TSA exhibit a high incidence of venous embolization during Humeral insertion and Shoulder reduction compared to non-cemented TSA. This paralells the experience in total hip arthroplasty. Patients with severe cardiopulmonary disease may benefit from specific anesthetic management and/or an alternate surgical procedure (non-cemented TSA).
References:
1. BMJ. 1971; 3(772): 460-61.
2. J Bone Joint Surg Am. 1998; 80-A(3): 389-96.

S-125.

A COMPARISON OF THE MONITORING QUALITIES BETWEEN ENTROPY AND BISPECTRAL INDEX VALUES DURING ORTHOGNATIC SURGERY UNDER SEVOFLURANE ANESTHESIA

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Introduction: The BIS-XP platform improved the utility of the monitor during electrocautery usage. A recently introduced brain monitor is The Entropy Module that generates both a state entropy (SE) and a response entropy (RE) values. We evaluated the difference related to the susceptibility of the EEG signal to interference by electrocautery between two monitors. The other objective was to compare the fluctuation of the displayed values within BIS, SE and RE.
Methods: Ten consenting patients scheduled for major orthognatic surgery were enrolled following written informed consent. Both BIS-XP and Entropy sensors were simultaneously applied. BIS, SE and RE indices were continuously recorded by a computer. Anesthesia was induced with propofol, fentanyl and vecuronium. Following tracheal intubation, anesthesia was maintained with sevoflurane, oxygen, air and fentanyl. The displays on both monitors were recorded continuously by video camera. The incidence of electrocautery interference with BIS or Entropy reading was determined by visual inspection of the recorded data as that the displayed variables were absent each time during surgery. The percentage of time determined to be blank was calculated. The fluctuation of each value was determined by the average differences between each value and the value 5 seconds before. Data was expressed as mean ± SD. Statistical analysis was performed by the unpaired t-test. $P < 0.05$ was considered significant.
Results: Two patients were excluded from statistical analysis because of the recording failure of the video tape. Therefore we analyzed eight patients, and found out that significantly fewer patients had blanking with the Entropy (0.04 %) compared to BIS (0.42 %). There were significant differences in fluctuation of the indices (BIS 1.0 ± 0.2, SE 2.0 ± 0.3, RE 4.0 ± 0.7).

Discussion and conclusion: Present study demonstrated that the electrocautery unit less interfered with the Entropy indices. On the other hand, there were fewer fluctuations on the displayed values of BIS, suggesting that BIS is superior to SE and RE to reflect stable hypnotic states. Therefore we have to recognize the differences of the monitoring qualities between Entropy module and BIS monitor.

S-126.

VARIABILITY OF BIS IS INCREASED IN RESPONDERS TO SKIN INCISION AND CORRELATES WITH PREINCISION ANALGESIC LEVEL

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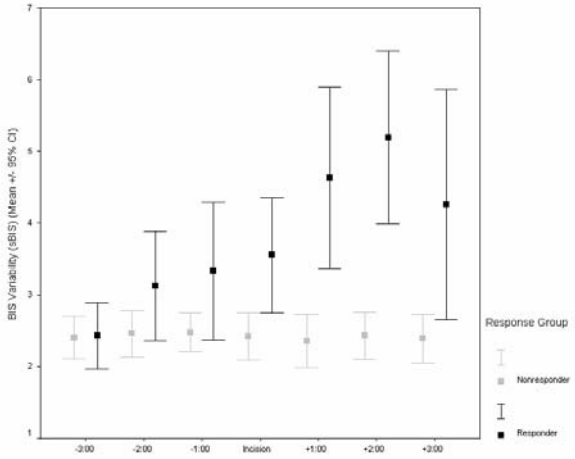
Introduction: Increased variability of BIS during surgery may be a reflection of arousal due to painful stimulation. Pain can increase BIS, and the size of the change is decreased by opioids[1]. Prior reports demonstrate that a composite index of BIS and EMG variability predicts the occurrence of intraoperative somatic responses [2] and correlates with the intensity of initial postoperative pain[3]. In this study we explored the hypotheses that BIS variability would correlate with preincision analgesic level and would increase in patients who responded to initial skin incision.
Methods: We analyzed data obtained during a previously published, IRB-approved multicenter trial of BIS as a predictor of movement[4]. Patients received one of the following maintenance anesthetic regimens: Propofol/N2O, Propofol/ Alfentanil/± N20, Isoflurance/O2, Isoflurance/Opioids, Isoflurane/N2O/Opioids. Pharmacokinetic/dynamic models (SIMINHALE, STANPUMP software, S. Shafer, Stanford U.) were used to estimate effect-site anesthetic concentrations from measured gases, recorded drug doses, and patient demographics (age, sex, weight). Alfentanil and sufentanil doses were converted to fentanyl equivalents in the ratio 75:0.11:1, respectively. An estimate of aggregate 'analgesic level' was developed using multivariate non-linear logistic regression as described previously[5]. A median split of the model-predicted analgesic level was used to create 2 groups: Less and More Analgesia. Standard deviation of BIS (sBIS) was calculated at 15-second intervals using BIS assessments recorded within the prior minute. Pearson correlation coefficients were used to measure association. Differences between groups were compared using Student's T-tests.
Results: 57 (32%) of the 181 patients moved in response to skin incision. Immediately before incision, sBIS correlated weakly with modeled level of analgesia ($R = -0.180$, $p=0.026$). Following skin incision sBIS increased markedly in responders but not nonresponders ($p<0.001$ at 1 min, see Figure). Similarly, sBIS increased in patients with Less Analgesia but not with More Analgesia ($p < 0.001$ at 1 min).
Conclusions: These data confirm our previous findings [2] with a different patient population. BIS variability was increased before and after incision in the patients who moved. Intraoperative variability of BIS may reflect instances of inadequate intraoperative analgesia.



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[2] Anesth 2006; 105:A1027.
[3] Anesth 2006; 105:A1042.
[4] Anesth Analg 1997:84:891-899.
[5] Anesth Analg 1995: 80(2S):S160.

S-127.

RELIABILITY OF TEMPERATURES MEASURED AT STANDARD MONITORING SITES AS AN INDEX OF BRAIN TEMPERATURE DURING DEEP HYPOTHERMIC CARDIOPULMONARY BYPASS

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Introduction: During induction of deep hypothermia with cardiopulmonary bypass (CPB) and subsequent circulatory arrest, it is essential to estimate brain temperature to ensure that the brain, the most vital organ vulnerable to decreased O_2 delivery, actually receives the benefit of the desired degree of hypothermia, and is not on the verge of hazardous hypothermia. In this study, using jugular vein temperature (JVT) as a standard for brain temperature, we evaluated the accuracy and precision of five standard temperature monitoring sites (i.e., pulmonary artery, nasopharynx, forehead deep-tissue, urinary bladder, and fingertip skin-surface tissue) during deep hypothermic CPB conducted for thoracic aortic reconstruction. The preliminary results obtained from 9 patients were previously presented at the IARS 79th Clinical and Scientific Congress.
Methods: In 20 adult patients with thoracic aortic aneurysms, the above temperatures were recorded every one-minute during deep hypothermic (<20°C) CPB. The accuracy was evaluated by the difference from JVT, while the precision was evaluated by its standard deviation, as well as by the correlation with JVT. Since the injection of cardioplegic solution (4°C) appeared to influence the PAT, we also evaluated the effects of cardioplegic injection on the difference and correlation between JVT and PAT. In addition, since the data on urinary bladder temperature (UBT) were relatively variable, we also evaluated the relation between urine volume and changes in UBT during either cooling or rewarming, using simple (either linear or non-linear) regression analyses. ANOVA, Scheffe F test, Fisher's Z-transformation, Student's t test and Welch's t-test were also used to determine significance ($p<0.05$), as appropriate.
Results: Pulmonary artery temperature (PAT) and JVT began to change immediately after the start of cooling or rewarming, closely matching, while the other temperatures lagged behind the two temperatures. During either situation, the accuracy of PAT measurement (0.3-0.5°C) was much superior to the other measurements, and its precision (standard deviation of the difference from JVT = 1.5-1.8°C; correlation coefficient = 0.94-0.95) was also best among the measurements, with its rank order being pulmonary artery > nasopharynx > forehead > bladder > fingertip. However, the accuracy and precision of PAT measurement was significantly impaired during and for several minutes after injection of cold cardioplegia. The urine volume, transformed to a logarithmic scale, correlates with the change in UBT both during the first 20 min of cooling (P =0.009) and during the first 30 min of rewarming (P=0.03).
Conclusions: PAT measurement is recommended to estimate brain temperature during deep hypothermic CPB even if it is conducted with the sternum opened, however caution needs to be exercised in its interpretation during periods of the cardioplegic injection. The results also suggest dependence of UBT on urine flow rate, consistent with the previous proposal (1).
Reference: 1. Anesthesiology 1988; 69: 986-989

S-128.

TRACHEAL INTUBATION USING THE AIRWAY SCOPE SYSTEM FOR PATIENTS WITH A SIMULATED DIFFICULT AIRWAY

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Introduction:
The Airway Scope System (ASS) consists of the Airway Scope AWS-S100 (AWS, Pentax Corp., Tokyo, Japan) and the Intlock ITL-S (ITL, Pentax Corp., Tokyo, Japan). ASS is a newly developed intubation device which allows visualization of the vocal cords without alignment of the oral, pharyngeal and tracheal axes. AWS has an imaging CCD and LED light attached to its tip. These features allow the operator to verify conditions in the oral cavity and the intubation status during tracheal intubation on a 2.4-inch color LCD monitor. ITL is a specialized laryngoscope blade with curved shape. With this system, there is no need to extend the patient's neck or apply excessive force. By placing ITL under the epiglottis and raising it lightly, it is possible to insert an endotracheal tube into the trachea. We evaluated the utility and safety of orotracheal intubation in adult patients with simulated difficult airways using ASS.
Methods:
Institutional review board approval was obtained and all study patients gave informed consent. Five ASA class I and II patients scheduled for elective surgery under general anesthesia requiring tracheal intubation were recruited. A rigid cervical collar was used to simulate the difficult airway as Cormack grades 3 or 4. All tracheal intubation were performed by an anesthesiologist, who had previously performed more than 10 normal intubations with ASS. Following induction of anesthesia, a rigid cervical collar was applied and the laryngoscopic grade assessed. General anesthesia was induced with 2 $mg.kg^{-1}$ propofol supplemented by 2 $\mu g.kg^{-1}$ fentanyl. After confirmation of effective mask ventilation, muscle relaxation was achieved using 0.1-0.15 $mg.kg^{-1}$ vecuronium. The total time to intubate, number of attempts, failures, hemodynamic changes during intubation were recorded.
Results:
The rigid collar effectively simulated a difficult airway. The success rate for tracheal intubation using ASS was 100%. The average time to intubation was 20.6 ± 13.6 sec. Although there were minor hemodynamic changes, mucosal bleeding and sore throat following intubation, there were no major complications in any of the study patients
Discussion:
ASS is an effective and safe intubating device for patients with simulated restricted cervical spine movement. Further studies are needed to elucidate the effectiveness and safety of this technique in managing patients with a difficult airway.
References: Can J Anaesth. 1999 Aug; 46(8):760-5.

ANESTH ANALG
2007; 104; S-1–S-271

S-129.

PILOT STUDY OF FORE-SIGHT CEREBRAL OXIMETER IN CARDIAC PATIENTS

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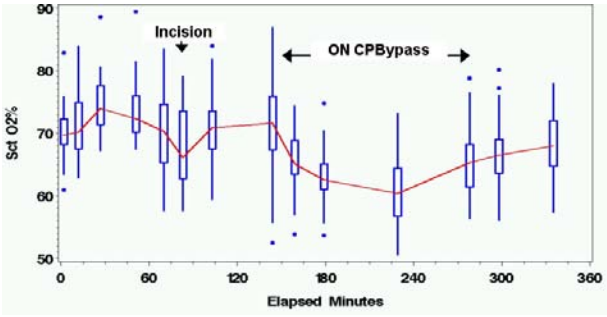
Introduction:
Cerebral oximetry is a non-invasive, optically-based technique to monitor brain oxygenation continuously by determining cerebral tissue oxygen saturation ($SctO_2$). The CAS Medical FORE-SIGHT^{TM} Absolute Cerebral Oximeter has been validated in a recent study of awake human volunteers during controlled oxygen desaturation (SpO_2 70-100%) and showed a strong correlation between oximeter and calculated cerebral tissue oxygen saturation [ref]. This observational pilot study was designed to determine the range of $SctO_2$ during stages of cardiac surgery.
Methods:
With written consent, patients undergoing CABG and/or valvular surgery (VS) with CPB were enrolled. Two FORE-SIGHT Cerebral Oximeter Sensors (left/right) were placed on the patient's forehead prior to induction. $SctO_2$ were recorded at 2-sec intervals; the 1-minute median value (derived from the 30 measures per minute) was calculated for both sensor readings. The average of left & right cerebral tissue oxygen saturations was used for analysis. At 14 pre-determined events the 5-minute median $SctO_2$ was reported. The length of time $SctO_2$ below 55, 60 and 65% was calculated and tested for association with gender, race, diabetes and procedure type.
Results:
33 patients (median age 68, years of education 13, gender 23M/10F, 29 W/4 AA, 8 diabetics, 27 CABG & 6 VS ± CABG [median cross-clamp time 73 v 123 mins, CPB time 112 v 178 mins]. The mean, IQR and range of 5-minute median $SctO_2$ for the Median Left/Right Average $SctO_2$ at the standardized event times are shown in figure



.The median durations of time below 55/60/65% thresholds were 0/21/105 mins [CABG] and 88/131/191 mins [VS ± CABG]. Five of 8 VS patients (63%) had >5 minutes below 55% $SctO_2$, compared to just 3/25 (12%) CABG-only patients (p=0.01).
Discussion:
In this study, the median $SctO_2$ value of awake patients was 70%. Awake $SctO_2$ variability was small (SD 3.9%) independent of age, skin color and gender. The pre-CPB median $SctO_2$ 72% dropped to 60% during CPB before returning to 68% at chest closure. VS patients showed longer periods below all 3 thresholds of $SctO_2$ values. This group did have significantly longer cross-clamp and CPB times; this may have contributed to greater times below the thresholds. Further study is ongoing to evaluate the significance of this observation with regard to clinical outcome.
Reference:
Anesthesia Analgesia 2006; 102(2S):S162

S-130.

COMPARISON OF THE EFFECT OF LINGUAL TRACTION VERSUS THE OVASSAPIAN PHARYNGEAL AIRWAY ON GLOTTIC VISUALIZATION DURING FIBEROPTIC INTUBATION

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Introduction
Fiberoptic bronchoscopic intubation (FOI) is a valuable tool for securing the airway. In the patient that has been rendered unconscious and paralyzed under general anesthesia, FOI can be made difficult by muscle relaxation and the resulting upper airway obstruction. Adjuncts and maneuvers are commonly used to facilitate this process. Two such adjuncts include the Ovassapian pharyngeal airway, and lingual traction. Our aim was to compare the quality of the first view of the glottis through the fiberoptic scope when combined with each of these two adjuncts.
Methods
Institutional Review Board approval was obtained. Following induction of general anesthesia, 24 ASA I-III volunteers having non-emergent surgery underwent two sequential fiberoptic glottic visualizations with video capture. All visualizations were performed by the same experienced operator using the same equipment. The Ovassapian airway and lingual traction were used sequentially in random order. In the case of lingual traction, gentle traction was applied to the tongue by an assistant while the operator performed the glottic visualization. Intubation over the fiberoptic scope was performed following the second visualization. The video obtained was edited such that a grader would be blinded to the airway method being presented. That grader then assigned a Cormack-Lehane score of I-IV to the first view of the glottis that was obtained.
Results
The average Cormack-Lehane view in the Ovassapian airway group was 3.21, compared with 2.04 in the lingual traction group. The lingual traction technique yielded better scores in twenty instances, poorer scores in two instances, and equivalent scores in two instances. The relative effectiveness of these two techniques was evaluated using the nonparametric Wilcoxon Signed Ranks test. A significant effect ($p<0.001$) indicated that fiberoptic glottic visualization with lingual traction was superior to fiberoptic glottic visualization with the Ovassapian airway.
Discussion
Some of the inherent challenges of fiberoptic endotracheal intubation include the presence of secretions and the anatomical obstruction encountered in the oropharynx and hypopharynx. Obtaining the first view of glottic structures is an important step in successfully advancing the fiberoptic scope towards and through the vocal cords. Any adjunct potentially serving to assist visualization and thus identification of the glottis is an asset. We found that in anesthetized patients undergoing fiberoptic intubation, lingual traction is an easy adjunct to employ and resulted in a significantly better first view of glottic structures than the Ovassapian pharyngeal airway.

S-131.

COMPARISON BETWEEN THE AIRWAY SCOPE AND THE BULLARD LARYNGOSCOPE FOR ENDOTRACHEAL INTUBATION IN PATIENT WITH NORMAL AIRWAY

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Introduction: Airway Scope (AWS: Pentax, Japan) is a rigid video laryngoscope with built-in 2.4 inch color CCD monitor paired with disposal blade. It is developed for management of both normal and difficult airway. Owing to its anatomically shaped blade including tube channel , there is no need to extend the patient's neck or apply excessive force during intubation. Unique feature is a target sign on the monitor. With this, operator only needs to manipulate the blade to "lock-on" the vocal cord on the monitor and just advance the tube into the trachea to complete intubation. We compare the intubation quality between AWS and the Bullard laryngoscope (BLS).
Methods: Thirty patients scheduled for elective anesthesia using orotracheal intubation were randomly assigned into two groups, group AWS, and group BLS. The time to take successful ETT placement, and number of attempted intubation were counted. After intubation, blood stain on the blade, incidence of postoperative hoarseness and sorethroat was examined. For statictics, the Unpaired Student's t-test and chi-square test were employed where appropriate, and $p<0.05$ considered significant.
Results: Although overall intubation time was shorter but not significant in AWS group, the use of the AWS significantly reduced the time required for successful ETT placement after the best laryngeal view obtained. All the patient In AWS group, tube was placed at first attempt, and no blood stain was observed on the blade tip. Incidence of postoperative hoarseness and sorethroat was not significantly different.
Discussion: Our result show that in comparison with BLS, the AWS provides comparable intubating conditions in patients with normal airway. Moreover, the CCD monitor with target provide greater view and orientation resulted in shorter time for intubation. Also, AWS seemed to be less traumatic due to its tube channel covering tip of the ETT without stylet unlike BLS's naked ETT with introducing stylet.

	Results		
	Airway Scope (n=15)	**Bullard** (n=15)	**P value**
Total time for intubation (sec)	33±14	38±12	0.29
Time for intubation after best laryngeal view obtained (sec)	6±2	15±6	<0.01
Number of intubation attemped	1±0	1.3±0.6	0.08

S-132.

VALIDATION OF CARDIAC OUTPUT MEASUREMENTS WITH THE LIDCO PULSE CONTOUR SYSTEM IN HEART SURGERY PATIENTS WITH REDUCED LEFT VENTRICULAR FUNCTION

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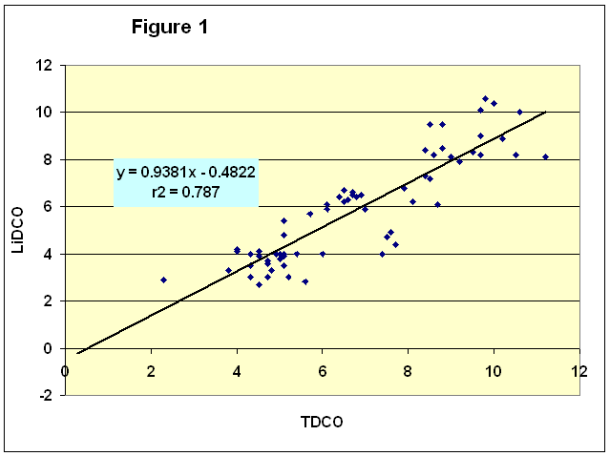
Introduction: The LiDCO™ is a new continuous, minimally invasive and user friendly method that employs the pulse contour technique to determine cardiac output (CO). In swine (1) and patients (2,3) with normal left ventricular systolic function there seems to be a strong relationship and good agreement between LiDCO™ and the thermodilution CO method using a pulmonary artery catheter (TDCO). However, LiDCO™ has not yet been validated in patients with reduced left ventricular ejection fraction (LVEF) although these patients would benefit the most from a goal directed therapy.
Methods: After institutional approval and having obtained informed consent we studied nine patients with a LVEF < 40% after cardiac surgery. In the course of their ICU treatment multiple CO measurements were carried out in various hemodynamic states simultaneously with the TDCO and the LiDCO™ technique. The correlation coefficient was determined by a simple regression analysis.
Results: TDCOs ranged from 2.3 to 11.2 l/min. The correlation coefficient r^2 we determined between these two methods was 0.79 ($P < 0.05$). Yet, LiDCO™ technique systematically underestimated TDCO by about 0.9 l/min (Fig 1).
Discussion: These preliminary results suggest that LiDCO™ seems to correlate well with TDCO even in patients with a reduced pump function after cardiac surgery. However, in the management of these patients, one has to bear in mind that it consistently gives lower CO values than TDCO over a broad range of TDCOs.
References: 1) Kurita T, et al. Br J Anaesth (1997) 79 : 770-775. 2) Linton RA, et al. Intensive Care Med (2000) 26: 1507-1511. 3) Hamilton TT, et al. Ann Thorac Surg (2002) 74: S1408-1412.



S-133.

AN ACTIVE PATIENT WARMING SYSTEM THAT UTILIZES CONDUCTIVE TEXTILE MATERIAL TO TREAT PERIOPERATIVE HYPOTHERMIA

AUTHORS: **M. K. Loushin**, J. S. Johnson, J. C. Iaizzo, P. A. Iaizzo;
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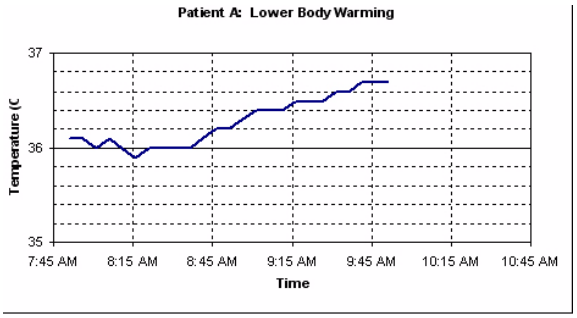
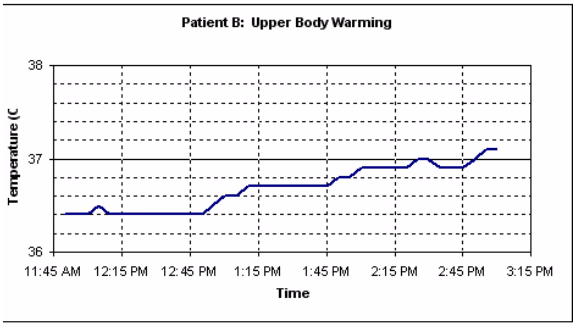
Introduction: Perioperative hypothermia is a common occurrence and is associated with complications such as coagulopathy, alteration in drug metabolism, shivering, and increased risk of wound infection1. Multiple peripheral active warming devices have been utilized during the perioperative period to minimize and/or prevent hypothermia. We present preliminary results for a new active warming system that utilizes conductive textile warming technology (Hot DogTM Warming System, Augustine Biomedical and Design; Eden Prairie, Minnesota).
Methods: After obtaining IRB approval and informed consent, patients who participated in the study were actively warmed with either an upper or lower body conductive textile warming blanket during general anesthesia. Intraoperative core body temperatures were recorded every five minutes utilizing an esophageal or nasopharyngeal temperature probes; skin temperatures were recorded from the chest and left upper arm; ambient operating room temperatures were also recorded throughout the study. For all patients, active warming was initiated 20-30 minutes after induction of general anesthesia and continued until the patient was extubated in the operating room. All patients were observed in the post-anesthesia recovery unit.
Results: Preliminary data results are from 11 adult patients, of which seven were in the upper body warming group and four were in the lower body warming group. After induction of general anesthesia, all patients had an initial core body temperature that was below 37oC. After initiation of the conductive textile warming device, almost all of the patients displayed a trend toward rewarming as evidenced by an increase in core body temperature. None of the patients displayed any adverse effects from the conductive textile warming system.
Discussion: Our preliminary findings indicate that conductive textile warming devices can be used safely and effectively to actively warm patients during the perioperative period.
Reference: 1. Sessler D. I. Mild Perioperative Hypothermia N Engl J Med 1997; 336:1730-1737.





S-134.

MATHEMATICAL MODEL EXPLAINS REDUCTION OF METABOLIC GAS EXCHANGE DURING ONSET OF GENERAL ANESTHESIA

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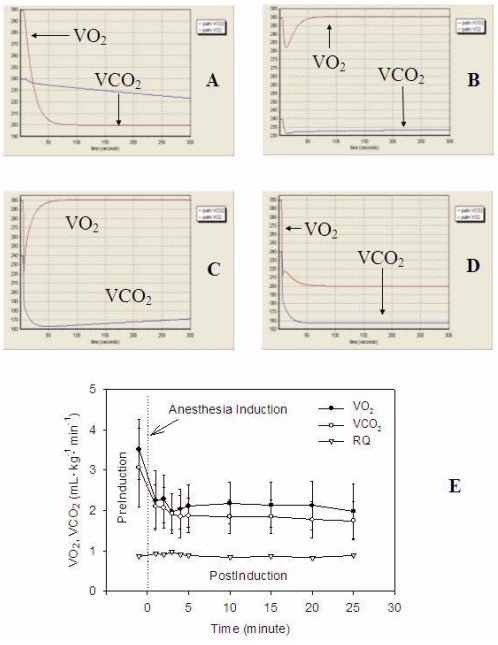
Introduction: We have designed a new metabolic gas exchange measurement system incorporating a bymixer[1] and fast response humidity sensor[2]. Using this system in 19 patients[3], we found that anesthesia induction caused an abrupt and sustained decrease of 38.6±11.5%, in airway O_2 uptake (VO_2) and CO_2 elimination (VCO_2) (Figure, panel E). We present a numerical analysis model to explain these findings. We hypothesized that anesthesia induction should decrease cardiac output (Q_T), decrease pulmonary artery pressure (Ppa), and increase high V_A/Q lung regions.
Methods: The computer model incorporates a small central compartment (5 lung units of V_A/Q = 0, 0.1, 1, 10, and infinity) and a large peripheral tissue compartment, connected by cardiac output and venous return. Algorithms describe solubility of gases in blood and tissue. The model allows independent perturbation of any parameter.
Results: In the Figure, Panel A displays the effect of 33% decrease of tissue metabolism on airway VCO_2 and VO_2 in the computer model; Panel B shows the effect of a 20% reduction in Q_T; and Panel C shows the effect of an increase in the high V_A/Q (=10) lung compartment from 5% to 40%. In Panel D, all three perturbations are combined to generate VCO_2 and VO_2 data, similar to the data measured in patients (Panel E).
Discussion: The slower decrease of airway VCO_2 during decreased tissue metabolism (Panel A), and the slower recovery of VCO_2 during decreased Q_T (Panel B) or increased high V_A/Q (Panel C), are due to the much larger peripheral stores and buffering capacity of CO_2 compared to . When we simultaneously executed all 3 different perturbations in the computer model, we obtained reductions in VCO_2 and VO_2 (Panel D) similar to our clinical study (Panel E). We conclude that anesthesia induction, in addition to decreasing tissue metabolism, reduces Q_T and Ppa to increase high V_A/Q lung regions which cause the overall effects of abrupt and sustained reduction in airway VCO_2 and VO_2.
Support: Committee on Research and Graduate Academic Programs, University of California Irvine, May 2005 and NIH grant HL-42637.
References: 1. Anesthesiology 2004; 100: 1427-37. 2. U.S. Patent Number 6,014,890; 2000. 3. Abstract, 2006 ASA, A474



S-135.

AIRWAY O_2 UPTAKE AND CO_2 ELIMINATION, MEASURED WITH A NEW BYMIXER-FLOW SYSTEM, ARE DECREASED IN MORBIDLY OBESE PATIENTS

AUTHORS: **A. Rosenbaum**, P. H. Breen;
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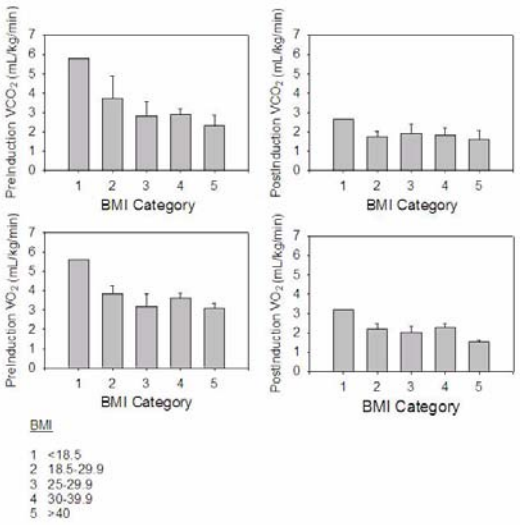
Introduction: Measurement of airway O_2 uptake (VO_2) and CO_2 elimination (VCO_2) can contribute to preoperative risk evaluation[1] and detection of critical events. We developed a noninvasive measurement system, specifically designed for anesthesia, based on the principle of indirect calorimetry. The system incorporates a bymixer[2], for the measurement of mixed gas fraction, and a fast response temperature and humidity sensor[3], for STPD correction of gas volumes. In this study, we hypothesized that VO_2 and VCO_2 will be depressed in obese patients undergoing anesthesia, due to lower metabolism of fat tissue.
Methods: After IRB approval, 17 patients were studied. Preoperative VO_2 and VCO_2 were measured with a spontaneous breathing device. In a second phase, we measured VO_2 and VCO_2 after anesthesia induction, using inspiratory and expiratory bymixers connected to the anesthesia circle circuit. Measurements were conducted until incision time (average of 10 measurements over 15 minutes).
Results: Of the 17 patients (Table, Figure), 1 was underweight (body mass index, BMI<18.5) 2 were normal weight (BMI 18.5-24.9), 7 were overweight (BMI 25-29.9), 5 were obese (BMI >30) and 2 were morbidly obese (BMI>40). The Table summarizes the pre and post anesthesia induction values of VO_2 and VCO_2 (mg/kg/min) and grouped by BMI. There was no significant statistical difference between the groups. However, in the morbidly obese group, VO_2 and VCO_2 were 20-30% lower than the less obese groups of patients.
Discussion: These preliminary data suggest that VO_2 and VCO_2 in morbidly obese patients are lower than less overweight patients, due to the decreased tissue metabolism of fat. We did not detect a specific effect of BMI on VO_2 and VCO_2 during induction of anesthesia. We plan further patient studies to clarify these findings.
References: 1. Chest 1999; 2: 355-62. 2. Anesthesiology. 2004; 100: 1427-37. 3. United States Patent No. 6,014,890, January 18, 2000.



VCO2 and VCO2 in correlation to BMI

BMI	n	PreVCO$_2$ mL/kg/min	PostVCO$_2$ mL/kg/min	PreVO$_2$ mL/kg/min	PostVO$_2$ mL/kg/min
<18.5	1	5.81	2.66	5.61	3.19
18.5-54.9	2	3.72+-1.15	1.74+-0.31	3.84+-0.41	2.19+-0.29
25-29.9	7	2.82+-0.75	1.91+-0.49	3.19+-0.65	2.01+-0.34
30-39.9	5	2.90+-0.28	1.84+-0.35	3.61+-0.26	2.27+-0.23
>40	2	2.31+-0.55	1.62+-0.46	3.09+-0.26	1.55+-0.05

S-136.

EFFECT OF CRICOID PRESSURE ON PLACEMENT OF THE LARYNGEAL TUBE

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Introduction: The Laryngeal Tube (VBM, Medizintechnik, Germany) consists of an airway tube with proximal pharyngeal and distal esophageal cuffs. It creates a gas tight seal within the pharynx, and has a ventral opening between the two cuffs for ventilation of the lungs. Its tip and esophageal cuff are intentionally inserted into the hypopharynx, and it may provide some protection from regurgitation when correctly placed. But patients at risk of regurgitation usually require the application of cricoid pressure during induction of anesthesia. In this study, we examined the effect of cricoid pressure on placement of the laryngeal tube.
Methods: We recruited 25 patients undergoing general anesthesia with neuromuscular blockade for elective surgery. The size of the laryngeal tube was chosen according to the patient's height. We used a randomized crossover design, the laryngeal tube was applied with cricoid pressure on one occasion, and without cricoid pressure (sham pressure) on the other occasion. After confirming the ability to bag mask ventilate the patients, a trained assistant applied bimanual cricoid pressure and sham pressure, in turn. The assistant's hand was covered by a cloth to blind the investigator as to whether cricoid pressure was applied. After every insertion, we graded the ease of insertion (easy, moderately easy, difficult or impossible) and the time of achieving ventilation. We tested the leak pressure up to a maximum of 30 cmH_2O. The McNemar (paired proportion) test was used to compare the success rate of adequate ventilation, and Wilcoxon signed rank test to compare the ease of insertion.
Results: Placement was successful in all 25 patients with sham pressure compared to only 6 (24%) patients with cricoid pressure ($P < 0.001$). Insertion was significantly more difficult under cricoid pressure than under sham pressure ($P < 0.001$). In patients in whom ventilation was adequate, the median time taken to achieve adequate ventilation was 10 (range 5 - 26) s for sham pressure, and 25 (15 - 33) s for cricoid pressure. The median leak pressure was 30 (range 20 - 30) cmH_2O (with no gas leak at 30 cmH_2O in 22 patients) for sham pressure and 15 (12 - 22) cmH_2O for cricoid pressure.
Discussion: This study showed that cricoid pressure impeded effective placement of the laryngeal tube and prevented successful ventilation. This suggests that the laryngeal tube may be inappropriate if cricoid pressure is required, and that cricoid pressure should be released in order to achieve successful placement. This will limit the application of the laryngeal tube in patients at risk of regurgitation.

Genetics/Genomics

S-137.

THE EFFECTS OF 5-HYDROXYTRYPTAMINE 3B RECEPTOR PROMOTER POLYMORPHISMS ON POSTOPERATIVE VOMITING

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Introduction: The introduction of 5-hydroxytryptamine (5-HT3) receptor antagonists for the treatment of postoperative nausea and vomiting (PONV) and chemotherapy-induced nausea and vomiting (CINV) has revolutionized the care of surgery and chemotherapy patients. However, more than 30% of patients still develop PONV even after the use of 5-HT3 antagonists (1). In the past several years genomic variations have been shown to account for inter-individual differences in 5HT3 efficacy. Specifically noted have been changes in drug metabolism (CYP2D6) (2) and 5HT3 receptor polymorphisms (PM) (3). In this study, we hypothesized that the promoter variants of the 5-HT3B subunit gene might affect the frequency of postoperative vomiting (POV) as has been noted in patients receiving chemotherapy.
Methods: A group of 93 high risk female patients undergoing standardized general anesthesia were given 4 mg of ondansetron 30 minutes before extubation. Patients were observed for symptoms of nausea and vomiting for 24 hours. DNA was extracted from whole blood in all patients. The 5'-upstream region of the 5-HT3B receptor promoter gene was sequenced.
Results: Sequencing of the DNA for the promoter region for the 5-HT3B receptor gene in the 93 patients (35 with vomiting and 58 without) demonstrated 3 known PMs in the promoter region of the 5HT3B subunit. The PMs and the prevalence in all the patients include: -761G to A (heterozygote, 17%); -381 T to C (heterozygote, 42%; homozygote, 13%); -102_ -104 AGA deletion (heterozygote, 13%; homozygote, 1%). Compared to patients with postoperative vomiting, patients without postoperative vomiting carried a significantly higher frequency of the -381C homozygote [11in 58 (19%) vs 1 in 35 (2.8%), $p < 0.05$]. There was no significant difference in the distribution of other genotypes between patients with and without postoperative vomiting.
Discussion: Recently it has been reported that variations in the 5HT3 receptor promoter region correlate with the incidence of chemotherapy induced vomiting (3). In our current study, we demonstrated that the 5HT3B receptor promoter PM -381 T> C was associated with a decrease in the frequency of POV. We theorize that decreased expression of the 5-HT3B receptor subunit may alter serotonin binding. Additionally, we found no effect for the other 2 polymorphisms encountered. Based on this preliminary data we believe that further studies are warranted.

Reference:
1. Kovac AL, et al. *J Clin Anesth*. 1999;11:453-459.
2. Candiotti KA, et al. Anesthesiology. 2005 Mar;102(3):543-9.
3. Tremblay PB, et al. J Clin Oncol. 2003 Jun 1;21(11):2147-55.

S-138.

CHROMOSOMAL SUBSTITUTION-DEPENDENT DIFFERENCES IN CARDIOPROTECTION BY ISOFLURANE -INDUCED PRECONDITIONING IN RATS

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Introduction: Isoflurane produces a delayed anesthetic preconditioning (APC) against myocardial ischemia and reperfusion injury.[1] The objective of this study was to compare cardioprotective effects afforded by APC in two genotypically distinct parental strains of rats (Dahl Salt Sensitive [SS] and Brown Norway [BN]) and in a consomic (chromosomal transfer) strain ($SS\text{-}18^{BN}$). The latter was a strain available from a larger panel of consomics in which single chromosome from the BN strain has been introgressed into an otherwise unchanged SS genetic background.[2]
Methods: APC trigger was achieved *in vivo* by 120 min exposure to isoflurane (1.0 minimum alveolar concentration) with an inspired oxygen concentration of 30% in five male adult (9-12 weeks-old) animals of each strain. Respective control groups were not subjected to above treatment. Twenty-four hours later hearts were isolated and subjected to 30 min of global, no-flow ischemia, followed by 120 min of reperfusion. On the end of the reperfusion, hearts were rapidly removed from the perfusion apparatus and sliced across the long axis of the left ventricle, from apex to base, into 2-mm-thick transverse sections and then incubated in 1% triphenyltetrazolium chloride in phosphate buffer (pH 7.4) at 38 C for 20 min. Infarct areas were visually enhanced by storage in 10% formaldehyde solution for 24 h before final measurement. Data are means ±SEM ($p < 0.05$; * vs. BN).
Results: Isoflurane significantly reduced infarct size as a percentage of the left ventricle in BN and $SS\text{-}18^{BN}$ strains (22 ± 5% and 23 ± 5%, respectively) as compared with SS strain(49 ± 7%*). There were no significant differences in infarct size between three control groups.
Discussion: The major significance of these results is the demonstration of a significant and reproducible difference in cardioprotective effects afforded by APC between two inbred strains that can be changed by a single chromosomal substitution. This knowledge provides a basis for selectively studying genetic factors associated with mechanisms of delayed anesthetic preconditioning related to this chromosomal substitution.

References:
1) *Anesthesiology* 100: 525-31, 2004.
2) *J Clin Invest* 97: 522-7, 1996.
Acknowledgments:
Supported in part by grant No.0360042Z from the American Heart Association-Greater Midwest Affiliate and PO1GM066730 from the National Institutes of Health.

ANESTH ANALG
2007; 104; S-1–S-271

S-139.

IMPACT OF BETA2 ADRENERGIC RECEPTOR SIGNALING UPON MURINE CARDIAC REMODELING AND GENE EXPRESSION

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AFFILIATION: Stanford University, Stanford, CA.

Introduction: Continuous beta1 adrenergic receptor (b1AR) stimulation is toxic to the myocardium and is believed to play a role in the development and progression of congestive heart failure. In contrast, stimulation of b2ARs has been shown to protect cardiomyocytes. We investigated the effect of continuous b1AR stimulation in vivo in the presence and in the absence of b2AR activation. Our goal was to assess the impact of b2AR signaling upon cardiac remodeling and gene expression.
Methods: We performed magnetic resonance imaging analyses of wild type (WT) and b2AR knockout (b2KO) mice before and after two week infusions of the non-specific bAR agonist isoproterenol. We also analyzed cardiac gene expression in WT and b2KO mice with and without isoproterenol infusions using Affymetrix 430A gene arrays and GeneSpring 7.2 software.
Results: Changes in both left ventricle end diastolic volume (LVEDV) and stroke volume (SV) were observed after isoproterenol infusion (See Table).
Two-way ANOVA anaylsis of cardiac gene expression revealed significant increases of four-and-a-half LIM domain protein, p38, and extracellular-regulated kinases (ERKs) after isoproterenol infusion in both WT and b2KO animals. Downregulation of the b1AR and sarcoplasmic reticulum calcium ATPase (SERCA) was observed after isoproterenol infusion for both genotypes. Two-way ANOVA also demonstrated a significant genotype effect with respect to the expression of cJun N-terminal kinase (JNK) and the b2AR. In b2KO mice, we observed greater expression of JNK as well as the b2AR gene (a non-translatable b2AR mRNA fragment in the b2KO animals). Two-way ANOVA also revealed genotype-treatment interaction effects for atrial natriuretic peptide (ANP), uncoupling protein 2 (UCP2), and phospholamban. ANP and UCP2 expression levels were greatest in WT mice who received isoproterenol infusions while phospholamban expression levels were lowest in these animals.
Conclusions: We observed differences in cardiac structure and gene expression during a comparison of WT and b2KO mice after isoproterenol infusion. Inability of b2KO mice to increase expression of protective substances like ANP implied that the absence of b2AR signaling was disadvantageous. However, structural analyses using MRI did not support this conclusion. In fact, increases in stroke volume among b2KO animals after isoproterenol administration suggested that b2AR activation could be detrimental. Direct assessment of cardiac inotropic performance in WT and b2KO mice using pressure-volume catheters may help to clarify this issue.

Changes in Structural/Physiologic Parameters after Isoproterenol Infusion

Structural/Physiologic Parameter	Wild Type	beta2KO
Left Ventricle End Diastolic Volume (cubic mm/gram body weight)	Increased (p=0.0002, t-test)	Increased (p=0.0003, t-test)
Stroke Volume (cubic mm/gram body weight)	Decreased (p=0.04, t-test)	Increased (p=0.002, t-test)
Ejection Fraction (%)	Trended Down (78% to 60%)	Trended Down (85% to 77%)

S-140.

ANALYSIS OF CARDIAC GENE EXPRESSION IN MICE WITH DISRUPTION OF THE BETA2 ADRENERGIC RECEPTOR PDZ BINDING MOTIF

AUTHORS: **E. Fung**[1], T. Samad[1], C. Chen[2], J. Wong[1], R. Agrawal[1], A. J. Patterson[1];
AFFILIATION: [1]Stanford University, Stanford, CA, [2]University of California, San Francisco, San Francisco, CA.

Introduction: Both beta1 and beta2 adrenergic receptors (ARs) contain PDZ binding motifs. The b1AR PDZ binding motif facilitates interaction between the b1AR and proteins like PSD-95 that anchor the receptor to the cell surface after agonist activation. In contrast, the b2AR PDZ binding motif interacts with ezrin-binding protein 50 (EBP50), which associates with A-kinase-anchoring protein (AKAP) ezrin. In vitro studies demonstrate that the b2AR PDZ binding motif helps direct the b2AR to microdomains within the cell after agonist-induced activation and, therefore, plays a role in linking this receptor subtype to signaling pathways that distinguish it from the b1AR.
We sought to assess the role of the b2AR PDZ binding motif in vivo. Specifically, we investigated the impact of b2AR PDZ binding motif disruption upon cardiac gene expression in mice.
Methods: We compared gene expression profiles of b2KO, b2PDZ, and WT mice before and after infusions of the non-specific bAR agonist isoproterenol. We used Affymetrix 430A gene arrays and GeneSpring 7.2 software to complete our investigation.
Results: Two-way ANOVA analysis of cardiac gene expression revealed a genotype-treatment interaction effect for heat shock protein 70 (HSP70). HSP70 levels were significantly elevated in b2PDZ mice after isoproterenol administration when compared to other isoproterenol-treated and untreated mice. Two-way ANOVA analysis also demonstrated a significant genotype effect with respect to expression of the b2AR. In b2KO mice (but not b2PDZ mice), we observed greater expression of the b2AR gene (a non-translatable b2AR mRNA fragment in the b2KO animals). Two-way ANOVA also revealed an isoproterenol treatment effect for b1AR expression. b1AR gene expression was significantly lower after isoproterenol treatment in WT, b2KO, and b2PDZ mice. Finally, two-way ANOVA revealed signficant increases in type I collagen, c-Jun N-terminal kinase (JNK), and FADD-like interleukin 1beta converting (FLICE) inhibitory protein in b2KO mice compared to b2PDZ animals.
Conclusions: We found that b2PDZ mice do not increase expression of the mutated b2AR gene, as b2KO mice do. These results suggest that mutated b2ARs in b2PDZ mice retain some capacity to function as b2ARs. However, we also observed a significant rise in HSP70 expression in the hearts of b2PDZ mice after isoproterenol infusion. In vitro data from Dr. Brian Kobilka's laboratory suggest that disruption of the b2AR PDZ binding motif causes b2ARs to behave like additional b1ARs by impairing coupling to Gi but not to Gs and by disrupting receptor trafficking to intracellular subdomains after agonist activation. We hypothesize that in vivo b2ARs with disruption of the PDZ binding motif signal like additional b1ARs whose gene expression is not downregulated like normal b1ARs during continuous agonist activation. Increased HSP70 expression in b2PDZ mice may represent a response to increased myocyte apoptosis induced by enhanced signaling through Gs pathways.

S-141.

THE DIFFERENTIAL EFFECTS OF ANESTHETIC-INDUCED PRECONDITIONING: DEPENDENCE ON RAT STRAINS

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Introduction: Anesthetic-induced preconditioning (APC) has cardioprotective effects against ischemia by reducing infarct size. However, the efficacies of the cardioprotective effects are dependent on the animal model used. For example, it has been reported that the Dahl S strain of rats are resistant to APC, unlike the Wistar rats. The goal of our research was to investigate the impact of APC on cardiac electrophysiology, which is not well established. Previous studies using Wistar rats showed that APC increased the cardiac sodium current (INa) density and accelerated the L-type calcium current (ICa) inactivation kinetics. In the present study, we characterized the effects of APC on the cardiac INa and ICa in the Wistar and Dahl S rats.
Methods: The study was approved by the Institutional Animal Care and Use Committee. The whole-cell configuration of the patch clamp technique was used to record INa and ICa from ventricular myocytes isolated from adult Wistar and Dahl S rat hearts. In the APC group, rats were exposed to 1.4% isoflurane (1.0 MAC) for 30 minutes with a 30-minute recovery period prior to cell isolation. In the non-APC group, rats were not exposed to isoflurane. Current-voltage relationships were obtained using standard protocol. Current amplitude was normalized to cell capacitance to yield current density. A double-exponential function was used for the analysis of ICa inactivation kinetics. Data are reported as mean±SEM. Statistical analysis was performed using unpaired Student's t-test and $P<0.05$ was considered as a significant difference.
Results: In the Wistar rats, APC induced a significant increase in peak INa density from -8.7±0.5 pA/pF (non-APC, n=13) to -13.2±1.2 pA/pF (APC, n=12). ICa inactivation kinetics exhibited significant decreases in the slow time constant (at test voltages ranging from -20 to +40mV) and the fast time constant (from -20 to +10mV) in the APC group (n=19-20/group). In contrast, in the Dahl S rats, there were no significant differences in the INa density between non-APC and APC groups (-10.7±0.6 pA/pF vs -10.7±0.9 pA/pF, respectively; n=10/group). Furthermore, no significant differences in ICa inactivation kinetics were observed between the two groups in the Dahl S rats (n=9/group).
Discussion: Anesthetic-induced preconditioning resulted in persistent changes in the cardiac Na and Ca channels in the Wistar rats. In contrast, these changes were not observed in the Dahl S rats. These results show that in the APC-resistant Dahl S rats, the functional changes in the cardiac ion channels associated with APC are not observed. Furthermore, the APC-associated changes in INa and ICa may contribute to maintenance of cardiac excitability and reduction in calcium overload, respectively, contributing to the cardioprotective effects.

S-142.

SEVOFLURANE AT SEDATIVE DOSES PREVENTS ENDOTHELIAL DYSFUNCTION AND ACTIVATION OF LEUKOCYTES AFTER ISCHEMIA/REPERFUSION INJURY IN HUMANS AND MODULATES MRNA EXPRESSION IN PERIPHERAL BLOOD

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Introduction: Endothelial dysfunction leading to neutrophil infiltration of tissues has been implicated in tissue injury caused by ischemia-reperfusion (I/R) [1]. Experimental data suggest that volatile anesthetics (VA) protect the endothelium against I/R injury [2-5]. However, whether this occurs in humans in vivo is still unknown. We tested whether inhalation of sevoflurane at subanesthetic concentrations provides protection against post-occlusive endothelial dysfunction induced by ischemia-reperfusion injury of the forearm in humans. Furthermore, we hypothesized that sevoflurane suppresses proinflammatory gene transcription in leukocytes.
Methods: Five healthy men (age 25-45) were enrolled in a study with cross-match design. Each subject was randomly exposed to 15 min of forearm ischemia in the presence or absence of sevoflurane. Sevoflurane was administered by mask 10 min before ischemia, during ischemia, and during the first 5 min of reperfusion at doses of between end-tidal 0.5-0.75 vol.-%. Hyperemic reaction, an indicator of ischemic injury and endothelial function, respectively, was determined at 15 min and 30 min of reperfusion using venous occlusion plethysmography. Blood samples were collected at baseline, 2, 5, 10, and 30 min after reperfusion from both forearms and used to determine markers of leukocyte activation (CD11b) using flow cytometry. Additional five volunteers received the volatile anesthetic sevoflurane at sub-anesthetic concentrations during 60 minutes. Venous blood was drawn at baseline (before sevoflurane inhalation), 15 min after starting sevoflurane application, at the end of the inhalation period (60 minutes), and 3, 6, and 24 hours after sevoflurane application. The blood samples were immediately transported on ice to the laboratory for RNA isolation and determination of CD11b and L-selectin expression after N-formylmethionyl-leucyl-phenylalanine (fMLP) stimulation.
Results: Exposure to 15 min of test ischemia followed by reperfusion markedly reduced hyperemic reaction, indicating endothelial dysfunction. Administration of sevoflurane at sedative doses prevented the reduction in hyperaemic blood flow response. In accordance with this observation, leukocyte activation, as measured by CD11b expression, was abolished by sevoflurane. Moreover, exposure to sedative concentrations of sevoflurane substantially altered gene expression in peripheral blood.
Conclusions: Sevoflurane preserves endothelial function and prevents leukocyte activation in an established model of endothelial ischemic injury in healthy volunteers. Our findings are of utmost importance because they provide evidence that the human endothelium, a key component of all vital organs, is receptive to protection by sevoflurane in vivo at even low sedative concentrations (<1 vol.-%). Inhibition of leukocyte adhesion is likely to be involved in the protection.
References:
[1] Circulation 103: 1624-30 (2001)
[2] Anesthesiology 99: 896-903 (2003)
[3] Anesthesiology 91: 521-30 (1999)
[4] Anesthesiology 90: 1372-81 (1999)
[5] Anesth Analg 95: 583-7 (2002)
Funding: Supported in part by the IARS 2005 Frontiers in Anesthesia Research Award

S-143.

MOLECULAR MECHANISM OF GLUTAMINE-MEDIATED INDUCTION OF HSP70 INVOLVES ACTIVATION OF THE O-LINKED-N-ACETYLGLUCOSAMINE PATHWAY IN MURINE EMBRYONIC FIBROBLAST CELLS

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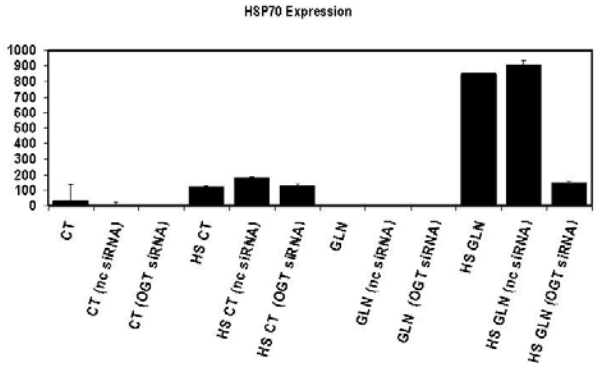
Introduction: Glutamine (GLN) can protect against critical illness. Data from our laboratory suggests that GLN protects via induction of HSP70. However, the molecular mechanism by which GLN enhances HSP70 expression is unknown. GLN can increase gene activation by O-linked-N-acetylglucosamine (O-glcNAc) glycosylation. The aim of this study was to investigate glutamine's effect on cellular levels of O-glcNAc and nuclear translocation of the transcription factors SP1 and HSF-1, which are vital to HSP70 expression. To determine the importance of this post translational modification in the production of HSP70, we used silencing RNA (siRNA) against O-linked-N-acetylglucosamine transferase (OGT), the enzyme that catalyzes the addition of O-glcNAc to proteins.
Methods: Heat stress was induced in a 43 degree C water bath for 45 minutes for all experiments. Visualization of cellular HSF-1, SP1 and O-glcNAc was performed following treatment with 0 mM GLN (CT) or 10mM GLN (GLN) with and without heat stress (HS). Immediately after HS, cells were fixed and stained. Mean fluorescent intensities (MFIs) were measured for each experimental group. OGT silencing was carried out in MEF cells were transfected with either no siRNA, siRNA to OGT, or negative control siRNA (nc siRNA) (with a comparable GC component to the OGT oligos). Cells were then treated with GLN or CT as above and HSP70 evaluated by Elisa. Results: Microscopy showed GLN-treatment increased nuclear MFI for HSF-1 by 40% (HS-CT: 1005±146 vs. HS-GLN:1403±102, $p < 0.05$) and SP1 by 54% (HS-CT:214±14 vs. HS-GLN:330±13, $p<0.05$). Total cell HSF-1 and SP1 MFIs did not change. Total cellular O-glcNAc levels showed a 44% increase in mean fluorescence intensity in the HS-GLN group compared to controls (HS-CT:360±24 vs. HS-GLN:518±51, $p<0.05$) Following OGT silencing, HS-GLN treated groups showed a seven fold increase in HSP70 production vs. HS-CT and the HS-GLN negative control siRNA groups showed a five-fold increase in HSP70 production. These increases were completely attenuated by OGT silencing ($p<0.05$ versus non-siRNA treated GLN groups). (See figure).



Conclusion: These results indicate GLN can activate the O-glcNAc pathway and enhance nuclear translocation of HSF-1 and SP1. Inhibition of OGT activity blocked GLN-mediated induction of HSP70. Thus, it appears the molecular mechanism of GLN-mediated HSP70 expression is dependent on enhanced O-glcNAc pathway activation.

S-144.

GLUTAMINE'S ATTENUATION OF MORTALITY AND THE INFLAMMATORY RESPONSE FOLLOWING SEPSIS IS DEPENDENT ON HSP70 EXPRESSION

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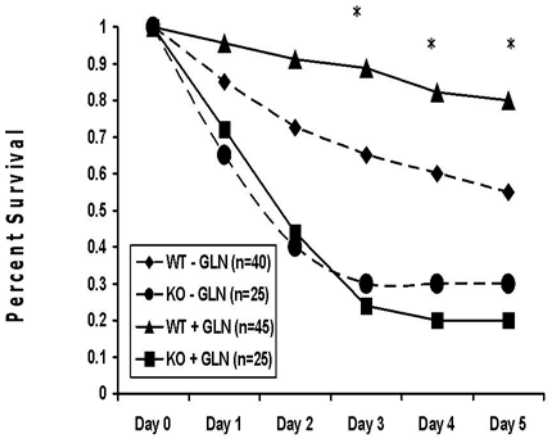
Introduction: The heat shock response has been implicated in attenuating NF-kB activation and pro-inflammatory cytokine expression following experimental illness and injury. Likewise, Glutamine (GLN) can improve outcomes following clinical and experimental illness and recently has been shown to be a novel enhancer of heat shock protein 70 (HSP70). The aim of this study was to evaluate the hypothesis that GLN's attenuation of the inflammatory response, tissue injury, and mortality following sepsis is dependent on HSP70 expression.
Methods: Sepsis was induced in $HSP70^{-/-}$ (KO) and $HSP\text{-}70^{+/+}$ (WT) mice via cecal ligation and puncture (CLP) and a dose of 0.75 g/kg GLN was administered IV 1 h post-CLP. Lung tissue NF-kB activation and inflammatory cytokine response was evaluated at 1, 2, 6, and 24 h post-CLP. ARDS was assessed using histopathology. Survival was assessed for 5 days post-CLP.
Results: NF-kB activation and cytokine expression in lung tissue was increased in $HSP70^{-/-}$ mice at all time points following CLP. Deletion of HSP70 prolonged NF-kB activation in lung tissue ($p < 0.01$ versus WT). GLN administration had no effect in $Hsp70^{-/-}$ mice, but led to a significant attenuation of NF-kB activation and inflammatory cytokine response in $HSP70^{+/+}$ mice ($p < 0.01$ versus KO). GLN attenuated lung injury in $HSP70^{+/+}$ mice following sepsis, however this protection was lost in $HSP70^{-/-}$ mice. Finally, GLN significantly improved survival in $HSP70^{+/+}$ mice, however this survival benefit was lost in $HSP70^{-/-}$ mice (see figure, *-$p< 0.05$ versus all other groups via anova).



Conclusion: Thus, HSP70 expression is required for GLN's protective effects on survival, tissue injury, and the inflammatory response in a murine sepsis model.

Liver/Transplantation

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S-145.

LIVER OUTFLOW IN LRLT PATIENTS IS NOT HARMED BY INCREASED PEEP!

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Introduction: Intensive care interventions like use of vasoactive drugs and artificial ventilation with higher positive end expiratory pressure (PEEP) levels might impair liver function . However some recent reports challenged this topic . As a reference center for living related liver transplantation (LRLT) we performed a clinical trial on patients after LRLT with special interest to hemodynamic, liver in- and outflow at different PEEP levels.
Methods: 30 patients following LRLT were enrolled in this study. All patients were mechanical ventilated with biphasic positive airway pressure (BIPAP). The effects of two randomly chosen PEEP levels (0 and 10 mbar) were studied in the immediate postoperative period in every patient. We obtained the systemic hemodynamic, using a pulmonary arterial catheter and simultaneously the flow velocities of the hepatic artery (HA), the portal vein (PV) and the right hepatic vein (RHV).
Results: Changes in the flow velocities of the RHV, the PV and HA between PEEP of 0 and 10 mbar did not reach statistical difference. There was no impact of increased PEEP of 10 mbar on mean arterial pressure (83 mmHg (0 mbar) vs 81 mmHg (10 mbar)), mean pulmonary arterial pressure (22 mmHg at both levels), and cardiac index (CI, 5.7 $L/min^{-1}*m^2$ vs. 5.4 $L/min^{-1}*m^2$). However, the central venous pressure increased significantly from 7 mmHg to 10 mmHg while increasing the PEEP from 0 to 10 mbar, and the pulmonary capillary wedge pressure increased significantly from 10 mmHg at 0 mbar to 13 mmHg at a PEEP of 10 mbar.
Discussion: The most striking feature of our study is that even in LRLT patients the liver outflow is not impaired at a PEEP of 10 mbar. Moreover, the unchanged blood flow velocities for HA and PV and RHV with an unchanged CI at a PEEP of 10 mbar indicates that the blood flow throughput the liver is unaffected by this PEEP level. In conclusion, short term ventilation with PEEP up to 10 mbar in LRLT patients does not impair the liver outflow.

S-146.

ISOFLURANE PRETREATMENT PROTECTS RAT LIVERS FROM ISCHEMIA/REPERFUSION INJURY BY INDUCTION OF HEME OXYGENASE-1

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Introduction: The heme oxygenase (HO) enzyme is responsible for the maintenance of liver perfusion and hepatocellular integrity especially under pathological conditions (1). Previous data could show that the volatile anesthetic isoflurane (ISO) leads to an expression of the inducible isoform of HO (HO-1) in the liver and thus improves hepatic blood flow (2,3). It was the objective of this study to characterize the influence of ISO induced HO-1 expression on hepatocellular integrity after partial ischemia/reperfusion (IR) in the rat.
Methods: After institutional approval rats were randomised into four groups: 1) pentobarbital (PEN, 40 mg/kg/h i.v.) + vehicle; 2) ISO (2.4 MAC) + vehicle; 3) PEN + SnPP IX (50 µmol/kg, i.v.); 4) ISO + SnPP IX. A tracheotomy was performed and animals were mechanically ventilated. After injection of SnPP IX or vehicle, six hours after onset, partial hepatic ischemia was induced for 1h, followed by 1h of reperfusion. At the end of each experiment, blood and liver tissue were obtained for molecular biological, histological and immunohistochemical analyses. Statistical analysis was performed with ANOVA and Student-Newman-Keuls tests. Differences were considered significant when $p<0.05$.
Results: Partial hepatic IR increased ALT, AST and α-GST plasma activity compared to sham operated animals ($p<0.05$). ISO pretreatment increased hepatic HO-1 mRNA, HO-1 protein, HO enzyme activity and decreased transaminases and α-GST after IR ($p<0.05$). Administration of SnPP IX inhibited HO activity and increased markers of hepatocellular injury to control levels of PEN anesthetized animals. Histological analysis of livers obtained from ISO pretreated rats showed a reduction of necrotic areas particularly in the perivenular region, the predominant site of ISO induced HO-1 expression. HO-blockade abolished the ISO induced protective effects.
Discussion: This study provides first evidence that pre-treatment with the non-toxic and clinically approved anesthetic isoflurane induces hepatic HO-1 expression, and thereby protects rat livers from ischemia/reperfusion injury. This may offer a new potential for hepatic organ protection.

References: 1.) Pannen BHJ et al. J Clin Invest 1998;102:1220-1228. 2.) Hoetzel A et al. Anesthesiology 2002;97(5):1318-1321. 3.) Schmidt R et al. J Hepatol 2004;41:706-713.

S-147.

A COMPARISON OF PRETRANSPLANT MELD SCORES AND MORTALITY OF ADULTS RECEIVING LIVING RELATED LIVER TRANSPLANTS VERSUS CADAVERIC LIVER TRANSPLANTS: A SINGLE CENTER STUDY.

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Introduction:
The MELD (model for end stage liver disease) score, which was developed by UNOS, was originally designed to be used as a way to determine which patients were in the most need of liver transplantation. However, recently, its use as a predictor of post transplant survival in adults receiving liver transplantations has been studied (Habib et al, 2006). We intended to examine and compare whether pretransplant MELD scores were useful determinants of post transplant mortality in adults undergoing living related liver transplants versus cadaveric transplants at our facility.
Methods:
We retrospectively analyzed all adult living related and cadaveric liver transplantations undergone at the University of Minnesota Medical Center-Fairview from 8/23/1999-12/31/2005. MELD scores were calculated prior to transplantation by the transplant team. These scores were then correlated with the five year survival rate of both living related recipients and cadaveric recipients. We also determined and compared the one, three, and five year survival rates of living related recipients and cadaveric recipients.
Results:
There were 340 total patients that underwent liver transplantation during this period. There were 290 cadaveric recipients and 50 living related recipients. Of the 290 cadaveric recipients 5 (3 living and 2 dead) recipients did not have pretransplantation MELD scores. Of the 50 living related recipients 1 living recipient did not have pretransplantation MELD score and thus was excluded from the study. The one, three, and five year survival rates of living related liver transplant recipients was 97.96%, 95.92%, and 93.88% respectively. The one, three, and five year survival rates of cadaveric liver transplant recipients was 84.21%, 74.74%, and 73.33% respectively. The mean MELD score of living related liver transplant recipients was 14.63 and of dead living related liver transplant recipients was 10.66. The mean MELD score of living cadaveric recipients was 23.82 and of dead cadaveric recipients was 21.48.

Discussion:
In conclusion, this study illustrates that at our center living related liver transplant recipients have lower MELD scores and increased survival rates than those patients undergoing cadaveric liver transplantation. However, the mean pretransplantation MELD score in both the cadaveric and living related liver transplant recipients was greater in those recipients that were living at five years compared to those who had died at five years post transplant.
References
1. Habib S. et al. Liver Transplantation. 2006; (3): 440-447.

S-148.

NON-INVASIVE MONITORING OF INTRACRANIAL PRESSURE IN PATIENTS WITH ACUTE LIVER FAILURE

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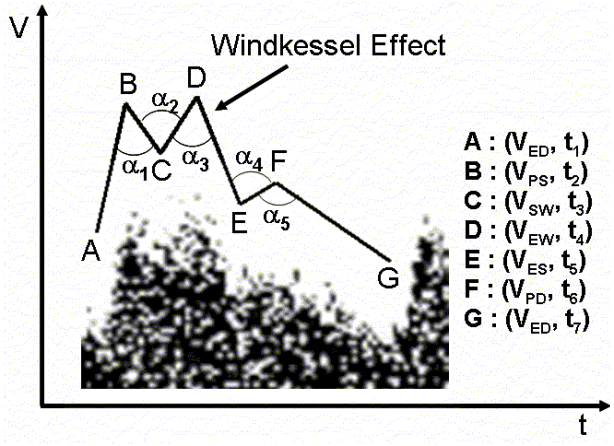
A reliable non-invasive monitoring procedure for intracranial pressure (ICP) will help prevent the complications of hemorrhage and/or infection associated with conventional techniques for measuring ICP in patients with acute liver failure (ALF).
PURPOSE: Preliminary demonstration that noninvasive transcranial doppler (TCD) waveform analysis can be used to monitor the development of elevated ICP in patients with ALF. The primary goal of this study was to determine whether linearized TCD waveforms could discriminate normal ICP (<20 mmHg) from elevated ICP (≥20 mmHg). TCD waveforms are characterized by a Windkessel effect during systolic deceleration that dampens as ICP increases. The systolic peak narrows and sharpens as ICP increases.
METHODS: Following IRB approval, 218 coupled ICP-TCD observations from 16 ALF patients were retrospectively identified. The TCD waveforms were digitally scanned and linearized as simplified waveforms consisting of seven coupled (V,t) pairs, as shown in the figure. TCD waveform features including mean velocity over a cycle (MV), pulsatility index (PI = V_{PS}/MV), fraction of cycle in systole, acceleration (deceleration) in each region, and angles associated with changes in acceleration were calculated. After dividing the ICP-TCD observations two groups (ICP < 20 mmHg and ICP ≥20 mmHg), simple stepwise linear discriminant analysis was used to identify which, if any, TCD waveform features discriminated between the two groups.
RESULTS: The analysis isolated four primary features that distinguished between the two ICP groups (in order): A_{FD}, forward acceleration during diastole; α_2, angle associated with beginning Windkessel effect; τ_S, fractional time spent in systole; and α_3, the angle associated with ending Windkessel effect. The linear discriminant analysis was able to properly classify between the groups with 67% accuracy ($\chi^2_{Yates} = 23.64$, $p < 0.01$).
DISCUSSION: The Windkessel effect during reverse systole occurs because the compliant arterial tree, which dilates during forward systole, contracts and returns energy to the flow. Rising ICP lessens the extent of arterial dilation during forward systole decreases, reducing energy that can be returned to the flow during reverse systole. Loss of arterial compliance due to external pressure (ICP) also leads to narrowing and sharpening of the systolic peak. The preliminary analysis provided here indicates alterations in compliance as reflected in the Windkessel effect and shape of the systolic peak are the primary discriminating features between the two ICP groups.



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S-149.

IMPACT OF PRESERVATION SOLUTION AND ISCHEMIA TIME ON REPERFUSION INSTABILITY IN ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction
Intraoperative reperfusion instability can occur due to hepatocyte injury and accumulation of lactate, potassium or other substances during cold ischemia. Many major transplant centers have adopted histidine-tryptophan-ketoglutarate solution (HTK) in place of University of Wisconsin solution (UW) as a cost saving measure for organ preservation. This study compares immediate post-transplant transaminase values in patients receiving either HTK or UW, as an indicator of hepatocyte injury.
Methods
Indiana Organ Procurement Organization records were reviewed to determine liver preservation solution in all patients undergoing whole organ liver tranplantation between 2001 and 2006. Liver aspartate- and alanine-amino transferase (AST and ALT) levels were measured immediately post-transplant. A Mann-Whitney test was used to compare values based on preservation solution.
Results
There were 699 cadaveric, whole organ liver transplants performed at our center between 2001 and 2006; 328 received UW (47%) and 371 received HTK (53%). AST and ALT values are reported in the table. Ninety-nine livers had cold ischemia time of 10 hours or greater. There were 23 perioperative deaths, 13 UW and 10 HTK (p=NS), of which 16 had short ischemia time (<10 hrs) and 7 had longer ischemia time (p=0.03).
Conclusions
Preservation with UW resulted in significantly lower post-transplant AST and ALT values, indicating better protection from hepatocyte injury during cold ischemia. However, at prolonged cold ischemia times, the solutions did not differ in their protection against hepatocyte injury. Perioperative mortality was not influenced by preservation solution, but was influenced by duration of cold ischemia time. The anesthesiologist should be aware of organ preservation solution and cold ischemia time and how these factors may impact patient stability at reperfusion.

Post-transplant AST and ALT based on preservation solution and total cold ischemia time

	AST	p-value	ALT	p-value
OVERALL	709		486	
UW	611	0.001	421	<0.01
HTK	809		543	
< 10 hours ischemia	651	0.01	466	0.02
>= 10 hours ischemia	962		619	
UW and <10 hours ischemia	556	<0.01	353	<0.01
HTK and <10 hours ischemia	811		548	
UW and >=10 hours ischemia	935	NS	626	NS
HTK and >=10 hours ischemia	1068		566	

S-150.

MORTALITY IN ADULT PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION IS PREDICTED BY INTRAOPERATIVE TRANSFUSION OF PACKED RED BLOOD CELLS AND FRESH FROZEN PLASMA BUT NOT BY MODEL FOR END STAGE LIVER DISEASE (MELD) SCORE

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Introduction: The purpose of our study was to evaluate whether transfusion of blood products or the Model for Endstage Liver Disease (MELD) score is predictive of mortality for primary adult orthotopic liver transplantation (OLT) patients.
Methods: Retrospective chart review of all patients undergoing primary OLT at a single center between January 2004 and February 2006. Statistical analysis of intraoperative blood product administration, MELD and surival data was performed.
Results: Our institution performed 101 primary liver transplants during the period Jan 04 to Feb 06. The average number of packed red blood cells (PRBC) and fresh frozen plasma (FFP) transfused intraoperatively per case was 11.1 (median 9) and 11.3 (median 9), respectively; average MELD score was 24.8 (median 24). There were 14 deaths during 1086 patient-months of follow-up, with a mean follow-up of 10.7 months.
A significant correlation was found between mortality and intraoperative transfusion of PRBC (P=0.005) and FFP (P=0.006).
Patient mortality was unrelated to pre-transplant MELD score (P=0.97). With respect to the individual components of MELD, only pre-transplant creatinine correlated with patient mortality, but not statistically significantly so. Transfusion of both PRBC and FFP were noted to increase with increasing MELD score, but again the relationship did not reach statistical significance.
Discussion: In our series of 101 consecutive adult patients undergoing primary OLT, increasing intraoperative transfusion of either PRBC or FFP was associated with increased patient mortality. Previous work has shown that increasing red blood cell transfusion is independently associated with patient survival,[1] but no mention is made of fresh frozen plasma. Our finding of correlation between patient mortality and FFP usage is not surprising, however, as the average number of units of PRBC and FFP transfused per case was nearly identical (11.1 vs 11.3). The finding that pre-transplant MELD score showed no relationship whatsoever to patient survival was somewhat surprising, as MELD has been shown to reliably predict mortality risk in end-stage liver disease (ESLD) patients before transplantation.[2] However, other factors that can greatly influence mortality associated with OLT, such as donor organ quality, ischemic time, rejection and/or infection, are independent of pre-transplant MELD values.
Increasing MELD score being associated with increasing transfusion of PRBC and FFP was an expected finding, as MELD essentially is an index of ESLD severity,[2] and it stands to reason that a patient with more advanced liver disease would probably be more coagulopathic and therefore need more blood products. For our patients, when looking at the components of MELD and blood product usage, the strongest correlation was between International Normalized Ratio (INR) and platelets (P=0.08), while the weakest was between INR and PRBC (P=0.64).
References: 1. Arch Surg 1999; 134: 25-9
2. Hepatology 2001; 33: 464-70

S-151.

HISTADINE-TRYPTOPHAN-KETOGLUTARATE (HTK) VERSUS UNIVERSITY OF WISCONSIN(UW) SOLUTION FOR INTESTINAL AND MULTIVISCERAL GRAFTS : INTRA-OPERATIVE OBSERVATIONS

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Introduction: The University of Wisconsin (UW) solution is currently the gold standard for preservation of all of the abdominal visceral organs. Recent data showed that Histadine-Tryptophan-Ketoglutarate (HTK) solution is as effective as UW for vascular flushing and preservation of abdominal solid organs. Accordingly, a nonrandomised controlled study was initiated to compare the intra-operative hemodynamic and metabolic changes observed with each solution particularly the incidence of the Post Reperfusion Syndrome (PRS)(MAP<70% of baseline on reperfusion) among visceral allografts with intestine alone or en-bloc with liver.
Methods:After IRB approval, 51 adult patients (44 ± 8 years), 20 males and 31 females undergoing first Intestinal or multivisceral Tx were prospectively studied. They were divided into two groups: Group 1(n=22) with HTK and Group 2 (n= 29) with UW as graft preservative solution. The liver was part of the composite visceral graft in 50% and 42% of each group, respectively. The measured intra-operative 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), serum potassium (K^+), ionized calcium (Ca++), base deficit (BE), and serum lactate. Variables were measured at 60 minutes after skin incision (A), 30 seconds (B), 5 minutes (C), and 60 minutes after reperfusion (D) and end of surgery (E). Data is presented as mean ± standard deviation and group analysis is done using ANOVA.

Results: The results among each group are shown in Table 1.

Table 1: Hemodynamic and metabolic changes using HTK/UW solution during abdominal visceral Tx

Variables	Groups	A	B	C	D	E
MAP	I	77±9	59±7[a]	70±7[a]	72±5	74±8
mmHg	II	79±11	62±8[a]	72±9	68±20[a]	75±6
K^+	I	3.6±0.3	4.2±1.6[a]	3.7±0.6	3.3±0.6	3.2±0.4
mmol/l	II	3.4±0.4	4.2±1[a]	4.2±0.9[a]	3.5±0.4	3.5±0.4
Lactate	I	3.7±1.9[b]	9.4±3.7[a]	9.0±3.8[a]	9.3±3.2[a]	8.3±4.8[ab]
mmol/l	II	1.6±0.9	8.8±5[a]	8.4±4.6[a]	9.0±3.6[a]	6.8±3[a]

a=p<0.05 from baseline, b=p<0.05 between the groups

PRS with the need for administration of epinephrine boluses and/or infusion was higher among group I (90%) compared to group II (40 %). In addition, patients in group I required epinephrine support for a longer duration compared to group II.
Conclusion: Patients with HTK preserved graft demonstrated higher 1) incidence of PRS and 2) increase in serum lactate on reperfusion which persisted for longer duration possibly indicating more graft injury. Despite recent published data on HTK, UW solution is still the solution of choice for preserving Intestinal and multivisceral grafts.

S-152.

PITUITARY APOPLEXY PRECIPITATING DIABETES INSIPIDUS AFTER LIVING DONOR LIVER TRANSPLANTATION

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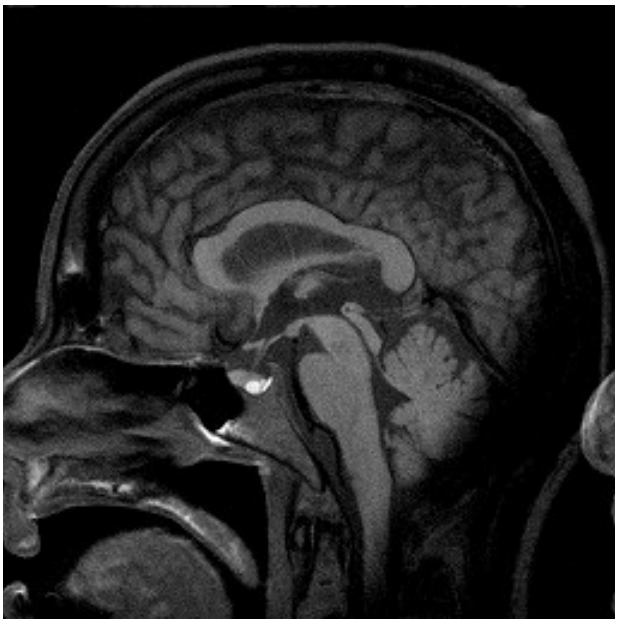
Pituitary apoplexy (PA) occurring after surgery is a rare but life-threatening acute clinical situation following extensive haemorrhage or necrosis within a pituitary adenoma. Pituitary apoplexy has been reported to occur spontaneously in the majority of cases or in association with various inducing factors. One of the pathophysiological mechanism that has been postulated is the fall of arterial blood pressure inducing ischaemia followed by infarction of the pituitary gland. We report a case of pituitary apoplexy complicated by diabetes inspidus following living donor liver transplantation. To our knowledge, this has not been previously reported. A 56-year female, who had liver transplantation from her daughter due to nonalcoholic steatohepatits, complained of severe headache, accompanied by thirst and frequent urination at postoperative 13th. She was in the absence of progressive neuro-ophthalmic signs. Her laboratory findings were significant for a serum sodium level of 150 mEq/L and urine specific gravity of <1.005. A magnetic resonance imaging (MRI) showed a haemorrhagic sellar mass. She was treated conservatively with desmopressin. In our case, intraoperative hemodynamic unstability and postoperative coagulopathy could have been the precipitating factor.



Neuroanesthesia

S-153.

IN VIVO GENE SILENCING OF PROTEIN KINASES IN THE RAT RETINA ELUCIDATES MECHANISMS OF ISCHEMIC PRECONDITIONING

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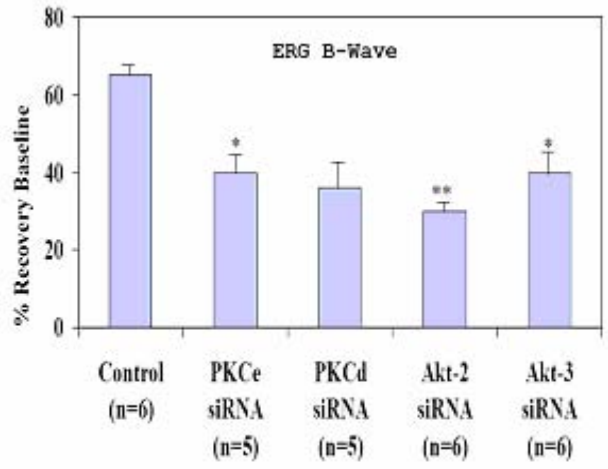
Introduction: Opening of mitochondrial K_{ATP} (mitoK_{ATP}) channels is a critical effector of retinal ischemic preconditioning (IPC)[1], an intrinsic process that robustly prevents injury after a subsequent prolonged, damaging ischemia in retina. Protein kinase C (PKCε) and PKBδ (Akt) are intracellular mediators in IPC signal transduction. We hypothesize that PKC and Akt are downstream to the opening of mitoK_{ATP} channels in IPC and with isozyme-specific actions. We focused this study upon PKC, PKC, Akt-2 and Akt-3, based upon results shown in earlier studies.
Methods: Rats were subjected to retinal ischemia 24 h after injection of diazoxide, a pharmacologic opener of the mitoK_{ATP} channel which mimics the protective effect of IPC. The experimental group was treated intra-vitreally with small-interfering RNA (siRNA) to specifically antagonize gene expression of PKCε, PKCδ, Akt-2 and Akt-3, while the control received non-silencing siRNA sequences. Electroretinography (ERG) b-wave assessed functional recovery 7 days after ischemia. Unpaired t-test was used to compare the results between the treatment and the control. The specificity of blockade was tested in cultured neuronal cells using immunocytochemistry with specific antibodies. Uptake of siRNA into the rat retina was examined *in vivo* in retinal cyrosections after injection of rhodamine-labeled siRNA.
Results: The IPC-mimicking effect of diazoxide was significantly affected by the down-regulation of PKC-ε expression, evident by the reduction ($p<0.05$) of % recovery of ERG b-wave in the experimental group compared to the control . Similar significant ($p<0.05$) reduction was found for the groups treated with siRNA inhibiting Akt-2 and Akt-3 compared to the control. A marginally significant ($p=0.065$) reduction was found for the group treated with siRNA targeting PKC-δ compared to the control. (Figure).



*: p <0.05; **: p<0.005; All comparisons were made between the protein siRNA-injected group and the control (nonsense siRNA-injected) group using unpaired t-test.

Discussion: Down-regulation of PKCε, PKCδ, Akt-2 and Akt-3 by inhibiting their expression with specific siRNA, attenuated the protection afforded by the opening of mito-K_{ATP} channels induced by diazoxide. Thus, PKC-ε, PKC-δ, Akt-2 and Akt-3 are downstream to the opening of mitochondrial K_{ATP} in retinal IPC.
References: 1. Mitochondrial potassium ATP channels and retinal ischemic preconditioning. Invest Ophthalmol Vis Sci. 2006; 47(5):2114-24.
Funding sources: National Institutes of Health Grant EY10343 (SR) and our state Society for Prevention of Blindness (SR). YS received student research fellowships from the American Academy of Neurology, American Heart Association/Stroke Council and our medical school's Office of Medical Education.

S-154.

EFFECT OF ISOFLURANE-INDUCED HYPOTENSION ON THE CEREBROSPINAL FLUID CONCENTRATION OF FREE FATTY ACIDS IN PATIENTS UNDERGOING CLIPPING OF INTRACRANIAL ANEURYSM

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Objective Recent studies showed that change in cerebrospinal fluid (CSF) level of free fatty acids (FFA) was closely related to cerebral damage. The aim of this study was to investigate whether deliberate hypotension induced by isoflurane can increase the release of FFA in CSF during clipping of intracranial aneurysm.
Methods Thirty ASA I-II patients (14 male, 16 female) aged 26-67yr undergoing elective intracranial aneurysm clipping were randomly allocated into two groups: deliberate hypotension group (group A, *n*=15) and control group (group B, *n*=15) in which BP was maintained at normal level during operation. In both groups anesthesia was induced with midazolam 0.06mg.kg^{-1}, fentanyl 3-5μg.kg^{-1}, propofol 2mg.kg^{-1} and vecuronium 0.1mg.kg^{-1} and maintained with isoflurane and intermittent intravenous (i.v.) blouses of fentanyl and vecuronium. After tracheal intubation the patients were mechanically ventilated (V_T=8-10ml.kg^{-1}, RR=12bpm, I:E=1:2). $PaCO_2$ was maintained at 35-38mmHg. In group A deliberate hypotension was induced by increasing the inhaled concentration of isoflurane until MAP was reduced by 30-40% of the baseline value. After clipping of aneurysm MAP was restored to baseline level by decrease the inhaled concentration of isoflurane. In group B, the inhaled concentration of isoflurane was in the range of 1.1%-1.3%. CSF level of FFA was measured before deliberate hypotension and 0, 2, 4hr after aneurysm clipping.

Results (1) In group A MAP was decreased from (96.36±9.38) mmHg to (61.80±3.56) mmHg 30min after deliberate hypotension was started and restored to (77.60±11.38) mmHg 30min after aneurysm was clipped. Both systemic peripheral vascular resistance and myocardial contraction acceleration were decreased but cardiac output and HR remained stable. The circulation parameters in group B had no significant changes. (2) Concentration of FFA in CSF was significantly increased in both groups, the value is from (236.38±33.08) μmol.L^{-1} to (279.25±54.19) μmol.L^{-1} ($P<0.01$) in group A, and it is from (233.90±16.92) μmol.L^{-1} to (244.97±18.55) μmol.L^{-1} ($P<0.05$) in group B. CSF level of FFA was significantly higher in group A than that in group B during the operation ($P<0.01$).
Conclusion Deliberate hypotension induced by isoflurane increases the release of FFA. The effect on perioperative cerebral protection should be studied further.

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S-155.

SEVOFLURANE ANESTHESIA DECREASES CARDIAC VAGAL ACTIVITY AND HEART RATE VARIABILITY

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Introduction: Heart rate and heart rate variability are primarily determined by cardiac vagal activity(1,2). While some studies demonstrated that vagal tone was attenuated by exercise or sevoflurane and heart rate variability decreased, others found no decrease in vagal activity with sevoflurane(3). The purpose of this study was to evaluate the role of cardiac vagal activity in modulating heart rate variability during sevoflurane anesthesia.
Method: Ten neurosurgical patients were placed with electrocardiogram (EKG) and electroencephalogram (EEG) electrodes. Power spectral analysis of the EKG was performed in 30 second intervals with 5 minute measurement periods. Heart rate entropy percentage index (PI) of heart periods was performed using Shannon's formula: $- \Sigma P(i) \log_2 P(i)$(2). Tone is the average of the PI time series with a negative number representing vagal inhibition. Non-invasive blood pressure, Response Entropy of the EEG, and end-tidal sevoflurane concentrations were recorded with the patient awake and at 1, 10, 20, 30, 40, 50, and 60 minutes of sevoflurane anesthesia.
Results Blood pressure decreased and heart rate increased 10-15% during sevoflurane anesthesia. EEG Response Entropy decreased from 98 ± 1 to 46 ± 5 and sevoflurane concentration was 1.6 ± 0.4% during 60 minutes of anesthesia. During sevoflurane, high frequency power (0.15 - 0.50 Hz) and percent heart rate entropy decreased and the decrease in these variables was significantly correlated ($r = 0.69 \pm 0.20$, $P < 0.05$, figure 1). Tone was -0.23 ± 0.17 when the patient was awake, indicating vagal dominance and decreased to -0.04 + 0.02 during sevoflurane ($P < 0.05$).
Discussion There was vagal dominance in awake patients indicated by negative tone and this was attenuated by sevoflurane. Simultaneously high frequency heart rate variability decreased. The results confirm that cardiac vagal activity is the primary determinant of heart rate variability.
References
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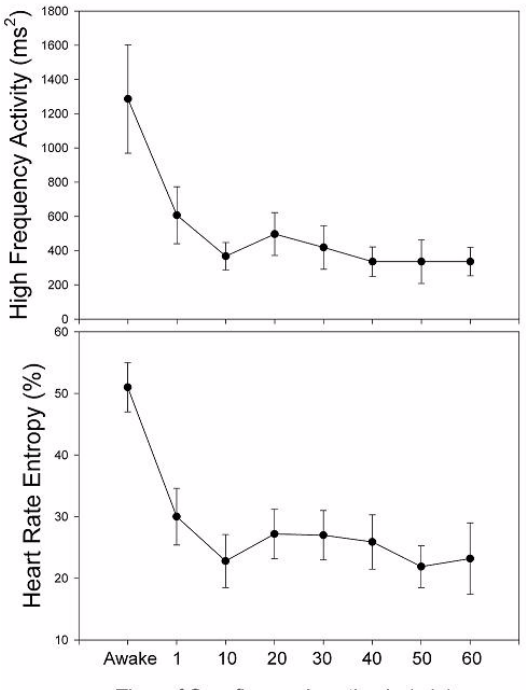
2. Oida E, Moritani T, Yamori Y. Tone-entropy analysis on cardiac recovery after dynamic exercise. J Appl Physiol 1997;82:1794-801.
3. Kanaya N, Hirata N, Kurosawa S et al. Differential effects of propofol and sevoflurane on heart rate variability. Anesthesiology 2003;98:34-40.
Figure 1. High frequency and entropy changes during awake baseline and 1-60 minutes of sevoflurane anesthesia.



S-156.

INCREASED PLASMA IL-1β LEVELS FOLLOWING HEMODILUTION IN RATS.

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Introduction: Acute hemodilution is associated with neurological injury in patients with cardiovascular disease and is best characterized in patients undergoing CPB during heart surgery (1,2). The mechanisms of injury may include cerebral tissue hypoxia, focal ischemia and inflammation. However, these mechanisms are undefined. This study assesses the systemic pro-inflammatory response to acute hemodilution by measuring plasma cytokine (TNFα, IL-1β and IL-6) levels in control and hemodiluted rats.
Methods: Isoflurane anesthetized and ventilated rats (50% O_2) underwent tail artery and vein cannulation to monitor MAP and perform hemodilution. Hemodilution was performed by simultaneously exchanging 50% of the estimated blood volume (30 $ml \cdot kg^{-1}$) with pentastarch (10 minutes).Control animals were not hemodiluted. Measurements continued for 3 hours (n=6 rats/group). Total hemoglobin concentrations (co-oximetry), ABG (Radiometer) and plasma samples were taken before and after hemodilution (Baseline, 1 and 3 hours). Animals were recovered for 18 hours and then anesthetized prior to blood sample collection for all endpoints before sacrifice. Plasma cytokines (TNFα, IL-1β and IL-6) were assessed at all time points in control and hemodiluted plasma by ELISA (Medicorp Inc.) Data was analyzed by ANOVA (mean ± SEM), with a significance of $p<0.05$.
Results: No baseline differences in physiological or biochemical data were measured. The hemoglobin concentration decreased from 134 ± 2 $g \cdot L^{-1}$ to 63 ± 3 $g \cdot L^{-1}$ ($p<0.001$). No other differences in co-oximetry or ABG data were observed between groups. TNFα levels increased in both groups (5801 ± 2058 vs. 5635 ± 1508 $pg \cdot ml^{-1}$) at 1 hour before returning to baseline levels at 3 and 18 hours. IL-1β levels increased progressively from baseline (9.0 ± 3.3 vs. 8.0 ± 5.5 $pg \cdot ml^{-1}$) at 1 and 3 hours (22.1 ± 5.4 vs. 21.6 ± 15.5 $pg \cdot ml^{-1}$), in control and hemodiluted groups. In control rats, the IL-1β levels returned to baseline by 18 hours. However, IL-1β levels remained significantly elevated in the hemodiluted rats (13.8 ± 4.8 $pg \cdot ml^{-1}$, $p<0.05$, relative to baseline and controls). There were no significant differences in IL-6 levels between groups.
Discussion: Serum TNFα and IL-1β levels were elevated early in both control and hemodiluted groups in response to the stress of anesthesia, ventilation and surgical manipulation. Serum IL-1β levels remained significantly elevated above baseline and control values in hemodiluted animals over 18hours. This sustained increase in IL-1β may contribute to inflammatory mechanisms of cerebral injury during acute hemodiluiton. Alternately, it may be a stimulus for activating cerebral homeostatic regulatory mechanisms, including HIF-1α. Defining the acute inflammatory response to acute hemodilution will help determine the mechanisms of cerebral injury in patients exposed to hemodilution in the clinical setting, such as those who undergo CPB during heart surgery (CAS, PSI support).
References: 1) Ann.Thorac.Surg. 2005; 80: 1381. 2) J Thorac Cadiovasc Surg 2003;126:1765

S-157.

RISK FACTORS AND OUTCOME OF EARLY POST-OPERATIVE REINTUBATION IN NEUROSURGICAL PATIENTS: A RETROSPECTIVE COHORT STUDY OF 5894 GENERAL ANESTHETIC ADULT NEUROSURGICAL CASES

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Introduction: Factors contributing to reintubation in spine surgery patients have been studied[1,2], however for neurosurgical patients as a group, early post-operative reintubation (EPOR) has not been as methodically addressed. We conducted a retrospective review to assess risk factors, incidence and outcomes for patients reintubated within the 24-hour period following neurosurgery.
Methods: After obtaining IRB approval, we queried the computerized medical records and IT databases of 5003 neurosurgical patients seen at Mount Sinai Hospital between the years 2000-2005, comprising 5894 general anesthetic adult neurosurgeries. Three hundred eighty-four cases were excluded because they were intubated preoperatively, reintubated greater than 24 hours after surgery, or were intubated and not extubated within a 24-hour period. Possible risk factors for reintubation included: age, gender, BMI, length of surgery, total fluids/blood products given, EBL, anesthesiologist working solo, anesthetic regimen, ASA status, emergency status, and procedure type. Outcome data included length of stay, tracheostomy, hospital discharge disposition and mortality. Univariate statistical analysis was performed using the t-test and chi-square test.
Results: The results are presented in Table I. 48.49% were male and the average age was 54.00 years. 2627 (44.57%) cases were craniotomies, while 2459 (41.72%) were spinal procedures. Fifty-seven (0.97%) cases were identified as EPOR. Of those cases that had been reintubated, outcome was statistically associated with the patient having been reintubated in the OR or within the first 24 hours of surgery outside the OR. Ninety-six (1.72%) of non-reintubated expired. Age, total RBCs, total fluids, EBL, length of surgery and anesthetic regimen were found to have significant association with EPOR.

Table 1: Descriptive Statistics

	Reintubated in OR			Reintubated < 24 hours			Reintubated in OR or <24 hours			Non-Reintubated		
	N=17			N=40			N=57			N=5837		
Age (mean ± SD)	56.63	±	13.44	59.37	±	19.17 *	58.11	±	17.80 *	53.96	±	15.72
Gender (% Male)	47.06			60.00			56.14			48.42		
BMI (mean ± SD)	27.42	±	3.39	26.11	±	4.72	26.35	±	4.42	27.72	±	5.87
Procedure Type (%)												
Craniotomy	41.18			45.00			43.86			44.58		
Spine	52.94			40.00			43.86			41.70		
Peripheral	0.00			0.00			0.00			0.87		
Other	5.88			15.00			12.28			12.85		
Length of Stay (mean ± SD)	4.64	±	5.27	26.10	±	27.99 **	20.18	±	25.84 **	7.44	±	12.34
Total RBCs (mean ± SD)	109.38	±	203.49	675.00	±	1404.40 *	505.80	±	1200.50 *	70.37	±	239.37
Total Fluids (mean ± SD)	1800.00	±	1299.74	3707.50	±	2535.81 *	3107.02	±	2418.43 *	2296.97	±	1588.86
Length of Surgery (mean ± SD)	2.26	±	1.13	4.89	±	3.54 **	4.10	±	3.27 *	2.84	±	1.92
EBL (mean ± SD)	131.25	±	174.28	960.63	±	1622.03 *	710.96	±	1410.67 *	312.38	±	452.63
Disposition (%)												
Expired	0.00			25.00		**	18.18		**	1.72		
Expired or Chronic Care Facility	0.00			42.50		**	30.91		**	6.80		
Trached (%)	0.00			15.00		**	10.53		**	0.74		

* p<0.05, ** p<0.001

Discussion: EPOR for neurosurgical patients is a rare event at our institution. For cases reintubated within the operating room, there was zero mortality, zero chronic care discharges, and zero tracheostomies; length of stay was not increased either. This is in marked distinction to the 25% mortality, 17.5% chronic care discharges, 15% tracheostomy rate and 350% increase in length of stay for EPOR outside the OR. While factors contributing to EPOR are multi-factorial, this study highlights that anesthesiologists must be meticulous in the assessment of recently-extubated neurosurgical patients prior to transfer from the operating room.
References:
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2. Canadian Journal of Anesthesia 1999;46:7-14.

S-158.

THE CHANGING FACE OF SPINAL FUSION SURGERY: ANALYSIS OF THE NATIONAL INPATIENT SAMPLE (NIS) DATABASE

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Introduction: Anesthesia for spinal fusion (SF) surgery requires careful management of positioning, fluids, anesthetic depth, blood pressure, among other factors. SF is one of the most rapidly increasing forms of inpatient surgery in the U.S. (1). Epidemiological data, however, do not demonstrate an increasing rate of spinal disorders (2). One possibility for this discrepancy is that elderly and medically complicated patients now more frequently undergo these procedures. If so, postoperative complications, potentially related to anesthesia, would also be expected to increase. To examine this possibility, we studied SF surgery in the National Inpatient Sample (NIS) database (3).
Methods: Data collection methods for the NIS (> 37,000,000 hospital discharges) are at ahrq.gov. Our IRB approved this study as "exempt." We compared spinal fusion (SF) to the less complex laminectomy/disc excision (LAM) for 1993-2004. Number of discharges, length of stay, hospital charges, and in-hospital mortality were compared between the procedures using the Z-test for proportions, with $P < 0.05$ considered signficant. Using data from 4 individual years (1997, 2000, 2002, and 2004), we examined the relationship between in-hospital deaths associated with SF procedures and age, insurance carrier (commercial, medicaid, medicare), hospital size, and teaching affiliation.
Results: From 1993 to 2004, LAM declined 30% (353,291 to 241,782), and SF increased 400% (60,972 to 303,374). Mean total charges for both nearly doubled while mean hospital stay significantly decreased ($24,045 to 53,290 and 7.7 to 4.1 d for SF, and $11,477 to 20,806 and 4.6 to 2.8 d for LAM). In-hospital mortality declined significantly for SF from 0.68% in '93 to 0.26% in '04, but mortality remained higher for each year examined for SF. The proportion of SF patients who were > 65 y of age or on Medicare increased significantly. Although yearly mortality did not increase over time in the 65-84 y old SF population, this group represented a larger proportion of in-hospital deaths than any other age group (3.6% in 2002 and 5.2% in 2004) In the 4 individual years studied, higher in-hospital mortality was associated with: Medicare status, age > 65, male gender, and surgery in a teaching or larger hospital.

Discussion: Anesthesiologists should expect to encounter spinal fusion surgery with increasing frequency. Elderly patients are at greater risk of death after the surgery possibly due to higher medical co-morbidity or the need to undergo more complex surgery. As with cardiac surgery, the higher mortality in larger or teaching hospitals may represent treatment of more complex patients (4). Outcome studies related to medical co-morbidity and surgical and anesthetic factors are needed in the SF population.
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3. http://www.hcup-us.ahrq.gov/nisoverview.jsp
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S-159.

FEASIBILITY OF PUPILLOMETRY AND RETINAL DIGITAL PHOTOGRAPHY DURING HIGH DOSE REMIFENTANIL INFUSION FOR PRONE SPINE SURGERY

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Introduction: The physiologic cascade leading to postoperative visual loss is largely unknown. Herein we describe two recent innovations that allow real-time measurement during prone spinal surgery that should contribute to physiologic modeling of optic nerve ischemia.
Methods: Following a 5 hour study of healthy volunteers, we continue to prospectively enroll major spine surgery patients in a study using the modified Dupaco "Proneview" helmet system frame which (1) affords access to the eyes from beneath the Jackson table in the prone position. Intraoperative hourly measurements included intraocular pressure (IOP) (Medtronic TonoPen XL) with contact lens, dilated (tropicamide 1%) retinal digital photography (RDP) (Nidex NM200), and light flash evoked pupillometry (LFEP) (NeurOptics).
Results: A 32 yo female (163 cm, 71 kg), requiring L3-S1 re-instrumentation, underwent induction with midazolam, fentanyl, lidocaine and propofol followed by cisastracurium. Maintenance anesthesia consisted of remifentanil (0.05-0.16 mcg/kg/min) and cisastracurium (1.5 mcg/kg/min) infusions with isoflurane (0.5-0.8% ET). The patient remained hemodynamically stable, requiring 5.1L crystalloid and 500 ml albumin with EBL of 1.6L and 400 cell saver return over the 6:30 hr duration of surgery. IOP rose steadily from 9 (supine, anesthetized initial) to 22 (prone, anesthetized final). RDP produced clear retinal images until hour 4 when the ocular refractive power exceeded the camera's dioptric refractive correction. LFEP latencies and amplitudes (degree of pupillary constriction following standardized light flash) remained stable throughout (Fig.1)

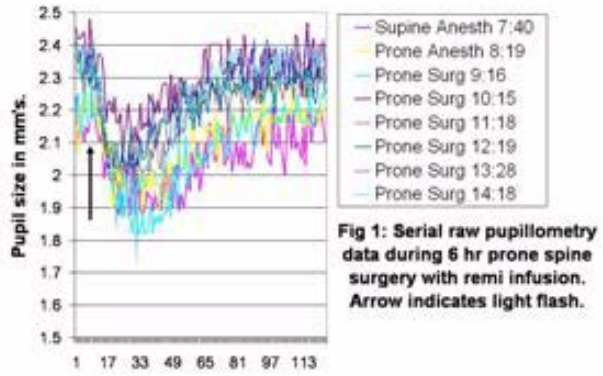

Fig 1: Serial raw pupillometry data during 6 hr prone spine surgery with remi infusion. Arrow indicates light flash.

Discussion: The modified headpiece allows real time measurement of prone, intraoperative IOP, RDP and LFEP. LFEP is feasible despite miosis induced by remifentanil infusion. LFEP provides a noninvasive method to monitor optic nerve function during prone surgery, and has the potential to signal ischemia through latency and amplitude changes. The profound intraoperative refractive changes that were also seen to a lesser extent in a prolonged study of prone volunteers requires further characterization.
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1. AnesthAnalg, 103(2):499, 2006.

S-160.

GOGGLES AND FOAM HEADRESTS: ANOTHER HAZARD IN PRONE-POSITIONED SPINE SURGERY PATIENTS

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AFFILIATION: University of Chicago, Chicago, IL.

Introduction: Eyes should be protected from injury during anesthesia, which includes, most commonly, corneal abrasion, but the most serious risk in the prone position is blindness. Some advocate eye goggles to prevent these injuries. However, goggles may be associated with their own set of risks. We report here on cases of eye injury due to use of goggles in patients who underwent prone position spine surgery.
Methods: A 53 year old man positioned prone on an Andrews frame underwent an L3-L4 posterior lumbar interbody fusion with Dupaco Opti-Gard goggles over the eyes. His head was in an OSI Gentle-touch foam headrest. Six hours postoperatively, he had a corneal abrasion over 70% of the surface of the left eye, prominent ciliary injection, no light perception and a non-reactive pupil, a pale retina, blood in the vitreous, and a cherry-red spot in the macula. The right eye was normal. A U-shaped abrasion was present over the left superior eyelid. Central retinal artery occlusion was confirmed by flourescent angiography. He subsequently developed optic disc pallor and never regained vision. This case was reported by the hospital's risk manager to FDA Medwatch. We reviewed the FDA Medwatch database for Adverse Event Reporting, covering the time from 1982 to present. Including this case, there are four reports of eye injury from the Opti-Gards.
Results: In all cases, patients were positioned prone with their faces in a foam headrest. The least serious injuries included post-operative keloid scarring from suspected pressure of the Opti-Gard on the side of the nose, and another with a superficial linear abrasion on the right upper cheek. In addition to the blindness sustained by the above patient, another sustained eyelid abrasions, and neurpraxia of the supraorbital nerve due to suspected pressure of the goggles on the supraorbital notch from which the nerve exits. Depending upon the patient's facial structure, there could be as little as 1 cm or less clearance between the clear plastic lens of the device positioned over the eyes and the opening for the eyes in the foam of the OSI Gentle-Touch. The lens could be deformed by downward pressure.

Discussion: According to Dupaco, Opti-Gards were designed to prevent damage due to corneal abrasion from drying of the eyes or from foreign body or other unintended materials contacting the eye during surgery. Because of these reports of serious injury including nerve damage and blindness, before using the Opti-Gards in prone-positioned patients on foam headrests, anesthesia providers should weigh the risks of using them against the suspected small gains in patient safety. We believe that taping the eyes and intermittent palpation of them during anesthesia, without use of goggles, is adequate for protecting eyes from injury intraoperatively.

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S-161.

ARE INTERMITTENT EPIDURAL INJECTIONS PROTECTIVE AGAINST EPIDURAL INTRAPARTUM FEVER?

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Introduction: Labor epidural analgesia (LEA) may be associated with maternal intrapartum fever. The mechanisms are thought to be physiological, partly from loss of sweating in the lower half of the body [1,2]. Most studies reporting the fever were in parturients who received continuous epidural infusions. We hypothesized that *intermittent* injections might be protective, because they may allow intermittent recovery of the sympathetic blockade and sweating mechanisms.
Methods: IRB approval was obtained. Healthy nulliparous women in spontaneous labor at term with a singleton fetus in vertex presentation were randomly assigned to one of two groups- Continuous LEA (CLEA) and Intermittent LEA (ILEA), 46 in each group. In both groups, epidural analgesia was established with fentanyl 100 ugm, and 8 ml of either 0.125% bupivacaine or 0.1% ropivacaine. Maintenance in the CLEA group was with a continuous infusion of either 0.125% bupivacaine plus 0.0002% fentanyl or 0.1% ropivacaine plus 0.0002% fentanyl, at 10-12 ml/hr. In the ILEA group, bolus doses of 10-15 ml of one of the above solutions were given at first maternal request for more analgesia. In both groups, additional rescue medications of the anesthesiologists' choice were given for breakthrough pain. A T-8 to T-10 level was desired. Maternal tympanic temperature was checked at the time of catheter insertion, and then at 4-hourly intervals until 4 hours post-partum. Fever was defined as temperature ≥ 38 ^{0} C. *Statistics*: Student's *t* test and chi-square were used as appropriate. A *p* value of < 0.05 was considered statistically significant.
Results: Three subjects in the ILEA group dropped out of the study before it was completed. There was no difference between the two groups in demographic data, baseline cervical dilatation and baseline temperature. The overall incidence of intrapartum fever in the CLEA group was 14/46 (30.4%), and in the ILEA group, 11/43 (25.6 %) (Table). There was, however, a significantly lower incidence of fever in the ILEA group at the 4-hour time point.

Time from Epidural insert	CLEA		ILEA		*P* value
	Fever	n	Fever	n	
4 hours	9	40	2	39	0.047
8 hours	7	23	7	21	0.91
Delivery	4	24	6	23	0.67
Any time intrapartum	14	46	11	43	0.79
4 hrs post partum	3	46	2	43	0.94

Discussion: Our study shows that intermittent labor epidural injections may be protective against intrapartum fever at 4 hours but not later in labor. The reasons for this are not clear.
References: 1. *Lancet*. 1989. 1: 1250-1252 2. *Anesthesiology* 1999. 90 (5) 1271-1275.

S-162.

LABOR OUTCOME WITH INTERMITTENT VS CONTINUOUS LABOR EPIDURAL ANALGESIA

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Introduction: Labor epidural analgesia (LEA) may be associated with more instrumental/operative deliveries and prolonged second stage of labor. Studies that compared continuous with intermittent epidural medications did not see any difference in the above parameters [1-3]. Here we report our findings of a study that compared continuous with intermittent LEA.
Methods: This was part of another study that compared the effects of continuous and intermittent LEA, on epidural fever. IRB approval was obtained. Healthy nulliparous women in spontaneous labor at term with singleton fetus in vertex presentation were randomly assigned to one of two groups- Continuous LEA (CLEA) and Intermittent LEA (ILEA), 46 in each. In both groups, epidural analgesia was established with fentanyl 100 ugm plus 8 ml of either 0.125% bupivacaine or 0.1% ropivacaine. Maintenance in the CLEA group was with 0.125% bupivacaine plus 0.0002% fentanyl or 0.1% ropivacaine plus 0.0002% fentanyl, at 10-12 ml/hr. In the ILEA group, bolus doses of 10-15 ml of one of the above solutions were given at first maternal request for more analgesia. In both groups, pain relief and a T-8 to T-10 level were aimed for. Additional rescue medications were given for breakthrough pain. *Statistics*: Student's *t* test and chi-square were used as appropriate. A *p* value of < 0.05 was considered statistically significant.
Results: Three subjects in the ILEA group dropped out of the study before it was completed. There was no difference between the two groups in demographic data and baseline cervical dilatation. The other results are given in the table. When considering instrumental/operative delivery, only cases that were secondary to dystocia (excluding fetal distress) were considered for analysis. We found that instrumental/operative delivery, and duration of second stage were significantly higher with CLEA compared to ILEA.

	CLEA Mean ± 1 SD where applicable	Valid n =	ILEA Mean ± 1 SD where applicable	Valid n =	p value
AROM	30	46	29	43	1.0
Oxytocin augmentation	32	46	37	43	0.11
Instrumental/operative delivery	15	41	4	41	0.009
Instrumental delivery	5	41	1	41	0.20
C/Section	10	41	3	41	0.070
ROM to "Complete" (min)	369.5 ± 267.2	38	404.2 ± 260.6	39	0.57
"Complete" to del (min)	133.1 ± 91.83	39	79.9 ± 64.8	40	0.004
Epidural to "Complete" (min)	289.8 ± 158.1	39	299.7 ± 167.8	40	0.83
Epidural to delivery (min)	426 ± 187	46	393 ± 199	43	0.42

Discussion: Our findings differ from the studies quoted below. This may be from a higher concentration of bupivacaine used (0.25%) in the intermittent group [2], or the methodology (retrospective study and definition of prolonged second stage > 3 hours [1], or combined spinal-epidural analgesia) [3]. The findings in our study might be because of ineffective pushing in CLEA group secondary to continuous perineal analgesia and decreased pelvic floor tone.
References: 1. Int J Obstet Anesth. 2003;12(1)9-11
2. Obstet Gynecol 2005;106(2)301-6
3. Anesth Analg 2006; 102: 904-9.

S-163.

THE EFFECT OF INTUBATION TECHNIQUE ON CORD GASES

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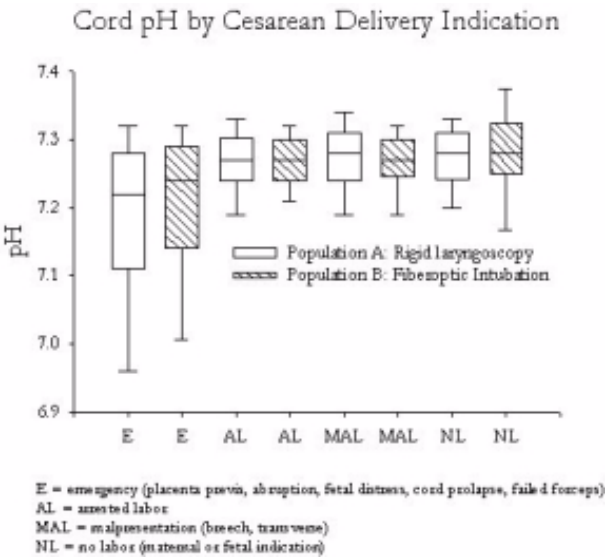
Introduction: Raising gastric pH with drugs is an accepted form of prophylaxis against aspiration pneumonitis. However, difficult intubation during general anesthesia for cesarean section accounts for the majority of aspirations. Would pre-emptive sedated fiberoptic intubation of the parturient decrease the incidence of failed intubation and aspiration without increasing fetal acidosis?
Methods: We searched the years 1974 through 2005 with our IRB approved obstetrical database for: (1) intubation technique of rigid rapid sequence or flexible fiberoptic (2) umbilical artery pH (3) cases of gastric aspiration. Since 1984, parturients with difficult appearing airways (hypoplastic mandible, limited mouth opening, enlarged tongue, or swollen oropharynx) were intubated with a fiberoptic prior to induction of general anesthesia.
Results: From 1974 - 1983, the incidence of failed intubation was 10/2000, there were six cases of aspiration confirmed by chest x-ray. After 1984, failed intubation fell to 1/2500, there were no aspirations. When analyzed by indication for c-section, there was no difference in cord gases between rapid sequence and fiberoptic groups (see figure).
Discussion: Using only a Mallampati score rather than a comprehensive airway exam would provide a sensitivity of 90% at a false positive rate of 60%[1]. We achieved a sensitivity of 90% with a fiberoptic rate of 14% (350/2500).
Reference: 1. Anesthesiology 103; 429, 2005.



S-164.

ANAESTHESIA FOR CAESAREAN SECTION IN A UNIVERSITY HOSPITAL IN GERMANY FROM 1999 - 2004

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Introduction
WHO estimates that 529,000 women die each year from complications of pregnancy or child-birth. This amounts to more than one death per minute. Fourteen percent of live births but less than 1% of maternal deaths take place in developed countries while 99% of all maternal deaths occur in developing countries[1]. The number of deaths due to anaesthesia has decreased in developed countries largely because of improved methods, monitoring and the emergence of consultant-led obstetric anaesthesia subspecialty. With the decline in the number of anaesthesia related maternal deaths in developed countries as reported in the CEMD and by various centres maternal mortality data offer fewer opportunities for directing further improvement in obstetric care[2,,3]. Useful alternative indicators might be severe morbidity, critical-incident reporting of near misses, or severe maternal morbidity-mortality ratio.
The purposes of this study are aimed at determining the effect of choice of anaesthetic technique on maternal morbidity and their relationship to anaesthetic management.
Methods
The anaesthetic charts of all obstetric patients who had a caesarean section in the University hospital of Goettingen Germany during the period June 1, 1999 to May 31, 2004 were reviewed. Data were also assessed from the surgical records for caesarean section from the same institution. Data obtained were compared with those from the total statistics for deliveries from Lower Saxomy and German Federal statistics office.
Results
During the period under review, a total of 4,453 births occurred in the hospital. Caesarean section accounted for 1,418 deliveries giving a caesarean section rate of 31.8%. Regional anaesthesia was performed in 618 (43.6 %) cases and 800 (56.4 %) patients had general anaesthesia. General anaesthesia was the commonest technique employed for caesarean section. Anaesthesia did not result in any mortality.
Conclusion
General anaesthesia in obstetric anaesthesia continues to be required in extreme emergencies and where there are contraindications for regional technique. The declining use of GA in obstetrics may leads to relative lack of experience in this technique by trainee anaesthetist. Safety of GA in obstetrics can be improved by teaching of obstetric anaesthetic and improved assistance for trainee anaesthetist.
References
1.Maternal Mortality in 2000: World Health Organization, 2004.
2.Curr Opin Anaesthesiol 1999; 12:277-281.
3.Br J Anaesth 2002; 89:499-508.

S-165.

A COMBINED SPINAL EPIDURAL NEEDLE REDUCES THE INCIDENCE OF POST DURAL PUNCTURE HEADACHE FOR CAESAREAN SECTION

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Introduction : Spinal anesthesia is one of the useful and typical anesthetic methods for Caesarean section. In addition to spinal anesthesia, epidural anesthesia could be a useful method for postoperative analgesia. There are two methods typically used for both spinal and epidural anesthesia. One is the needle-through-needle single interspace method, and the other is the double-needle separate-interspace method. At present, there is a high incidence of post dural puncture headache (PDPH) reported among young females. This study retrospectively examined the incidence of PDPH after these two combined spinal epidural anesthesia methods for Caesarean section.
Methods: The subjects were two hundred and thirty-four patients who underwent Caesarean section in our institution between 2003 and 2005. These two hundred and thirty-four subjects underwent surgery under combined spinal epidural anesthesia. The subjects were divided into two groups : A CSE-1 group (26 patients) and a CSE-2 group (208 patients). The CSE-1 group received anesthesia by the needle-through-needle single interspace method with a Combined Spinal Epidural needle (27 gauge pencil point type spinal needle and 16 gauge epidural needle), and the CSE-2 group received anesthesia by the double-needle separate-interspace method with a 25 gauge Quinke type spinal needle and 17 gauge epidural needle. We compared the incidence of PDPH between the two groups. Significance was assessed by two-sample t-test. $P < 0.05$ was considered significant.
Results: There was no significant difference between the backgrounds of the two groups. PDPH occurred in 8.5% of CSE-2 group, but none of the CSE-1 group developed PDPH. The difference between the two groups was significant ($p<0.05$).
Conclusions: These findings suggest that a CSE needle which is available as a 27 gauge pencil point type spinal needle reduces the incidence of PDPH compared to that after the double-needle separate-interspace method.

S-166.

ACUTE FATTY LIVER OF PREGNANCY: CLINICAL PRESENTATION, COMPLICATIONS AND OUTCOME.

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Introduction: Acute fatty liver of pregnancy (AFLP) is a rare but potentially fatal complication of the third trimester of pregnancy. The aim of this study was to determine clinical presentation, biochemical findings, complications and the maternal - perinatal outcomes in patients who were diagnosed with AFLP.
Methods: Retrospective study over a period of nine years (1996 - 2005). Records were reviewed for presenting symptoms, laboratory findings, complications and maternal and perinatal outcomes.
Results: Nine cases of AFLP were identified; the mean age was 26.4 $\pm$ 7.7 years and gestational age 35.3 $\pm$ 4.1 weeks. Six patients (66%) were primigravid. In 7 patients (78 %) AFLP presents with a prodrome of malaise, nausea and vomiting, followed by jaundice within about a week, epigastric pain and pruritis occurred in 5 patients (56%). All patients had hypoalbuminemia (27 -56 g/L) and raised transaminases and serum bilirubin (36 - 281 µmol/l), hypoglycaemia (< 3 mmol/l) was founded in 3 patients (33%), hypofibrinogenemia (< 1 g/l) in 5 patients (56%) and prolonged prothrombin time in 7 patients (78%).
The most common maternal complication was: renal insufficiency (n=6; 66%), disseminated intravascular coagulation (n = 5; 56%), ascites (n = 4; 45%), preeclampsia (n = 4; 45%), hemorrhage (n = 3; 33%), hepatic encephalopathy (n = 2; 22%) and one patient had seizure (11%). All our patients required blood or blood products. Emergency cesarean section was performed in 5 patients (56%). Diagnosis was confirmed by liver biopsy in 8 patients (89 % one of them in post-mortum). There were two (22%) maternal deaths and three (33%) fetal deaths.
Discussion: Patients with persistent nausea, vomiting, or epigastric pain in the third trimester must receive evaluation of liver enzymes, renal function, and a complete blood count to rule out the diagnosis of AFLP. Otherwise, the treatment consists of early termination of pregnancy and aggressive supportive care with blood component therapy.

S-167.

LOW DOSE INFUSION OF DEXMEDETOMIDINE IS EFFECTIVE AND SAFE FOR POSTOPERATIVE GYNECOLOGICAL PATIENTS EVEN IN GENERAL WARDS - NOVEL DEX INFUSION METHODS -

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Introduction: Dexmedetomidine (DEX) has both sedative and analgesic effects with less respiratory depression and so it is quite useful especially for postoperative care in intensive care patients. However, loading dose of DEX sometimes causes excessive hypertension or bradycardia and high dose of DEX causes hypotension, then shows difficulties to use in general ward. Accordingly we hypothesized that giving DEX with low dose infusion method would provide adequate and safe postoperative pain management in the general ward.
Method: With IRB approval, 15 gynecological patients were randomly and double-blindly allocated into three groups: placebo (n=5), DEX-1 (0.3-0.4 μg/kg/hr infusion only, n=5) and DEX-2 (initial 1 hour 0.8 μg/kg/hr lording and then 0.3-0.4 μg/kg/hr infusion, n=5). Anesthesia was induced and maintained with propofol TCI and fentanyl with the off-line pK calculation method. During anesthesia, propofol was titrated to maintain BIS at approximately 50 and fentanyl was titrated to maintain BP and HR within 20% of baseline values. At the end of surgery, fentanyl infusion was set to achieve a simulated effect-site concentration of 1.5-2 ng/mL. Once the patient was extubated, we started an IV DEX infusion with the Syrinjector® infusion pump (Daiken Co. LTD., Osaka, Japan). The patients remained on the Syrinjector® for 20 hours. We measured NIBP, HR, and SpO2; we also recorded verbal rating scale (VRS) for pain and Ramsay Scale score for sedation at every 30 min after extubation till 2hr in PACU and every 3 hr thereafter in general ward. Also we evaluated incidence postoperative nausea and vomiting (PONV) and the total amount of analgesics and sedatives given until 20 hours postoperatively. We used repeated measures ANOVA and Turkey post hoc test with a 0.05 two-sided significance level.
Results: Demographic and morphometric data were similar in the groups, and there were no significant side effects with homodynamic and any others. Patients were given IV NSAID, IV pentazosine, IV hydroxyzine, or rectal NSAID for supplementary pain treatment as necessary. The total dose of drug was significantly less in the DEX-2 group than in the DEX-1 group and placebo group. Mean VRS for pain was significantly less in the both DEX group compared with placebo groups.
Discussion and Conclusion: Dexmedetomidine was effective and safe for postoperative pain management after gynecological surgery in the general ward at low dose infusion regimen 0.3-0.4 μg/kg/hr. Furthermore initial 1 hour 0.8 μg/kg/hr lording and then 0.3-0.4 μg/kg/hr infusion method could provide more adequate sedation and analgesia without any homodynamic instability for 20 hours after surgery using the Syrinjector®. This infusion method, thus, appears to be an economical and safe way to infuse dexmedetomidine in the general ward.

S-168.

PULMONARY DISORDERS DURING PREGNANCY: INCIDENCE, ETIOLOGY AND OUTCOME.

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Introduction: During pregnancy respiratory system undergoes changes and is subject to additional functional and anatomic stresses. Pathophysiologic processes may result in significant ventilatory compromise, adversely affecting maternal and foetal oxygenation [1].
Methods: We conducted a prospective study over 5 years (July 2000 to June 2005) involving 116 women with pulmonary disorders in pregnancy (PDIP). These patients were selected among 389 obstetrical patients admitted in our Intensive Care Unit (ICU). The diagnosis of pulmonary disorder was made on the basis of clinical data, arterial blood gas, and/or a pulmonary artery monitoring wedge pressure of at least 18 mmHg, findings that were confirmed by chest X-ray or CT-angiography.
Results: PDIP incidence in our series was 29.8%. Thirty seven percent of our patient were primigestous, 41% were primiparous, and 58% were multiparous. Matrenal age average was 32 years (19 to 44). Eighty percent of women underwent caesarean section; spontaneous delivery was observed in 17% and 32% were instrumentally delivered. Pre-existing medical consists of cardiovascular diseases (n=14; 12%), thromboembolic events (n=2; 1.7%), asthma (n=3; 2.5%), hypothyroidism (n=1; 0.8%) and diabetes (n=1; 0.8%). PDIP was attributes to eclampsia (55%), to obstetrical sepsis (19%) and to haemorrhage (26%). Eighty nine percent of patients required mechanical ventilation. Global maternal mortality was 14%. Causes of death was septic shock (n=5), intracerebral haemorrhage (n=3), cardiogenic shock (n=3) and pulmonary embolism (n=1) and inhalation syndrome (n=5).
Discussion: PDIP is a serious complication. Patient at risk should be delivered in appropriate conditions. Close collaboration between obstetrics and ICU department may improve prognosis of such patients.
Reference:
[1] Graves CR. Acute pulmonary complications during pregnancy. Clin Obstet Gynecol. 2002 Jun; 45(2):369-76.

Pain - Basic Science

S-169.

MINOCYCLINE DOES NOT REDUCE HYPERALGESIA IN A RAT PLANTAR INCISION PAIN MODEL

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Introduction: The antibiotic derivative minocycline hydrochloride crosses the blood brain barrier and is a potent inhibitor of microglial activation (Tikka et al , J Neurosci 2001;21:2580). Minocycline 40 mg/kg intraperitoneal (IP), given 60 min before surgery and continued daily, produced a decrease in the development of mechanical hyperalgesia in rats with L5 spinal nerve transection (Raghavendra et al, JPET 2003;306:624). Minocycline 90 mg/kg IP, given 30 min before injection of the inflammatory irritant carrageenan into the rat hindpaw, produced a decrease in the development of paw edema equivalent to that produced by 30 mg/kg ibuprofen (Cornet et al, Eur J Pharm 2004;505:111). Our study examines whether a single preemptive dose of minocycline can reduce mechanical and thermal hyperalgesia in a rat model of postoperative pain.
Methods: Following IACUC approval, male Sprague-Dawley rats (n=12) were tested for baseline mechanical sensitivity of the plantar hindpaw with calibrated von Frey filaments using the iterative up-down method (Chaplan et al., J Neurosci Meth 1994;53:55) and thermal sensitivity using the light-bulb hindlimb withdrawal test (Hargreaves, Pain 1988;32:77). Subsequently, minocycline hydrochloride 40 mg/kg (n=6) or water vehicle (n=6) was administered IP (0.5 mL) 60 min before incision. Under isoflurane anesthesia, a right plantar foot incision (Brennan model) was performed (Pain 1996;64:493). Animals were reassessed for mechanical and thermal hypersensitivity at 3 h, and 1, 2, and 5 days post-incision, and the minocycline and vehicle groups were compared with repeated measures analysis of variance.
Results: There was no difference in postoperative mechanical or thermal hypersensitivity in the minocycline treated animals compared to vehicle controls. Presurgery, the mechanical force thresholds were 15 g (cutoff) in all rats. At 3 h postsurgery, the force threshold was 4.53 ± 0.99 g in minocycline rats versus 5.98 ± 1.12 g in control injected rats. At 2 days, the force threshold was 5.85 ± 1.24 g in minocycline rats versus 5.22 ± 1.67 g in control injected rats. Presurgery, the right hindlimb withdrawal latency was 12.46 ± 0.26 sec in minocycline rats versus 12.14 ± 0.27 sec in control injected rats. At 3 h postsurgery, the latency was 3.55 ± 0.65 sec in minocycline rats versus 3.97 ± 0.82 sec in control injected rats. At 2 days, the latency was 4.48 ± 0.92 sec in minocycline rats versus 4.20 ± 0.29 sec in control injected rats.
Discussion: Unlike minocycline reducing mechanical allodynia and thermal hyperalgesia in the L5 spinal nerve transection model, preoperative minocycline 40 mg/kg did not influence pain development in the plantar foot incision model. Although higher doses of minocycline or multiple postsurgical injections could potentially influence hypersensitivity, it appears that microglial activation is not a critical element in initiating postoperative pain.

S-170.

NEUROIMAGING EVIDENCE FOR SUBJECTIVE ANALGESIC EFFECTS OF OPIOIDS AND IMMERSIVE VIRTUAL REALITY DISTRACTION.

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Introduction: The experience of acute pain following nociceptive stimulation is complex, modifiable, and commonly managed with both pharmacologic (e.g., opioid) and non-pharmacologic (e.g., cognitive distraction) techniques. Immersive virtual reality (VR) is a novel and effective form of distraction analgesia for mild/moderate pain, yet its effects on subjective and neuroimaging responses to pain, compared to opioids, are unknown. We used functional magnetic resonance imaging (fMRI) to assess and compare both pain-related brain activity and subjective pain ratings in subjects receiving opioid, VR distraction, or both.
Methods: Healthy subjects (n=9) received thermal pain stimulation to the dorsum of their right foot on two separate study days while in a 1.5T MRI system. On each study day, subjects were exposed to two intervention conditions (total of four intervention conditions) in a within-subjects design. Conditions included opioid administration (target-controlled hydromorphone infusion [plasma level of 4 ng/ml]) and/or distraction with immersive VR (3-D visual and integrated sound effects with user-environment interaction via trackball in the SnowWorld virtual environment). Specific conditions were (1) no opioid/no VR, (2) VR only, (3) opioid only, and (4) combined VR + opioid. In each condition subjects received three 30-sec pain stimulations alternating with three 30-sec rest periods. Outcomes included (1) subjective pain reports (0-10 labeled graphic rating scales) and (2) blood oxygen level dependent (BOLD) assessments of pain-related brain activity in five specific regions of interest (anterior cingulate cortex [ACC], insula, thalamus, and the somatosensory cortices [SS1, SS2]). A 2x2 factorial design, linear statistical model was used to analyze the subjective pain score and fMRI (z-score) results.
Results: Opioid or VR alone each reduced subjective pain ratings, while their combined use showed an additive analgesic effect. Patterns of BOLD activity in the insula, thalamus, and SS2 were consistent with subjective analgesic reports (see table summary).

Subjective and Neuroimaging Pain Outcomes (SD) *p<.05

OUTCOME (0-10 GRS or trans-formed z-score)	No opioid/ No VR	VR only	Opioid only	Combined VR + opioid
Worst Pain	8.3 (0.8)	5.9 (2.2) *	7.7 (1.9)	4.5 (1.9) *
Pain Unpleasantness	8.6 (0.5)	5.3 (2.2) *	7.2 (1.6) *	4.0 (2.0) *
Time Spent Thinking About Pain	8.7 (1.2)	4.6 (2.5) *	7.8 (1.8)	3.8 (1.7) *
ACC	3.2 (2.2)	1.6 (2.0)	2.1 (2.8)	0.7 (1.6) *
insula	5.8 (1.1)	3.7 (2.3) *	3.6 (1.9) *	3.0 (1.9) *
thalamus	4.8 (2.0)	2.6 (2.5) *	2.0 (1.7) *	0.6 (1.1) *
SS1	3.5 (2.6)	2.9 (2.9)	3.1 (2.3)	2.5 (2.1)
SS2	4.3 (2.1)	2.1 (2.2) *	2.6 (1.8)	1.0 (2.0) *

Discussion: These results provide neuroanatomic evidence supporting the comparative analgesic effects of opioid and VR distraction analgesia. When both are applied concurrently, the resulting reductions in both subjective pain scores and BOLD activity appear additive and not interactive. This result suggests that the analgesic actions of opioid and VR distraction are independent and unrelated. In addition, these results provide preliminary data to justify the clinical use of multimodal (e.g., combined pharmacologic and nonpharmacologic) analgesic therapies.
Funding: Supported in part by the IARS 2006 Clinical Scholar Research Award.

S-171.

NICORANDIL, A K^+_{ATP} CHANNEL OPENER, INHIBITS MUSCARNIC ACTIVATION OF EXTRACELLULAR SIGNAL-REGULATED KINASES (ERK) IN PC12 CELLS

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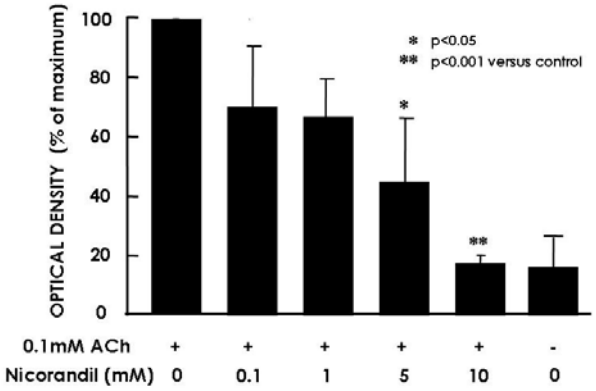
Introduction: Mitogen-activated protein kinases (MAPKs) family plays roles in regulating cell growth, differentiation, and synaptic plasticity. Extracellular signal-regulated kinases (ERK) activation has shown in dorsal root ganglion (DRG) and spinal neurons after noxious stimulation. In the central nervous systems, intracellular and extracellular movement of potassium ions plays an important role in regulating neuronal excitability and the release of neurotransmitters. Nicorandil, an adenosine triphosphate-sensitive potasium (K^+_{ATP}) channel opener, is reported to have an antinociceptive effect by hyperpolarization through K^+ channel, but the mechanisms are not clearly understood. We investigate the effects of nicorandil on muscarnic acetylcholine (ACh) receptor-mediated activation of ERK in rat pheocromocytoma PC12 cells, the model of neurons.
Methods: Using PC12 cells, we studied the effects of nicorandil on ACh-induced ERK activation by Western blot analysis. We also examined the effects of nicorandil on intracellular stimulants-induced ERK activation, such as fluoroalminate (AlF_4^-), the activator of G proteins, 4β-phorbol 12-myristate 13-acetate (PMA), the activator of PKC, or ionomycin, a calcium ionophore. Intracellular Ca^{2+} was visualized in fluo-3-loaded PC12 cells using fluorescence microscopy.
Results: Nicorandil inhibited ACh induced ERK activation in a concentration-dependent manner (Fig; mean ± SD). These inhibitions were recovered by glibenclamide, a K^+_{ATP} channel blocker. Nicorandil suppressed ERK activation induced by ionomycin and $_{AlF4}^-$, but not PMA. Pretreatment of nicorandil suppressed intracelluer luminescence by ACh.
Discussion: Nicorandil, a K^+_{ATP} channel opener, inhibits muscarnic activation of ERK via the action on G proteins or upstream of PKC at the target sites, especially effect on the influx of Ca^{2+}. This is the first observation that a K^+_{ATP} channel opener inhibits ERK activation. Since the K^+_{ATP} channel activity has been suggested to play a role in capsaicine-evoked acute nociception mechanisms, it is suggested that its inhibition of ERK activation could reflects some roles for the temporal suppression of neuropathic pain.

References:[1]Anesth Analg. 2000; 90(5): 1146-51
[2]Jpn J Pharmacol. 2001; 87(4): 268-76



S-172.

USE OF A KNEE SURGERY MODEL IN RATS TO ASSESS MODULATION OF POSTOPERATIVE PAIN-RELATED BEHAVIOR BY MORPHINE, KETAMINE, OR CLONIDINE

AUTHORS: **A. Buvanendran**, J. S. Kroin, K. J. Tuman;
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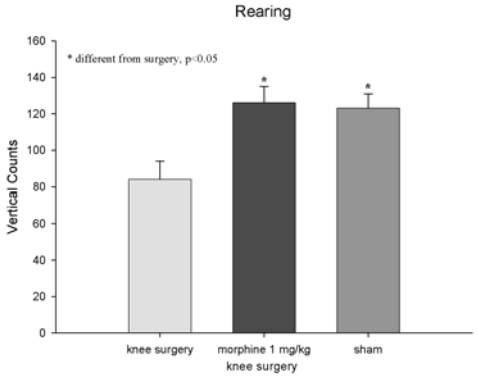
Introduction: Laparotomy in rats produces pain-related behaviors that can be attenuated with analgesics (Roughan&Flecknell, Pain 2001;90:65; Martin et al., Anesthesiology 2004;101:191). This observation in animals is of clinical relevance because it mimics aspects of postoperative pain-related behavior in humans (e.g. decreased locomotor activity). The present study uses a knee surgery model to characterize pain-related behavior in the rat, and its modulation with analgesics.
Methods: Following IACUC approval, isoflurane-anesthetized rats had an incision made over the left knee to expose the patella tendon. The tendon was reflected aside temporarily and a 1.4 mm diam, 0.5 mm deep hole was drilled in both the femur and tibia at 2 mm above and below the knee joint respectively. The holes were filled with dental cement and the wound closed. Sham surgery animals only had a skin incision. At 24 h after surgery, animals received one of the following doses of drug (0.5 ml i.p.): morphine sulfate 1 mg/kg, ketamine hydrochloride 5 mg/kg, clonidine hydrochloride 25 µg/kg, or saline vehicle (n=8/ group). Pain-related behavior was then assessed by recording exploratory locomotive activity (Martin, ibid) for 60 min. Animals were tested in clear plastic cages in which vertical and horizontal light beam interruptions are automatically recorded to access rearing activity and ambulation. Behavioral data were compared for the total number of counts (beam breaks) over 60 min among groups using analysis of variance with the Tukey-B *post hoc* test.
Results: The effect of morphine on rearing was significant (F=7.3, P=0.001), with morphine/surgery rats displaying as much activity as sham surgery rats, while vehicle/ surgery rats showed decreased activity (figure). Morphine also restored ambulation to normal (level of sham rats). Ketamine/surgery rats had as much rearing activity as sham surgery rats (F=10.6, P=0.001), and ambulatory activity was also improved compared to vehicle/surgery rats. Clonidine did not improve postsurgical locomotor activity.
Discussion: Morphine 1 mg/kg or ketamine 5 mg/kg had an analgesic effect in the knee surgery model as evidenced by reversal of the surgery-induced deficits in rearing and ambulatory behavior at 24 h post-surgery. Clonidine 25 µg/kg did not improve activity (50 µg/kg was sedating in control rats). This knee surgery model will be useful in evaluating postsurgical pain-related behavior, although some drugs may give anomalous results if they produce sedative effects.



S-173.

THE ROLE OF P38MAPK IN SPINAL CORD RELEASE OF THE INFLAMMATORY CYTOKINE TNF-α IN THE CCI RATS

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Background: Previous studies showed tumor necrosis factor α (TNF-α) expression increased in spinal after nerve injury. It is also documented that p38 mitogen-activated protein kinase (MAPK) plays an important role in the development of neuropathic pain. TNF-α and p38 MAPK activation in spinal could be linked at two points, of which TNF-α could trigger p38 activation or phosphorylated p38 could induce the upregulation of TNF-α. This study examined the hypothesis that chronic constriction injury (CCI) of the sciatic nerve could promote spinal cord releasing TNF-α and produces allodynia via the p38 MAPK pathway.
Methods: 118 SD rats were divided into 5 groups: 1) naïve control rats, 2) sham surgery rats, 3) CCI surgery rats without treatment, 4) CCI surgery rats with saline treatment and 5) CCI surgery rats with the p38 inhibitor SB203580 treatment. In group 4 and group 5, saline or SB203580 was given every day by intrathecal route starting 1d before or 1 or 7d after CCI. All rats were killed at different occasions following surgery to examine p38 activity and TNF-α releasing in spinal cord by western blot or immunohistochemistry; Mechanical allodynia was tested by von Frey hairs after surgery.
Results: Peripheral nerve injury induced dramatically mechanical allodynia and enhanced spinal cord releasing TNF-α. SB203580 inhibited p38 MAPK activity, resulting in reduction of TNF-α release in the spinal cord and attenuation of allodynia.
Conclusion: These data indicate that p38 MAPK activation is one aspect of the signaling cascade that culminates in TNF-α releasing and contributes to mechanical allodynia after peripheral nerve injury.

Fig1 Mechanical allodynia induced by CCI is attenuated by SB203580

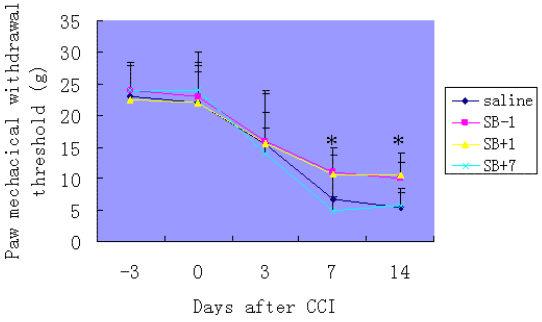
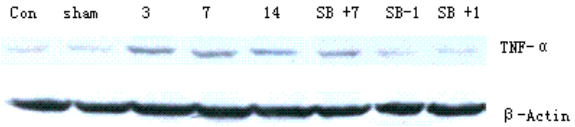


Fig2 Western bolt: Treatment with SB203580 starting 1 day (SB-1) before CCI and 1day (SB+1) but **not** 7days (SB+7) after CCI attenuates TNFα release in spinal



S-174.

ANALGESIC EFFECT OF LOW-LEVEL LASER THERAPY ON INFLAMED PAWS OF RAT

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Introduction: Low-level laser therapy (LLLT) was pioneered in Europe and Russia in the early 1960s. As the definition suggests, LLLT takes place at low irradiation intensities. Therefore, it is assumed that biologic effects are secondary to direct effects of photonic radiation and are not the result of thermal processes. In a double-blind controlled trial, LLLT and transcutaneous electric nerve stimulation significantly reduced pain scores and improved median sensory latency in patients with carpal tunnel syndrome (1). Pinheiro et al. (2) treated patients with disorders of maxillofacial pain, including trigeminal neuralgia, using laser therapy in a nonrandomized unblinded study, and demonstrated a reduction of painful symptoms. However, the pain relieving mechanism of LLLT is unknown. In painful inflammation, endogenous corticotropin-releasing factor (CRF) releases opioid peptides (mainly beta-endorphin) from various types of immune cells, and produces antinociception by activating opioid receptors on peripheral sensory nerve endings. Beta-endorphin is derived from propiomelanocortin (POMC). Immunocyte-derived beta-endorphin can activate peripheral opioid receptors on sensory neurons to inhibit pain within inflamed tissue (3). In case of inflammatory pain, the analgesic effects of LLLT may be attributed to the local release of endogenous opioids such as beta-endorphin. Therefore, we investigated the analgesic effect of LLLT with laser on acute inflammatory pain, verifying the contribution of endogenous opioids. Methods: In an in vitro study, POMC and CRF mRNA expression was investigated by reverse transcription polymerase chain reaction (RT-PCR) in the blood of the rat exposed to a semiconductor laser (830 nm) of 1000 mW for 5 min. Glyseraldehyde-3-phosphate dehydrogenase (GAPDH) was amplified with RT-PCR as an internal control. In an in vivo study, it was investigated whether the low-level laser irradiation on inflamed paws reduces the peripheral pain. Adult male Sprague Dawley rats weighing about 300 g were used. We injected Freud's complete adjuvant (FCA) into the sole planter, and a semiconductor laser (830 nm) of 1000 mW for 5 min was used for irradiation. The pain threshold was measured using a hot planter test. Results: POMC and CRF mRNA expression was markedly enhanced 4 h after laser irradiation. The laser irradiation of the sole planter provided a pain reduction effect. At this time, at the inflammatory spot, the manifestation and augmentation of Beta-endorphin was confirmed by the laser irradiation. Discussions: The present results demonstrate that POMC and CRF genes are activated by exposing the blood to the laser. Expression of endogenous opioid peptides by the immune cells is very important in the local analgesic effect. The current data suggests that the laser irradiation may reduce various types of pain (e.g., post-operative pain).
1: Arch Phys Med Rehabil 2002. 83:978-88.
2: J Clin Laser Med Surg 1997. 15:181-3.
3: Anesthesiology. 2001 Aug;95(2):500-8.

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S-175.

PELVIC ORGAN COLOCALIZATION WITHIN DORSAL ROOT GANGLIA OF RATS

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Introduction: Previous work has demonstrated convergent responses that suggest one organ's response to pain could influence another nearby neighbor organ. Could the now well appreciated human clinical syndromes of IC, VVS, IBS, and their co-occurrence be fostered by the phenomena of convergent responses? The stimulus to examine the possibility of shared neural signaling at the level of the peripheral nervous system grew out of previous studies by Berkley et al on cross system visero-visceral interaction.
One mechanism of pain perception underlying clinical presentation of pain syndromes may be through the interaction and sharing of putative nociceptive stimuli at the dorsal root ganglion level. The incidence of episodic or chronic pain disorders such as irritable bowel syndrome, fibromyalgia and interstitial cystitis, known as functional pain syndromes all lack a specific pathology. These conditions are associated with hyperalgesia and altered sensory nerve modulation. Clinically, they often coexist in the same patient. The dorsal root ganglions associated with pelvic pain are of low lumbar and sacral origin in the rat model; thus we directed our attention in this study at this level to observe anatomical and neurochemical changes in the dorsal root ganglion.
Methods: Flourogold dye was injected into the descending colon and TMR dye was injected into the myometrium of the uterus. In another set of experiments, both dyes were injected into their respective locations in a same animal. Flourogold alone was injected into the uterus to enable comparison of the two dyes for purposes of retrograde tracing.
In the dual labeled rats, (dye injected in both colon and uterus), the Flourogold and TMR dyes co-localized in the DGR neurons at the levels where neurons projected from the colon (Li, L2 and L6). . In the dual labeled rats, (dye injected in both colon and uterus), the Flourogold and TMR dyes co-localized in the DGR neurons at the levels where neurons projected from the colon (Li, L2 and L6).
Conclusions: We demonstrated that neural input from two different pelvic organs projected to the same cell body within the same DRG. The design of the these studies, using retrograde labeling from the uterus and colon addressed the possibility that the same primary afferent innervate both reproductive and gastrointestinal organs and it is plausible that this population of dichotomizing (branching) neurons plays a vital role in the mechanism of nociceptive transduction at the level of primary afferent neurons. This cross-sensitization would lower nociceptive thresholds of colonic afferent neurons producing allodynia and hyperalgesia in response to colon distension.

S-176.

SYSTEMIC BLOCKADE OF GLYCINE, GAMMA AMINOBUTYRIC ACID(GABA)$_A$ AND GABA$_B$ RECEPTORS INCREASES SEVOFLURANE MINIMUM ALVEOLAR CONCENTRATION IN RATS

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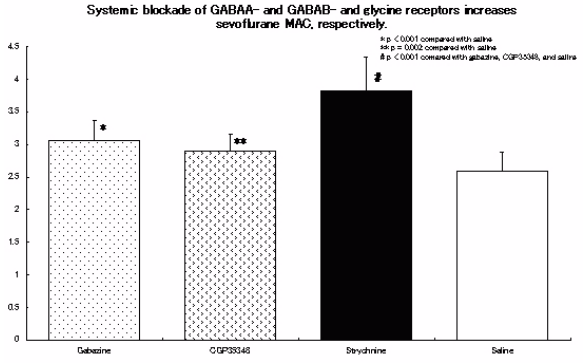
Introduction: Although blockade of glycine and GABA$_A$ receptors reportedly mediate the capacity of inhaled anesthetics to produce immobility during noxious stimulation (i.e., would underlie MAC, the minimum alveolar concentration required to suppress movement in response to a noxious stimulus in 50% of subjects) (1,2), no data are still available regarding the role of these receptors in determining sevoflurane MAC. In this study, we examined the effects of intraperitoneal strychnine (a blood brain barrier penetrating glycine receptor antagonist), gabazine (a blood brain barrier penetrating GABA$_A$ receptor antagonist), or CGP35348 (a blood brain barrier penetrating GABA$_B$ receptor antagonist) on sevoflurane MAC in rats.
Methods: Four groups of six male Wistar rats weighing 250-350 g each received one of the following drugs dissolved in the physiological saline solution intraperitoneally 30 min prior to testing: (1) strychnine 2 mg/kg; (2) gabazine 10 mg/kg; (3) CGP35348 10mg/kg; (4) no drug as vehicle control. MAC was defined as the average of the partial pressures that just prevented and permitted movement in response to clamping the tail for 30 sec. Data were analyzed by means of Dunnet T3 multiple comparison tests after a one-way analysis of variance. In all tests, a value of $p < 0.05$ was considered statistically different.
Results: Compared with vehicle control, intraperitoneal administration of strychnine, gabazine, and CGP35348 significantly decreased the sevoflurane MAC in rats, respectively. Furthermore, the MAC obtained after strychnine pretreatment was significantly greater than the MAC following gabazine and CGP35348, respectively.
Discussion: These findings suggest that systemically distributed glycine, GABA$_A$ and GABA$_B$ receptors may, at least in part, mediate the capacity of sevoflurane to produce immobility during noxious stimulation. Among these three receptors, glycine receptors may be the most prominent contributor to the immobilizing action of sevoflurane.



References:
1. Anesth Analg 2003; 96: 97-101
2. Anesth Analg 2003; 96: 706-12.

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S-177.

IMPROVING LONG-TERM OUTCOMES FOLLOWING ACL SURGERY: USE OF PREVENTATIVE MULTIMODAL ANALGESIA WITH COX-2 INHIBITION

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Introduction: Anterior cruciate ligament (ACL) reconstruction is associated with considerable postoperative pain (1). Unrelieved postoperative pain may delay discharge from the hospital, result in inability to participate in rehabilitation programs, delay recovery, and cause poor outcomes (2). Patients unable to participate in rehabilitation program following knee surgery are at increased risk for developing postoperative complications such as: delay in strength recovery, prolonged stiffness, anterior knee pain, and complex regional pain syndrome (CRPS) (3). Further, unrelieved acute pain may lead to a higher incidence of chronic post-surgical pain (4). The goal of this study is to assess the long-term analgesic efficacy of utilizing celecoxib in a preventative multimodal analgesic technique for patients undergoing outpatient ACL surgery.
Methods: 200 consecutive patients were randomized to receive acetaminophen 1000 mg and either celecoxib 400 mg or placebo 1-2 hours prior to surgery. Before awakening, all patients were administered 20 mL intraarticular bupivacaine 0.25% and morphine 5mg and an external cooling system was applied to the operative knee. After discharge patients were instructed to take acetaminophen 1000 mg every 6 hours and either celecoxib 200 mg every 12 hours or matching placebo (according to randomization) and oxycodone 5-10 mg every 3 h for the first 14 days postoperatively. All patients were enrolled in an accelerated rehabilitation program. Six months postoperatively, patients were evaluated for the presence of patellofemoral complications including: anterior knee pain, flexion contracture, quadriceps weakness, and CRPS. In addition, patients' postoperative level of activity was assessed according to the International Knee Documentation Committee (IKDC) (5).
Results: There were no differences between the groups with respect to demographic variables, operative times, or preoperative level of activity. Six months following surgery, significantly more patients in the control group developed patellofemoral complications compared to the celecoxib group (p=0.001). These included a higher incidence of anterior knee pain (14/96; 15%) vs (4/95; 1%), CRPS (7/96; 7%) vs (1/95; 1%), flexion contractures (9/96; 9%) vs (2/95; 2%), and scar tissue requiring re-arthroscopy ((8/96; 8%) vs (2/95; 2%). More patients in the celecoxib group returned to a Grade III or IV activity level (84% vs. 65%) ($p<0.01$), were able to participate at a more intense level ($p<0.02$), and return to full sports activity ($p<0.05$).
Conclusions:
The administration of celecoxib as a preventative adjunct in the multimodal approach for ACL reconstruction has results in a significant reduction in long-term patellofemoral complications and these patients are more likely to return to their pre-injury level of activity including full sports participation.
References:
1. Reuben SS, et al. JBJS 2000;82:1754-66.
2. Moffett H, et al. Clin Orthop 1991;262:210-26.
3. Reuben SS, et al. Acute Pain 2004;7:65-73.
4. Perkins F, et al. Anesthesiology 2000;93:1123-33.
5. Irrgang JJ, et al. Am J Sports Med 2001;29:600-13.

S-178.

ALVIMOPAN ACCELERATES GASTROINTESTINAL RECOVERY AND DECREASES LENGTH OF HOSPITAL STAY AFTER BOWEL RESECTION WITHOUT COMPROMISING OPIOID-BASED ANALGESIA

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Introduction: Postoperative ileus (POI) occurs universally after bowel resection (BR) and is exacerbated by exogenous opioids used for pain management. Gastrointestinal (GI) recovery and hospital length of stay (LOS) in patients undergoing BR and receiving alvimopan, a peripherally acting mu-opioid receptor (PAM-OR) antagonist, or placebo were analyzed in 4 multicenter, randomized, double-blind trials in the United States and Canada (14CL302, 14CL308, 14CL313, 14CL314).
Methods: Adult patients undergoing laparotomy for BR or total abdominal hysterectomy who were scheduled for postoperative intravenous patient-controlled opioid analgesia received oral alvimopan or placebo preoperatively and twice daily postoperatively until hospital discharge or for ≤ 7 postoperative days. This pooled post hoc analysis analyzed all patients who underwent BR and received alvimopan 12 mg or placebo. Treatment effects on time to events in the modified intent-to-treat (MITT) population were analyzed using the Cox proportional hazards model, and magnitude of treatment effects was expressed using differences in Kaplan-Meier means. Efficacy endpoints included GI-2 recovery (composite of time to first bowel movement and toleration of solid food) and postoperative LOS (supportive analysis of the prespecified secondary endpoint measured from the calendar day after surgery to the calendar day of hospital discharge order written). Mean daily opioid consumption was recorded in morphine sulfate equivalents (MSEs), and *P* values were calculated using an analysis of variance model. Safety was monitored by adverse event reporting.
Results: A total of 1,409 patients were included in the MITT BR population, and the majority were white (84%) and underwent large BR (92%).

	Placebo (n = 695)	Alvimopan 12 mg (n = 714)	
GI-2 recovery, hazard ratio	—	1.5	$P < 0.001$
Mean time to GI-2 recovery, hours	120.8	102.0	$\Delta = 18.8$
Postoperative LOS, days	6.6	5.6	$P < 0.001$
Postoperative LOS ≥ 7 days, patients (%)	239 (34.4)	134 (18.8)	% change = - 43.9%
Daily postoperative opioid consumption, MSEs (mg)	28.8	27.2	$P = 0.290$

Statistical significance was only assessed for hazard ratio measurements, postoperative LOS, and opioid consumption.

Nausea (placebo, 63%; alvimopan 12 mg, 54%) and vomiting (placebo, 25%; alvimopan 12 mg, 17%) were the most commonly reported treatment-emergent adverse events, and incidences of each were lower in the alvimopan group than in the placebo group.
Discussion: Alvimopan 12 mg was associated with significantly accelerated GI recovery, shorter postoperative LOS, and a lower proportion of patients with LOS ≥7 days. Opioid consumption was comparable between groups, and alvimopan was well tolerated with a lower incidence of nausea and vomiting in the alvimopan group than in the placebo group.

S-179.

ACUTE POSTOPERATIVE PAIN SERVICE IN AN ACADEMIC AND COMMUNITY HOSPITAL

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Introduction: Evidence supports the concept that pain is frequently poorly controlled in hospitalized patients, especially during the immediate postoperative period. Historically, surgeons have been empowered to manage acute surgical pain. Although, several models of acute pain services have been proposed, in the past few years, considerations have been given to an increase role of anesthesiologists in acute pain management. This study was designed to compare the changes in the activity of acute postoperative pain service activities over a period of 4 years in an academic and community hospital.
Methods: Using procedure codes, the number of procedures (62318, 62319, 64445, 64446, 6447, 64448,64449, 64520 and 64999), acute pain consult (99213, 99231, 99252, 99253) and follow up visit for continuous epidurals (01996) performed in fiscal year 20003 to 2006 were obtained from an academic (A) and a community (C) hospital with an established acute pain service.
Results: Table 1 presents the acute pain activities in A and C for fiscal year 2003 to 2006. During the study period the number of surgery performed in both hospital remained within 20% of the number recorded for 2003.

Table 1 presents the acute pain activities in A and C for fiscal year 2003 to 2006.

	Fiscal Year 06 A	Fiscal Year 06 C	Fiscal Year 05 A	Fiscal Year 05 C	Fiscal Year 04 A	Fiscal Year 04 C	Fiscal Year 03 A	Fiscal Year 03 C
Follow Up Visit for epi-dural	1,287	161	1,023	878	657	419	307	243
Thoracic Epi-dural	324	48	209	280	109	218	19	168
Lumbar Epi-dural	58	23	39	42	43	76	29	89
Peripheral Nerve Blocks	782	7,061	78	5,875	21	2,575	26	993
Acute Pain Consult	1,091	5	967	4	627	78	374	65
TOTAL	3,542	7,298	2,316	7,079	1,457	3,366	755	1,558

Discussion: Our data indicates that in the past 4 years we observed an increase contribution of the acute pain service in the postoperative management of acute surgical pain in both the academic and community hospitals, suggestive of an increase in the role plays by the acute pain service in the postoperative management of surgical patients.

S-180.

METHADONE IMPROVES PAIN MANAGEMENT AND PATIENT SATISFACTION IN AMBULATORY SURGICAL PATIENTS

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Introduction:
Long acting opioids such as morphine and methadone are considered undesirable for ambulatory surgical patients because of concern that these drugs prolong time to discharge. However, data suggests morphine compared to fentanyl can improve pain control without significantly increasing time to discharge from the PACU (1). We sought to determine if methadone provides better pain control and greater patient satisfaction in surgical outpatients.
Methods:
After IRB approval for this prospective, randomized, double-blinded study, we recruited 67 ambulatory surgery patients expected to require post-operative analgesia. After informed consent, patients were randomized to receive either methadone, 10 mg or fentanyl, 200 mcg (both diluted to 10 cc) intra-operatively. One half of the study drug was given on induction and the remaining half was given 30 minutes later. The anesthesia provider was blinded to the study drug and was instructed not to give additional analgesics during the surgery. Upon PACU arrival, a nurse blinded to opioid group evaluated the patient for pain and nausea and vomiting (using a VAS score). Discharge eligibility was determined using a Postanesthetic Discharge Scoring System (discharge eligibility achieved with score ≥ 9 out of 10) (2). Fentanyl was given (25 to 50 mcg) every 5 minutes as needed for complaints of pain. Patients were contacted postoperatively and asked to rank satisfaction with pain control and their least, worst, and average pain in the first 24 hours post-discharge on a VAS scale of 0 to 10. Wilcoxin's rank sum test was used to evaluate the pain and satisfaction scores and amount of fentanyl used in the PACU. Fisher's exact test was used for nausea and vomiting rates. The two-sided two-sample t-test was used to evaluate time to discharge. Analysis was on an intent-to-treat basis.
Results:
62 patients completed the study. The methadone group reported significantly greater satisfaction with their pain control than patients treated intraoperatively with fentanyl (median: methadone 10, fentanyl 8; p=0.0007). Methadone patients had significantly lower "least" pain scores compared to fentanyl (methadone 0, fentanyl 2; p=0.04). The "worst" pain scores were marginally lower in the methadone group (p=0.06). There was no significant difference in pain scores on PACU arrival (p = 0.54). There was no significant difference in discharge times from the PACU (methadone 113 ± 62 minutes, fentanyl 109 ± 46 minutes; p=0.76). There was no difference in nausea (p=0.85) and vomiting (p=1.00) after hospital discharge.
Discussion:
Patients receiving methadone for outpatient surgery reported significantly greater satisfaction with pain management and pain relief up to 24 hours after surgery. The combination of improved satisfaction with no delay in discharge times makes methadone a desirable drug for pain control in ambulatory surgery patients.
References:
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2 Anesth Analg 1995;80:896.

S-181.

ADVANTAGES OF PATIENT CONTROLLED EPIDURAL ANALGESIA (PCEA) FOR POSTOPERATIVE PAIN CONTROL AFTER LUMBAR SPINE SURGERY

AUTHORS: E. M. Noguera Chia, E. Farag, I. Kalfas, J. Na, E. Mascha;
AFFILIATION: Cleveland Clinic, Cleveland, OH.

Introduction: Recent trials show conflicting findings that suggest no advantage of Epidural over IV PCA after spine surgery(1,2,3). These studies focus on different populations. The purpose of this study is to evaluate the association of patient controlled epidural analgesia (PCEA) with good outcome after lumbar spine surgery.
Methods: Following IRB approval, 177 records of patients after lumbar spine surgery were reviewed. Outcome variables recorded: PCA mode, IV narcotics used, VAPS at rest, LOS in days, and DVT presence. Epidural catheters were place by surgical team under direct visualization and PCA method started in the postoperative period. Association between analgesia mode and outcomes was assessed using linear regression (pain score), logistic regression (low-medium-high morphine use, DVT, OR extubation) and Cox proportional hazards model (LOS). Each analysis was adjusted for baseline covariables age, ASA, re-exploration, levels instrumented, and chronic pain. The significance level for each hypothesis was 0.05.
Results: Our study involved n=95 Epidural and n=82 IV patients aged 60 ± 13 and 59 ± 14 yrs, respectively, *P*=0.59.
Epidural patients required less morphine (*P*< 0.001) and had lower mean pain score than IV patients (*P*= 0.01). See table 1.

Table 1. Association between epidural and pain control

Pain Control	*PCEA* N= 95	*IV PCA* N=78	*Association*	*P value*
	Median (Q1, Q3)	Median (Q1, Q3)	Odds ratio (95% CI)[a]	
Morphine equivalent	0 (0, 4.1)	24 (0, 110)	0.21 (0.11, 0.39)	<0.001
	LS Mean[b] (SE)	LS Mean (SE)	Difference (95% CI)	
Pain Score	3.5 (0.2)	4.3 (0.2)	-0.8 (-1.3, -0.2)	0.01

[a] odds of lower morphine requirement in PCEA vs IV PCA based on quartiles of the data
[b] LS Mean: Least Squares Mean

The incidence of DVT among PCEA and IV PCA patients was 3.2% and 4%, respectively, with the multivariable logistic regression odds ratio (95% CI) of 0.8, (0.14, 4.5), *P*=0.80.
Days to discharge (median (quartiles)) were 4 (3, 5) and 4 (3, 6) for the Epidural and IV groups, respectively. No significant association between LOS and epidural use was found using Cox multivariable regression; hazard ratio (95% CI) of Epidural vs IV (reference group) was 1.14 (0.83, 1.58), P=0.41.
Time to extubation was not associated with epidural use in a Cox multivariable regression; hazard ratio (95% CI) of 1.02 (0.74, 1.4), P=0.92.
Discussion: This study revealed a significant decreased use of narcotics and lower pain scores for patients treated with PCEA after lumbar spine surgery. There was no association between epidural or IV PCA and incidence of venous thrombosis, length of stay and time to extubation. This study suggests a slightly better patient satisfaction and decreased narcotic consumption in patients who had epidural analgesia after lumbar spine surgery.
References:
1. *Spine. 2006, 31(15):1646-51.*
2. Paediatric anaesthesia. 2004, 14 (2) 1009-15.
3 Spine 2003, 28 (8): 739-743

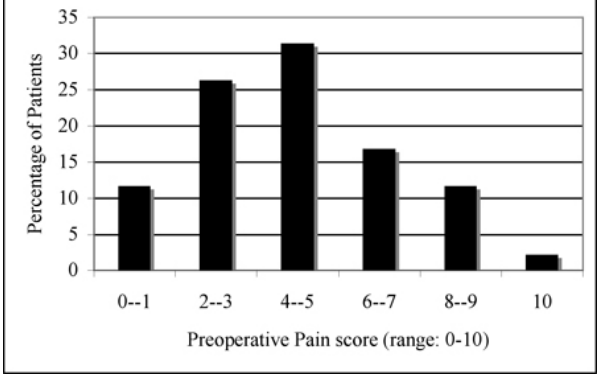
S-182.

THE BLOOD PRESSURE CUFF: A POTENTIAL NEW TOOL FOR ASSESSING PREOPERATIVE PAIN TOLERANCE

AUTHORS: E. T. Nielsen, A. Mellor, K. Ross, G. Neuman;
AFFILIATION: St Vincent's Catholic Medical Center New York, New York, NY.

Introduction: Several recent studies have focused on the employment of preoperative pain tolerance tests[1,2,3,4,5] to predict postoperative pain intensity. Pan et al[4] and Granot et al[3] showed thermal sensitivity tests are of predictive value for post-cesarean section pain and analgesic requirements while other studies have used pressure algometers[5] or ice water[1,2] as noxious stimuli to determine pain tolerance. This investigation proposes a method that does not require additional equipment, impose any deviation from the usual preoperative protocol or inflict significant discomfort on the patient. We hypothesized that non-invasive blood pressure cuff inflation can be used to evaluate pain tolerance and that this method might produce an appropriate distribution of pain scores.
Methods: A prospective cohort study was conducted with ambulatory patients age 18-65 years undergoing elective surgery. During the preoperative check-in, the patients had a blood pressure cuff inflated to 250mmHg for 5 seconds on one arm. The patients then identified their level of pain on a Wong/Baker faces scale, a visual analog scale with 0 representing no pain and 10 representing the most pain. The distribution of pain scores was examined to assess the potential of using the blood pressure cuff as a tool for indicating preoperative pain tolerance.
Results: From the 137 patients enrolled, pain scores ranged from 0-10, with a mean score of 4.2, standard deviation of 2.5, variance of 6.1, and a median of 4. The Kurtosis was (-0.50) with a skew of 0.25 (see Fig. 1)

Fig. 1. Distribution of preoperative pain score immediatly after blood pressure cuff pain test.



Discussion: BP cuff inflation produced pain scores ranging from zero to ten showing the variability of interpatient pain tolerance. Chen et al[2] suggested a dichotomy of pain responsivity as opposed to a natural Gaussian distribution which recent studies[1,3,4,5] likely assume. Our results are consistent with a Gaussian curve suggesting that pain tolerance might not be dichotomously distributed. Since this novel method of measuring pain tolerance is cost effective, easy to implement, and does not inflict substantial discomfort, it is our hope that with further study the blood pressure cuff pain test will prove to be a useful tool for predicting and managing perioperative pain.
References:
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S-183.

POSITRON EMISSION TOMOGRAPHY EVALUATION OF POSTOPERATIVE PAIN RESPONSES FOLLOWING TOTAL KNEE ARTHROPLASTY

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Introduction: Postoperative pain following total knee arthroplasty (TKA) is a common problem and impedes rehabilitation (Buvanendran et al, JAMA 2003;18:2411). However it is not clear how different analgesic regimes fundamentally reduce the sensation of pain. Positron emission tomography (PET) is an imaging technique that can quantify increases in nerve cell activity in selective regions of the brain. Earlier studies have examined the pattern of increased brain activity that follows experimentally-induced acute pain (Iadarola et al, Brain 1998;121:931; Coghill et al, J Neurophysiol 1999; 82:1934). However, no clinical study has investigated the change in brain activity associated with severe postoperative pain.
Methods: Following IRB approval, a 69 yo female patient having primary TKA was \for study. An MRI (T1-SPGR, 1.6 mm gapless axial) was performed preoperatively. Immediately after surgery, pain was controlled by patient-controlled epidural bupivacaine (1 mg/ml). The next morning, epidural infusion was temporarily stopped. Two hours later, in a quiet room with low ambient light , the patient was injected intravenously with 4.5 mCi ^{18}F-fluoro-2-deoxyglucose. After waiting 30 min, a 3-D brain PET scan performed. Prior to the PET scan the patient fasted for 8 h. No oral or parenteral opioids were administered. After the first PET scan, epidural infusion was immediately resumed, with a bolus dose of lidocaine to produce a prompt analgesic effect, followed by slow patient-controlled epidural infusion of bupivacaine. On the second day after surgery, another PET scan was performed with maintained epidural infusion, using the same PET protocol. Prior to each PET scan, pain scores were measured using the verbal rating scale, with 0=no pain, 10=worst imaginable pain. Digital files of PET scans were co-localized with the pre-surgery MRI. Pixel intensities in regions of interest were contrasted between scans: Day 1 postsurgery (maximum postoperative pain) minus Day 2 postsurgery (maximum analgesic effect). Z scores greater than 2.0 were considered statistically significant.
Results: The pain score on Day 1 postsurgery (with analgesia stopped) was 6. On Day 2 postsurgery (with epidural analgesia) the pain score was 0. After subtracting the PET scan of Day 2 postsurgery from that of Day 1 postsurgery, there was elevated activity in the contralateral primary somatosensory cortex (SI). Increased activity was not seen in anterior cingulate cortex (ACC), insular cortex, or secondary somatosensory cortex (SII). Other brain regions showing increased postsurgical activity were parietal cortex, pulvinar and medial dorsal nucleus of thalamus, putamen, superior temporal gyrus, fusiform gyrus, posterior and anterior cerebellar lobe.
Discussion: Pain after surgery can have elements of both acute and chronic pain. One area associated with the acute pain pathway, SI, was activated postoperatively. However, other areas that are considered integral parts of the acute pain network: SII, ACC, and insula did not show increased activation.

S-184.

ALVIMOPAN, A PERIPHERALLY ACTING MU-OPIOID RECEPTOR ANTAGONIST, IS ASSOCIATED WITH REDUCED POSTOPERATIVE NAUSEA AND VOMITING WITHOUT COMPROMISING OPIOID-BASED ANALGESIA

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Introduction: Postoperative ileus (POI), an impairment of bowel motility after surgery, is exacerbated by opioid drugs used to manage pain. Alvimopan, a peripherally acting mu-opioid receptor (PAM-OR) antagonist, accelerated gastrointestinal recovery in phase III trials. This pooled post hoc analysis investigates opioid consumption, visual analogue scale (VAS) pain scores, and incidences of nausea and vomiting by postoperative day (POD) in alvimopan trials. Differences in analgesia or opioid use could be suggestive of central opioid antagonism.
Methods: Alvimopan or placebo was administered orally preoperatively and twice daily postoperatively until hospital discharge or for ≤ 7 PODs to adult patients scheduled to receive opioid-based intravenous patient-controlled analgesia. This analysis assessed all patients who underwent bowel resection and received alvimopan 12 mg or placebo in 4 multicenter, randomized, double-blind trials in the United States and Canada (trials 14CL302, 14CL308, 14CL313, 14CL314). Total opioid consumption (morphine sulfate equivalents [MSEs], mg) (collected in 4 trials) and VAS pain scores (0 [no pain] to 100 mm [worst pain]) (collected in 3 trials) were recorded; *P* values were calculated from an ANOVA model. Incidences of treatment-emergent nausea and vomiting by day were also gathered from 4 trials; *P* values were calculated from Fisher's exact tests.
Results: Opioid consumption and VAS pain scores were comparable between groups. As compared with patients in the placebo group, patients in the alvimopan group experienced less nausea on PODs 3 and 4 less vomiting on PODs 3, 4, and 5.

	Placebo	Alvimopan 12 mg	*P* value
Opioid consumption, mean MSEs	(n = 695)	(n = 714)	
Preoperative (before scheduled surgery start)	18.9	19.9	0.308
Intraoperative	28.3	29.2	0.591
Daily postoperative	28.8	27.2	0.290
VAS pain scores, mean	(n = 383)	(n = 397)	
Daily postoperative	29.1	29.2	0.913
Nausea by POD, %	(n = 695)	(n = 714)	
POD 0	20.7	23.2	0.274
POD 1	20.7	19.7	0.691
POD 2	11.1	8.7	0.153
POD 3	9.9	5.2	< 0.001
POD 4	6.9	3.5	0.005
POD 5	3.2	1.7	0.082
Vomiting by POD, %	(n = 695)	(n = 714)	
POD 0	1.7	2.1	0.699
POD 1	5.0	5.2	0.904
POD 2	5.6	4.1	0.214
POD 3	6.5	2.9	0.002
POD 4	5.5	1.5	< 0.001
POD 5	2.7	0.8	0.008

Discussion: Alvimopan 12 mg did not compromise opioid-based analgesia as measured by opioid consumption and VAS pain scores supporting the hypothesis that alvimopan is a PAM-OR antagonist. Alvimopan treatment effect was more apparent later in the inpatient recovery period; incidences of nausea and vomiting were significantly lower later on PODs 3 through 5 for patients who received alvimopan 12 mg compared with patients who received placebo. Moreover, incidence of vomiting appeared to increase through POD 3 in the placebo population, possibly reflecting ongoing POI. The reductions in nausea and vomiting observed in the alvimopan 12-mg group warrant further investigation and may correspond to a period of higher risk for delayed gastrointestinal recovery (prolonged POI) or postoperative nausea and vomiting because of POI.

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S-185.

FEMORAL NERVE CATHETER INFUSION OF FENTANYL OR ROPIVACAINE FOR ANALGESIA IN KNEE REPLACEMENT SURGERY.

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Introduction: Continuous nerve catheter infusions are becoming increasingly popular for postoperative analgesia after surgery on both upper and lower extremities, including total knee replacement (TKR). Catheter guided post-operative pain control may also facilitate earlier ambulation and hospital discharge. The goal of this study was to compare the efficiency of fentanyl and ropivacaine in localized pain control administration versus standardized systemic pain control.
Methods: During this prospective, placebo-controlled, double-blinded, randomized study, patients were selected who were scheduled to undergo elective, non-traumatic TKR surgery. After consenting to the study, pre-operative FNS catheter placement was confirmed by electrical stimulation at a threshold of <0.6 and >0.2 mA. All subjects received a test dose of 20ml of 2% lidocaine through the catheter, and tested positive for nerve block. Post-operatively a randomly assigned infusion of fentanyl (3mcg/ml), ropivacaine (0.1%) or fentanyl and ropivacaine together (3mcg/ml and 0.1% respectively) or saline control, was initiated through the FNS catheter at a rate of 10ml/hour. Subjects were screened using a standard 0-10 Visual Analog pain Scale (VAS). Those with a VAS >5 received a 3ml bolus of study infusion, and the pump rate was increased by 2ml/hour, with a maximum pump rate of 14ml/hour. Standard of care intravenous morphine was given for analgesia throughout the post-operative course. Primary endpoints measured included quality of analgesia as assessed by the need for IV morphine, 24 hour post-operative bilateral knee strength for flexion and extension measured by isometric dynamometry, and 24 hour serum fentanyl concentrations.
Results: In 41 completed subjects, VAS scores were statistically identical between all four groups. Requirements for IV morphine analgesia were statistically identical between treatment groups. All treatment groups were significantly different from the control in morphine requirements (One Way ANOVA fentanyl $p = 0.004$, ropivacaine $p = 0.005$ and fentanyl with ropivacaine $p = 0.034$). Post-surgical muscle strength was significantly greater in the fentanyl treatment group when compared to the fentanyl plus ropivacaine ($p = 0.017$) and ropivacaine ($p = 0.006$). Comparable serum fentanyl levels were observed between fentanyl and fentanyl with ropivacaine groups. Assays yielded no measurable serum fentanyl in ropivacaine and control groups.
Discussion: Equal pain relief was provided to subjects as demonstrated by equal VAS scores. Post operative analgesia the using FNS catheter infused with 3mcg/ml fentanyl was comparable to that of ropivacaine (0.1%) or fentanyl with ropivacaine, requiring less IV morphine than a saline control group. Subjects receiving fentanyl alone through FNS catheters tended to have greater leg extension strength than those receiving ropivacaine, fentanyl with ropivacaine, or a saline control. The combination of sufficient analgesia with better leg strength should facilitate earlier stable ambulation, physical therapy and hospital discharge.
References: 1. Chelly EC et al. J Arthroplasty 2001;16:436-445.

S-186.

USE OF EPIDURAL DEXMEDETOMIDINE IN PATIENTS UNDERGOING POST-TRAUMATIC LOWER LIMB ORTHOPEDIC SURGERY.

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ABSTRACT: This double blind, randomised study tested the hypothesis that during epidural anesthesia for patients undergoing lower limb orthopedic surgery with bupivacaine, addition of Dexmedetomidine [DEX] effectively controls & prolongs postoperative pain and reduces analgesic requirements.
Methods: Following approval by the IRB, 26 ASA I - II male patients, undergoing surgery for traumatic fracture neck and shaft femur were selected.
The procedure was explained to them and informed consent obtained. All patients were premedicated with Inj. Ondansetron 4 mg IV & Inj. Tramadol 2 mg/kg IV and preloaded with 10 ml/kg of Ringer Lactate prior to epidural injection.
The patients were randomly divided into two groups of 13 patients each.
Under all aseptic precautions, anesthesiologist identified epidural space [L3-4 or L4-5] by loss of resistance technique to injection of saline in the sitting position. 3-5 cm of epidural catheter was placed in the space. The anesthesiologist injected the drugs via the catheter without knowing its contents.
Control Group A: received 20 ml of 0.5% bupivacaine epidurally + saline to make upto 23ml with saline via epidural catheter.
Study Group B: received 20 ml of 0.5% bupivacaine + 2 ug/kg DEX epidurally made upto 23ml with saline.
After the epidural injection, patients were placed supine in horizontal position. All patients received O_2 4-6L by Hudson mask.
In patients with inadequate or failed epidural analgesia intraoperatively, general anesthesia was administered and case deleted from the study and a new case inducted.
Postoperatively, any complaint of pain was treated with a 10 ml top-up of 0.125% bupivacaine with 50µg of fentanyl.
Pain free period: This was the period from initial epidural injection to 1st epidural top-up (Inj. Fentanyl 50µg with 10 ml of 0.125% bupivacaine). Patients were observed for 24 hrs to note the total number of top-up doses required.
Mean duration of analgesia and total number of top-ups in the two groups have been compared statistically using paired 't' test. Value of $p<0.05$ has been considered significant.
Result & Conclusion: Patients who received DEX epidurally had a significantly longer pain free period [$p<0.001$] and needed fewer number of subsequent epidural doses. Thus, addition of DEX not only enhances patient comfort but is also less labor intensive for acute pain service personnel during the postoperative period.

COMPARISON OF MEAN DURATION OF ANALGESIA AND EPIDURAL TOP-UPS *P<0.001

GROUPS	TIME (IN MINUTES)	NO. OF TOP-UP DOSES
A (CONTROL)	234.8 ± 68	3.3 ± 0.75
B (STUDY)	735.8 ± 137*	1.2 ± 0.43*

S-187.

COMPARISON OF SAFETY AND EFFICACY OF A FENTANYL TRANSDERMAL PCA SYSTEM TO MORPHINE PCA FOR POSTOPERATIVE ANALGESIA AFTER ABDOMINAL OR PELVIC SURGERY

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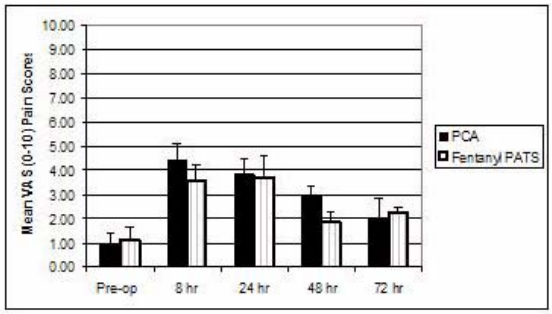
Introduction: The fentanyl HCl patient-activated transdermal system (PATS) is a needle free, credit card-sized, programmed system that eliminates the need for the cumbersome delivery of intravenous opioid analgesics by pumps.
The purpose of this study was to assess the safety and efficacy of fentanyl HCl PATS compared to intravenous (IV) Patient Controlled Analgesia (PCA) for post surgical pain management after abdominal or pelvic surgery.
Methods: 20 patients were randomized into fentanyl HCl PATS (n=10) or IV PCA (n=10) groups following IRB approval and informed consent. Fentanyl HCl PATS patients received fentanyl 40mcg (on demand dose) delivered over 10 min for a maximum of 6 doses/hr (240mcg/hr) or a maximum of 80 doses (32mg) in 24 hours. Patients randomized to IV PCA morphine received 1mg Morphine bolus with a 5 min lockout period, up to 10 doses/hr (10mg/hr) and a maximum of 240 doses/24hr. Rescue medications included morphine and fentanyl for the PCA and fentanyl HCl PATS patients, respectively. The duration of the open label treatment phase was 72 hours.
Patients were assessed for pain intensity obtained preoperatively and at 8, 24, 48, and 72 hours. Patients reported pain intensity scores on an 11-point numerical pain scale (0-10). Global assessment of pain control and an "ease of care" questionnaire to assess their experience with fentanyl HCl PATS were obtained, as well as respiratory and hemodynamic parameters. Data are reported as means ± SE and a $p<0.05$ was considered statistically significant.
Results: Demographic data were not significantly different between groups. There were no significant differences in respiratory rate, oxygen saturation (SpO_2), systolic, diastolic blood pressure, and heart rate. Pain scores were also not significantly ($p=0.62$) different between groups (See Figure). 20% of patients in the IV PCA group required rescue medication versus 10% in the fentanyl HCl PATS group. Mean IV PCA morphine dose was 85±61 mg and 1864±810 μg of fentanyl for fentanyl HCl PATS group.
Discussion: The fentanyl HCl PATS delivery system was effective for treatment of post-operative pain in patients undergoing major abdominal or pelvic surgery. The pain intensity scores of both treatment groups were similar as well as use of rescue medication. In this limited patient population fentanyl HCl PATS delivery was an equivalent therapy to IV PCA Morphine.



S-188.

THE EFFICACY OF INTRAVENOUS LIDOCAINE FOR ACUTE HERPETIC PAIN

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Introduction : Acute herpetic pain, which is considered not only nociceptive pain but also neuropathic pain, is often severe and intractable. Although there have been reported the efficacy and safety of intravenous lidocaine for neuropathic pain such as diabetic neuropathy and postherpetic neuralgia, the efficacy of lidocaine for acute herpetic pain is not known. Therefore, the effect of IL for acute herpetic pain was examined.
Method : The study included 69 patients (28 women, 41 men), with a mean age of 64-years-old (25 to 85-years-old), who consulted to our pain management office within 6 months after skin eruption of herpes zoster between May 2004 and April 2006. A lidocaine test was done with a bolus injection of 1 mg/kg of lidocaine followed by a continuous infusion of 1 mg/kg for 30 min. Visual analogue scale (VAS) was assessed before and after a lidocaine test. When VAS after a lidocaine test decreased to less than one half of VAS before a test, it was considered as positive. A patients with a positive test was treated with intravenous lidocaine once, twice or three times a week as an outpatients according to an attending physicians. The initial dose of lidocaine was 2 mg/kg and was changed according to VAS.
Results : A lidocaine test was positive of 65 patients (94%) and negative inonly 4 patients (6%). A mean value of VAS decreased siginificantly from74±20 (mean±SD) mm before treatment to 14±12 mm after treatment ($P<0.01$). The mean value of dose of lidocaine was 2.2±0.6 mg/kg. There were no severe adverse events.
Discussion : Intravenous lidocaine demonstrated a significant analgesic effect in patients with acute herpetic pain. Smaller doses of lidocaine may be enough for relief of acute herpetic pain compared with other nuropathic pain.
References : Anesth and Analg ; 101 : 1738-49, 2005.

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S-189.

HEART AND RESPIRATORY RATE CHANGES ARE PREDICTIVE OF PAIN IN PATIENT MONITORED WITH CONTINUOUS OXIMETRY/CAPNOGRAPHY DURING PCA THERAPY

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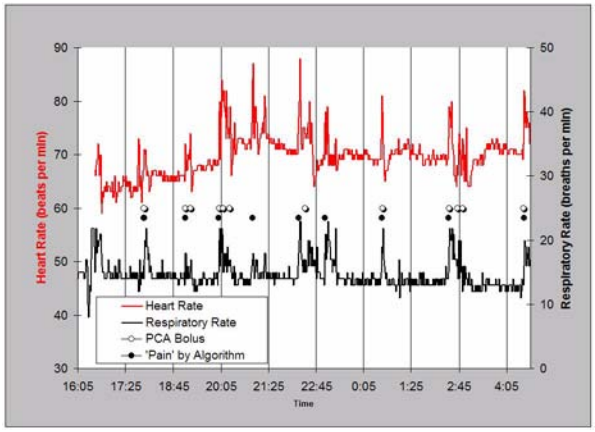
INTRODUCTION: Postoperative pain often manifests as tachycardia and tachypnea[1]. We examined heart rate (HR) and respiratory rate (RR) tracings from a patient monitored continuously with sidestream capnography and oximetry during patient controlled analgesia (PCA). Noting HR and RR rate 'spikes' preceded self-administered boluses of meperidine, an algorithm to predict the need for additional opioid was desired.

METHODS: With IRB approval, continuous HR and RR data from a 76 y.o. female after laparoscopic surgery and receiving meperidine PCA was processed. The mean HR/RR during 20 minutes preceding a two minute test window established the baseline HR/RR. The test window was passed over the data stream in chronological order. A mean HR increase of >=10 beats per minute (bpm) from baseline, or a mean HR increase >=5 bpm from baseline coupled with an increase in RR of >=4 breaths per minute during the test window was considered vital sign 'spike' attributed to pain. A pain bolus administered within 5 minutes after a 'spike' was considered a true positive, a spike without a bolus was a false positive, and a bolus without a 'spike' a false negative. Boluses immediately following the 8 min PCA lockout were attributed to insufficient pain relief and counted as single bolus events.

RESULTS: The algorithm detected 9 vital sign 'spikes' (Figure), 7 of which were true positives, two were false positives. There were no boluses without a preceding vital sign 'spike' (false negatives). In this patient, the point estimate for sensitivity of this algorithm was 100 % and vital sign 'spikes' were 78% (7/9) predictive of a meperidine bolus within five minutes. Specificity could not be assessed.



CONCLUSION: This patient had consistent HR and RR changes prior to a bolus of opioid. A PCA pump with an embedded algorithm that uses a patient's vital sign 'signature' as a condition for allowing further opioid boluses may enhance the safety of PCA by minimizing 'PCA by proxy'.[2] Future research will validate the detection algorithm and including healthy (i.e., without pain) controls will allow specificity to be determined. These limitations not withstanding, this study supports the hypothesis that pain may be detectable physiologically and the synergy of multi-faceted measurements may improve patient safety.

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2. http://www.jointcommission.org/SentinelEvents/SentinelEventAlert/sea_33.htm

S-190.

THE USE OF EXTENDED RELEASE EPIDURAL MORPHINE (DEPODUR™) LEADS TO DECREASED LENGTH OF STAY IN PATIENTS UNDERGOING TOTAL HIP ARTHROPLASTY

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INTRODUCTION: Post-operative pain following Total Hip Arthroplasty (THA) impacts negatively on patient satisfaction, rehabilitation, and hospital length of stay. Epidural analgesia provides significantly better pain relief compared to parenteral narcotics (1). However, the need for post-operative anti-coagulation following THA complicates the use of indwelling epidural catheters. The use of extended release epidural morphine, (DepoDur™; Endo Pharmaceuticals Inc, Chadds Ford, PA) decreases pain scores, narcotic consumption, and allows patients to transition directly to oral narcotics following hip surgery, without the need for an indwelling catheter (2). One would expect these effects to translate into a shorter hospital stay. We therefore evaluated the effects of DepoDur™ on the narcotic consumption, pain scores, and length of stay in patients undergoing THA.

METHODS: We retrospectively studied 111 consecutive patients who underwent THA over a six-month period and divided the patients based on peri-operative pain regimen: pre-operative DepoDur™ versus intravenous patient controlled analgesia (IV PCA). We then compared the effects of DepoDur™ versus IV narcotics on total narcotic consumption, visual analogue pain scores and length of hospital stay.

RESULTS: Of the 111 patients, 45 received DepoDur™ for post-operative pain relief and 66 used IV PCA. Patients who received DepoDur™ demonstrated significantly less visual analogue scores in the first 24 hours following THA, and required almost no supplemental IV narcotics in the first 48 hours compared to the IV PCA group. Likewise, those patients who received DepoDur™ experienced a significantly shorter (p =0.01) hospital stay of 3.4 days versus 3.8 compared to IV PCA.

CONCLUSION: Our data demonstrates that extended release epidural morphine provides superior pain control and obviates the need for a PCA, allowing the patient to transition directly to oral analgesics. Furthermore, these effects directly lead to a decreased length of stay, presumably by facilitating rehabilitation.

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1. Anesthesiology. 2005 May;102(5):1014-22.2. JAMA. 2003 Nov 12;290(18):2455-63.

S-191.

EFFECT OF PREOPERATIVE AND POSTOPERATIVE ULTRASOUND GUIDED RECTUS SHEATH BLOCK AND ILIOINGUINAL/ILIOHYPOGASTRIC NERVE BLOCK IN COMBINATION ON POSTOPERATIVE PAIN RELIEF IN PATIENT UNDERGOING ABDOMINAL GYNECOLOGICAL SURGERY.

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Introduction: Ultrasound guided rectus sheath block (RSB) combined with the ilioinguinal/iliohypogastric nerve block (II/IH block) can provide long-lasting analgesia using long-acting local anesthetics (1) (2). The aim of this study was to compare combined RSB and II/IH block performed before skin incision with at the end of surgery on postoperative pain relief in patient undergoing abdominal gynecological surgery.
Method: With IRB-approval, 20 patients classified as ASA physical status I-II, who underwent abdominal gynecological surgery, were divided into two groups randomly. In Group 1(n=10), RSB and II/IH block were performed before skin incision. In Group 2(n=10), done at the end of surgery. Anesthesia was induced with propofol and maintained with sevoflurane. Fentanyl was administered using off-line pharmacokinetic simulation model and kept at 2.0-3.0 ng/ml effect site concentration (Ce) during surgery. Ultrasound guided RSB and II/IH block were performed with a local anesthetic mixture which contains 1% ropivacaine 20ml, 1% lidocaine 20ml with epinephrine, and saline 20ml. Patients of both groups were awakened at 1.0-2.0ng/ml Ce of fentanyl. After extubating tracheal tube, continuous IV-fentanyl infusion with 0.65mcg/kg/hr and 1.5mg/day of droperidol was initiated to provide postoperative analgesia. A supplemental diclofenac suppository (50mg) was administered when patients complained of progressive pain at rest. The visual analogue scales (VAS) at rest and at cough were recorded at 0, 6, 12, 18, 24, 30, 36, and 48 hr after surgery. The number of patients administered supplemental diclofenac suppository was recorded. Statistical analysis consisted of student's t-test, repeated measures analysis of variance, $\chi 2$ test. P value <0.05 was considered significant.
Result: There were no significant differences between the two groups in age, height, weight, anesthetic time, operating time, total amount of fentanyl and fentanyl Ce at emergence. The VAS at rest was not significantly different between the two groups at 0, 6, 12, 18, 24, 30, 36, and 48 hr after surgery (Group1: 0±0, 16.8±6.7, 6.0±2.8, 1.5±1.7, 10.1±3.9, 2.5±3.95, 0±0, and 0±0, vs. Group2: 0±0, 12.4±6.7, 0±2.8, 2.0±1.76, 0±3.9, 5.0±3.95, 0±0, and 0±0, respectively). The VAS at cough was not significantly different between the two groups at all phase (Group1: 0±0, 30.8±20.4, 31.9±18.9, 23.6±16.1, 26.3±17.6, 25.0±14.2, and 25.1±14.2, vs. Group2: 0±0, 27.4±20.3, 20.9±16.3, 30.3±18.1, 26.2±11.7, 27.8±17.4, 20.1±10.5, 20.7±9.9, respectively). The number of patients who requested diclofenac suppository was not significantly different (Group1: n=8, vs. Group2: n=9, respectively).
Discussion: We did not find preemptive effect of combined RSB and II/IH block in patient anesthetized with sevoflurane and fentanyl underwent abdominal gynecological surgery. These results might be affected by fentanyl administration to suppress nociceptive stimuli although extended good postoperative analgesic effects of combined RSB and II/IHblock was shown.
Reference:
(1) Anaesthesia 1999; 54:475-478
(2) Br J Anaesth 2006; 23:1-6

S-192.

AURICULAR ACUPUNCTURE NEEDLES FOR POSTOPERATIVE PAIN CONTROL IN TOTAL HIP AND KNEE REPLACEMENT SURGERIES

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In this study we present our observation on the role of auricular acupuncture (AA), as a non pharmacological modality of treatment[1], in postoperative pain control after total hip and knee arthroplasty operations (THA /TKA).
A control group (Group I) comprised of 25 patients and a series of 10 sequential patients (Group II) undergoing total hip and knee arthroplasty operations were enrolled in this study. After receiving a balanced general anesthesia, all patients were transferred to the post anesthesia care unit (PACU) and a PCA pump was connected to the patient and set to deliver 2 mg hydromorphone /hour with a 0.2 mg dose, 6-min lock-out period, no basal dose. If the patients complain of pain on the second postoperative day, oral analgesia was administered (oxycodone 5 mg/ Tylenol 325 mg twice a day). Patients in group II received auriculotherapy in addition to the regular pain medication. ASP-AS_{gold} implantable sterile ear needles were utilized after examining the ears for signs of skin pathology. The duration of AA needle retention was up to 4 days after the surgery.
The incidence of the side effects, pain score using the visual analog scale (VAS), 10 cm visual analog Scale, (0=No pain; 10=Intolerable pain) at 0, 3, 6, 12, 24, 48, and 72 hour, duration of stay in PACU and hospital discharge, and the total amount of medications given to the patient from the PCA pump and orally were recorded in both group of patients.
Our results shows that the pain intensity on VAS from 0-10 was almost similar in both groups in 0, 3, 6, 12, and 24 hours evaluation postoperatively, although it was observed that the pain score is insignificantly lower in patients with AA. At 48 and 72 hours postoperatively there was a significant lower (P<0.5) pain score in GII (PCA+AA) when compared with GI. .
The duration of stay in PACU and the total requirement for the opioid analgesic after 72 hours postoperatively were significantly lower in GII (PCA pump + AA). There was no significant difference in the other measured parameters between the two groups except that the time to first request for analgesic medication was longer in GII than GI (47.8±0.63 V/S 24.32±0.34 minuets). No patients reported side effects from the AA needles.
We concluded that auricular acupuncture could be used to reduce postoperative analgesic requirements, cost effectiveness and can be easily learned and used by anesthesiologists/pain management practitioners who have no previous acupuncture knowledge. Further large-scale randomized investigation of this treatment modality comparing it with standard therapy and placebo acupuncture (non-inserted needle) appears to be necessary.
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S-193.

ADMINISTRATION OF LOW-DOSE ORAL NALTREXONE TO ENHANCE ANALGESIA IN PATIENTS RECEIVING CONTINUOUS INTRATHECAL MORPHINE FOR CHRONIC PAIN: A RANDOMIZED, DOUBLE-BLIND, PROSPECTIVE PILOT STUDY

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Introduction: Observations over many years suggest that very low-doses of opioid antagonists (naltrexone) block excitatory opioid receptor pathways and may paradoxically enhance morphine analgesia.[1,2] The **purpose** of this pilot study was to evaluate and compare the analgesic efficacy and safety of two different low doses of oral naltrexone added to chronic intrathecal morphine infusions in patients with chronic pain.
Methods: After IRB approval, 15 patients with chronic non-malignant pain receiving continuous intrathecal morphine were admitted into a prospective, randomized, double-blind, placebo-controlled 7-day pilot study. Patients were randomized into 3 groups: naltrexone 100 mcg (group A, 3 pts), naltrexone 10 mcg (group B, 7 pts), or placebo (group C, 5 pts). All patients continued with their constant IT morphine infusion and received one capsule of the study medication every 12 hours for 7 days. Other analgesics or co-analgesics were kept at a constant dose level throughout the study. Patients monitored pain scores (VAS, 0=no pain; 10=worst pain) and rated side effects 3 times daily for the study period.
Results: 15 patients (6M, 9F) completed the study with a mean (SD) age of 55 (10) yrs and weight of 81 (21) kg. The mean (SD) baseline VAS pain intensity rating of 6.8 (1.5) was very similar in all 3 groups. Baseline pain VAS score minus the lowest daily pain VAS score gave a peak pain intensity difference (PID) score such that positive scores indicate a reduction in pain intensity, and a negative score indicates worsening of pain. The peak PID score from day 1 was statistically ($p<.05$) highest (median PID score 5.9) in group A (naltrexone 100 mcg) compared with placebo group. There was a trend in PID scores across days 2 through 7, with median PID scores higher (ie. pain relief; $p=.07$) in group A. In the daily global pain assessments, the pain scores across days 2-7 trended lowest (least pain) in group A compared to placebo ($p=.07$) or group B ($p=.08$). Side effects were common (93% of pts), minor (headache, nausea, sedation, dry mouth), and similar across treatment groups. No serious adverse events were observed and no evidence of opioid withdrawl was seen.
Conclusions: 1) Patients receiving oral naltrexone 100 mcg BID added to chronic intrathecal morphine infusions tended to have the greatest improvement in their pain scores. 2) Side effects were common, minor, and similar across treatment groups. 3) No serious adverse events were recorded. 4) No evidence of opioid antagonist toxicity or opioid withdrawal was observed.
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S-194.

FACTORS OF FAILURE IN EPIDURAL BLOOD PATCH FOR PATIENTS WITH CSF LEAK

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<Introduction> Epidural blood patch (EBP) is one of successful treatment for patients with cerebrospinal fluid leak (CSF leak). However, the success rate of EBP in patients with intracranial hypotension is considerably lower than that in patients with post-dural puncture headache. Conventional EBP is generally performed with blind technique at the lumber region and the injected volume is controversial. There is a possibility that blind EBP at the lumber region results in failure because of inaccuracy of puncture site and unidentified spread of blood. There is a report even if skilled anesthesiologists can operate inaccurate needle displacement in up to 30% of cases (1). We are describing here a prospective case-control study of the differences between “blind EBP” and “visible EBP” under fluoroscopic measurement.
<Methods> Subjects were 32 patients with a lumber epidural blood patch for CSF leak. All participants underwent a lumber epidural puncture blindly with a 17-gauge epidural needle. Using fluoroscopic guidance, a 30 ml of autologous blood with contrast medium as target volume was injected into the epidural space. The injection was stopped, if the patient complained of lower back pain or radicular pain. Epidurograms were obtained at the point of 10, 20, and 30 ml injection. Distance of a needle tip from midline, spread of the solution and amounts of injected volume were recorded. After that, the patients were divided into two groups regarding a tip of needle displacement, in midline puncture (Group M) and unilateral puncture (Group U).
<Results> Of 32 patient, unilateral tip of epidural puncture was obtained in 18 (56%). The injected solution could reach to target volume because of pain in 6 (Group M, 43%) and in 5 (Group U, 28%) (n.s). Although unilateral spread was seen in 1 (Group M, 7%) and in 11 (Group U, 61%) at 10 ml ($P<0.01$), all cases except 3 in group U have been corrected bilaterally at 20 ml. No injected solution reached above T4 level in this study.
<Discussion> Our study indicates that more than 20 ml injection is recommended preventing from inadequate spread due to laterality at the lumbar level. On the other hand, unilateral puncture may not be a main cause of failure of EBP in case injected volume achieves more than 20 ml.To achieve an effective EBP, to inject close to the site of leak is very important. EBP under fluoroscopic guidance is very useful for preventing from “blind spread”.
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S-195.

SACROILIAC JOINT DENERVATION OF THE L4-L5 MEDIAL BRANCH AND S1-S3 LATERAL BRANCH RADIOFREQUENCY THERMOCOAGULATION : A STUDY OF OVERALL EFFICACY OF TECHNIQUE AND COMPARISON OF PULSED VERSUS HIGH TEMPERATURE RADIOFREQUENCY THERMOCOAGULATION

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Background: Treating sacroiliac joint pain has been limited to injection/bipolar radiofrequency lesioning without results (8). A small retrospective study has proposed ablation of the L5 medial and S1-S3 lateral branch as a option (1) although the innervation of the sacroiliac joint is variable with different studies quoting from L3-S4 (2-7). The previous study (1) was not prospective and did not ablate L4 medial branch. No study has compared pulsed versus high temperature radiofrequency in the sacroiliac joint .
Study Design: Prospective double-blind
Objective: Two outcomes reviewed: 1) VAS after radiofrequency of L4-L5 medial S1-S3 lateral branch 2) VAS between pulsed versus high temperature radiofrequency of L4-L5 medial S1-S3 lateral branch..
Method: Twenty-one patients. Inclusion criteria: unilateral pain > 3 months < one year, age > 18 < 65 , no litigation/ back surgery, MRI negative for stenosis or compressive disc disease, positive Patrick's/ Gaenslens, > 50% pain reduction at least 24 hours from two sacroiliac joint injections. Responders randomized to receive pulsed (42 degrees C/120 seconds) or high temperature(75 degrees C/75 seconds) radiofrequency of the L4-L5 medial S1-S3 lateral branch by a single blinded physician. VAS measured preoperatively, 1 hours, 1 week , 1month, 3months, 6 months.
Results:
1) All 21 patients showed significant reduction in mean VAS from baseline at all time points through the use of one-sample t-tests ($p < .0001$). Mean percentage VAS reduction: 1 hour (46.456 %), 1week (56.078 %), 1month (59.729%), 3 months (44.907%), 6 months (39.977%) .
2) 11 patients in pulsed radiofrequency group versus 10 patients in the high temperature group compared . Multivariate analysis of variance used for the assessment of both a time and group effect. Wilks' lambda statistic used to test for a possible time, group and time x group interaction. Results significant for time ($p < 0.001$), but not for an interaction ($p = 0.83$), nor group ($p = 0.49$). The time and interaction effects were also assessed with univariate tests within subjects. Time was significant using an F-test ($p < 0.01$) and the interaction was not significant ($p = 0.79$). No significant difference
between groups were noted at each time point
Conclusion: 1) Radiofrequency of L4-L5 medial S1-S3 lateral branch showed significant pain reduction for 6 months. 2) No significant difference in pain relief between pulsed versus high temperature radiofrequency ablation.
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S-196.

WILLED VISUOMOTOR IMAGERY ALLEVIATES DEAFFERENTATION PAIN: POSSIBLE THERAPEUTIC IMPLICATIONS OF MIRROR VISUAL FEEDBACK

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Introduction Following lesions in somatosensory pathways, deafferentation pain often occurs. Patients report that the pain is of a complex nature, and its treatment can be difficult. Anecdotal evidence has suggested that mirror visual feedback (MVF) can alleviate phantom limb pain, so we examined the possibility of using MVF to treat deafferentation pain. We also sought to classify the nature of the pain to understand more specifically the potential analgesic effect of MVF.
Methods Twelve patients with phantom limb pain, or pain associated with spinal cord or nerve injury, performed MVF once a day for a given period (17.9±13.7 weeks). Before and after the MVF treatment period, we evaluated phantom limb awareness, movement representation of phantom or affected/paralyzed-limb, and pain intensity on an 11-point numerical rating scale, and the nature of the pain (exteroception-associated or proprioception-associated) that included pain descriptor items for each of the two categories.
Results Reported pain intensity decreased significantly (before, 6.4±1.6; after, 4.1±2.4; 0 = no pain and 10 = pain as bad as it could be). After MVF, the patients' use of proprioception- but not exteroception-associated pain descriptors decreased significantly. The pain amelioration and the decrease of proprioception-associated pain descriptors were closely linked to the emergence of willed movement representation of the phantom or affected/paralyzed limb.
Discussion We confirmed the empirical usefulness of MVF followed by willed visuomotor imagery for treating deafferentation pain, and we roughly classified the pain descriptor items into two types for evaluating the qualities of pain and implicating its mechanisms. Our findings suggest that MVF may reconcile the sensorimotor loop and consequently MVF can ease certain types of pathological pain.

Acknowledgments: We thank Dr. Candy S McCabe, The Royal National Hospital for Rheumatic Disease for her critical and constructive comments on this study.

S-197.

TREATMENT OF CHRONIC COMPLEX REGIONAL PAIN SYNDROME TYPE I TUNNELED EPIDURAL INFUSION OF MARCAINE ALONE VIA I-FLOW FIXED RATE BALLOON PUMP FOR CONTINUOUS SYMPATHETIC BLOCKADE: PROSPECTIVE STUDY OF LONG TERM PAIN RELIEF AND FUNCTIONAL OUTCOMES.

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Background: CRPS I involves symptoms including allodynia, autonomic dysfunction, edema, atrophy,sympathetic hyperactivity. Short term epidural injections of various drugs have been tried with variable success: local anesthetic, morphine/fentanyl, clonidine, corticosteroids (1-13). Only one study used prolonged epidural infusion via tunneled catheter with external pump but this study was retrospective and used fentanyl mixed with marcaine (14). Our study looked at prospective pain relief and function from continuous epidural sympathetic blockade using marcaine alone and a low cost fixed rate hydrostatic I-flow balloon pump.
Method: (8 patients total) Inclusion criteria: evidence of CRPS I of a single limb for at least 6 months, >18 but <65, >50% temporary relief with two lumbar sympathetic blockade, no litigation. Tunneled epidural catheter was placed under fluoroscopic guidance to the side of symptoms with the catheter tip at C7 or L3 level . A 2 cc/hr I-flow balloon pump for cervical or 5 cc/hr for lumbar with initial concentration of marcaine .0625% was used. VAS and SF-8 measurements were done preoperatively,1 week, 1month, 3 month intervals. Changes between each of the three time points versus baseline were assessed with paired t-tests.
Outcome: Changes between each of the three time points versus baseline were assessed with paired t-tests. All data was seen to be normally distributed. **SF-8:** There were few statistically significant results for the SF-8 functional parameters, perhaps due to the extremely small sample size. The only differences observed from baseline were 1 month BP ($p = 0.04$), 3 month BP ($p = 0.02$), and a marginal difference for GH at 1 month ($p = 0.08$). **VAS scores:** Results were either statistically significant or marginally significant. . The mean drop in VAS and p-values compared to baseline were: 2 Weeks (17.25; p-value =0.06), 1 Month (22.88; p-value = 0.03), and 3 Months (16.38; p-value = 0.06).
Conclusion: Continuous Epidural Infusion of Marcaine does not significantly improve function in CRPS type I. but it may decrease self--reported pain
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140 Sami ,Pain Practice 2002 pp 81-86

S-198.

ANALYSIS OF URINE DRUG SCREEN TESTING IN AN INNER CITY PAIN MEDICINE CLINIC

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Introduction Our facility is a 617 bed tertiary medical center. We provide medical care to 28,000 inpatients and 150,000 outpatients annually.
The Pain Clinic at our institution began random urine drug screening (UDS) in 2005. We screened one in twenty patients. As of January 2006, 81% (n=43) of our patients were in violation of their narcotic agreement. We decided (for ethical and medicolegal reasons) to test all of our patients. All of our patients who are prescribed opioids have signed a narcotic agreement.
Methods Beginning February 1, 2006 we have tested or will test every third follow up patient in the clinic who is prescribed opioids until all patients have been tested. If the patient has an inappropriate (any use of drugs or alcohol not described as appropriate) UDS in the chart, they will be tested for cause. Each subject is identified only by age and sex, reason for screening (random or cause), drugs prescribed and drugs (or alcohol) found in the urine.
Results to date (n=197)

# of patients	Description
46 (23%)	Using prescribed drugs/not using anything else
19 (10%)	Using prescribed drugs/using nonprescribed legal drugs or alcohol
14 (7%)	Using prescribed drugs/using illegal drugs
11 (6%)	Using prescribed drugs/using nonprescribed legal drugs or alcohol/using illegal drugs
32 (16%)	Not using prescribed drugs/not using other drugs (legal or illegal)
21 (11%)	Not using prescribed drugs/using illegal drugs
14 (7%)	Not using prescribed drugs/using nonprescribed legal drugs or alcohol/ using illegal drugs
14 (7%)	Not using prescribed drugs/using nonprescribed legal drugs or alcohol
15 (8%)	Not using some prescribed/using some prescribed drugs
6 (3%)	Not using some prescribed drugs/using some prescribed drugs/using other nonprescribed legal drugs or alcohol
1 (1%)	Not using some prescribed drugs/using other prescribed drugs/using illegal drugs
4 (2%)	Not using some prescribed drugs/ using some prescribed drugs/using nonprescribed legal drugs/using illegal drugs

Discussion 77% of the tested patients are in violation of their narcotic agreement. 54% of the screened patients are not using some or all of their prescribed drugs. We assume that these patients not taking prescribed drugs are diverting these drugs. We cannot allow this ethically or legally. We have discharged (or will discharge at the next visit) the 77% of patients screened in violation of their narcotic agreement.

S-199.

MORPHOLOGICAL FINDINGS OF THE CAUDA EQUINA IN CHILDREN DURING THE LATERAL DECUBITUS POSITION

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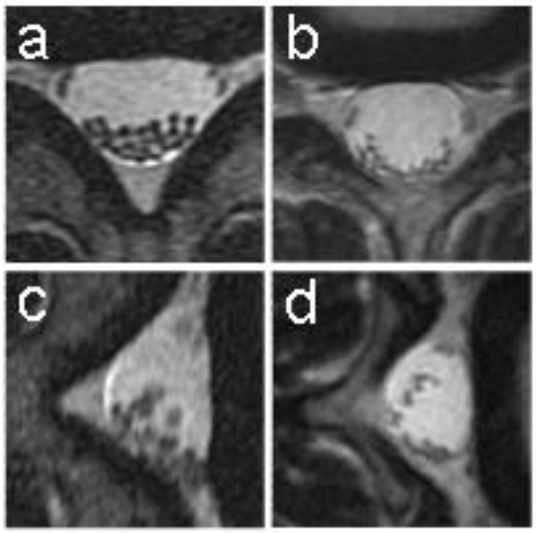
Introduction: It is very important for performing spinal anesthesia, to know detailed information about the cauda equina in the lateral decubitus position. In our previous studies (1,2), we demonstrated via magnetic resonance (MR) imaging how changed positions affect the mobility of the cauda equina's nerve roots in adults. In the lateral decubitus position, gravity caused the cauda equina to shift and sag. In the present study, we examined the movement of the cauda equina in children during the lateral decubitus position, using MR.
Methods: After obtaining the approval of the hospital ethics committee and informed consent from healthy volunteers (three pairs of father and child), the present study was scheduled. MR images of the cauda equina were obtained in the supine and lateral decubitus position.
Results: The dynamical movement of the cauda equina was observed by changing position in adults, but not in children. Figures show the cauda equina at each L3/4 inter vertebral level in adult and child during the supine and lateral decubitus position. The nerve roots of the cauda equina in adult (fig. a) and child (fig.b) lay symmetrically and aligned in the spinal canal. The nerve roots of the cauda equina in adult dynamically shifted to the gravity dependent side in the lateral decubitus position (fig. c). However, it was not obvious in children. (fig. d).



Discussion: The differential growth between the vertebral column and spinal cord during childhood may contribute to the limitation of the movement of the cauda equina in children. Our results using MR imaging may help us to better visualize where to administer local anesthesia for spinal anesthesia in children.
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S-200.

COMPARISON OF KETAMINE AND FENTANYL FOR POSTOPERATIVE ANALGESIA AFTER TONSILLECTOMY IN CHILDREN

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Perioperative use of Ketamine as an adjunct to general and regional anesthesia and to postoperative pain relief and its role in prevention of opiate-tolerance has been of interest lately [1].
This prospective, randomized double blind study was designed to compare fentanyl and preemptive Ketamine and their effect on postoperative analgesia after tonsillectomies in children as fentanyl is the opioid most commonly used during anesthesia for these surgeries.
Sixty children aged between 2 and 7 years with ASA status I & II scheduled for elective tonsillectomy with or without adenoidectomy, were enrolled in the study.
Children were randomly assigned to one of four groups to receive either fentanyl 1μg/Kg **(F1 group)**, fentanyl 2μg/Kg **(F2 group),** ketamine 0.5mg/Kg **(K group)**, or fentanyl 1μg/Kg plus ketamine 0.5mg/Kg **(FK group)**. A blinded physician gave the medications after induction of anesthesia but before the surgical incision. The anesthetic technique consisted of inhalational induction with sevoflorane in nitrous oxide/oxygen followed by initiation of an iv line, endotracheal intubation with or without muscle relaxants and maintenance with sevoflorane in oxygen and nitrous oxide.Upon conclusion of surgery and discontinuation of anesthesia, the time to eye opening to command, was noted and the patients were extubated fully awake and transferred to the post anesthesia care unit (PACU).
A blinded observer scored the post operative pain by using the pediatric behavioral pain scale [2](FLACC scale) on arrival
to PACU and at 30, 60, and 90 minutes after.
Any child with a pain score > 5 was given supplemental analgesia and that child was excluded from further analysis of pain scores. Any incidence of nausea and vomiting as well as the time patient stayed in PACU, were recorded.
Our results showed that the four groups of our patients are similar with respect to age, weight, and durations of surgery and recovery time from anesthesia. The FLACC PAIN SCORE showed that patients in K and FK groups have a significant decrease in their pain score ($p < 0.05$) than the F1 and F2 groups on arrival to recovery room and insignificant decrease after 30, 60 and 90 minutes. The F2 and K groups had a shorter duration of stay in recovery room.
We concluded that ketamine when given preemptively in sub-anesthetic doses in children undergoing tonsillectomy operation has a better postoperative pain control. The benefit of fentanyl and kitamine combination needs further investigation.
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Pediatric Anesthesia

S-201.

SEVOFLURANE PROTECTION DURING BRAIN ISCHEMIA IN NEONATAL MICE IS SUSTAINED INTO ADULTHOOD

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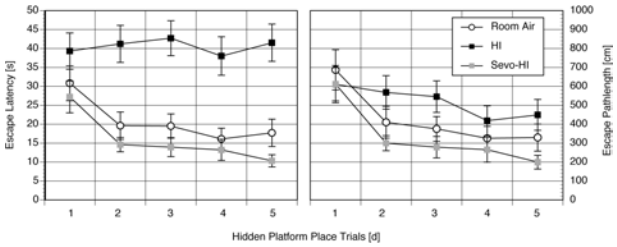
Introduction: Hypoxic-ischemic brain injury in neonates causes prolonged developmental impairment, such as documented in up to 55% of survivors of neonatal cardiac surgery, demanding better neuroprotective strategies during periods of inadequate brain perfusion. (1) Volatile anesthetics have been shown to protect during brain ischemia, but protection was thought to be only transient. (2-3) The long-term effects of volatile anesthetics during neonatal brain ischemia have not been studied. Therefore, we examined the effects of sevoflurane administration during brain ischemia in 10 day-old mice, equivalent to term human neonates, on neuronal structure and neurocognitive function in adulthood.
Methods: After IACUC approval, 10 day-old mice were briefly anesthetized for right carotid artery ligation, followed by a 2-hour recovery, and then randomized to one of three groups with controlled pericranial temperatures: HI) 60 minutes of 10% oxygen breathing spontaneously, unanesthetized (4), SEVO-HI) 60 minutes of sevoflurane 3.5% in 10% oxygen, orotracheally intubated and mechanically ventilated, or ROOM AIR) 60 min of room air breathing spontaneously. Anesthetic exposure is not survivable with spontaneous breathing during hypoxia-ischemia. (5) Arterial blood gases were obtained after sixty minutes of ischemia or room air (n=24). Right/left (R/L) brain hemispheric weight ratios and brain damage scores were determined 7 days after ischemia (n=38). To test spatial memory in adulthood, Morris water maze (MWR) performance was evaluated ten weeks post-ischemia (n=61). Groups were compared using repeated measures general linear models with Tukey's posthoc analysis for multiple comparisons. Significance was accepted at $P<0.05$.
Results: Arterial blood gases and glucose were similar during HI or SEVO-HI. Seven days after hypoxia-ischemia, R/L brain hemispheric weight ratios were significantly higher in SEVO-HI compared with HI (1.05±0.13 and 0.9±0.14, $P=0.003$), but similar to ROOM AIR (1.09±0.12). MWR hidden platform escape latency and pathlength, measures of neurocognitive function, were significantly better after SEVO-HI compared with HI ($P<0.001$, figure).



Discussion: Previously, in the adult brain, isoflurane administration during ischemia has failed to show long-term protection. (3) In the present study, in the developing brain, sevoflurane administration during ischemia demonstrates sustained protection of neurocognitive function in adulthood. This finding warrants a greater role for volatile anesthetics in perioperative brain protection in neonates.
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S-202.

USE OF A HANDHELD VIDEO GAME PRIOR TO PEDIATRIC ANESTHESIA: EFFECTS ON EMERGENCE DELERIUM AND POSTOPERATIVE PAIN

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Introduction: Higher preoperative pediatric anxiety is associated with difficult mask induction and a higher incidence and severity of emergence agitation (1).A recent study showed that preoperative distraction with a hand held video game resulted in no increase in pediatric anxiety at anesthesia induction when compared to baseline, as measured by the modified Yale Preoperative Anxiety Scale (mYPAS) (2). The present study sought to determine the effect of reducing preoperative anxiety with a video game on emergence delerium(ED) or postoperative pain (Pain) following pediatric surgery.
Methods: In a randomized, prospective study of 119 children ages 4-12 yrs undergoing outpatient surgery, anxiety was assessed after admission (Base) and again at mask induction of anesthesia (Preinduction), using the modified Yale Preoperative Anxiety Scale (mYPAS). Patients were randomly assigned to three groups: parent presence (P), P+ a handheld video game (VG), and P+ 0.5 mg/kg oral midazolam (M) given >20 min prior to entering the operating room. Patients assigned to VG were allowed to play the game through the mask induction of anesthesia. In the PACU, nurses blinded to the intervention rated postoperative pain (faces pain scale) and emergence delerium on a five point scale at 5 and 10 minutes and then at 10 minute intervals for up to 60 minutes (3).
Results: Data were analyzed with SPSS (v.13.0).119 children mean age 6.6 yrs (st. dev. 2.47 yrs) participated. A positive effect of VG playing on preoperative anxiety was demonstrated: patients in the VG group had a median mYPAS change score of zero (from Base to Preinduction) while P patients increased +5 and M patients increased +8.5 mYPAS units (p=0.08). By logistic regression, preinduction mYPAS scores were higher for P and M than VG (p=0.05). Younger age and increase in pulse at induction were significant covariates to mYPAS preinduction scores. No effect of pre-anesthetic interventions on ED or Pain was observed. ED and Pain were highly intercorrelated (p<0.001).
Discussion: Emergence delerium and postoperative pain were not affected by the pre-anesthetic intervention despite the anxiety alleviating effect of VG playing on preoperative anxiety. Limitations of the study include not controlling for type of surgery. ED and pain may be difficult to distinguish from one another, yet several studies have reported ED in presumably pain free patients (1). Although a potential relationship between ED and preoperative anxiety has been suggested, reports are conflicting.(4) Pre-anesthetic intervention with a handheld video game does not appear to affect ED and Pain which remain stubborn issues in pediatric anesthesia.
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3.Pediatr Anaesth;12:442-447,2002
4.Anesth Analg; 96:1625-30,2003

ANESTH ANALG
2007; 104; S-1–S-271

S-203.

THE EFFECT OF HYPOXIA ON THE DEVELOPING RAT BRAIN: A FUNCTION OF AGE

AUTHORS: L. Wise-Faberowski[1], **P. Robinson**[1], D. Warner[2];
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Introduction: The N-methyl-D-aspartic acid (NMDA) receptor subunits undergo age related changes during human hippocampal development.(1) This developmental effect is dependent on the partial pressure of oxygen and allows the fetus to tolerate hypoxic conditions in utero.(2) *We hypothesized that these age related differences to hypoxia are related to the NMDA receptor subunit composition.*
Methods: Organotypic hippocampal slices were prepared from Sprague-Dawley rat pups post natal day 4, 7, 14 and 21 (PND) as described by Stoppini et al. Hypoxia (<5% oxygen) was administered via a hypoxic chamber and maintained for 10 minutes. Neuronal cell death was assessed 3 days after exposure to hypoxia using Sytox staining and expressed as mean optical density. NMDA receptor subunit composition was determined using western blot analysis after exposure to hypoxia.
Results: In slices from PND 4 and 7 pups, less than 10% of CA1 neurons (relative to controls exposed to air) were lost after a 10 min exposure to 5% oxygen. The greatest effect on cell death was noted in PND 21 slices (>50% neuronal cell loss), exposed to 5% oxygen for 10 min ($p < 0.001$) and was similar to the amount of neuronal cell death observed in the PND 14 slices *(Figure 1)*. The NR2B subunit composition decreases and the NR2A subunit composition increases with increasing age as occurs with nero-ontogenetic development. *Hypoxia decreases the NR2B subunit composition and increases the NR2A subunit composition*

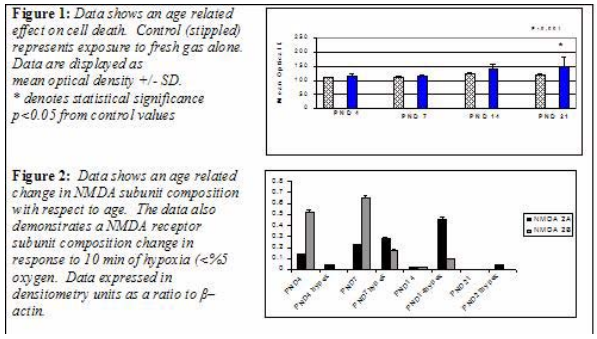

Figure 1: *Data shows an age related effect on cell death. Control (stippled) represents exposure to fresh gas alone. Data are displayed as mean optical density +/- SD. * denotes statistical significance p<0.05 from control values*

Figure 2: *Data shows an age related change in NMDA subunit composition with respect to age. The data also demonstrates a NMDA receptor subunit composition change in response to 10 min of hypoxia (<%5 oxygen. Data expressed in densitometry units as a ratio to β–actin.*

Discussion: This investigation demonstrates an age-related response to hypoxia that is dependent on the NMDA subunit composition of the developing tissue. It also demonstrates that the NMDA subunit composition changes in response to hypoxia.
References: 1. Neuroscience 118:25-35;2003 **2**. Dev Brain Res 60; 235-240;1991

S-204.

COMPARISON OF CONVENTIONAL BALANCED GENERAL ANESTHESIAVERSUS PROPOFOL BASED TOTAL INTRAVENOUS ANESTHESIA FOR VITREORETINAL SURGERY IN CHILDREN

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Introduction: Vitreoretinal (VR) surgery can engender severe pain and postoperative nausea and vomiting (PONV) in children and adults (1-3). No information was found on the use of total intravenous anesthesia (TIVA) in children undergoing VR surgery compared to conventional general anesthesia (GA) regarding PONV and pain.
Methods: A prospective, randomized single blind study was carried out on 40 ASA grade I and II children 6-16 years of age undergoing elective VR surgery. Children were pre-medicated with oral diazepam 0.2mg/kg, 2 hours prior to surgery. After routine monitoring anesthesia was induced with propofol 2.5-3mg/kg, fentanyl 2µg/kg and vecuronium 100µg/kg, and the trachea intubated. Children were randomly allocated to one of 2 groups. In group I (conventional GA) anesthesia was maintained with 60% nitrous oxide in oxygen and isoflurane with hourly boluses of 0.5µg/kg fentanyl. Group II patients received 40% oxygen in air with propofol infusion (10mg/kg/hr for 10 min decreased to 8 mg/kg/hr) and fentanyl infusion at 0.5µg/kg/hr. All children were mechanically ventilated to maintain normocarbia. Numbers of episodes of oculo-cardiac reflex (OCR) were recorded. IOP was recorded before, after instillation of silicone oil and at completion of surgery.
Pain (using AIIMS Pain Score) and PONV were monitored at 2, 2-6 and 6-24 hours. Rescue analgesia was with fentanyl for the first 2 hours and then oral paracetamol. PONV was treated with IV ondansetron.
Results: The demographic data of the two groups was comparable. The incidence of OCR was 30% in Group I and 50% in Group II ($p = 0.089$). IOP was comparable in both groups. The mean pain scores at 0-2, 2-6 and 6 -24 hours were comparable in both groups. (Group I: 2.65±1.04, 3.80±1.67 and 1.95±1.15; Group II: 3.05±1.05, 3.45±1.90 and 1.60±1.10 respectively). Ten patients in group I (10/20, 50%) had postoperative vomiting (POV) compared to 1 patient in group II (5%) in the first 2 hours after surgery ($p < 0.05$), and required ondansetron (4 in Group I versus none in Group II, $p < 0.05$). Eleven patients in group I (11/20, 55%) had POV compared to four patients in group II (4/20, 20%) in the 2- 6 hours postoperatively ($p = 0.022$). Incidence of PONV was comparable in the remaining period.
Discussion: The high incidence of emesis observed with the use of conventional GA in VR surgery has been reported earlier (1,2). Use of TIVA with short-acting opioids has been seen to reduce PONV in strabismus surgery (4). Avoidance of inhalational agents could have contributed to reduced PONV as reported earlier (5).
References: 1.Reg Anesth Pain Med, 28: 43-7, 2003.
2. J Postgrad Med, 49:123-6, 2003.
3. Retina, 21: 627-32, 2001.
4. Acta Anaesthesiol Scand, 36: 182-6, 1992.
5. Br J Anaesth, 88: 659-68, 2002.

S-205.

VIDEO-BRONCHOSCOPIC COMPUTER-ASSISTED ANALYSIS OF GLOTTIC AND CRICOID DIMENSIONS: IS CRICOID THE NARROWEST PART OF THE PEDIATRIC AIRWAY?

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AFFILIATION: [1]Penn State Milton Hershey Medical Center, Hershey, PA, [2]Washington University School of Medicine, St Louis, MO, [3]Kaiser Foundation Hospital, Oakland, CA.

Introduction: Previous studies have explored the laryngeal dimensions in children using indirect methods such as MRI (1). Only video-bronchoscopy allows direct visualization of the larynx (2). The aim of this study was to introduce a direct measure of the airway dimensions in children combining videobronchoscopy with computer analysis and to explore the relationship between the glottic and cricoid dimensions in children.
Method: Approval from the Institutional Review Board was obtained. In the first part of the study, validation experiments were performed on circular structures of various diameters using videobronchoscopy. A size 5 suction catheter was first passed through a rigid bronchoscope such that a fixed length of the catheter protruded from the tip of the bronchoscope. A video-bronchoscopic image of a graph paper with the tip of the catheter touching the graph paper was then obtained. This manoeuvere was necessary to calibrate number of pixels per mm. Images of the circular structures were then obtained with the bronchoscope-suction catheter assembly with the catheter tip touching the circular structures. A blinded observer analyzed the cross-sectional areas and the diameter of these images off-line using the ImageJ (1.33u, NIH, USA) software. This technique was validated by another blinded observer who directly calculated the diameter of the circular structure using a linear scale by applying the formula the 'area of the circle' = πr^2. In the second part, 11 ASA physical status 1 or 2 children were anesthetized and paralyzed using a standard technique. Video-bronchoscopic images of the glottis and the cricoid of these children were obtained using the bronchoscope-suction catheter assembly and off-line analysis as described above. Statistical analysis was performed using the SigmaStat 3.1 for Windows.
Results: A total of 11 children were enrolled in the study. The mean age was 5.7 years (± 2.2), mean weight was 23.3 kg (± 9.6) and the mean height was 116.5 cm (±14.7). The results are as shown in table 1.

Table 1:

Parameter	Glottis (mean ± sd)	Cricoid (mean ± sd)
Antero-posterior diameter (mm)	7.6 ± 1.1	6.6 ± 2.1
Transverse diameter (mm)	2.9 ± 0.5 *	8.1 ± 2.5
Cross-sectional area (mm^2)	17.6 ± 13.4 **	41.6± 16.9

*p<0.05, **p<0.001

Discussion: Our results suggest that in anesthetized paralyzed normal children, the glottis is the narrowest part of the pediatric airway. This study has implications on selection of cuffed vs uncuffed tube and the application of this technique in obtaining real-time measurements of the stenotic airway.
References: (1) Anesthesiology 2003; 98(1):41-45, (2) Thorax 2005; 60:652-658

S-206.

VALIDATION OF THE PEDIATRIC EMERGENCE DELIRIUM SCALE

AUTHORS: C. Lin, J. Sobol, **C. Galiza**, S. Lo, M. Carson, L. Sun;
AFFILIATION: Columbia University, New York, NY.

Introduction: Emergence delirium (ED) is a postanesthetic complication occurring in young children with behaviors including: confusion, delusions, incoherence, and inconsolable crying. One scale used to determine the presence of ED is the Pediatric Anesthesia Emergence Delirium (PAED) scale validated in children 18 months to 6 years of age[1]. We have developed the Pediatric Emergence Delirium Scale (PEDS) to evaluate infants and children aged six months to six years. The aim of this study was 1) to test the validity of each scale in diagnosing ED, and 2) to assess the reliability in applying the two scales.
Methods: All scheduled patients aged six months to six years admitted to the post-operative recovery area (PACU) were eligible for this IRB-approved prospective, observational study. Two observers independently scored each patient on the PEDS and PAED scales 5 and 30 minutes after their arrival in the PACU. At the same time, an experienced anesthesia nurse determined whether the patient had ED or not (gold standard). All observers were blinded to each other's scores. Data were pooled from both time points for analysis.
Results: 52 patients were enrolled in this study. Their average age was 2.19±1.46 years (range 0.58 to 6 years, 47% 6-18 months). The interobserver correlations and average scores were calculated for both scales (Table 1). Each scale was then validated against the gold standard. For the diagnosis of ED, a cutoff score of 14 was used for the PEDS and a score of 10 for the PAED scale as determined previously[1]. Sensitivities and specificities were calculated for both scales based on these cutoff values (Table 1).
Table 1

	Interobserver Correlation	Average Scores (mean±SD)		Sensitivity	Specificity
		ED	no ED		
PEDS	0.84	15.1±2.98	10.3±4.1	0.79	0.70
PAED	0.65	14.7±3.5	8.7 ±4.5	0.88	0.50

Discussion: Our results illustrate that in children between 6 months and 6 years both PEDS and PAED have good interobserver reliability generating comparable scores validated against our gold standard. PEDS and PAED have similar sensitivities, but PEDS has greater specificity for diagnosing ED. A common problem with both scales is the possibility of a patient receiving high scores in the absence of ED. This is likely due to the well-known difficulty in differentiating pain-related behaviors from ED in infants and young children. Further refinement of the PEDS to improve its ability to make this distinction is planned.
References: [1] Anesthesiology 2004,100(5),1138-45.
The study was supported in part by NIH5T32GM008464.

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S-207.

THE EFFECTS OF "VIRTUAL" PARENTAL PRESENCE ON THE POST-ANESTHETIC EXPERIENCE OF CHILDREN

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AFFILIATION: University of Chicago, Chicago, IL.

Introduction: The post-anesthetic experience can be a frightening time for children emerging from anesthesia. The anxiety and disorientation that can accompany awakening in a strange place with unfamiliar faces is often characterized in children as emergence delirium (ED). The incidence of ED can vary from 25 to 80% depending on the definition of ED used to establish its presence.(1) Although efforts have been made to examine different drug combinations that might decrease this incidence, no optimal solution has been found. The calming effect of parental presence at induction has previously been demonstrated.(2) Unfortunately, the character of emergence from anesthesia makes parental presence at that juncture inconvenient at best and potentially unsafe. Previous studies in this area have shown that having a "virtual" parent present at emergence is viable and may lessen the incidence and severity of ED.(3,4) This study looked to validate those claims by comparing the agitation levels of children with and without "virtual" parental presence to their previous anesthetic experiences.
Methods: Parents of subjects aged 6 months to 8 years undergoing general anesthesia for an MRI between June and August 2006 were invited to record a personal message for their child. All willing participants recorded their message, and it was then randomly determined whether or not it would be played for their child at emergence. Parents were not told whether or not their recordings were used. Children were induced and maintained with sevoflurane and/or propofol. When applicable, a short survey was used to compare the patient's level of agitation after this anesthesia experience to previous anesthetics.
Results: Nineteen children aged 6 months to 8 years were enrolled in the study from June to August 2006. One patient randomly assigned to awaken with a "virtual" parental presence was removed from analysis due to audio difficulties. With that exclusion, 10 patients did not have their parents' messages played for them upon emergence from anesthesia while 8 patients were played their parents' recordings. Among those awakening to the parental recordings that had experienced anesthesia in the past, 80% (4/5) reported less agitation with the recording. Just under 30% (2/7) of the children in the control group who had undergone general anesthesia in the past had less agitation this time around according to their parents.
Discussion: "Virtual" parental presence for children emerging from anesthesia appears to be a viable way to avoid the complications involved with parental presence at emergence while maintaining some of its benefits and creating a more pleasing post-anesthetic experience.
References: 1. Sikich N, Lerman J. Anesthesiology 2004: 100; 1138-45. 2. Himes M, Munyer K, Henly S. AANA J. 2003: 71; 293-8. 3. Bryan Y, Glick D. SPA. 2002. 4. Trinh MA, Glick DB. SPA 2005.

S-208.

SUBSPECIALTY IMPACT FACTORS: CONTRIBUTION OF PEDIATRIC ANESTHESIA ARTICLES

AUTHORS: **R. Ramsdell**, J. Lerman;
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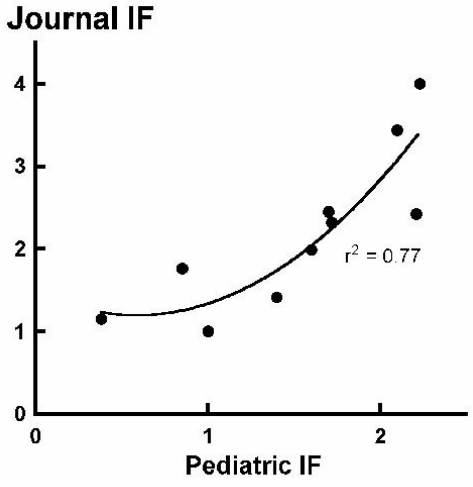
Introduction:
The **journal impact factor** (Journal IF) is the ratio of the citation counts in a given year (from articles published in the preceding two years) to the number of articles published in the preceding two years for that journal.[1] Currently, it is the most widely accepted method for comparing the quality of articles published in a journal. The IFs for anesthesia journals are widely reported, however the IFs for subspecialty sections of those journals have not been reported. Therefore, we sought to compare the IFs of the pediatric anesthesia articles (Pediatric IF) from four prominent anesthesia journals (*Anesthesiology*, *Anesthesia and Analgesia*, *British Journal of Anaesthesia*, and *Canadian Journal of Anesthesia*) to that of the dedicated pediatric anesthesia journal, *Pediatric Anesthesia*.
Methods:
An article by article search for pediatric anesthesia articles published in the years; 1998, 1999, 2003, and 2004 was performed in each of the printed journals. The results were cross-referenced with a medline search. The following types of articles were included in the analysis: clinical trials, bench research, reviews, and case reports. Two types of articles were specifically excluded: letters to the editor and editorials. The citation counts for the articles were then determined by searching the Web of Science. The ratio of the citation counts to the total number of articles published in each journal was used to calculate the Pediatric IF for 2000 and 2005 for the five journals. The relationship between the Journal IF and Pediatric IF was determined.
Results:
We found that the Pediatric IFs for 2000 and 2005 were: *Anesthesiology* 2.1, 2.23; *Anesthesia and Analgesia* 1.72, 1.7; *British Journal of Anaesthesia* 1.61, 2.21; *Canadian Journal of Anesthesia* 0.38, 0.85; and *Pediatric Anesthesia* 1.00, 1.41; respectively.



The figure displays the second order polynomial relationship between the Journal IFs and the Pediatric IFs for 2000 and 2005 combined.
Discussion:
The Pediatric IFs in 2000 and 2005 were consistently less than the Journal IFs (Figure). Journals with greater IFs published pediatric anesthesia articles that were more frequently cited than journals with smaller IFs. These findings may have implications for authors, readers and journal editors in anesthesia.
References:
1. Garfield, E. Journal Impact Factor: a brief review. *CMAJ 1999* 161 (8): 979.

Pharmacology - Basic Science

S-209.

ACTIVATING THE THALAMIC CONSCIOUSNESS SWITCH: THALAMIC MICROINJECTION OF NICOTINE REVERSES SEVOFLURANE-INDUCED UNCONSCIOUSNESS IN THE RAT

AUTHORS: **M. T. Alkire**, J. McReynolds;
AFFILIATION: Univ of Calif, Irvine, Orange, CA.

Introduction: Neuroimaging of anesthesia in humans reveals a common suppressive effect of most agents on regional thalamic activity **[1]**, prompting some to propose a thalamic consciousness switch **[2, 3]**. In support of this concept, microinjection of GABA agonists into the intralaminar central medial (CM) thalamus induces a loss of righting in rats **[4]**. This suggests the CM may be the site of an arousal switch. However, confirming the CM is a critical locus for an arousal state switching mechanism requires demonstrating that activating such a switch blocks the unconsciousness component of anesthesia. Here we determine whether microinfusion of nicotine directly into the CM thalamus can reverse anesthetic-induced unconsciousness.
Methods: Following IACUC approval cannula were implanted in rats and aimed at the CM or control locations. The following week, rats were anesthetized past the loss of righting reflex point with sevoflurane (1.4 ± 0.2%). The arousal effects of a single infusion of nicotine (150 µg/0.5 µl over 1 min) were behaviorally determined and histologically localized (n=73). EEG effects were determined in a subset of animals (n=8) using a PowerLab/4s system (ADInstruments, Milford, MA). Resumption of consciousness was behaviorally defined as restoration of righting.
Results: Nicotine demonstrated a site specific ability to temporarily restore righting and mobility in those animals whose cannula placements were within about 1 mm of the anterior (AP -3.0 mm) CM thalamus ($p < 0.0001$, Chi-squared; See Figure). Righting occurred despite continued systemic exposure to anesthesia. Righting occurred on average (± SD) 290 ± 183 sec following the end of the infusion and lasted a median time of 103 sec (interquartile range: 65 - 144 sec). Control infusions were without effect. EEG changes always preceded arousal responses, but they did not necessarily indicate resumption of wakefulness.
Conclusions: Intrathalamic nicotine reverses anesthetic-induced unconsciousness. The CM thalamus is a critical component of the arousal state switching mechanism. Anesthetic-induced unconsciousness appears to occur in large part through a mechanism whereby anesthetics competitively inhibit thalamic nicotinic receptors.

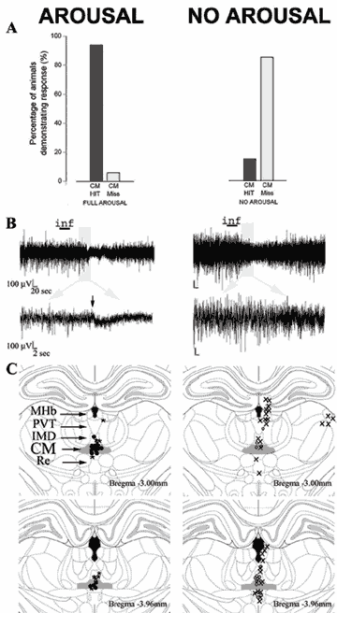


Figure: (A) Percentage of arousal responses. (B) EEG responses. (C) Histology of infusion tips: filled circle = full arousal, * = partial arousal, open circle = seizure, x = miss.

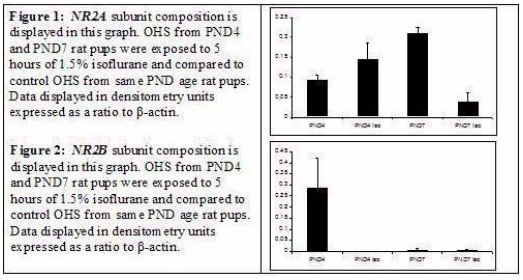
References:
[1] Prog Brain Res. 2005;150:229.
[2] Conscious Cogn. 2000;9:370.
[3] Anesthesiology. 2005;102:447
[4] Neuropharm. 1990;29:649.

S-210.

THE AGE-DEPENDENT EFFECTS OF ISOFLURANE ON RAT NMDA RECEPTOR SUBUNIT COMPOSITION

AUTHORS: S. Rich[1], P. Robinson[2], **L. Wise-Faberowski**[2];
AFFILIATION: [1]Indiana University, Indianapolis, IN, [2]University of Colorado, Denver, CO.

Introduction: Anesthetic neurotoxicity has been demonstrated in a 7 day old rat pup (PND7) model. This effect of anesthetic neurotoxicity is age-dependent, being demonstrated in PND7 rat pups as compared to rat pups of other ages(1,2). Changes in the NMDA receptor subunit composition occur as function of age; being NR2B predominant early in development and NR2A predominant later in development (3). *We hypothesized that isoflurane may change the subunit composition in an age-dependent manner.*
Methods: Organotypic hippocampal slices (OHS), prepared according to the methods of Stoppini, were prepared from PND4 and PND7 rat pups. The OHS were maintained in culture for 7 days. At such time, the OHS were exposed to 1.5% isoflurane for a period of 5 hours. After 5 hours, the OHS were harvested and later western blot analysis of the NR2B and NR2A receptor subunits was performed.
Results: Exposure to isoflurane decreased the NR2A subunit composition in OHS prepared from PND7 rat pups (Figure 1) and decreased the NR2B subunit composition in OHS prepared from PND4 rat pups (Figure 2). Furthermore, isoflurane increased the NR2A subunit composition in OHS prepared from PND4 rat pups (Figure 1).



Discussion: This investigation demonstrates the age-related changes in the NR2B and NR2A subunit composition in response to a 5 hour exposure to 1.5% isoflurane. The vulnerability of OHS prepared from PND7 rat pups to isoflurane neurotoxicity may be in response to the decrease in the NR2A subunit composition. Furthermore, the absence of isolfurane neurotoxicity in OHS prepared from PND4 rat pups may in part be explained by the increase in the NR2A subunit composition. The mechanism for such an effect remains to be further elucidated.

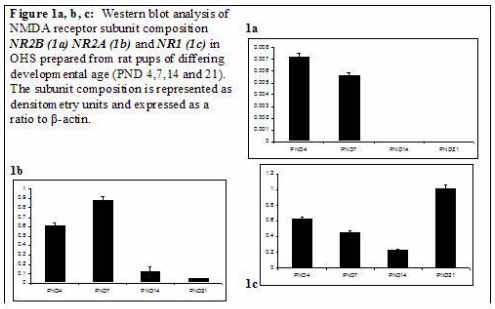
1. J Neurosci 23(3); 876-82, 2003
2. Anesth Analg 100(3); 651-7, 2005.
3. J Child Neurol 219(3) ; 236-9, 2006

S-211.

NMDA RECEPTOR SUBUNIT COMPOSITION: A FUNCTION OF RAT DEVELOPMENTAL AGE

AUTHORS: P. Robinson[1], S. Rich[2], L. Wise-Faberowski[1];
AFFILIATION: [1]University of Colorado, Denver, CO, [2]Indiana University, Indianapolis, IN.

Introduction: In evaluating the response of neuronal tissue to isoflurane, one must have an understanding of the NMDA receptor (NR) neuro-ontogeny in the model system being evaluated (1). The seven day old (PND7) rat pup is the most frequently used model for evaluating responses of developing brain to injury and treatment. Anesthetic neurotoxicity is an example of a developmental response to isoflurane (2). We hypothesized the NMDA receptor subunit composition changes as a function of developmental age in PND 4-21 rat pups.
Methods: Organotypic hippocampal slices (OHS), according to the methods of Stoppini, were prepared from PND4, 7 14 and 21 rat pups. The OHS were maintained in culture for 7 days. At such time, the OHS were harvested and later western blot analysis of the NR1, NR2B and NR2A receptor subunits was performed.
Results: The NMDA receptor subunit composition changes as follows: The NR1, NR2B and NR2A subunit decrease as function of increasing age **(Figure 1a, b, c)**. Noted exceptions are the increase in NR2A at PND7 and increase in NR1 at PND21 **(Figure 1a, b, c).**



Discussion: An understanding of the mechanism of anesthetic neurotoxicity can be gained by this investigation. The transition from NR2B to NR2A receptor subunit composition predominance occurs at PND7. However, based on the NR2B predominance in OHS prepared from animals of younger developmental age, one may infer that the presence of the NR2B subunit composition places the developing brain at risk of anesthetic neurotoxicity.

1. J Child Neurol 219(3) ; 236-9, 2006
2. J Neurosci 23(3); 876-82, 2003
3. Anesth Analg 100(3); 651-7, 2005.

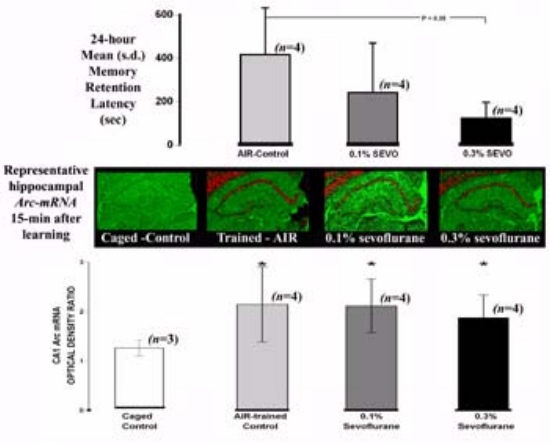
S-212.

HIPPOCAMPAL MRNA LEVELS OF THE PLASTICITY RELATED IMMEDIATE-EARLY GENE *ARC* ARE NOT SUPPRESSED BY AN AMNESIC DOSE OF SEVOFLURANE IN THE RAT

AUTHORS: T. Beydoun, T. Miyashita, J. McReynolds, J. Guzowski, **M. T. Alkire**;
AFFILIATION: Univ of Calif, Irvine, Orange, CA.

Introduction: The amygdala plays a role in the memory consolidation effects of anesthesia **[1]**. Recently, the mechanism by which the amygdala influences memory consolidation has been linked to hippocampal synaptic plasticity changes involving the immediate-early gene *Arc* (activity-regulated cytoskeletal associated protein) **[2]**. Post-learning amygdala manipulations that enhance memory also enhance hippocampal *Arc* and conversely manipulations that impair memory decrease *Arc*. Here we determine whether the memory consolidation effects of anesthesia might also be mediated via an *Arc*-related hippocampal mechanism.
Methods: Following IACUC approval, 27 well-handled rats learned the inhibitory avoidance paradigm during exposure either to air, 0.1 or 0.3% sevoflurane. Hippocampal *Arc* mRNA (as a potential marker for *Arc* protein) was determined using *in situ* hybridization at 15-min following the learning experience in a subset of animals. In the remaining rats, memory was assessed at 24 h. *Arc* mRNA signal was imaged at the cellular level with a Typhoon Trio+ Variable Mode Imager (Amersham Biosciences). Hippocampal *Arc* mRNA was quantified using ImageQuant TL (Amersham Biosciences). Signal intensity changes were compared using ANOVA with post-hoc t-tests. $P < 0.05$ was considered significant.
Results: Memory at 24 hours showed a dose-dependent reduction, reaching significance for animals trained in the presence of 0.3% sevoflurane. Memory enhancement was not seen, nor expected with the 0.1% dose because of the learning parameters used. Representative hippocampal *Arc* mRNA signal is shown in the figure. Quantitative *Arc* mRNA analysis revealed that mean (SD) *Arc* mRNA was induced with learning mainly in the CA1 region, as expected. However, *Arc* mRNA did not significantly differ between the Air-trained and the sevoflurane exposed animals.
Conclusions: Hippocampal *Arc* mRNA levels did not differ between amnesic and non-amnesic doses of sevoflurane. This establishes that the amnesic effect of low dose sevoflurane is NOT primarily due to an anesthetic-induced failure of encoding. Rather, sevoflurane-induced amnesia must occur through the disruption of memory consolidation at a mechanistic site downstream from hippocampal *Arc* mRNA induction. The next plausible target now becomes *Arc* protein synthesis, itself. *Arc* mRNA cannot serve as a marker for sevoflurane-induced amnesia. Alternatively, the possibility is raised that *Arc* may not be a key protein in the memory consolidation effects of anesthetics.

References:
[1] Anesthesiology 2005, 102:754-60.
[2] PNAS 2005, 102:10718-23.
Funded by NIH RO1GM065212 and MH060123-to-JG.

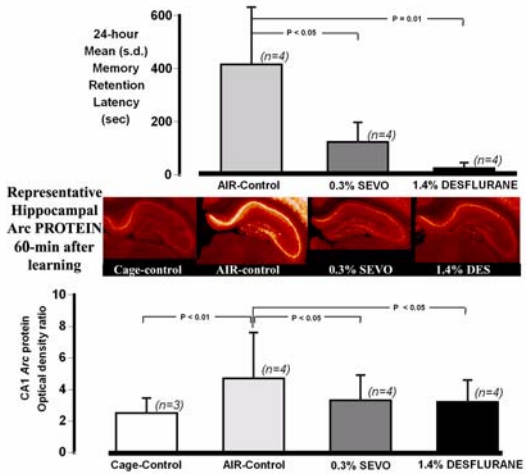


S-213.

TOWARD THE MECHANISM OF ANESTHETIC-INDUCED AMNESIA: ANESTHETICS SHUT DOWN MEMORY CONSOLIDATION BY INHIBITING HIPPOCAMPAL *ARC*-PROTEIN SYNTHESIS IN THE RAT.

AUTHORS: **M. T. Alkire**, T. Beydoun, T. Miyashita, J. McReynolds, J. Guzowski;
AFFILIATION: Univ of Calif, Irvine, Orange, CA.

Introduction: The amygdala plays a role in the memory consolidation effects of anesthesia [1]. Recently, the mechanism by which the amygdala influences memory consolidation has been linked to hippocampal synaptic plasticity changes involving the immediate-early gene *Arc* (activity-regulated cytoskeletal associated protein) [2]. Post-learning amygdala manipulations that enhance memory also enhance hippocampal *Arc* and conversely manipulations that impair memory decrease *Arc*. Here we determine whether the memory consolidation effects of anesthesia might also be mediated via an *Arc-protein*-related hippocampal mechanism.
Methods: Following IACUC approval, 27 well-handled rats learned the inhibitory avoidance (IA) paradigm during exposure either to air, 0.3% sevoflurane or 1.4% desflurane. Hippocampal *Arc*-protein was measured using immunohistochemistry at 60-min following the learning experience in a subset of animals. In the remaining rats, memory was assessed at 24 h. *Arc*-protein was imaged at the cellular level with a Typhoon Trio+ Variable Mode Imager (Amersham Biosciences). Hippocampal *Arc*-protein was quantified using ImageQuant TL (Amersham Biosciences). Signal intensity changes were compared using ANOVA with post-hoc t-tests. $P < 0.05$ was considered significant.
Results: Memory at 24 hours was significantly suppressed by both anesthetics, see figure. Representative hippocampal *Arc*-protein signal is also shown in the figure. Quantitative *Arc*-protein analysis revealed that mean (SD) *Arc*-protein levels in the hippocampal CA1 region were significantly enhanced with learning, as expected. However, *Arc*-protein in anesthetic exposed rats was not significantly different from the levels found in caged-controls and was significantly reduced compared with levels found in the air-trained rats ($P < 0.05$ for sevoflurane and $P < 0.05$ for desflurane, but one-tailed only).
Conclusions: Hippocampal *Arc*-protein synthesis is suppressed by low amnesic doses of volatile anesthetics that block long-term memory consolidation. Taken together with other results demonstrating that hippocampal *Arc*-mRNA is not suppressed by anesthesia, these findings offer strong pin-point evidence that anesthetics block long-term memory consolidation through a mechanism localized to the direct (translation inhibition) or the indirect (amygdala mediated) suppression of *Arc*-protein synthesis.
References:
[1] Anesthesiology 2005, 102:754-60.
[2] PNAS 2005, 102:10718-23.
Funded by NIH RO1GM065212 and MH060123-to-JG.



S-214.

THE EFFECTS OF VOLATILE ANESTHETICS ON THE INDUCTION OF LONG-TERM POTENTIATION IN THE MOUSE HIPPOCAMPUS.

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Introduction: Volatile anesthetics are known to produce amnesia; however, possible mechanisms underlying memory disruption by volatile anesthetics still remain unknown. The purpose of the current study was to examine the effects of isoflurane and sevoflurane at clinical concentrations on excitatory synaptic transmission and on long-lasting changes in synaptic efficacy induced by high frequency afferent stimuli in the CA1 region of rat hippocampal slices.
Methods: Field excitatory postsynaptic potentials (fEPSPs) in the CA 1 area were recorded with extra-cellular electrodes following electrical stimulation of Schaffer-collateral-commissural (SCC) fiber inputs. Volatile anesthetics at concentrations ranging from subanesthetic to anesthetic levels were applied to slices in an artificial cerebro-spinal fluid (ACSF) solution using a carrier gas (95%-O_2/5%-CO_2) and calibrated commercial vaporizers. Paired pulse facilitation was used as a measure of presynaptic effects of the anesthetic. Long-term potentiation (LTP) was induced using titanic stimulation (100 Hz, 1 s) of the SCC pathway. Electrical stimuli consisted of square wave paired pulses were delivered by a stimulus generator to electrodes every 15 s to minimize frequency-dependent changes in synaptic transmission. The stimulus intensity was set to evoke 50-70 % of the maximal amplitude of the responses.
Results: Isoflurane depressed the amplitude of fEPSPs in a dose-dependent manner. Clinically relevant concentration of isoflurane, but not subanesthetic concentration, increased paired-pulse facilitation, suggesting that isoflurane affects the probability of glutamate release. A brief titanic stimulation induced stable LTP. Isoflurane (2.8 vol. %) blocked the induction of LTP. Isoflurane did not block LTP induction in the presence of picrotoxin, a specific antagonist of gamma aminobutyric acid type A (GABAA) receptors, suggesting that modulation of GABAA receptors play an important role for LTP inhibition produced by isoflurane.
Discussion: In accordance with our previous studies (1, 2), isoflurane depressed excitatory synaptic transmission in the CA1 region of rat hippocampal slices by acting presynaptic- and postsynaptic sites. In the present study, we found that isoflurane (2.8 %) inhibited the induction of LTP; however, picrotoxin overcomes the effects isoflurane on LTP induction. These data suggests that modulation of GABAA receptors contributes significantly to LTP inhibition. Understanding how general anesthetics affect LTP can be useful for assessing molecular mechanisms by which anesthetic agents disrupt memory function.
Conclusions: Clinically relevant concentrations of volatile anesthetics inhibit the induction of LTP, at least in part, by modulating GABAA receptors.
References: 1) Anesthesiology 92:228-36, 2000; 2) J Neurosci 20:5915-23, 2000

S-215.

EFFECTS OF PROPOFOL ON PHOSPHORYLATION OF GLUTAMATE AMPA RECEPTORS IN RAT STRIATAL NEURONS

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AFFILIATION: Univ of Missouri-Kansas City Sch of Med, Kansas City, MO.

Introduction: The excitatory neurotransmitter glutamate is involved in the regulation of various synaptic and cellular activities throughout the CNS. The regulation is achieved through interactions with both ionotropic and metabotropic glutamate receptors which are densely expressed in the CNS. One subtype of these glutamate receptors, the ionotropic α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid receptor (AMPAR), has been shown to undergo active phosphorylation at Ser831 and Ser845 sites of the intracellular C-terminus of the GluR1 subunit. The phosphorylation at these sites may represent an important mechanism for regulating receptor function. In this study, a working hypothesis that the general intravenous anesthetic propofol may affect phosphorylation of AMPARs at GluR1-Ser831 and/or GluR1-Ser845 was determined in cultured rat striatal neurons.

Methods: The standardized procedure preparing primary striatal neuronal cultures from day 18 rat embryos was used in this study. Cells were cultured 8-12 days before use. In a time-course study, propofol at 10 μM was incubated in cultures for different durations (1, 2, 5, 15, or 30 min) to examine the effect of propofol on AMPAR phosphorylation at GluR1-Ser831 and GluR1-Ser845. Propofol (2,6 di-isopropylphenol, Sigma) was dissolved in 0.1% DMSO which itself had no effect on GluR1 phosphorylation at either Ser831 or Ser845. Western blots were performed with a phospho-specific antibody against phosphor-GluR1-Ser831 or phosphor-GluR-Ser845. Blot data were measured and analyzed using a one-way ANOVA.

Results: Propofol (10 μM) incubated for different durations did not significantly alter basal levels of GluR1-Ser831 phosphorylation. In contrast, propofol (10 μM) seemed to increase GluR1-Ser845 phosphorylation as evidenced by a significant increase in basal GluR1-Ser845 levels at 5 and 30 min. At all time-points surveyed, propofol did not alter basal levels of GluR1 subunits and control protein actin.

Discussion: Propofol is well-known to activate GABA-A receptors to inhibit synaptic transmission and produce anesthesia. However, the effect of propofol on glutamate receptor activity is poorly understood. In this study, we found that propofol can elevate AMPAR GluR1 phosphorylation at a specific site. While the functional significance of this effect is unclear, this result might indicate a new avenue to study the influence of anesthetics over ionotropic glutamate receptor function in relation to excitotoxicity and other actions.

Reference:

1. Mol Neurobiol 32: 237-249, 2005.

S-216.

MOLECULAR ANALYSIS OF ALPHA2A AND ALPHA2C ADRENERGIC RECEPTORS IN CULTURED MOUSE SYMPATHETIC NEURONS

AUTHORS: P. Brum, C. Hurt, O. Shcherbakova, B. Kobilka, **T. Angelotti**;
AFFILIATION: Stanford University, Stanford, CA.

Introduction:

Previous research suggested that α2A and α2C adrenergic receptor (AR) subtypes have overlapping but unique physiological roles in neuronal signaling; however the basis for these dissimilarities is not completely known (1). To better understand the observed functional differences between these autoreceptors, we investigated targeting and signaling of endogenously expressed α2A&C ARs in cultured sympathetic ganglion neurons (SGN) (2).

Methods:

Trafficking and signaling of endogenously expressed α2A&C ARs were studied in primary mouse SGN cultures. To differentiate between α2A&C ARs, SGN were cultured from wild-type (WT), α2A AR, and α2C AR knockout (KO) mice. Cultured SGN were examined by immunocytochemical analysis with α2A&C AR subtype specific antisera and calcium influx ($[Ca^{2+}]_i$) imaging.

Results:

At Day 1 and 4, α2A&C ARs could be readily detected in cultured SGN from wild-type mice. By Day 8, α2A ARs were targeted to cell body, as well as axonal and dendritic sites, whereas α2C ARs were primarily localized to an intracellular vesicular pool within the cell body and proximal dendritic projections. Expression of synaptic vesicle marker protein SV2 did not differ at Day 8 nor co-localize with either subtype. By Day 16 however, α2C ARs had relocated to somatodendritic and axonal sites and, unlike α2A ARs, co-localized with SV2 at synaptic contact sites (Figure 1). Consistent with a functional role for α2 ARs, we also observed that dexmedetomidine-stimulation of cultured SGN more efficiently inhibited depolarization-induced calcium entry into older, compared to younger, cultures.

Conclusions:

Though α2A and α2C AR are highly homologous proteins, and have similar pharmacologic properties, they have different localization patterns at nerve terminals where they act as presynaptic autoreceptors. These results provide direct evidence of distinct developmental patterns of endogenous α2A&CAR targeting and function in a native cell system and that maturation of SGN in culture leads to alterations in neuronal properties required for proper targeting. More importantly, the co-localization at Day 16 of α2C ARs at sites of synaptic contact may partially explain the differential modulation of neurotransmitter release and responsiveness to action potential frequency observed between α2A and α2C ARs in SGN.

References:

1. Hein L, Altman JD, Kobilka BK *Nature* (1999) 402:181-4.
2. Brum PC, Hurt CM, Kobilka B, Angelotti T. *Neuropharmacology* (in press)

This work was supported in part by NINDS K08 NS050654-01A1

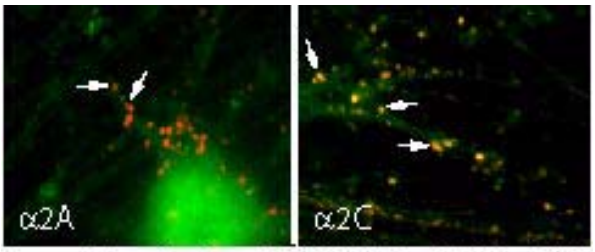

Fig. 1. Co-localization of α2A&C AR and SV2 in SGN. Immunocytochemical staining for α2AR (green) and SV2 (red) reveal co-localization (yellow) with α2C but not α2A ARs in cultured SGN (arrow).

S-217.

TITRATED DOBUTAMINE REVERSES THE VASOPRESSIN-ASSOCIATED IMPAIRMENT IN CARDIAC INDEX AND SYSTEMIC OXYGEN SUPPLY IN OVINE ENDOTOXEMIA.

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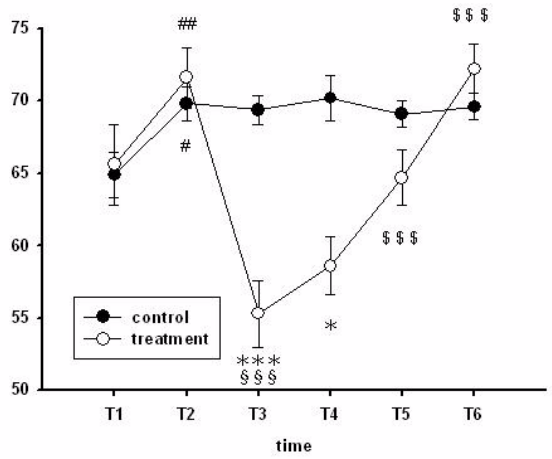
Introduction: Arginine vasopressin (AVP) is increasingly used to treat sepsis-related vasodilation and to reduce catecholamine requirements [1]. However, AVP infusion may be associated with a marked reduction in systemic blood flow and oxygen transport [2]. The purpose of the present study was to evaluate whether dobutamine may be titrated to reverse the AVP-related reduction in cardiac index (CI) and systemic oxygen delivery index (DO_2I) in an established model of ovine endotoxemia.
Methods: Eighteen adult ewes were chronically instrumented to determine cardiopulmonary hemodynamics and global oxygen transport. All ewes received a continuous endotoxin infusion that contributed to a hypotensive-hyperdynamic circulation and death of four sheep. After baseline measurements in the healthy state (T1) and following 16 hours of endotoxemia (T2), the surviving ewes (n = 14; 34.6 ± 1.2 kg) were randomized to receive either AVP (0.04 $U \cdot min^{-1}$; n = 8) or the vehicle (normal saline; n = 6) for 2.5 hours. After 1 hour of AVP infusion (T3), dobutamine was simultaneously infused in AVP-treated sheep. Dobutamine infusion was started with an initial rate of 2 $\mu g \cdot kg \cdot min^{-1}$ (T4) and was increased to 5 (T5) and 10 $\mu g \cdot kg \cdot min^{-1}$ (T6) after 30 and 60 minutes, respectively.
Results: AVP infusion increased mean arterial pressure (MAP) and systemic vascular resistance index (SVRI) at the expense of a markedly reduced CI, DO_2I and S_vO_2. Dobutamine dose-dependently reversed the reductions in CI, DO_2I and S_vO_2 and further increased MAP (figure 1; $^{\#}p<0.05$ vs. T1, $^{\#\#}p<0.01$ vs. T1, $^{\S\S\S}p<0.001$ vs. T2, $^{\$\$\$}p<0.001$ vs. T3, *p<0.05 vs. control, ***p<0.001 vs. control)



Discussion: This study employs dobutamine as a useful catecholamine to reverse the AVP-associated impairment in systemic blood flow and global oxygen transport.
References: [1]Circulation 2003; 107:2313-2319. [2]Crit Care Med 2003; 31:1502-1508.

S-218.

ENHANCEMENT OF ALPHA2C ADRENERGIC RECEPTOR SURFACE EXPRESSION BY REEP FAMILY MEMBERS

AUTHORS: C. Hurt, S. Bjoerk, B. Kobilka, **T. Angelotti**;
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Introduction:
As regulators of sympathetic neuron function, α2A and α2C adrenergic receptors (ARs) have different neuronal localizations (1, 2). In non-neuronal cell lines, α2A ARs target readily to the plasma membrane, however, α2C ARs have little plasma membrane expression (Fig. 1). However, α2C ARs readily target to the plasma membrane in neuronal cell lines. We investigated if two new families of interacting proteins, Receptor Transporting Proteins (RTPs) and Receptor Expression Enhancing Proteins (REEPs) were modulators of α2C AR surface expression in neuronal cells.
Methods:
Expression of RTP 1-4 and REEP 1-6 proteins were examined in various non-neuronal (NRK, Rat 1) and neuronal (PC12, AtT20) cells lines, using RT-PCR techniques with specific primers. RTP and REEP family members that showed differential expression were then studied for their ability to regulate cell surface expression of α2C ARs. Stable NRK clones expressing individual modulator proteins and α2A&C ARs were examined by immunofluorescence microscopy and cell-surface ELISA assays. Direct interactions between α2A&C ARs and modulator proteins were examined by immunoprecipitation assays.
Results:
RT-PCR analysis revealed that REEP 1, REEP 2, and REEP 6 mRNAs were found to be differentially expressed, being present in PC12 and not NRK cells. NRK stable clones expressing each REEP protein were created. Immunocytochemical staining of surface and total expression of α2A&C ARs in each stable cell line demonstrated enhanced surface expression of α2C ARs following co-expression of REEP 2 and REEP 6 cDNAs; α2A AR surface expression was not affected by any REEP family member tested. Quantitative cell surface expression by ELISA assay revealed similar results. Immunoprecipitation assays revealed that REEP1 and 2 proteins could co-precipitate α2C ARs, suggesting a biochemical interaction *in vitro*.
Conclusions:
Targeted cell surface expression of α2C ARs in neuronal cell lines may be due to expression of interacting proteins of the REEP family, thus accounting for differential expression and targeting seen in native neuronal systems (2). Such biochemical distinctions may underlie physiological and pharmacological differences between α2A&C ARs. Experiments to delineate α2A&C AR domains involved and proof of direct protein-protein interactions are underway.
References:
1. Hurt CM, Feng FY, Kobilka B. *J Biol Chem* (2000) 275:35424-31.
2. Brum PC, Hurt CM, Kobilka B, Angelotti T. *Neuropharmacology* (in press)
This work was supported in part by NINDS K08 NS050654-01A1

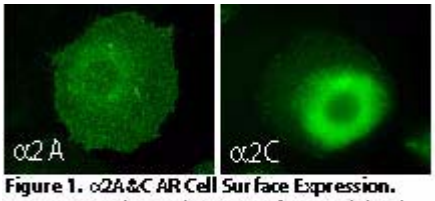

Figure 1. α2A&C AR Cell Surface Expression. Immunocytochemical staining of permeabilized NRK cells revealing predominant cell surface (α2A) and intracellular (α2C) staining.

S-219.

LIDOCAINE MODULATES VOLTAGE-GATED PROTON CHANNELS IN RAT MICROGLIA

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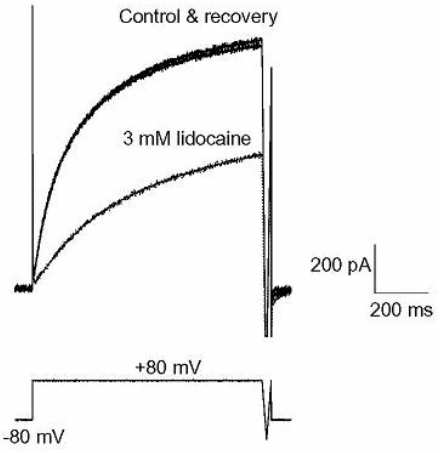
Introduction. Microglia, immune cells widely distributed in the CNS, can initiate repair of injured regions by phagocytosis of cell debris and secretion of biologically active substances in response to acute brain insult. Voltage-gated proton channels expressed on microglia are thought to be essential for the process of phagocytosis and respiratory burst (1). Local anesthetics are known to have a variety of anti-inflammatory profiles which include suppression of phagocytosis in monocytes (2). However, the effects of local anesthetics on microglia proton channels remain to be determined.
Methods. Lidocaine action on proton channels was studied in rat microglia using the whole-cell recordings (3). To analyze proton currents, major ions were removed from the solutions and the external and internal pHs were set to be 7.3 and 5.5. The pH of lidocaine (0.1 - 10 mM) test solutions were adjusted to 7.3.
Results. The current traces show that lidocaine (3 mM) reversibly inhibited proton channels (Figure). Lidocaine decreased the current amplitude of proton channels in a dose-dependent manner. Significant inhibition was observed at 300 μM ($p < 0.05$). The effective concentration to inhibit the currents to 50% of the control was ~5 mM. The current-voltage relationship obtained from voltage ramps revealed that lidocaine dose-dependently shifted the reversal potential of the channel to more positive voltages. This suggested that exogenously applied lidocaine might increase the intracellular pH (pHi) as the pHo was kept to be constant. The resulting reduction of the driving force for H^+ efflux could explain only ~25% of total inhibition. The pHi increase by lidocaine estimated from the reversal potential shift was ~0.2 with 1 mM. The time constant of the activation process on depolarization was dose-dependnetly increased by lidocaine.
Discussion. The present results indicated that lidocaine inhibited proton channels by at least two different mechanisms, one is related with pHi increase and the other is not. The latter effect was much greater than the former. In conclusion, lidocaine inhibits proton channels, leading to suppression of phagocytic action of microglia.
References: 1. Prog Neurobiol 64:277-305, 2001. 2. Anesthesiology 93:858-75, 2000. 3. J Neurosci 20:7220-7227, 2000.



S-220.

VERIFICATION OF THE TISSUE ACIDIFICATION HYPOTHESIS FOR LOCAL ANESTHETIC FAILURE ASSOCIATED WITH ACUTE INFLAMMATION

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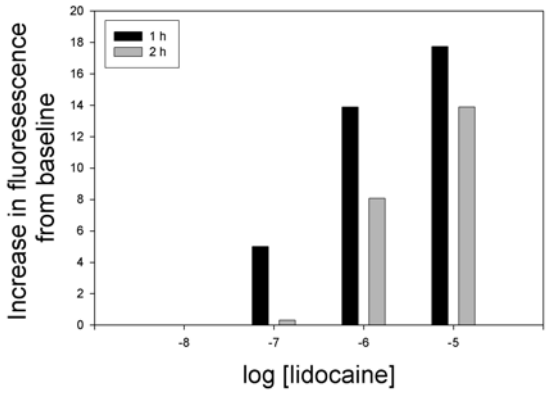
Introduction: It is well-known that local anesthetics do not successfully work in the patients with acute inflammation. Such a clinical phenomenon is explained by the theoretical decrease of non-ionized membrane-active drug molecules due to inflammatory tissue acidification. However, the hypothetic pH-lowering mechanism has not been experimentally proven especially in relation to the mode of local anesthetic action. We studied the pH-dependent interaction of local anesthetics with lipid membranes to discuss the pharmacological background for anesthetic failure associated with acute inflammation.
Methods: DPH-labeled liposomal and nerve cell model membranes were prepared with various phospholipids (1,2-dipalmitoylphosphatidylcholine, 1-palmitoyl-2-oleoylphosphatidylcholine, 1-palmitoyl-2-oleoylphosphatidylethanolamine, 1-stearoyl-2-oleoylphosphatidylserine, sphingomyelin and/or cardiolipin) and cholesterol [1]. Their suspensions in 25 mM phosphate buffer containing 100 mM NaCl (pH 2.0, 5.9, 6.4, 6.9, 7.4 and 7.9) were treated with either DMSO or diluted HCl solutions (pH 4.0) of lidocaine (1.0 mg/ml), procaine (2.0 mg/ml), prilocaine (1.0 mg/ml) and bupivacaine (0.5 mg/ml). After incubation for 10 min at 37ºC, membrane fluidity changes were determined by measuring DPH fluorescence polarization [2]. Lidocaine pretreated with peroxynitrite (2-40 μM) for 10 min was also applied to nerve cell model membranes at pH 6.4-7.4.
Results: 1,2-Dipalmitoylphosphatidylcholine membranes were fluidized by all anesthetics in DMSO and the fluidization decreased with lowering the pH from 7.9 to 5.9. Such a pH-dependence became more significant by applying lidocaine as an aqueous acidic solution similar to marketed anesthetic solutions. The membrane fluidization potency was correlated with the relative concentration of non-ionized lipid-interactive molecules, which was obtained by the Henderson-Hasselbach equation. However, nerve model membranes were fluidized by lidocaine at pH 6.4, showing the fluidizing degree comparable to that at pH 7.4. Cationic lidocaine fluidized the membranes consisting of cholesterol and 1-stearoyl-2-oleoylphosphatidylserine or cardiolipin at pH 6.4, but not at pH 2.0 where the anionic groups of acidic phospholipids were in non-ionized form. The membrane-fluidizing effect of lidocaine was significantly decreased by its treatment with peroxynitrite.
Discussion: The anesthetic-induced fluidization of 1,2-dipalmitolyphosphatidylcholine membranes decreased at lower pH, seemingly supporting the conventional hypothesis. Even under acidic conditions (pH 6.4) corresponding to inflamed tissues [3], however, lidocaine was able to fluidize nerve model membranes with different phospholipids. Such fluidization is speculated to occur through the ion pair formation of lidocaine with membrane acidic phospholipids from its characteristic membrane-interaction at pH 2.0 and 6.4. Local anesthetic failure associated with acute inflammation is not necessarily explained by the pH-dependent mechanistic interaction between drugs and lipid membranes. Inflammatory peroxidation by-products like peroxynitrite with the ability to influence the membrane effect of lidocaine may be responsible for anesthetic tolerance.
References:
[1] J. Chromatogr. A, 1073: 303-308, 2005.
[2] Fundam. Clin. Pharmacol., 16: 325-330, 2002.
[3] J. Oral Pathol., 16: 36-44, 1987.Supported by JSPS grant #15592145.

S-221.

LIDOCAINE ACTIVATES DIHYDROETHIDIUM - IMPLICATIONS FOR FLOW CYTOMETRY

AUTHORS: A. Ploppa, **M. E. Durieux**;
AFFILIATION: UVA Health System, Charlottesville, VA.

Introduction: Dihydroethidium (DHE) is used frequently as a flow cytometry dye to measure intracellular superoxide release by neutrophils. Since local anesthetics (LA) have been shown to affect superoxide release in neutrophils (1,2), use of DHE might be considered to investigate this LA effect. However, it is possible that LA might interact directly with DHE, and that any changes observed might therefore not be due to alterations in superoxide release, but instead to direct LA-DHE interactions. Therefore, we investigated the effect of lidocaine, as a representative LA, on DHE-induced fluorescence.
Methods: We used whole blood from human volunteers, to which the recommended amount of DHE was added, as well as lidocaine (10E-8 to 10E-5 M). No additional activating compounds were added. Fluorescence was determined using flow cytometry after 1 or 2 h incubation.
Results: Lidocaine did not affect fluorescence of blood in the absence of DHE (data not shown). In the presence of dye, lidocaine increased DHE-induced fluorescence. At the greatest lidocaine concentration tested (10 μM), fluorescence was increased almost 50% from basteline. The lowest concentration of lidocaine (100 nM) did not appreciably affect fluorescence. The effect appears to dissipate over time, as DHE activation by lidocaine was less after 2 h than after 1 h.
Discussion: Our results indicate a direct interaction between lidocaine and DHE. This should be taken into account when designing flow cytometry studies involving these compounds, as it might potentially confound results from such experiments.
References: 1. Hollmann MW et al: Anesthesiology 2004; 100: 852-860
2. Kiefer RT et al: Anesthesiology 2003; 98: 842-848



S-222.

LIDOCAINE INHIBITS DEPHOSPHORYLATION OF BRAIN SODIUM CHANNEL NAV 1.2 BY PROTEIN PHOSPHATASE-1

AUTHORS: **H. Hemmings**, D. Zachary, H. Tung;
AFFILIATION: Weill Cornell Medical College, New York, NY.

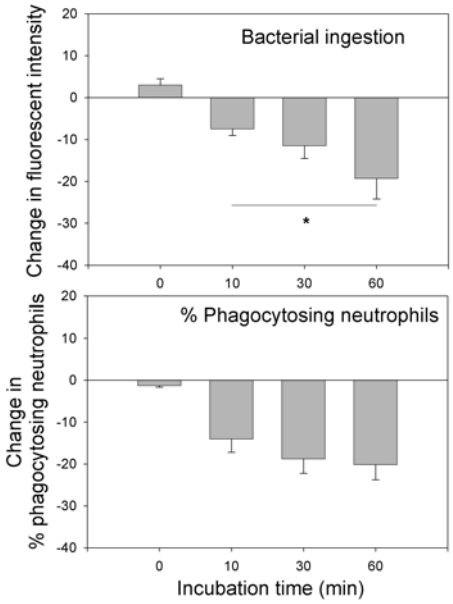
Introduction: Voltage-gated sodium channels (Na_v) control neuronal excitability and signaling. Na_v function is regulated by phosphorylation of multiple sites in the cytoplasmic linker domains L_{I-II} (aa 428-753) and L_{III-IV} (aa 1474-1526) by PKA and PKC. The role of protein phosphatases in the regulation of these sites is largely unknown. We examined regulation of dephosphorylation of S1506, a major PKC phosphorylation site[1] in the human $Na_v1.2$ L_{III-IV} domain, by the major CNS protein phosphatases, protein phosphatase-1 (PP1) and protein phosphatase-2A (PP2A). The effect of lidocaine, which binds to the L_{III-IV} region and modulates Na^+ channel gating,[2,3] was also examined.
Methods: Recombinant $Na_v1.2$ fragments and PP1 and PP2A catalytic subunits ($PP1_{cat}$ and $PP2A_{cat}$) were cloned from a human brain cDNA library, overexpressed as C-terminal His-tagged or GST-fusion proteins in *E. coli*, and purified by affinity chromatography. Native PP1 and PP2A holoenzymes were purified from pig brain. ^{32}P-labeled phosphoprotein substrates (L_{III-IV} or phosphorylase *a*) were prepared using [γ-^{32}P]ATP and PKC or phosphorylase kinase, respectively. L_{III-IV} was phosphorylated exclusively at S1506 as determined by site-directed mutagenesis. Phosphatase activity was measured as [^{32}P]phosphate release in the presence or absence of lidocaine and known phosphatase inhibitors. Data analysis employed GraphPad Prism v4.0 software.
Results: Native brain PP1 was ~70-fold more active than PP2A in dephosphorylation of the $Na_v1.2$ L_{III-IV} domain. Initial rates of dephosphorylation were 175 and 2.5 μmol/min/mg for PP1 and PP2A, respectively, compared to 77 and 55 μmol/min/mg for phosphorylase *a*, respectively. Recombinant catalytic subunits were more active on L_{III-IV} than their holoenzymes (638 μmol/min/mg for $PP1_{cat}$ and 34 μmol/min/mg for $PP2A_{cat}$). The K_m of $PP1_{cat}$ for L_{III-IV} was 9.6 μM, and of native PP1 was 8.8 μM. Dephosphorylation of L_{III-IV} by PP1 was inhibited by lidocaine in a concentration-dependent manner; the IC_{50} for inhibition of L_{III-IV} dephosphorylation was 10 μM for $PP1_{cat}$ and 27 μM for native PP1, with calculated K_i values of 6.5 μM and 17 μM. Kinetic analysis of lidocaine inhibition of $PP1_{cat}$ and native PP1 revealed that lidocaine decreased v_{max} with no change in K_m, consistent with a noncompetitive mechanism. Lidocaine did not inhibit $PP1_{cat}$ or native PP1 activity for the standard substrate phosphorylase *a*, indicating a substrate-specific mechanism.
Discussion: PP1 was much more active than PP2A in dephosphorylating S1506 of $Na_v1.2$. Lidocaine inhibited S1506 dephosphorylation by PP1 at clinically relevant concentrations via a substrate-mediated mechanism, consistent with the observation that L_{III-IV} binds lidocaine[2]. These findings may contribute to the Na^+ channel blocking effects of local anesthetics by inhibiting dephosphorylation of $Na_v1.2$ S1506 to down-regulate brain Na^+ channel function[4].
References: 1. *Science*. 1991;254:115-8. 2. *Br J Pharmacol*. 2004;142:222-8. 3. *J Physiol*. 2005;546:21-31. 4. *Br J Anaesth*. 2003;90:199-211.

S-223.

TIME-DEPENDENT INHIBITION OF NEUTROPHIL PHAGOCYTOSIS BY LIDOCAINE

AUTHORS: A. Ploppa[1], **M. E. Durieux**[2];
AFFILIATION: [1]University of Tuebingen, Tuebingen, Germany, [2]UVA Health System, Charlottesville, VA.

Introduction: Local anesthetics (LA) have been shown to inhibit priming of neutrophil respiratory burst in a time-dependent manner, i.e. with increasing potency after prolonged exposure (1). This may make these inflammatory modulating effects particularly relevant during e.g. epidural analgesia. Although other neutrophil actions are known to be sensitive to local anesthetics, it is not known if such sensitivity is also time-dependent. We therefore analyzed data obtained in our previous investigation of LA effects on neutrophil functions (2), to determine a possible time-dependent effect on phagocytosis.
Methods: Neutrophils from volunteers were exposed to calcein-labeled S. aureus, and fluorescent intensity of intracellular bacteria, as well as % of phagocytosing neutrophils, was assessed by flow cytometry after 0, 10, 30 and 60 minutes in the absence and presence of lidocaine (2 mM). Time course of the effect was then compared using ANOVA.
Results: In the presence of lidocaine, intracellular fluorescence decreased with a significant time effect ($p<0.05$). Although a similar trend was observed for the % phagocytosing neutrophils, this did not reach statistical significance.
Discussion: Our results indicate that lidocaine inhibits neutrophil phagocytosis in a time-dependent manner, similar to its effect on priming of superoxide release. This suggests that a LA effect on this neutrophil function may be relevant in the context of prolonged LA administration, such as postoperative epidural analgesia, but it remains to be investigated whether more prolonged exposure leads to a sufficient increase in potency to make this action clinically relevant. If µM concentrations of LA are able to inhibit phagocytosis after prolonged exposure, this suggests that LA might potentially interfere with the host response to bacterial invasion.
References: 1. Hollmann MW et al: Anesthesiology 2004; 100: 852-860
2. Kiefer RT et al: Anesthesiology 2003; 98: 842-848



S-224.

QUANTITATIVE ANALYSIS OF APOPTOTIC RESPONSES TO A-EPO AFTER ISCHEMIC BRAIN INJURY.

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Introduction: Erythropoietin (EPO), both in vitro and in vivo, has demonstrated anti-apoptotic properties in models of ischemia, hypoxia, serum withdrawal, and kainite exposure. More specifically, systemic administration of EPO has been shown to reduce the amount of TUNEL positive cells and histological damage in the surrounding penumbra region of injury after the induction of a stroke-like insult in rats[1]. AsialoEPO (a-EPO) is a derivative of EPO that is nonerythropoietic, thereby reducing the possibility of recurrent injury in models of stroke[2]. The goal of this study was to determine the effect of a-EPO on apoptotic-specific cellular death after ischemic brain injury in rats.
Methods: Focal cerebral ischemia was surgically induced in Sprague Dawley rats by inserting a 4.0 polypropylene suture into the region of the middle cerebral artery (MCA), occluding blood flow to the striatum. Following 90 minutes of occlusion, rats were implanted with a continuous-flow mini-pump (Alzet) and treated with a-EPO (20 µg/kg/day) or saline control for four days. On day four, rats were perfused with saline and brains were fixed with 10% formalin, followed by TUNEL immunostaining for detection of apoptotic activity. Apoptosis was semi-qualitatively analyzed by an investigator blinded to treatment groups and quantitatively analyzed by blinded counting techniques of the same immunostained sections.
Results: Levels of a-EPO in CSF measured by ELISA assay were significantly higher in the a-EPO group ($p<0.05$). Hematocrit was not significantly different between groups, supporting the lack of hematopoietic activity. The saline control group (n=9) demonstrated TUNEL-positive results in an average of 24.4% (qualitative) and 24.1% (quantitative) of the total brain field, as compared with the a-EPO group (n=9), which demonstrated TUNEL positive results in an average of 3.2% (qualitative) and 5.9% (quantitative) of the total brain field ($p\leq0.01$ for both comparisons) .

Conclusion: Qualitative as well as quantitative analysis suggests that a continuous subcutaneous infusion of low-dose a-EPO is capable of reducing the amount of apoptotic-induced cellular death in the region of insult and surrounding areas after an ischemic stroke-like injury to the brain.
References: 1. Siren et al. *Proc. Natl. Acad. Sci. USA*. 2001 (98) 4044-4049; 2. Erbayraktar et al. *PNAS* 2003; 100(11):6741-6746.

S-225.

SYSTEMIC BLOCKADE OF 5-HYDROXYTRYPTAMINE$_{2A,2B,2C}$ RECEPTORS DECREASES SEVOFLURANE MINIMUM ALVEOLAR CONCENTRATION IN RATS

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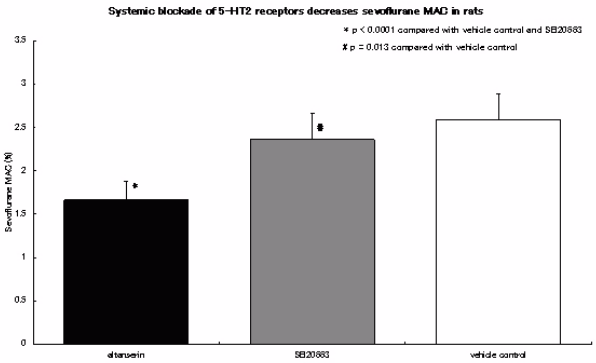
Introduction: Although blockade of 5-hydroxytryptamine(5-HT)$_{2A}$ receptors reportedly mediate the capacity of inhaled anesthetics to produce immobility during noxious stimulation (i.e., would underlie MAC, the minimum alveolar concentration required to suppress movement in response to a noxious stimulus in 50% of subjects) (1), no data are still available regarding the role of this receptor in the immobilizing action of sevoflurane. In this study, we examined the effects of intraperitoneal altanserin (a blood brain barrier penetrating 5-HT$_2$ receptor antagonist) or SB20663 (a blood brain barrier penetrating 5-HT$_{2B-,2C-}$ receptor antagonist) on sevoflurane MAC in rats.
Methods: Three groups of six male Wistar rats weighing 250-350 g each received one of the following drugs dissolved in dimethyl sulphoxide (DMSO) intraperitoneally 30 min prior to testing: (1) altansein 10 mg/kg; (2) SB20663 10 mg/kg; (3) no drug as vehicle control. MAC was defined as the average of the partial pressures that just prevented and permitted movement in response to clamping the tail for 30 sec. Data were analyzed by means of Bonferroni's multiple comparison tests after a one-way analysis of variance. In all tests, a value of $p < 0.05$ was considered statistically different.
Results: The rank order of MAC values obtained after intraperitoneal drug pretreatment and sevoflurane exposure was altanserin < SB20663 < no drug.
Discussion: These findings suggest that systemic blockade of 5-HT$_{2B,2C}$ receptors as well as 5-HT$_{2A}$ receptors may, at least in part, mediate the capacity of sevoflurane to produce immobility during noxious stimulation.
References:
1. Anesth Analg. 2003; 97: 475-9.



S-226.

INHALATION OF CARBON MONOXIDE IMPROVES MICROCIRCULATION AND INHIBITS EARLY INFLAMMATION AFTER PANCREATIC ISCHEMIA/ REPERFUSION IN RATS

AUTHORS: **R. Schmidt**, M. Scholtes, U. T. Hopt, K. K. Geiger, E. von Dobschuetz, B. H. Pannen;
AFFILIATION: University Hospital Freiburg, Freiburg, Germany.

Introduction: Microcirculatory dysfunction plays a major role in ischemia/ reperfusion (IR) induced pancreatic injury (1). Ample evidence suggests that induction of the heme oxygenase pathway has the potential to protect organs from IR injury (2). It was the objective of this study to determine the influence of carbon monoxide, a product of the heme oxygenase metabolism, on pancreatic microcirculation and the early inflammatory reaction after IR.
Methods: After institutional approval, male Sprague-Dawley rats (200-300 g) were randomly assigned to three groups: 1) sham controls; 2) animals subjected to 1 hour of pancreatic ischemia followed by 2 hours of reperfusion; 3) animals treated with 250 ppm carbon monoxide and subjected to 1 hour of pancreatic ischemia followed by 2 hours of reperfusion. Ischemia was induced by clipping the pancreas supplying arteries for 1h. Functional capillary density (FCD) and leucocyte-endothelial-adherence (LEI) were measured by intravital epifluorescence microscopy after 2 hours of reperfusion. Statistical analysis was performed with ANOVA followed by Student-Newman-Keuls tests. Data are expressed as mean ± SEM. Differences were considered significant when $p<0.05$.
Results: Analyses of microcirculation after 2 hours of reperfusion showed a significant decrease of FCD (216,89 + 11 cm/cm²) as compared to sham operated control animals (274 + 3 cm/cm²). Administration of carbon monoxide in IR treated animals led to an increase of FCD up to control values (266,57 + 9 cm/cm^2). LEI was significantly increased after 2 hours of reperfusion (128,45 + 21 mm^2) compared to sham controls (52,40 + 9,71 mm^2). Carbon monoxide treatment of animals subjected to IR decreased LEI to control levels (54,26 + 8 mm^2).
Discussion: Our results indicate that inhalation of low dose carbon monoxide improves microvascular blood flow and reduces the early inflammatory reaction in the pancreas after warm IR. This may offer a new potential for pancreatic organ protection.
References: 1.) Vollmar B, Menger MD Pancreatology 2003; 3:181-190. 2.) Ryter SW et al. Physiol Rev 2006; 86(2):583-650.

S-227.

ACTIVE GLUCURONO-CONJUGATED MOLECULES CAN BE PRODUCED IN LARGE AMOUNTS FROM PORCINE URINE EXTRACTION

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INTRODUCTION: The development of morphine-6-glucuronide, the first glucuronidated molecule to reach late stage clinical development (1), has shown that pharmacological activity of a glucuronide may be higher than that of the parent compound. FP0153 is the glucuronidated metabolite of FP0011, an antiglutamate compound currently developed (phase II) for neurological indications (2).
Investigating antiglutamate properties of FP0153 is prevented by its challenging chemical synthesis. An alternative strategy to produce large amounts of the FP0153 is to use the *in vivo* metabolization of FP0011 by the UDP-glucuronosyltransferases and to collect the FP0153 in the urines. A porcine model aimed at the production of FP0153 was set up in our experimental anaesthesia unit and the antiglutamate activity of this compound was then controlled in rats.
MATERIALS AND METHODS: With institutional animal protection committee approval, a Foley catheter was inserted under general inhaled anesthesia (ketamine, azaperone, propofol, pancuronium, isoflurane) in 3 Large White pigs, tunnelled and connected to a urine bag sewed and secured on the abdominal wall. Upon recovery, the animals were fed FP0011. The urine from the bag was collected under sedation 24h later. FP0153 was extracted by preparative HPLC. Its antiglutamatergic activity was tested in freely moving rats by microdialysis with enzymatic assessment of the glutamate in the dialysates (3).
RESULTS: 1) all pigs underwent uneventful anesthesia and recoveries, 2) the amount of FP0153 collected after each experiment is shown in the table, 3) F0153 decreased the glutamate activity by 65% over the baseline in rats (n=3)**.**

Experiment	**1**	**2**	**3**
Pig weight (kg)	22	31	49
Oral FP0011 intake (mg/kg)	100	1000	1000
Urine collected at 24hr (mL)	2100	630	3660
Diuresis (mL/kg/24h)	95.40	20.30	74.70
Total FP0153 extracted (g)	1.37	4.97	26.48*
FP0153 concentration in urine (g/L)	0.70	7.90	7.20
Ratio FP0153/FP0011	62%	16%	54%

*extrapolated : 7.31g/1.01L
DISCUSSION: Unlike pigs 1 and 3, pig 2 had no free post op access to water, explaining the lower urine production and the lower amount of FP0153 collected. Our study shows the possibility to collect large amounts of pure and active glucuronoconjugate FP0153 in the urine of pigs fed the parent compound. Pure FP0153 could be obtained by simple and efficient extraction method. This process is simpler and allows for better control than the *in vitro* alternative using isolated pig hepatocytes in a bioreactor. The development of this experimental animal model opens the way for the production of clinical batches of FP0153 and more generally of any glucuronidated compound difficult to synthesize otherwise.
References: (1)Anesth.Analg.(2006);102(6):1789-1797; 2)http://www.faustpharma.com/html/Development/Projects/FP0011; (3)Neurochem.Int.(1993);22(1):53-58

S-228.

COBALT PROTOPORPHYRIN TREATMENT INDUCES PANCREATIC HEME OXYGENASE-1 THEREBY IMPROVING MICROVASCULAR BLOOD FLOW AFTER ISCHEMIA/ REPERFUSION IN RATS

AUTHORS: **R. Schmidt**, E. von Dobschuetz, M. Scholtes, U. T. Hopt, K. K. Geiger, B. H. Pannen;
AFFILIATION: University Hospital Freiburg, Freiburg, Germany.

Introduction: Microcirculatory derangements caused by ischemia/reperfusion (IR) play a pivotal role in acute and graft pancreatitis (1,2). The inducible isoform of heme oxygenase (HO-1) has been shown to decrease IR injury influencing capillary perfusion in other organs (3). It was the goal of this study to evaluate the effect of HO-1 on the pancreatic microcirculation after IR.
Methods: After institutional approval, rats (200-300 g) were randomly assigned to four groups: 1) sham controls; 2) IR + vehicle; 3) IR + cobalt protoporphyrin IX (CoPP, 5mg/kg; HO-1 inducer); 4) IR + CoPP + tin protoporphyrine IX (SnPP, 50 µmol/kg; HO-inhibitor). Ischemia was induced by clipping the pancreas supplying arteries for 1h. Functional capillary density (FCD) was measured by intravital epifluorescence microscopy after 2 hrs of reperfusion. Expression of HO-1 mRNA, HO-1 protein and HO enzymatic activity were assessed by northern blot, western blot and activity assay. Statistical analysis was performed with ANOVA followed by Student-Newman-Keuls tests. Data are expressed as mean ± SEM for n=7 animals per group. Differences were considered significant when $p<0.05$.
Results: CoPP treatment induced pancreatic HO-1 mRNA and protein levels and increased HO enzyme activity, while SnPP decreased HO activity to baseline levels. Comparison of FCD showed a significant decrease in IR treated animals (173 + 10 cm/cm²) as compared to control (267 + 10 cm/cm²). Preinduction of HO-1 with CoPP increased FCD after IR to control values (257 ± 10 cm/cm²). HO activity inhibition of CoPP treated animals decreased FCD significantly (217 ± 10 cm/cm²) as compared to sham controls and CoPP treated animals.
Discussion: Preinduction of HO-1 improves pancreatic microcirculation after normothermic IR. Given this improvement, we hypothesize that HO-1 could be of clinical relevance in postischemic pancreatitis by decreasing acute IR during the early onset of reperfusion.
References: 1.) Obermaier R et al. Clin Exp Med 2001; 1:51-59. 2.) Benz S et al. Transplantation 2001; 71: 759-763. 3.) Katori M et al. Transplantation 2002; 7: 905-912.

S-229.

THIOPENTAL PROTECTS HUMAN T LYMPHOCYTES FROM APOPTOSIS VIA EXPRESSION OF HEAT SHOCK PROTEIN 70 IN VITRO.

AUTHORS: **M. Roesslein**, D. Schibilsky, K. K. Geiger, H. L. Pahl, B. H. Pannen, T. Loop;
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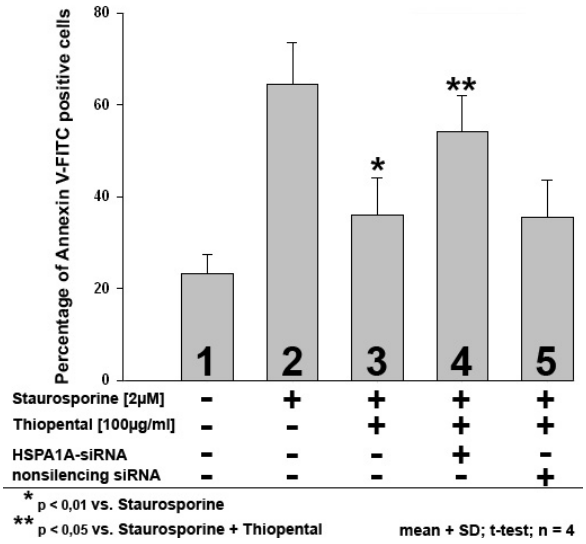
Introduction:
Thiopental, a widely used anesthetic, is known to have modulatory effects on immune functions and cyto-protection (1;2). Heat shock protein (Hsp) 70 has been shown to convey cell protection by inhibiting nuclear factor (NF-) κB, a central regulator of the immune response (3). The aim of this study was to determine whether thiopental, a known inhibitor of NF-κB (4), is able to confer protection from apoptosis, effected by caspase-3, by inducing Hsp70 expression in human T lymphocytes in vitro.
Methods:
Human T lymphocytes (Jurkat or primary) were incubated with thiopental [0.5-4h at 100-1000 µg/ml]. Expression of Hsp-70 was analyzed by Northern (mRNA) and Western blot (protein). Cells were transfected with either small interfering (si) RNA specifically targeting HSPA1A, one of the major genes coding for Hsp70, or nonsilencing siRNA with no homology to any known mammalian gene.
Apoptosis was induced with staurosporine [4h at 2µM] and assessed by flow cytometry using Annexin V-FITC (Annexin) staining. In addition, caspase-3 activity and processing were assessed by activity assay and Western blot.
Results:
Thiopental time- and dose-dependently induced the expression of hsp70-mRNA and Hsp70-protein. Transfection of cells with siRNA targeted at HSPA1A resulted in a pronounced decrease in expression of hsp70-mRNA.
Incubation of cells with staurosporine lead to a significant augmentation in caspase-3 activity and processing, and also increased the number of Annexin-positive cells (bar #2 vs. #1). Pre-treatment of cells with thiopental significantly decreased caspase-3 activity and processing, and also significantly reduced the number of Annexin-positive cells (bar #3 vs. #2). This reduction was suspended in cells transfected with HSPA1A-siRNA (bar #4 vs. #3). Conversely, the number of Annexin-positive cells remained low in cells transfected with nonsilencing siRNA (bar #5).



Discussion:
Thiopental induces the expression of Hsp70 in human T lymphocytes and protects the cells from staurosporine-induced apoptosis. Hsp70 seems to be critical in this protection, since its silencing on mRNA-level offsets the protective effect. These results provide a possible molecular mechanism by which thiopental may exert its cytoprotective effects.
References:
(1) AANA J. 2005 Aug;73(4):297-302. (2) Eur J Anaesthesiol 2005; 22(8):616-623. (3) Circulation 2004; 110(23):3560-3566. (4) Anesthesiology 2002; 96(5):1202-1213

S-230.

EFFECTS OF RHO-KINASE INHIBITORS ON ANESTHETICS-INDUCED RELAXATION OF RAT BRONCHIAL SMOOTH MUSCLE

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AFFILIATION: [1]Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan, [2]Hoshi University, Tokyo, Japan.

Introduction: Smooth muscle contraction in response to physiologic agonists is associated with an increase in the cytosolic Ca^{2+} concentrations ($[Ca^{2+}]i$). However, contractile force is not determined by $[Ca^{2+}]i$ alone because membrane receptor stimulation with agonists increases the force at a constant $[Ca^{2+}]i$ (=increases Ca^{2+} sensitivity). This Ca^{2+} sensitization is reportedly mediated by small G-protein Rho and its target Rho-kinase (ROCK). We have previously showed that selective ROCK inhibitors decrease the force produced by muscarinic receptor stimulation with acetylcholine (ACh) in rat airway smooth muscle (ASM), suggesting that ROCK inhibitors may act as bronchodilator. In this study, we examined the effects of ROCK inhibitors on anesthetics-induced relaxation of rat ASM.
Methods: Ring strips (width 200µm, diameter 500µm) from the intrapulmonary bronchus of male Wistar rat were placed in 400µl organ baths containing Krebs-Henseleit solution (bubbled with 95%O_2/5%CO_2) at a resting tension of 50mg. After equilibration period, isometric force was measured. [1] After obtaining a stable contraction with 30µM ACh, propofol (1µM-1mM) was cumulatively applied. H-1152 (0.03 µM), Y-27632 (0.03 and 1µM) or vehicle was added to propofol. [2] After obtaining a stable contraction with 30µM ACh, isoflurane (0.5-4.0%), with 1 µM Y-27632 or vehicle, was cumulatively applied.
Results: [1] 0.03 µM H-1152 significantly caused the leftward shift of the concentration-response curve for propofol and decreased EC_{50}, while 0.03µM Y-27632 had no effect. 1µM Y-27632 significantly shifted the concentration-response curve for propofol leftward and decreased EC_{50}.
[2] Y-27632 caused a leftward shift of concentration-response curve for isoflurane.
Discussion: In the first study, H-1152 at a very low concentration augmented the inhibitory effect of propofol on rat ASM contraction. Y-27632 did not affect the propofol-induced relaxation of ASM at the same concentration as H-1152. However, 1µM Y-27632 shifted the concentration-response curve leftward, suggesting H-1152 is more potent than Y-27632 in ASM, as we previously reported. Intravenous anesthetics relax ASM solely by decreasing $[Ca^{2+}]i$ without affecting Ca^{2+} sensitivity. In this study, ROCK inhibitors augmented the inhibitory effect of propofol, and this augmentation is supposed to be mediated by decreasing Ca^{2+} sensitivity, resulting in a synergistic effect. In the second study, Y-27632 augmented isoflurane-induced relaxation of ASM. Volatile anesthetics relax ASM by decreasing both $[Ca^{2+}]i$ and Ca^{2+} sensitivity. The result of this study suggests that addition of ROCK inhibitor to volatile anesthetics produces the further bronchodilation, probably by potentiation of inhibitory effects on Ca^{2+} sensitivity.
Conclusion: ROCK inhibitors augment the inhibitory effects of both volatile and intravenous anesthetics on rat ASM contraction. Addition of ROCK inhibitors to anesthetics may be useful for anesthetic managements of asthmatic patients.
References:
1) Hanazaki M et al. Anesthesiology 2000; 92: 133-139
2) Akao M et al. Am J Physiol 1996; 271:L719-L725

S-231.

APROTININ INFLUENCES DISPARATE MECHANISMS TO EFFECT LV CONTRACTILITY AND CYTOKINE ACTIVATION IN A MOUSE MODEL OF I/R

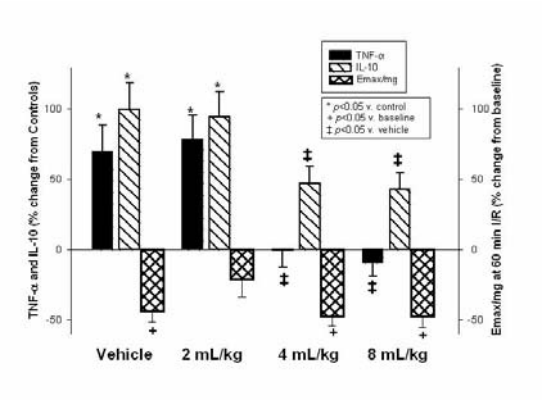
AUTHORS: **M. D. McEvoy**, A. B. Taylor, J. A. Zavadzkas, I. M. Mains, R. E. Stroud, S. T. Reeves;
AFFILIATION: MUSC, Charleston, SC.

Ichemia-reperfusion (I/R) in cardiac surgery is associated with left ventricular (LV) dysfunction and cytokine release, which aprotinin (APRO) has been posited to modulate. However, the direct relationship of APRO to these parameters has not been examined. Thus, this study tested the hypothesis that APRO effects LV contractility and cytokine release following a period of I/R in a dose-dependent manner.

An intact mouse model of LV I/R (30 min LAD occlusion, then 60 min reperfusion) was used in which LV function was measured by a pre-calibrated high-fidelity microtransducer-volumetry catheter at baseline, 30 min ischemia, and 30 and 60 min of reperfusion. Following baseline measurements, mice were randomized as follows:(a) APRO 2mL/kg (n=11);(b) APRO 4mL/kg (n=10);(c) APRO 8mL/kg (n=10) and (d) Vehicle (saline, n=10). APRO doses were calculated to be reflective of the Hammersmith doses of half, full or 2Xfull, respectively. APRO (1mL=10,000 Kallikrein Inhibiting Units) or saline was given by intraperitoneal injection immediately after baseline measurements. Upon completion of I/R, plasma measurements for tumor necrosis factor-α (TNF) and interleukin-10 (IL-10) were performed with a calibrated and validated enzyme-linked flow cytometric system (Multiplex Suspension Array®) which provided high sensitivity and specificity (TNF of 0-400 ,IL-10 of 0-200 pg/ml). Data are reported as Mean±SEM.

Results expressed as a percent change from baseline (Emax) or reference controls (cytokines) are shown in the Figure. Emax normalized to LV mass (Emax/mg) fell from baseline (0.78±0.06 mmHg/µl*mg) with I/R in the Vehicle group. However, for APRO 2mL/kg, LV contractility returned to baseline values after 60 min of I/R, an effect not observed for APRO 4 or 8mL/kg. TNF increased from controls (24.47±1.80pg/mL) in Vehicle and APRO 2mL/kg following I/R, whereas TNF was suppressed for higher doses. IL-10 increased from control (4.32±0.24pg/mL) for Vehicle and APRO 2mL/kg, but was reduced at higher APRO doses with I/R.

The unique findings of this study were 2-fold. First, only a dose of APRO reflecting half-Hammersmith provided protective effects on LV contractility following a period of I/R. Second, computed full and double Hammersmith doses suppressed TNF and IL-10 release, but failed to facilitate recovery of LV contractility with I/R. These results demonstrate 2 potentially distinct and independent mechanisms of action of APRO in the context of I/R with respect to the effects on LV contractility and cytokine activation.



Pharmacology - Clinical

S-232.

COMPARISON OF PROPOFOL AND ISOFLURANE DURING EXTUBATION UNDER DEEP ANAESTHESIA

AUTHORS: **Q. Fan**[1], B. Yu[1], R. Eltringham[2];
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Inrtoduction The aim of this study was to compare the emergence characteristics of unpremedicated patients when extubated while deeply anaesthetized ("deep extubation") with propofol or isoflurane and to record the maintanance dosage of propofol and isoflurane during deep extubation. **Methods** Sixty healthy patients (ASA physical status I or II) were enrolled in the study. They ranged in age from 26 to 58 years and were scheduled for elective surgical procedures below the umbilicus under general anaesthesia. They were randomly assigned to one of two groups, Group P or Group I. All patients received an intravenous induction with midazolam 0.03mg·kg^{-1}, fentanyl 2μg·kg^{-1} and propofol 2mg·kg^{-1} followed by vecuronium 0.1mg·kg^{-1}. Endotracheal intubation was performed by one of the investigators approximately 2 minutes after induction. Anaesthesia was maintained with a combination of fentanyl, vecuronium and isoflurane. During the final 10 minutes an infusion of propofol replaced the administration of isoflurane in patients in group P, whereas isoflurane administration continued in group I. The infusion rate of propofol and the inhaled concentration of isoflurane were adjusted as necessary to achieve same level of BIS (BIS70±5). The infusion rate of propofol and the concentration of inhaled isoflurane were recorded. The emergence characteristics and the arousal scores were recorded during endotracheal extubation in the operating theatre, during transport and in the recovery room. Any complications including excessive secretions, breath-holding, laryngospasm, coughing, bronchiospasm, desaturation, nausea, vomiting and involuntary muscle movement were noted during each time period. **Results** The average infusion rate of propofol and the minimum alveolar concentration of isoflurane for deep extubation were 2.8±0.6mg·kg^{-1}·h^{-1} and 0.42±0.11MAC, respectively. Patients in group P were arousable sooner than patients in group I (8.1±3.5vs16.3±8.9min). However, the later arousal scores and times to discharge were the same. There were no serious complications in either group. Breath-holding and emergence delirium were more common in group I. The overall incidence of airway problems and desaturation episodes were similar in the two groups. **Discussion** Deep extubation can be safely performed with either propofol or isoflurane. Return to an arousable state occurred more quickly with propofol, although the time to reach the criteria for discharge was the same in both groups. After deep tracheal extubation, airway problems can occur but are easily managed.

References

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2 Kearse LA, Rosow C, Zaslavsky A, et al. Bispectral analysis eletroencephalogram predicts conscious processing of information during propofol sedation and hypnosis. Anesthesiology, 1998, 88: 25.

S-233.

THE EFFECT OF PROLONGED HIGH TEMPERATURE STORAGE ON TETRACAINE CONCENTRATION.

AUTHORS: **C. H. Shields**, S. Bina, R. Kyle, M. Chernofsky, C. C. Buckenmaier;
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Introduction: Local anesthetics are used in a variety of austere and combat environments. Medications used in such environments are often exposed to temperatures that exceed the manufactures recommended storage temperatures. There is a clinical impression that after local anesthetics are persistently stored at high temperatures they are less effective (1). The daily temperature in the Middle East can reach 135 °F (57 °C). No studies have looked at the degradation of local anesthetics after prolonged storage at very high temperatures. We hypothesized that tetracaine stored for a prolonged period at high temperature would undergo significant degradation. Clinical significance was defined as a 10% or greater reduction in the concentration of the drug, when mixed as a 0.5% solution with normal saline.

Methods: 27 vials each of tetracaine 20mg/ml, (Abbott) from the same lot were maintained at 42 °C or at 57 °C in temperature controlled ovens (Precision Gravity Convection). Vials were tested prior to temperature elevation and study vials were tested after 15, 36, 60, and 90 days of high temperature storage. 3 vials were tested in each condition. A U.S Pharmacopeia tetracaine reference standard was run, before and after each group of samples was analyzed. All samples were analyzed via HPLC in triplicate. HPLC analysis was done using Waters Model 2690 Separations Module equipped with Waters Model 996 Photodiode Array Detector.

Results: The concentration of 0.5% tetracaine was not decreased after prolonged storage at either 42° C or 57° C. None of the samples showed any relevant decrease in concentration by HPLC analysis. The intra sample testing reproducibility was excellent as indicated by the very low standard error of the mean (SEM) for each sample.

Table 1

Mean measured [mg/ml] 0.5% tetracaine	Days stored at high temperature				
	0	**15**	**36**	**60**	**90**
Sample 1 at 42° C	4.96±0.01	4.95±0.00	4.99±0.00	5.01±0.003	5.04±0.00
Sample 2 at 42° C	4.99±0.00	4.89±0.01	4.98±0.02	5.12±0.001	5.07±0.01
Sample 3 at 42° C	4.96±0.00	4.92±.03	4.98±0.01	5.10±0.001	5.04±0.01
Average at 42° C		**4.93±0.00**	**4.99±0.01**	**5.10±0.01**	**5.05±0.01**
Sample 1 at 57° C		4.94±0.00	5.02±0.01	5.12±0.002	5.02±0.00
Sample 2 at 57° C		5.02±0.01	5.02±0.02	5.11±0.003	5.01±0.00
Sample 3 at 57° C		4.97±0.01	5.01±0.01	5.10±0.003	5.01±0.01
Average at 57° C		**4.96±0.01**	**5.01±0.01**	**5.10±0.003**	**5.01±0.00**

Mean measured tetracaine concentrations in mg/ml ± SEM.

Discussion: A clinically significant decrease in concentration was defined as a 10% or greater reduction in tetracaine concentration of a 0.5% solution. None of the samples had a significant reduction in concentration below baseline levels. Reduction in concentration of tetracaine after high temperature storage, detectable by HPLC, is not the cause of any perceived reduction in clinical efficacy.

1. Regional Anesthesia and Pain Medicine, 2003; 28: 321-327

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S-234.

DYSKALAEMIA DURING THIOPENTONE COMA FOR REFRACTORY INTRACRANIAL HYPERTENSION

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Introduction
The induction of barbiturate coma for treatment of refractory intracranial hypertension (ICH) and the subsequent weaning off have been reported to cause life-threatening hypokalaemia and hyperkalaemia respectively[1, 2]. We sought to study if these observations were also found in our patients on thiopentone coma (TC), and to identify potential predictors of these changes in serum potassium levels.
Methods
We conducted a retrospective analysis of all patients receiving TC for treatment of refractory ICH in a tertiary neurosurgical intensive care unit over an 18-month period. Logistic regression analysis was performed to identify predictors of hyperkalemia and hypokalemia. All results are reported as mean ± SD or median (IQR) as appropriate.
Results
There were 47 patients who had TC for treatment of refractory ICH in our institution from Jan 2004 to June 2005 (18-month period). 32 out of 47 (68%) developed significant hypokalaemia (K+ < 3.0 mmol/L) after induction of TC. The lowest potassium level recorded was 2.1 ± 0.5 mmol/L occurring at 25.5 hrs (20.3 - 40.5) after induction of TC. The median potassium replacement given per day was 60 mmol (24 - 158). Significant hypokalaemia refractory to replacement (K ≤ 3.0 mmol/L) was found in 16 out of 47 (50%) patients.
Independent predictors for the development of hypokalaemia were the cumulative total dose of thiopentone given and the rate of insulin infusion required during TC to maintain euglycaemia (P values 0.038 & P 0.041 respectively).
There were 16 (34%) patients who developed rebound hyperkalaemia (K+ > 5.0 mmol/L) on weaning from TC. Except for one patient, all others had normal potassium levels before tailing down the thiopentone infusion. The highest potassium level recorded was 6.1 mmol/L (5.5 - 7.0) occurring 31.5 hrs (28.0 - 55.5) after weaning TC. In 12 patients (26%), hyperkalaemia persisted for up to 27.5 hrs (9.3 - 41.3) after termination of TC.
We found that the cumulative dose of potassium replacement during TC was an independent predictor for development of hyperkalaemia (Pp = 0.001).
Discussion
Hypokalemia is common following induction of TC for treatment of refractory ICH. Higher total dose of thiopentone used and insulin infusion required during TC appear to predict development of significant hypokalaemia. Rebound hyperkalaemia during weaning from TC appears to be related to the amount of potassium replacement given. Frequent monitoring of serum potassium and judicious replacement of potassium is therefore recommended in all patients receiving TC for treatment of refractory ICH.
References
[1]Intensive Care Med 2002; 28: 1257 - 60[2]Acta Anaesthesiol Scand 1992; 36: 367 - 77

S-235.

DEFINING DRUG INTERACTION FOR COMBINATION ANTIEMETICS. A SYSTEMATIC REVIEW.

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Introduction: Many studies have shown that a combination of antiemetic drugs provides better protection against postoperative nausea and vomiting (PONV) compared with monotherapy. However, it is unclear how drug interaction may affect treatment response. The aim of this quantitative systematic review was to compare the observed response to combinations of two drugs with that predicted from additivity of the response to each drug alone.
Methods: We searched the MEDLINE (from 1966), EMBASE (from 1982), Cochrane Library and other relevant database using different strategies without language restriction. We only included full reports of randomized, placebo controlled trials that tested the antiemetic efficacy of combining two commonly prescribed antiemetics (including droperidol, serotonin antagonists, metoclopramide, antihistamines) with either drug alone. We excluded trials that did not have a placebo group, because the relative efficacy cannot be determined. The predicted incidence of PONV after drug combination was calculated as the product of the individual drug response, normalized to that of the controls. The drug combination is defined as synergistic if the observed incidence is less than that predicted. The reverse is considered as antagonistic. The drug interaction for side effects was also determined using a similar model. A pooled estimate was calculated by combining the effect sizes according to the DerSimonian-Laird random effects method.
Results: A total of 19 trials, involving 6,734 patients were analyzed. Overall, there was no difference between predicted and observed incidence of PONV after a combination of two antiemetics (Table 1). These data suggested that the interaction was additive in nature. Only nine studies (1,312 patients) reported adverse events after study drug administration. The chief complaints were headache and pruritus. The difference between observed and predicted incidence of side effects (95% confidence intervals) was -0.2 (-18.5 - 18.0)%, indicating the interaction for side effects was also additive.

Pooled estimates (95%CI) of predicted & observed incidence of PONV after combination antiemetics

	Incidence of postoperative nausea and vomiting after combination antiemetic therapy (95% confidence intervals)		
	Observed	Predicted	Observed - Predicted
Serotonin antagonists and droperidol (*n*=9)	18.8 (12.4-25.2)	16.5 (8.0-25.0)	2.5 (-3.7 - 8.8)
Serotonin antagonists and Dexamethasone (*n*=3)	26.1 (6.9 - 45.4)	31.8 (20.0 - 43.6)	2.3 (-2.2 - 6.8)
Droperidol and dexamethasone (n=1)	40.7 (37.7 - 43.8)	37.8 (34.4 - 41.4)	2.9 (-1.7 - 7.5)
Metoclopramide and droperidol (*n*=3)	26.1 (16.6 - 35.5)	24.3 (9.2 - 39.3)	-0.6 (-16.5 - 15.2)
Ondansetron and metoclopramide (*n*=1)	44.0 (24.4 - 65.1)	33.3 (15.6 - 59.1)	10.7 (-20.9 - 37.7)
Dimenhydrinate and metoclopramide (*n*=2)	23.6 (4.6 - 42.5)	22.4 (7.4 - 37.4)	-3.1 (-20.7 - 14.6)
Promethazine and ondansetron (*n*=1)	29.2 (12.6 - 51.1)	25.3 (9.8 - 48.4)	3.9 (-25.3 - 28.8)
Dimenhydrinate and droperidol (*n*=2)	8.6 (1.8 - 23.1)	10.6 (2.6 - 26.7)	-2.0 (-20.0 - 11.4)

Discussion: This meta-analysis demonstrated that a combination of two commonly administered antiemetics for preventing PONV after a wide variety of surgery had an effect that was consistent with an additive interaction of the two drugs. At these dosages, there was no excessive side effect after drug combination

S-236.

USE OF DEXMEDETOMIDINE INFUSION DURING LAPAROSCOPIC BARIATRIC SURGERY: A DOSE-RANGING STUDY

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Introduction: Dexmedetomidine (Precedex®) is a selective alpha$_2$-adrenoceptor agonist with hypnotic, sedative, sympatholytic and analgesic properties. In previous studies, it has been shown that dexmedetomidine (Dex) is associated with both anesthetic and analgesic-sparing effects. The objective of this study is to test the hypothesis that an optimal infusion rate of Dex would improve control of acute autonomic responses during bariatric surgery and decrease postoperative pain, leading to improved clinical outcomes.
Methods: A total of 20 patients (ASA II-III) undergoing laparoscopic bariatric surgery were enrolled to date in this ongoing randomized, double-blind, placebo-controlled study. After obtaining written informed consent, these patients were randomly separated into one of the four groups: Control (saline infusion), Dex 0.2 μg/kg/min, Dex 0.4 μg/kg/min and Dex 0.8μg/kg/min. The study drug infusion was started when the patients arrived in the operating room and was discontinued at the end of the surgery. Postoperative pain was treated with fentanyl (25μg IV boluses) upon emergence from anesthesia, and IV-PCA was started after the patients arrived in the PACU. IV fentanyl (25μg IV) was also used to supplement PCA morphine in the PACU. Heart rate (HR) and mean arterial blood pressure (MAP) values were recorded at specific intervals. Pain scores were evaluated using an 11-point verbal analog scale (VAS, 0=none to 10=maximal) postoperatively. The need for postoperative pain medication, rescue antiemetics, and times to discharge from PACU were also evaluated.
Results: The demographic and preliminary findings are summarized in Table 1 and Figures 1 and 2. There were no significant difference in the intraoperative HR and MAP values while the mean end-tidal desflurane concentrations for Group 4 was significantly reduced compared to the Control group (3±0 vs 5±1**,** $p<0.05$). The groups were also similar with respect to postoperative pain scores on emergence from anesthesia and during their stay in PACU. Group 3 received significantly less "rescue" fentanyl in the PACU compared to the control group (42±52 vs 155±76 μg, respectively).
Conclusions: Dexmedetomidine infusion, 0.4 μg/kg/min, during laparoscopic bariatric surgery procedures significantly decrease the need for rescue pain treatment in PACU. However the preliminary findings suggest that the use of dexmedetomidine, 0.2-0.8 μg/kg/min, failed to improve intraoperative hemodynamic control or reduced the length of stay in the PACU after bariatric surgery.

S-237.

THIOPENTAL POTENCY ASSESSED BY BIS

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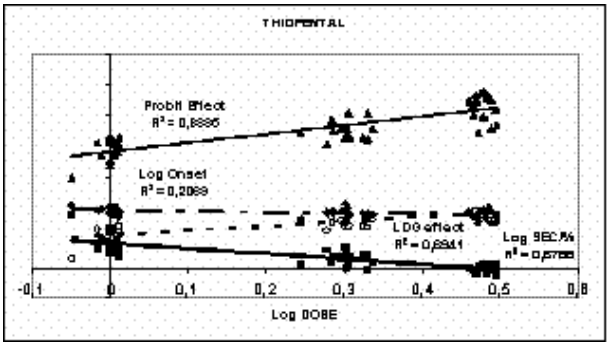
Introduction: *Thiopental* (**THP**) dose response has been established using end point clinical evaluation[(1)]. Subjectiveness introduces important distortion to these methods. *Bispectral index monitoring* (**BIS**) has been specifically introduced to evaluate hypnosis during anesthesia. The aim of present trial is to recalculate THP potency by using BIS.
Material & Methods: After institutional signed consent and special induction conditions, undisturbed patients, free from any sedatives, were randomly assigned to 3 groups according to the dose of THP: 1, 2 or 3 mg.Kg^{-1} (15e/a) administered in 10 seconds. BIS electrodes were previously secured and monitor (Aspect ®) calibrated. *Maximal depression* (**MAX**) and *onset time* (**OT**) were assessed. After log dose/probit effect transformation, a regression line was developed and slope obtained. Solving Hill equation for each patient, ED_{50}, $_{90}$ and $_{95}$ were calculated. *Speed of action* (**SA**) was considered as OT/MAX ratio (seconds/%). After log transformation for dose, MAX, OT and SA, regression line were obtained and equation used for predictions.Values are mean±standard deviation.
Results: Doses were 0,9±0.03, 2±0.1 and 3±0.07 mg.Kg^{-1}, for groups 1, 2 and 3. MAX was 13±6, 32±10 and 55±18%. OT: 80±21, 67±22 and 55±18 seconds. SA: 10±14, 2.3±1.2 and 0.95±0.2 sec/%. ED_{50}, $_{90}$ and $_{95}$, were 2.4±0.6, 5±1, and 6.9±1.8 mg.Kg^{-1} respectively. R^2 for log dose/probit effect, log dose/log MAX and log SA were in the same order: 0.678 to 0.694. Poor correlation was found for log dose/log onset. Non significant differences were noticed for predictions of MAX, OT and SA (p range 0.173 to 0.701) using regression line equation for every group and pharmacodynamic parameters (Fig. 1).



Discussion: Due to poor correlation between dose and OT, a need to include MAX seems necessary to restore dependence, which was accomplished by introducing SA. Notorious variability in reported potency for THP can be linked to highly subjective methodology used to assess end point[(2, 3, 4)]. As BIS is a consistent figure, present results should be considered as a reliable measure for THP potency. A 10% BIS depression is reported as loss of consciousness[(5)], using actual 1xED_{50} should be enough for anesthesia induction.

References: 1) Br J Anaesth 1992; 68: 308.- 2) J Clin Anesth 1991; 3: 367.- 3) Anesth Analg 1988; 67: 342.- 4) Br J Anaesth 1991; 66: 13.- 5) Anesthesiology 1997; 86: 613.

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S-238.

INTERACTION OF MORPHINE EFFECT SITE CONCENTRATION AND INFUSION MODE ON RESPIRATORY DEPRESSION DURING PATIENT CONTROLLED ANALGESIA

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Introduction: Continuous background infusions (CBI) have been implicated as a risk factor for respiratory depression (RD) during patient controlled analgesia[1]. We applied pharmacokinetic modeling to PCA dosing data to determine whether effect site concentrations account for differences in RD between patients receiving CBI and those receiving only bolus dosing.

Methods: With IRB approval, continuous sidestream capnography monitoring of postsurgical patients on morphine PCA yielded longitudinal measurements of respiratory rate (RR) and morphine dosing, from which plasma and effect site concentrations (C_e) were derived using Dahan's kinetics[2]. RD is defined as a RR less than or equal to 10 breaths per minute maintained for at least 2 consecutive minutes. An arbitrary C_e 'high threshold' was chosen as the empirical 75th percentile of C_e. This threshold was applied to individual patient data to dichotomize individuals as C_e 'never *below threshold*' (BT) vs. C_e '*above threshold*' at least once (AT). The interrelationships of this classification, the method of infusion (CBI vs. bolus only) and the occurrence of episodes of respiratory depression (RD) were examined.

Results: Fifty-three (69.7%) of 76 subjects had at least one episode of RD. 47 (61.8%) were never above the Ce 'high threshold' which was 134.05 nm. Classification of AT was related to increased odds for the occurrence of RD (OR=3.0; p=0.058). Furthermore, there was a significant interaction of method of infusion with the C_e high threshold for the association with RD ($p<0.01$). In patients on CBI, the odds of RD were >10 times higher for AT patients when compared to CBI-BT patients (p=0.003). For CBI-BT patients, the odds of RD were less than 1/10 that of patients on bolus only, for either Bolus-AT (OR<0.10, p=0.012) or Bolus-BT (OR<0.10, p=0.011). There was a tendency for patients on CBI-AT patients to have higher odds of RD when compared to either bolus-AT (OR=4.0, p=0.24) or bolus-BT (OR=4.7, p=0.15).

Conclusion: CBI was protective for RD provided the C_e remained under the 75% percentile; however, the odds of RD appear to be much higher in CBI patients above the high threshold. This interaction of CBI and high effect site concentrations may pose a clinical risk to patients. Further research is needed to examine the occurrence of RD in conjunction with the longitudinal trends in effect site concentration.

References:

1. Sidebotham D. et.al. The safety and utilization of patient-controlled analgesia. Journal of Pain & Symptom Management. 14(4): 202-9, 1997 Oct.
2. Dahan A. Romberg R. Teppema L. Sarton E. Bijl H. Olofsen E. Simultaneous measurement and integrated analysis of analgesia and respiration after an intravenous morphine infusion. Anesthesiology. 101(5):1201-9, 2004 Nov.

S-239.

ELECTROPHYSIOLOGIC MONITORS AS PREDICTORS OF NOCICEPTION DURING SEVOFLURANE ANESTHESIA IN VOLUNTEERS

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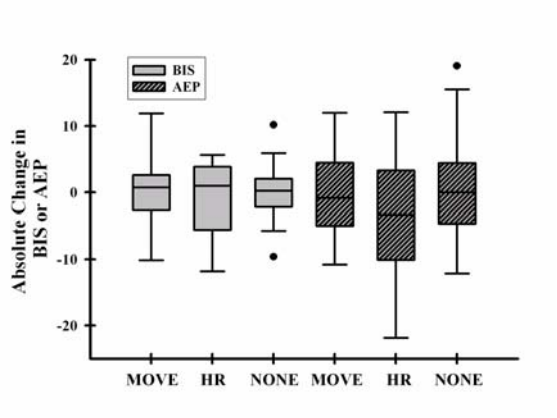
Introduction: Opioids decrease the dose of volatile or intravenous anesthetics needed to produce sedation and provide immobility to surgical incision. Electrophysiologic monitors can characterize the sedative effects and predict surgical immobility when a sedative/hypnotic is administered alone or in combination with nitrous oxide. However, electrophysiologic monitors are not able to adequately characterize the increase in sedation observed when opioids are added to sedative/hypnotics. This study was designed to investigate the ability of electrophysiologic monitors to predict adequate nociception during opioid-hypnotic combinations that produce clinically adequate sedation (Observer's Assessment of Alertness/Sedation, OAA/S ≤ 1).

Methods: Utilizing remifentanil-sevoflurane combinations (0-80 ng/mL remifentanil and sevoflurane 0-6 % atm) that were designed to characterize pharmacodynamic response surfaces; the data from 24 volunteers with an OAA/S score ≤ 1 were analyzed. The change in Bispectral Index™ (BIS, Aspect Medical Systems) or Auditory Evoked Potential (AEP, Alaris, Inc.) observed when an electric tetanic stimulation of ≥ 45 milliamps was applied for 5 seconds were categorized for those volunteers who moved and had a heart rate increase (Move), those who did not move but had an ≥ 20% increase in heart rate (HR), and those who demonstrate no somatic or autonomic responses (None). A Kruskal-Wallis one-way ANOVA with $P< 0.05$ considered significant was used to compare the electrophysiologic responses for each monitor between the response categories.

Results: The peak electrophysiologic response occurred 50 milliseconds (BIS) and 40 milliseconds (AEP) after electrical stimulation. The BIS and the AEP were unable to demonstrate a statistically significant difference in the change of the index for any of the response categories.

Discussion: Although others have demonstrated that the BIS is able to predict movement responses during single drug anesthetics, there was no difference in the change in BIS or the change in AEP between any of the response categories for sevoflurane-remifentanil anesthetics spanning a large combination of concentration pairs. Therefore, in patients who receive neuromuscular junction blockers and beta-adrenergic antagonists, the magnitude of change of either of these electrophysiologic monitors after skin incision may not be able to discriminate between adequate and inadequate nociception.



S-240.

PHARMACODYNAMICS OF MIVACURIUM-METOCLOPRAMIDE INTERACTION

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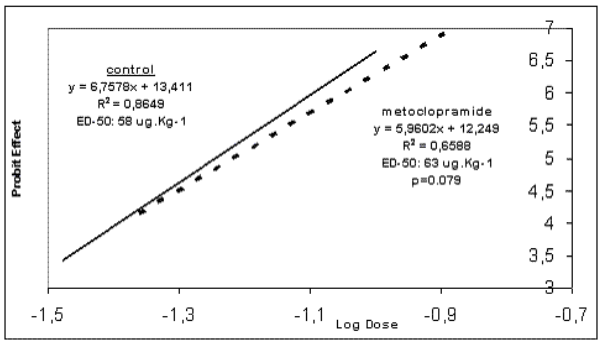
Introduction: Prolongation on mivacurium's (**MIV**) effect has been reported following metoclopramide (**MTC**) administration[1-3]. Although infusion rates of MIV to maintain 95% block are reduced after MTC[3], a comprehensive pharmacodynamic study on the MIV-MTC interaction has not been undertaken. This is the aim of present trial.
Material & Methods: In part one: two groups (n=11e/a) of elective and consenting adult patients were randomly assigned to receive MIV small fractional successive doses during induction with intravenous agents and nitrous oxide, either alone (control) or preceded by MTC as a preanesthetic medication. Using electromyography, maximal effect (%) (**MAX**) was assessed. A *cumulative* dose-response curve was calculated after slope was obtained from the log dose/probit effect transformation regression line. In part two: two different groups (n=22e/a) received MIV 100 µg.Kg^{-1} or preceded by MTC. *Initial onset time* (seconds), up to 80% blockade (**INT**), *onset time* (**OT**), MAX, *early recovery index* (seconds) (between 10 and 25% spontaneous recovery) (**ERI**) and *clinical duration* (minutes) (up to 25% spontaneous recovery) (**DUR**), assessed by the same monitoring system. T test and $p<0.05$ level as significance, were used for statistical comparisons.
Results: Neither zero nor 100% effect was noticed. Final amount and blockade for cumulative assessment as well as ED_{50}'s didn't reach statistical significant difference among groups (Fig. 1). Non significant differences between control and study group were noticed for INT (192vs184'', p=0.657), OT (267vs276'', p=0.697) MAX (89vs95%, p=0.135), ERI (208vs242'', p=0.297), respectively. DUR was significantly shorter in control group (14 vs 20 minutes, p=0.027).
Discussion: Prolonged recovery both in present and reported trials[1-3], should be considered as a pharmacokinetic phenomenon in nature. Correlation between longer DUR and plasma cholinesterase inhibition by MTC is not clear[1]. Lack of differences in MAX, OT and recovery index have been observed after MTC[1]. During similar clinical conditions MTC failed to alter succinylcholine's action although OT was accelerated and DUR prolonged for a subsequent MIV dose[4].
In *conclusion*: non-significant modifications on MIV potency and pharmacodynamics other than DUR, should be expected after previous administration of MTC. As no changes ocurred during ERI, causes for longer DUR should take place after initial recovery.
References: 1) Br J Anaesth 1999; 82:542.- 2) Acta Anaesthesiol Scand 2002; 46:214.- 3) Eur J Anaesthesiol 2005; 22:197.- 4) Anesthesiology 2003; 99:A1138



S-241.

SIMULATION OF THE PRIMING PRINCIPLE

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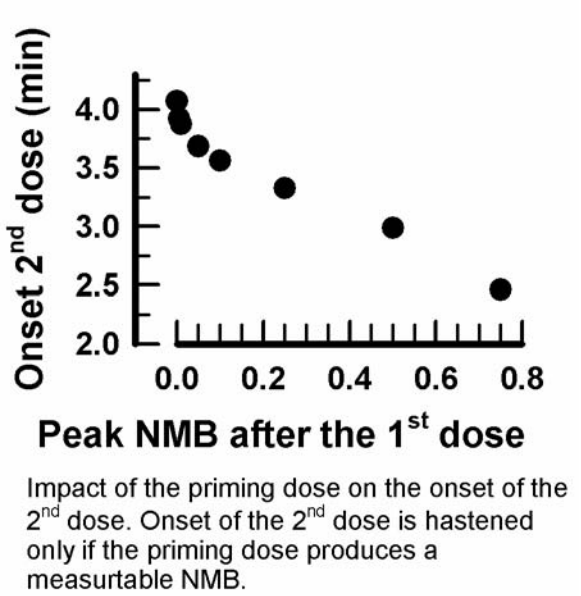
Introduction: Injection of a small dose of a muscle relaxant (MR) has been proposed as a method to hasten the onset of neuromuscular block (NMB) of the second dose ("priming principle" (1)). To be safe, the first dose should produce no NMB. Investigations of the priming technique to speed NMB have yielded contradictory results. The goal of the current study was to examine in simulations the impact of a priming dose on the time course of the subsequent main dose.
Methods: The hypothetical MR D was assigned pharmacokinetic properties resembling those of clinically used MRs (V_C=50 and V_{SS}=250 mL·kg^{-1}, clearance = 10 mL·kg^{-1}· min^{-1}). In the effect compartment, D binds to two sites on the postsynaptic receptors (2). Synaptic clefts within the effect compartment contain D in equal concentrations. Within the clefts, D competes with acetylcholine (ACh) for binding to the two sites at the postsynaptic receptors (3). Twitch strength was calculated from the peak concentration of the receptors with both sites occupied by ACh and NMB as the difference in twitch strength in the absence and the presence of D. The first dose of D varied from (0 to 0.695)·ED95. The second dose, injected at the time of the peak concentration of D in the effect compartment, was the difference between ED95 and the first dose. The time difference between the injection of the second dose and the peak NMB was defined as onset time. In a second series of simulations, the first dose was 0.1·ED95 and the second dose 2·ED95. The time to reach NMB=0.95 (NMB95) was taken as onset time.
Results: The first dose of 0.1·ED95 occupies ~45% of the receptors and does not produce NMB. Onset times following the second dose decreased only if the first dose produced NMB>0.01 (Figure). The extent of shortening was related to the magnitude of NMB established by the first dose (Figure).



NMB95 was reached 0.85 min after 2·ED95 as a single bolus and at 0.75 min following 2·ED95 as a second dose.
Discussion: A priming dose that does not produce a measurable NMB does not markedly hasten the onset of the subsequent dose
References: (1) Brit J Anaesth 56: 663, 1984. (2) J Pharmacokinet Pharmacodyn 33: 461, 2006. (3) J Pharmacokinet Pharmacodyn 30: 23, 2003.

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S-242.

THE EFFECT OF CISATRACURIUM AND SUCCINYCHOLINE UPON INTRAOCULAR PRESSURE FOLLOWING PROPOFOL INDUCTION OF GENERAL ANESTHESIA: *DOES IT MATTER?*

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Introduction: Numerous studies have shown an increase in intraocular pressure (IOP) upon administration of succinylcholine (Sch). The increase in IOP is by direct effect on extraocular extrafusal muscle tension and contraction of orbital smooth muscle[1]. This untoward effect of Sch raises concern of its use in glaucomatous patients as well as those with traumatic eye injuries. It is also known that nondepolarizing muscle relaxants have either no effect on, or result in a decrease in IOP[2]. Additionally, numerous studies have shown that propofol induction is associated with a decrease in IOP[1]. The purpose of our study was to prospectively determine if there is a difference in the change in intraocular pressure upon administration of succinylcholine versus cisatracurium after propofol induction of general anesthesia.
Methods: Following IRB approval and informed consent, 40 patients (ages ranging from 46 years to 76 years) undergoing elective Vatikutti Institute Prostatectomy (VIP)[3] were included in this prospective trial. Patients with glaucoma, visual defects, blindness, and prior corneal abrasions were excluded. Induction medications were standardized to lidocaine (2mg/kg), fentanyl (1mcg/kg), and propofol (2mg/kg) without premedication. Following loss of verbal response, cisatracurium (0.2mg/kg) or succinylcholine (1mg/kg) was administered; 17 and 23 patients were administered cisatracurium and Sch respectively. Endotracheal intubation was performed in the cisatracurium group after 3 minutes and in the succinylcholine group after 60 seconds, or as clinically indicated. Intraocular pressure was measured in the supine position before induction and just prior to intubation. A Medtronic Tono-Pen XL® was used to measure IOP in one eye. Measurements in the 95th percentile, as displayed by the tonometer, were recorded. A paired t-test was used to evaluate the change in IOP from baseline to pre-intubation in the entire cohort. A students' t-test was used to evaluate the change in IOP among the cisatracurium group versus the Sch group between the two aforementioned time points.
Results: Mean baseline IOP was 16.3(±5.7). Following induction and administration of either cisatracurium or succinylcholine the mean IOP was 10.6(±5.0). The mean change in IOP between the two time points was -5.7(±5.5. There was a statistically significant decrease in IOP for the entire cohort ($P<0.0001$). The mean change in IOP in the cisatracurium group versus the succinylcholine group was -6.7(±4.6) and -5.0(±6.2) respectively. The decrease in IOP between the succinylcholine group and the cisatracurium group was not significantly different ($P>0.33$).
Discussion: The effect on IOP of succinylcholine in the presence of propofol, lidocaine, and fentanyl is similar to cisatracurium. Induction, with succinylcholine, is a viable option in patients where a decrease of intraocular pressure is desired, and a short acting muscle relaxant is needed.
References: 1) Anesthesia Analgesia 1996;83:814-7
2) European Journal of Anesthesiology 2002; 19: 823-28
3) J. Urology 2003 June;169(6):2289-92

S-243.

DOSE-RESPONSE RELATIONSHIP OF NONDEPOLARIZING MUSCLE RELAXANTS: COMPARISON OF SINGLE VERSUS CUMULATIVE DOSE TECHNIQUE USING SIMULATIONS

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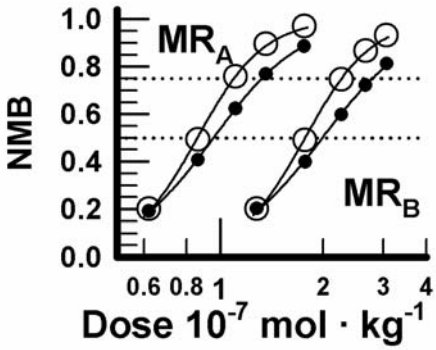
Introduction: The cumulative dose-response technique for nondepolarizing muscle relaxants (MRs) offers advantages over the single-dose technique. Elimination of a fraction of the previous dose(s) up to the time when the second or subsequent doses achieve their peak effect confounds the cumulative dose technique. While some investigators found that the two methods yield similar results, others found that the cumulative dose technique underestimates the potency. Therefore, we have evaluated the two techniques using simulations.
Methods: Two hypothetical MRs were assigned identical initial and steady state volumes of distribution (V_C=50 and V_{SS}=250 mL·kg^{-1}), but different systemic clearances, either 10 or 44 ml·kg^{-1}·min^{-1}. A 3-compartment model was constructed for each MR. Transport of the MR from the central to the effect compartment was defined as diffusion governed by the gradient of the free concentrations and the transport rate constant k_{e1}, k_{e1}=0.2 min^{-1} for either MR. The details of binding of a MR to the postsynaptic receptors in the effect compartment and diffusion of the MR into the synaptic cleft were presented earlier (1). In the synaptic cleft, acetylcholine (ACh) released by a stimulus was assumed to bind to two sites at the postsynaptic receptor and is rapidly hydrolyzed (2). Twitch strength was calculated from the peak concentration of the receptors with both sites occupied by ACh and neuromuscular block (NMB) from the difference between the twitch strength in the absence and in the presence of a MR. We assumed that ten stimuli are delivered per min. Sequential doses of either MR increased the peak NMB to approximately 0.2, 0.4, 0.6, 0.75, and 0.90. These doses were injected when three consecutive estimates of NMB following the previous dose increased by <2%.
Results: For both MRs, the dose-NMB curve obtained by the cumulative technique was less steep than that obtained by the single dose technique (Figure). The ED50 and ED75 doses estimated by the cumulative technique were about 12% and 21% larger than those estimated by the single dose technique for either MR (Figure).



The dose-response relationship for MR_A and MR_B using either the single dose (empty circles) or cumulative technique (solid circles). The cumulative technique yields a less steep curve.

Discussion: We have confirmed that the cumulative technique underestimates the potency of a MR. The underestimation is independent of the pharmacokinetic properties of the MRs.
References: 1. J Pharmacokinet Pharmacodyn **33:** 461, 2006. 2. J Pharmacokinet Pharmacodyn **30:** 23, 2003.

S-244.

PRIMING MIVACURIUM: A COMPREHENSIVE EVALUATION

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Introduction: Lack of convincing results leading to lost of interest on *priming* (**PRM**) left several gaps in clinical pharmacology of this technique. *Mivacurium* (**MIV**) was about less studied drug. Tools as *early onset time* (**80%**), *train-of-four* (**TOF**) assessment, *speed of action index* (**SAI**) and *restrictive* method (**RST**) for evaluation of *onset time* (**OT**) were seldom or not used by existing works. This is the aim of present trial.
Material & Methods: Consenting patients received MIV 100 $\mu g.Kg^{-1}$ either by bolus (**BOL**, group 1) or PRM: 10+90 $\mu g.Kg^{-1}$, 3 minutes apart (group 2) during induction. (n=15e/a). Using electromyography, time to 80%, OT (seconds), *maximal blockade* (**MAX:**%), *clinical duration* (**DUR**:minutes) and TOF fade at 80% block were assessed. SAI was calculated as the ratio between fractional OT and MAX during *initial* phase (up to 80%) (**INI**), *final*: between 80%-MAX (**FIN**) and global: OT/MAX ratio (**GLB**) (**sec/%**). Only patients with final MAX 93-95% in both groups (3 and 4), were picked for RST evaluation of the same parameters (n=8e/a). T test, analysis of variance and Student-Neuman-Keuls with $p<0.05$ level for significance, were used for comparisons.
Results: Significant fade were noticed by PRM in comparison to BOL (47±9 vs 35±18%: p=0.047) but not statistical difference was observed during RST method (44±14 and 39±26% respectively, p=0.744). There was not significant differences neither among methods (p=0.242), first twitch height (16-19%, p=0.675) or time to reach it (3-4 minutes, p=0.698). Groups 3 and 4 had longer OT and slower GLB than group 2, and FIN than group 1. Not additional significant findings were noticed (Table 1).

Table 1

	80%SEC	MAX%	OTSEC	DUR-MIN	INIsec/%	FINsec/%	GLBsec/%
1)MIVBOL	200±63	93±4	279±48	14±7	2,5±0,7	6±2	3±0,5
2)MIVPRM	152±62	96±4	253±52	15±6	1,9±0,7	6±2	2±0,6
-p=	0.050	0.092	0.159	0.685	0.050	0.693	0.144
RST							
3)MIVBOL	196±25	94±0,5	323±43	13±3	2±0,3	8±1	3±0,4
4)MIVPRM	204±48	94±0,5	332±63	13±6	2±0,6	8±1	3±0,6
.p=	0.696	0.250	0.775	0.863	0.696	0.934	0.780
SIG	p=0.079	p=0.219	2)vs:3-4	p=0.791	p=0.079	1)vs:3-4	2)vs:3-4

Discussion: Due to dependence between OT and MAX, both, non-paralyzing doses and SAI were included in present trial for adequate evaluation of a method intending to increase speed. Shorter OT for PRM reported by others comes from larger amount of drug, longer interval period, different monitoring method and unclear statistical analysis[1-3]. In *conclusion*: actual results poorly support main purpose for priming MIV. As a preferential pre-synaptic action is a proposed mechanism for increasing speed by PRM[1], actual reduced TOF fade observed could be pointed responsible for failed findings. RST methodology resulted useful to clarify inconsistent results.
References: 1) Anaesth Pharmacol Rev 1995, 3:209.- 2) Can J Anaesth 1994: 41:902.- 3) J Clin Anesth 1996: 8:276.-

S-245.

SUCCINYLCHOLINE PRETREATMENT WITH ATRACURIUM: USE OF SPEED OF ACTION AND RESTRICTIVE METHOD FOR ASSESSMENT

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Introduction: When *succinylcholine* (**SCH**) is used, a pretreatment with a non depolarizing muscle relaxant, *atracurium* (**ATR**) among them, is commonly accepted as standard clinical practice for prevention of undesirable side-effects. According to previous reports, the resulting interaction significantly reduces potency and delay SCH *onset time* (**OT**)[1-3]. The incidence of *final effect* (**MAX**) on OT is well known, and makes mandatory its consideration. But existing clinical tools including the latter, and developed to clarify previous conclusions, as *restrictive* methods (**RST**) and *speed of action index* (**SAI**) have never been used. This is the aim of present trial.
Material & Methods: Two similar groups of elective consenting patients (n=21e/a), with no contraindication, received either a bolus of SCH 1 $mg.Kg^{-1}$ or preceded by ATR 50 $\mu g.Kg^{-1}$ 3 minutes apart, for tracheal intubation, during induction with intravenous agents and nitrous oxide. Using electromyography and train of four stimulation, time to achieve 80% block, OT (**seconds**) and MAX (**%**) were assessed. In addition SAI was calculated as the ratio between fractional OT and MAX (**SEC/%**) during *initial* phase: up to 80% (**INI**), *final* between 80% and MAX (**FIN**) and *global* as the OT/MAX ratio (**GLB**) for the *regular method* (**REG**). Only patients with 98% MAX were picked for RST evaluation by the same parameters. T test and statistical comparison for proportions with $p<0.05$ were used for analysis.
Results: For REG, ATR significantly slowed and reduced SCH effect. All statistical differences were lost by using RST. FIN was about 60 and 40% slower than INI, according to the method (Table 1).

Table 1

	$80\%^{SEC}$	$MAX^{\%}$	OT^{SEC}	$INI^{SEC/\%}$	$FIN^{SEC/\%}$	$GLB^{SEC/\%}$
Regular						
SCC	38±15	99±1	72±21	0,46±0,17	1,67±0,73	0,69±0,16
^{ATR}SCC	60±15	93±9	96±23	0,77±0,19	2,77±2,21	1,06±0,31
.p=	0.0001	0.012	0.001	0.0001	0.019	0.0001
Restrictive						
SCC	48±17	98±0	76±8	0,6±0,2	1,5±0,8	0,77±0,09
^{ATR}SCC	68±20	98±0	108±30	0,85±0,25	2,22±1,11	1,1±0,3
.p=	0.139		0.053	0.138	0.312	0.053

Discussion: Results coming from the REG are qualitatively similar to those reported previously[1-3]. None of these figures could be confirmed by the RST. Claimed significant antagonism is not supported by present results, explaining unaltered clinical conditions during tracheal intubation after ATR-SCH sequence[2]. Differences between INI and FIN have been described as a biphasic OT[4], and present results shows that pretreatment doesn't change that feature. In conclusion: SAI showed to be insufficient to assess correctly ATR-SCH interaction. Inclusion of RST method is necessary for complete interpretation as antagonism apparently doesn't exist.
References: 1) Anesth Analg 1985; 64:1010.- 2) Anaesthesia 1985; 40:642.- 3) Br J Anaesth 1987; 59:606.- 4) Anesth Analg 2005; 100:S421

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S-246.

ROCURONIUM-MIVACURIUM: CUMULATION-ELIMINATION RELATIONSHIP?

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Introduction: If *cumulative* (**CML**) characteristics of a *muscle relaxant drug* (**MRD**) is considered by residual effects, it may become apparent when pharmacodynamics of a *first dose* (**D1st**) is compared to that of the *second dose* (**D2nd**)(1). Potency of a MRD are underestimated when *single dose* response curves (**SGL**) is compared with CML technique due to *elimination* occurred during development(2). Close similarity of proportions between SGL/CML ratio for *mivacurium* (**MIV**) and *rocuronium* (**ROC**) was demonstrated(3). The aim of the present trial is to find any further relationship among these two properties.
Material & Methods: During first part, two groups of adult elective patients randomly received MIV (100 µg.Kg^{-1}) or ROC (400 µg.Kg^{-1}) as a D1st during the induction with intravenous agents and nitrous oxide. At 25% spontaneous recovery, D2nd a quarter in sizes was administered. Using electromyography, maximal effect was assessed. For both D1st and D2nd, ED_{50} from a SGL dose-response curve was calculated after slope was obtained from the log dose/probit effect transformation regression line.In part two, different groups received either 50, 100 and 200 µg.Kg-1 ROC, 20, 40 and 100 µg.Kg-1 MIV or small fractional successive doses and ED_{50} for SGL and CML were respectively obtained by the same method. ED_{50}'s D1st/D2nd and SGL/CML ratios were calculated. T test, comparison of proportions and $p<0.05$ significance were used for statistical analysis.
Results: Potency was increased after D2nd, but didn't reach statistical significance for MIV. CML significantly underestimated potency in comparison to SGL, for both MRD. Non significant differences were noticed among D1st/D2nd and SGL/CML ratio both for ROC as well as MIV (Table 1).

Table 1

ED_{50} µg.Kg^{-1}	D1st	D2nd	*D1st/D2nd*	SGL	CML	*SGL/CML*
Rocuronium	67±20 (α) (α):p=0.001	52±9 (α)	*0.779* (δ) (γ) (γ): p=0.509	169±52 (Ω)	232±58(Ω) (Ω):p=0.0001	*0.730* (δ) (ϕ) (δ):p=0.680
Mivacurium	82±4 (β) (β):p=0.229	74±3 (β)	*0.897* (ε) (γ) (ε):p=0.292	47±12 (ϖ)	58±8 (ϖ) (ϖ):p=0.0001	*0.808* (ε) (ϕ) (ϕ):p=0.884

Discussion: Lack of significant differences between D1st and D2nd for MIV could be explained by the non-cumulative properties of this drug(4). Due to differences in elimination ½β, D2nd for ROC was administered at an earlier stage than MIV, producing a certain degree of accumulation and explaining increased potency. Decreased potency by CML method is ascribed to elimination occurred during developing(2). In *conclusion*: close similarity and lack of statistical differences between D1st/D2nd and SGL/CML ratios could hypothetically reflect both accumulation and elimination for these MRD.
References: 1) Can J Anesth 2002; 49:353.- 2) Anesth Analg 1997; 85:667.- 3) Anesth Analg 2006; 100:S289.- 4) Anaesth Pharmacol Rev 1995; 3:156.-

S-247.

REVISED ALGORITHM FOR THE DELIVERY OF REMIFENTANIL BASED ON THE GRADIENT BETWEEN RESPONSE ENTROPY AND STATE ENTROPY

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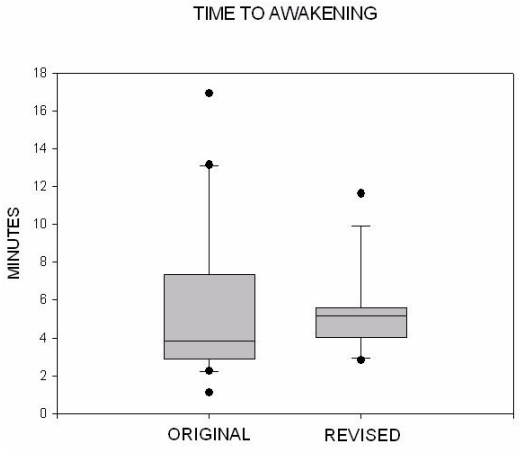
Introduction: Facial EMG (FEMG) may have utility in assessing adequacy of anti-nociception. We have previously described an advisory system for the administration of remifentanil based on the difference, or gradient, between response entropy (RE) and state entropy (SE) (GE Healthcare, Helsinki, Finland), an indirect marker of FEMG activity.[1] The underlying algorithm is designed to deliver a remifentanil infusion that results in a RE-SE difference that is neither too great nor too small. Following critical review, we modified system variables with the goal of improving performance.
Methods: After obtaining IRB approval and patient consent, 13 patients scheduled for anterior cruciate ligament repair were studied with the updated advisory system (REVISED) and data was compared to 20 patients cared for with the original system (ORIGINAL). The advisory system was constructed as a modular subcomponent of RUGLOOP (Michel Struys and Tom DeSmet, University of Ghent, Belgium) and utilized target controlled infusions of propofol and remifentanil. Propofol effect-site concentration (Ce) was adjusted to maintain a SE of 50. Remifentanil Ce was adjusted with the revised advisory algorithm. Data compared included time to awakening to verbal stimulation and orientation, incidence of movement during surgery and predicted remifentanil and propofol Ce at the end of surgery, end of closing and at awakening. Data was compared with t-test, Mann-Whitney Rank Sum test and Chi-Square analysis as appropriate with SigmaStat (Systat, Point Richmond, CA). A p value of 0.05 was considered significant.
Results: Median time to awakening to verbal stimulation (interquartile range) was 3.8 (2.9-7.2) and 5.1 (3.7-5.4) minutes for the ORIGINAL and REVISED groups, respectively (N.S, see graph).



Median time to orientation was 6.8 (4.7- 9.0) and 6.1 (5.5-7.1) min for ORIGINAL and REVISED, respectively (N.S). Predicted propofol and remifentanil Ce values were not significantly different at any surgical milestone. There was less patient movement in the REVISED group (0 of 13) compared with the ORIGINAL group (4 of 20, NS)
Discussion: The revised remifentanil advisory system showed possible improvement over the original with less patient movement. The times to awakening and orientation were similar, but the smaller interquartile ranges may reflect less patient variability with the revised algorithm.
[1]Anesth Analg 2006;102:S-291

S-248.

THE EFFECT OF METHODS OF ANESTHESIA ON GASTROINTESTINAL BOWEL FUNCTION AFTER COLONIC SURGERY.

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Introduction: Gastrointestinal bowel movement is reduced by opioid-based anesthesia. Recently remifentanil is popularly used for total intravenous anesthesia. We compared to the effect of anesthetic methods on gastrointestinal bowel movement after colon surgery.
Methods: Ninety patients were allocated randomly into three groups; Thirty patients received intraoperative inhalation anesthesia (desflurane+N_2O, Group I), thirty patients received intraoperative total intravenous anesthesia (propofol+remifentanil, Group II), thirty patients received intraoperative epidural anesthesia (epidural lidocaine+propofol, Group III). All patients received postoperative epidural analgeisa with a mixture of ropivacaine and morphine. Time to first passage of flatus, hospital stay and visual analog pain scale were recorded.
Results: There was no significant difference in first passage of flatus among groups (Group I: 92.7 ± 19.6, Group II: 86.9 ± 19.4, Group III: 81.9 ± 12.8 hours, p = 0.063). There were no significant difference in hospital stay and visual analog scale among three groups.
Discussion: Total intravenous anesthesia with remifentanil did not reduce gastrointestinal bowel movement compared to those of inhalation or epidural anesthesia.
References:
1. Condon RE, Cowles V, Ekbom GA, Schulte WJ, Hess G: Effects of halothane, enflurane and nitrous oxide on colon motility. Surgery 1987; 101: 81-5.
2. Scheinin B, Lindgren L, Scheinin TM: Perioperative nitrous oxide delays bowel function after colonic surgery. Br J Anaesth 1990; 64: 154-8.
3. Freye E, Sundermann S, Wilder-Smith OH: No inhibition of gastro-intestinal propulsion after propofol- or propofol/ketamine-N_2O/O_2 anaesthesia. A comparison of gastro-caecal transit after isoflurane anaesthesia. Acta Anaesthesiol Scand 1998; 42: 664-9.

S-249.

LACK OF EFFECT OF APREPITANT OR ITS PRODRUG FOSAPREPITANT ON QTC INTERVALS IN HEALTHY SUBJECTS

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Introduction:
Fosaprepitant is an intravenous prodrug that converts to the potent and selective NK1 receptor antagonist aprepitant, via phosphatase enzymes. The pharmacological effect of fosaprepitant is attributed to aprepitant. A single dose of 115-mg fosaprepitant is bioequivalent in terms of aprepitant AUC to a 125-mg dose of oral aprepitant.
In preclinical and clinical studies to date, fosaprepitant and aprepitant have not demonstrated a propensity to prolong QTc intervals. The purpose of the present study was to corroborate these earlier data and definitively demonstrate the lack of a meaningful effect by aprepitant or its prodrug fosaprepitant on QTc intervals.
Preclincal data suggest that conversion of fosaprepitant is not mediated by CYP450.
Methods:
This was a double-blind, double-dummy, placebo-controlled, randomized 3-period balanced crossover study in healthy young subjects to evaluate the potential effects of fosaprepitant 200 mg on QTc prolongation. In each period, subjects received a single oral dose of either 400-mg moxifloxacin, 200-mg fosaprepitant, or placebo in a randomized sequence.
The effect of fosaprepitant on QTc interval was assessed by 12-lead ECGs extracted from a Holter recorder by a blinded centralized laboratory. The baseline value for QTc interval for each subject during each period was defined as the average of 5 replicate baseline QTc intervals extracted from the predose ECGs. ECGs were performed at Predose, 2, 5, 10, 15, 20, 30, 45 minutes, 1, 1.5, 2, 3, 4, 6, and 8 hours post- initiation of 15- minute infusion.
Results: Following fosaprepitant 200 mg there was no increase in QTcf (corrected using Fridercia's correction) observed at the end of the infusion time (Tmax) or at any other point during the active fosaprepitant period for any subject. The mean (95% CI) QTcf change from baseline at Tmax was -1.45 (-4.67, 1.77), which was a change from baseline difference compared to placebo of -1.37 (-4.78, 2.05). Neither were significant changes. The active control in this study, moxifloxacin, was associated with an increase in QTcf. The mean (95% CI) QTcf change from baseline at 2 hours (moxifloxacin Tmax) was 9.71 (6.49, 12.93), which was a change from baseline difference compared to placebo of 10.50 (7.09, 13.92).
Maximum aprepitant concentrations after a single 200 mg dose of fosaprepitant was 6300 ng/mL. This is about 2-, 4-, and 9-fold higher than that achieved with fosaprepitant 115 mg (3095 ng/mL), aprepitant 125 mg (1600 ng/mL), and aprepitant 40 mg (675 ng/mL), respectively
Discussion:
In subjects receiving active fosaprepitant 200 mg, there were no clinically meaningful increases in QTc seen at any time point. The lack of a QTc increase at this high dose of fosaprepitant and resulting aprepitant plasma exposures supports the expectation that clinical doses of fosaprepitant or aprepitant will not be associated with significant QTc prolongation.

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S-250.

DEXMEDETOMIDINE REDUCES THE REQUIREMENT OF IV-PCA FENTANYL FOR THE POSTOPERATIVE PAIN MANAGEMENT OF ABDOMINAL AORTIC ANEURISM GRAFTING.

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Introduction: Dexmedetomidine is a selective alfa2-agonist, which induces anxiolysis and analgesic without respiratory depression. In our institution, intravenous patient-controlled-analgesia (IV-PCA) fentanyl had been used routinely for analgesia of the post abdominal aortic aneurysm (AAA) operation. In 2004 dexmedetomidine was approved for clinical use in Japan. Since then we started to administer dexmedetomidine combined with previously used IV-PCA fentanyl. We hypothesized that dexmedetomidine reduces the requirement of opiates and affects circulatory parameters of the post abdominal aorta aneurysm grafting.
Methods: Following ethical committee approval, we analyzed retrospectively the data from consecutive 26 patients who underwent an elective AAA grafting between 2003 and 2004 in our institution. All patients were given fentanyl through IV-PCA technique postoperatively. The first 13 patients (control group) were managed with no other analgesic agents. The latter 13 patients (dexmedetomidine group) were administered dexmedetomidine continuously in addition to IV-PCA fentanyl. The analgesic effect was monitored by the visual analog scale (VAS) score and IV-PCA dosing was recorded. To evaluate the circulatory and respiratory effects of dexmedetomidine, heart rate, blood pressure and blood gas were also monitored.
Results: Patients demographics, operative status, intraoperative fentanyl dose and catecholamine dose were similar. There were no significant differences in the length of ICU stay and intubation after the operation. Dexmedetomidine were administered 0.36-0.7 mcg/kg/hr and continued 12.3±5.4 hours after the operation. The requirement of IV-PCA fentanyl for 24 hours after the operation was significantly reduced in the dexmedetomidine group. (629±169 vs 995±337 mcg, $p<0.01$). Systolic blood pressure at 4 and 24 hours after the operation were not significantly different between groups. However heart rate at 4 hours in dexmedetomidine group was significantly lower than control group. (74±8.0 vs 87±10 bpm, $p<0.01$). There were no cases which developed bradycardia, heart rate < 50 bpm or hypercapnea, $PaCO_2$ > 50 mmHg. **Discussions:** Since Dexmedetomidine significantly reduces IV-PCA fentanyl, analgesic potency of dexmedetomidine was proved. Reduction of fentanyl requirement may contribute to reduce the incidence of adverse effects of fentanyl, such as respiratory depression, nausea and vomiting. As the incidence of ischemic heart disease and AAA concomitantly is high, and decreasing heart rate is important to prevent perioperative ischemic heart events, dexmedetomidine might have an advantage for AAA operation. The combination of fentanyl and dexmedetomidine did not affect weaning of the respirator and ICU stay. Respiratory depression due to fentanyl was not enhanced by dexmedetomidine. However, to verify the safety and efficacy of the combination of dexmedetomidine and fentanyl, further prospective studies are required.

S-251.

A STUDY OF PERI-INTUBATION & PERI-EXTUBATION HAEMODYNAMIC CHANGES AND POSTOPERATIVE ANALGESIC EFFICACY OF PERIOPERATIVE INTRAVENOUS INFUSION OF LIDOCAINE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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AFFILIATION: [1]University of North Carolina, Chapel Hill, NC, [2]Aligarh Muslim University, Aligarh, India.

INTRODUCTION: We tested the hypothesis that a fixed bolus and infusion regime of lidocaine effectively attenuates changes in perioperative hemodynamics and alleviates postoperative pain.
METHODS: After IRB approval and consent, 60 adult female ASA I and II patients undergoing elective laparoscopic cholecystectomy were selected. Patients with cardiorespiratory, renal or endocrine disease were excluded from the study.
The patients were randomly divided into two groups:
Group A: Patients received normal saline bolus and infusion at comparable volume and rate as the B group
Group B: Patients received 1.5mg/kg IV bolus of lidocaine over 10 minutes followed by its continuous infusion of 1.5mg/kg/hr until one hour postoperatively. Patients were induced using 2mg/kg of IV propofol & 0.1mg/kg of vecuronium bromide. Following relaxation, laryngoscopy & intubation were performed. Immediately after intubation, patients received a mixture of oxygen and nitrous oxide [40% and 60% respectively] and a step down infusion of propofol [10 mg/kg/hr for first 10 minutes, 8 mg/kg/hr for next 10 minutes followed by a continuous infusion of 5mg/kg/hr.] The propofol infusion was terminated 3-5 minutes prior to conclusion of surgery. Nitrous oxide was stopped at the conclusion of the surgery.
Residual neuromuscular blockade was reversed with neostigmine & glycopyrrolate, 0.04 mg/kg & 0.01 mg/kg respectively. Extubation was performed after having achieved TOF > 0.8 in a patient responsive to verbal command. All patients received 4l/min oxygen by Hudson mask for 30 min in the recovery room. Perintubation & periextubation hemodynamic parameters as well as pain free period [period from conclusion of surgery to the first requirement of analgesic for pain relief as demanded by the patient] was noted and recorded by a person blind to the nature of infusion [saline or lidocaine]. Study data was analyzed by using paired & unpaired Students t test.
Results & Conclusion: Patients receiving lidocaine had significantly less rise in MAP under the stimulus of intubation or extubation as compared to the saline group. A significantly longer pain free period [329 min vs 54 min] was also noted. An interesting finding was an attenuated fall in MAP under the stimulus of induction agent in patients receiving lidocaine infusion. Notably, lidocaine infusion does not attenuate the HR response to any significant level. A larger prospective trial is needed to confirm these findings.

Lidocaine infusion and post operative analgesia FALL(-) RISE(+) $p<0.05$*

Groups		Change Post Induction	Change Post Intubation	Change Post Extubation	Pain Free Period (Min)
A	HR	1.8 (-)	23.7 ± 13 (+)	28.1 ± 11 (+)	54.4 ± 99
Saline	MAP	15.7 ± 9 (-)	26.2 ± 12 (+)	21.8 ± 10 (+)	
B	HR	0.8 (-)	18.5 ± 14 (+)	24.4 ± 13 (+)	329 ± 372 *
Lidocaine	MAP	9.2 ± 7 (-)	9.9 ± 7 (+) *	12 ± 6 (+)*	

S-252.

EFFECT OF REPARIXIN ON PLASMA NEUTROPHIL COUNT IN PATIENTS UNDERGOING ON-PUMP CORONARY ARTERY BYPASS SURGERY

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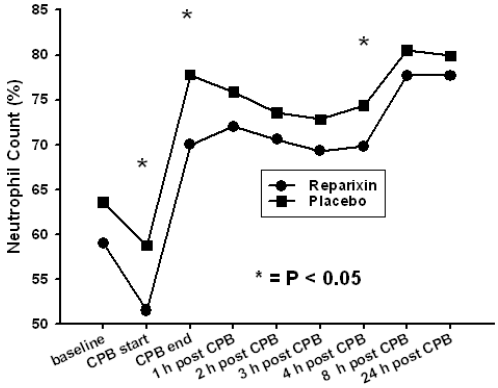
Introduction:
Ischemia-reperfusion injury after cardiopulmonary bypass is associated with an inflammatory reaction characterized by recruitment and activation of neutrophils, which are the primary target cells of the chemokine IL-8. We were interested if reparixin, a novel IL-8 inhibitor, attenuates neutrophilia induced by cardiopulmonary bypass (CPB) (1,2).
Methods:
After IRB approval and informed consent 32 patients undergoing elective on-pump coronary artery bypass graft surgery were included. Baseline blood samples were drawn through a newly inserted radial arterial catheter. After inducton of anesthesia the loading dose of reparixin (4.5 mg kg^{-1}) or an equal volume of placebo was administered over 30 min through a central venous catheter. After this loading dose, a continuous infusion of reparixin (2.8 mg kg^{-1} h^{-1}) or an equal volume of placebo was given until 8 hours after going off bypass. Besides baseline levels, blood samples were obtained after the start and the end of CPB, as well as 1, 2, 3, 4, 8 and 24 h after CPB end. Analysis of variance was employed for statistical evaluation of the data.
Results:
Neutrophil count declined in both groups with the beginning of CPB with higher levels being determined in the placebo group ($P > 0.05$). After CPB, neutrophil count exceeded baseline levels in the two groups with a greater increase in the placebo group as compared to the reparixin group ($P < 0.05$). Significant group differences were also detected at 4 hours post-CPB (Fig. 1).

Figure 1



Discussion:
The rise of the neutrophil count after CPB was less marked in the reparixin group. This may indicate that inflammatory induced ischemia-reperfusion injury is less severe in patients after surgery on CPB when IL-8 is inhibited.
References:
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S-253.

EFFECT OF PREGABALIN ON PREOPERATIVE ANXIETY IN PATIENTS UNDERGOING ELECTIVE SURGERY PROCEDURES

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Introduction:. Pregabalin, a new gabapentinoid compound, has been shown to be effective in reducing chronic neuropathic pain. Preliminary data suggest that this new drug may possess CNS properties (e.g., sedation, anxiolysis, analgesia) which could be useful in the perioperative period. In this placebo-controlled, dose-ranging study, we hypothesized that patients receiving oral pregabalin would experience less anxiety prior to induction of general anesthesia. Secondary objectives of this study were to evaluate if premedication with pregabalin would contribute to reduced postoperative pain and an improved quality of recovery.
Methods: A total of 120 consenting patients undergoing elective surgery will be randomly assigned to one of four groups: Placebo; Pregabalin 75 mg;Pregabalin 150 mg, and Pregabalin 300 mg. The study medication will be administered orally 60-90 min prior to induction of anesthesia in identical capsules.The effects of the study medication on anxiety, sedation, and pain will be assessed at specific intervals by using scales, with 0=none to 10=maximal. The need for postoperative pain medication and rescue antiemetics, and times to PACU discharge will also be evaluated.
Results: Preliminary results from the first 50 patients enrolled in the study are summarized in Table 1 and Figure 1. The four groups are similar with respect to demographic characteristics. Patients in Group 3 have lower mean anxiety scores at the time of induction, compared to the placebo group [3±3 vs 1±1]. Group 4 reports significantly more drowsiness at 120 min postoperatively compared to the placebo group [4±3(14) vs 9±3(4)]. The length of the PACU stay was prolonged in Group 4 compared to the other three treatment groups.
Summary: Preliminary data show that pregabalin decreases preoperative anxiety and increases perioperative drowsiness in a dose-related fashion. Pregabalin, 150 mg po, appears to be the optimal dose for reducing anxiety without producing unwanted sedation in the postoperative period.

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S-254.

THE STUDY ON FEASIBILITY OF LABETALOL AND NICARDIPINE AS A PART OF ANESTHETICS

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INTRODUCTION: The meaning of modern anesthesia is loss of consciousness and no recall of trauma and surgery. Even Prys-Roberts suggested that the concept of anesthetic depth is illusory, and the process of anesthesia is all or none. Nociceptive stimuli during general anesthesia are usually suppressed by increasing the inspired concentration of volatile anesthetic and/or administration of opioid analgesics. However, several studies[1,2]have suggested that sympatholytic drugs may be effective alternatives to opioid analgesics. To test the hypothesis that nicardipine and labetalol can maintain hemodynamic stability by replacing some volatile anesthetic and opioid analgesics during laparoscopic cholecystectomy with applying of BIS monitor, and to compare the recovery process between experiment groups and the contrast group, we designed this prospective study.
METHODS: Sixty-eight patients (20-60ys, ASAI-II), undergoing elective laparoscopic cholecystectomy, were randomly assigned to four groups: GroupI(control, n=16) varied the inspired concentration of desflurane to maintain hemodynamic stability, not received any sympatholytic drugs. Group II(labetalol, n=18), Group III(nicardiping, n=18) and Group IV(labetalol+ nicardiping, n=18) suppressed nociceptive stimuli mainly by the two sympatholytic drugs. During surgery, the mean arterial blood pressure (MAP) was maintained within ±20% of the baseline value. In addition to MAP and HR, the end-tidal concentrations of desflurane and BIS values were recorded throughout the perioperative period. Recovery times and qualities were assessed.
RESULTS: Compared with the control group, adjunctive use of labetalol and nicardipine attenuated the increase in HR (in Group II) and MAP (in Group III) after tracheal intubation. In Group IV,the combination of the two drugs controlled the hemodynamic changes effectively at the same time. The use of labetalol and nicardipine as an adjunct to desflurane reduced the end-tidal concentrations of desflurane. The anesthetic concentrations of experiment groups (5.00±0.73, 4.04±0.44, 3.71±0.22%) were significantly lower than that of the control group(6.50±0.72%), P<0.01. There was a significant correlation between orientation time and end-tidal concentrations of desflurane at the end of surgery. Compared with the control group, the use of labetalol and nicardipine shortened emergence times (15.7±2.7, 12.8±2.1, 11.5±2.5 vs 18.3±2.4min)and reduced the occurrence of pain after surgery in nicardipine groups (29%,24% vs 75%).
CONCLUSION: The use of labetalol and nicardipine as a part of anesthetics during laparoscopic cholecystectomy attenuates the hemodynamic response to stimuli. Furthermore, the use of labetalol and nicardipine reduces the end-tidal concentrations of desflurane. As much as this study shows, nicardipine's anesthetic-sparing action is more significant. Use of labetalol and nicardipine as an adjuvant to desflurane anesthesia does not increase the risk of awareness, and shorten the recovery times. Nicardipine's analgesic-sparing action decreases the occurrence of pain and the requirement of opioids after surgery.
REFERENCES:
[1] Pain 60: 83-90 1995
[2] Brain Research 818: 187-195 1999

S-255.

OXIDATIVE STATUS BIOMARKERS DURING HIGH VERSUS LOW DOSE PROPOFOL ANESTHESIA

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Introduction: Oxidative stress occurs when there is imbalance between generation of reactive oxygen species and antioxidant defense systems leading to cell damage [1]. Propofol resembles phenol-based antioxidants in chemical structure and proved to be scavenger of free oxygen radicals [2]. Some investigators claim it evident only at supramaximal blood levels [3] while others found that even at anesthetic blood concentrations, propofol inhibited peroxidation of lipids [4]. The aim of this study is to assess such impact by comparing the effect of high versus low dose propofol TIVA on the oxidative status using antioxidant and oxidative stress biomarkers.
Methods: Thirty adult patients (ASA I-II) of either sex scheduled for major abdominal surgeries were randomly allocated to one of two groups of fifteen patients each to receive TIVA with propofol 200 µg kg^{-1} min^{-1} (group HI) or 100 µg kg^{-1} min^{-1} (group LO), sufentanil (0.2 µg kg^{-1} hr^{-1}), vecuronium (1 µg kg^{-1} min^{-1}) in air:O_2. Five venous samples of 5 ml each were taken at preinduction (T0), ten minutes (T1), one hour (T2), end of surgery (T3) and 24 hours after recovery (T4) for detection of the antioxidant biomarkers superoxide dismutase (SOD), glutathione peroxidase (GPx), and total antioxidant status (TAO) as well as the oxidative stress biomarker malonaldehyde (MDA) .
Results: The HI group showed significant drop of blood pressure and heart rate till 15 minutes after recovery. SOD and TAO increased significantly by T1 and T4 in the LO group while GPx showed the same rise by T2. In contrast, MDA showed a significant drop by T3 in LO group.

	SOD (u/ml)		GPx (u/l)		TAO (mmol/l)		MDA (umol/l)	
	HI	LO	HI	LO	HI	LO	HI	LO
T0	176±46.2 b	270.8±102.3 a	8141±710 a	6955±1419 a	1.60±0.29 a	1.41±0.29 a	3.77±0.49 b	6.96±3.49 a
T1	216.5±64.5 b	338.4±119.1 a **	8867±1279 a	6645±1460 b	1.64±0.44 a	1.78±0.20 a **	4.99±2.07 a	4.93±1.85 a
T2	206.3±66.0 a	282.0±116.3 a	9276±1135 a **	7350±1259 b **	1.74±0.31 a	1.66±0.31 a	4.69±1.71 a	4.44±1.65 a
T3	208.9±67.4 a	265.4±85.4 a	9122±965 a **	7465±1600 b	1.79±0.39 a	1.49±0.33 a	4.94±2.24 a	3.50±1.16 a **
T4	196.5±34.7 b	374.7±146.3 a **	8230±595 a	6363±1119 b	1.54±0.28 b	1.78±0.08 a **	3.83±0.79 a	5.17±2.43 a

*Within group (** p<0.001) compared to T0*
Between groups (a,b) readings sharing same letter at same timing are not significantly different
Discussion: Propofol reduces the oxidative stress and enhances the antioxidant defense mechanisms expressed by larger concentrations of free radical scavengers. This was elicited and maintained with the use of low rather than high- dose propofol. These results may be related to higher lipid content of the propofol emulsion which promoted more lipid peroxidation as well as hypotension causing a potential hypoxic cell insult producing mitochondrial peroxides especially after restoration of cellular reperfusion.
References:
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Regional

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S-256.

THE EFFECTS OF THE HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY ACT (HIPAA) ON RESEARCH STAFF WORKLOAD DURING A PROSPECTIVE, RANDOMIZED CLINICAL TRIAL

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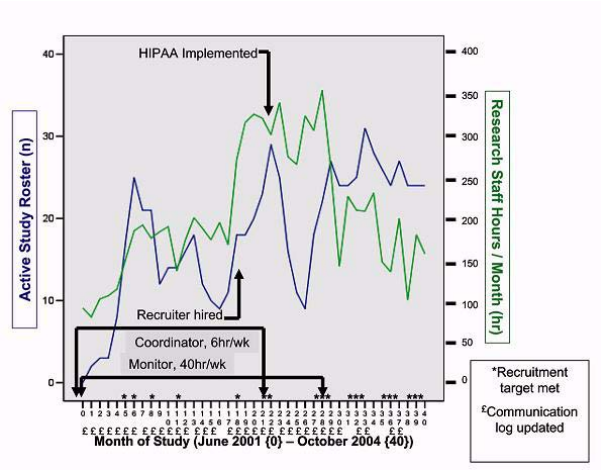
Introduction: In an IRB-approved, prospective clinical trial of surgical outpatients (n=270),[1] HIPAA regulations were enacted at the midpoint of enrollment. We retrospectively examined research staff hours per month before and after HIPAA.
Methods: 233 outpatients were retained throughout this 12-week prospective study (from May 2001 - October 2004); patients were followed daily for 4 days, then at 1, 3, 7, and 12 weeks after surgery. The recruitment target was 8 per month, to meet sample size requirements in 36 months. We determined: (i) months that the recruitment target was met, and (ii) months with evidence of study communications log updates. We then described each study month with the following dichotomous designations: "recruitment target met," "communication log updated," and "HIPAA implemented." These 3 factors were independent variables inserted into linear regression equations, to determine the number of hours per month of research staff time was required to accomplish the stated goals of recruitment, documentation, and compliance.
Results: The Figure shows a monthly time-line of study roster, research staff hours, communication log updates, and achieving recruiting targets. The study completed recruitment in the 40th month, 4 months later than originally targeted. In 19 months, the recruiting target was met. Four of the 6 "off-target" months after HIPAA were May-August 2003. In the regression model, the "research staff time" constant was 122 hours per month (for recruiting and follow-up), with 79 additional hours per month associated with communication log updates (P=0.007), and 57 additional hours per month associated with HIPAA implementation (P=0.012).
Discussion: Communication log updates were associated with a 65% increase in monthly hours over base workload (of recruiting and follow-up), and HIPAA was associated with a 47% increase in monthly hours over base workload. Meeting recruiting targets (as a dichotomous variable) did not influence work hours per month. Junior clinical investigators and their research mentors may find these calculations useful for forecasting study budgets and hiring the correct mix of research staff to specifically address recruitment, follow-up, documentation, and compliance. When preparing the budget involving clinical research in anesthesiology, it appears that staff-hour budgets should be significantly increased, when compared with staff-hour budgets before HIPAA.
Supported by NIH/NIAMS (K23 AR47631) and IARS Clinical Scholar Research Award (2001)
Reference: 1. *Anesthesiology* 104(2): 315-327, 2006



S-257.

HOW TO DO ANESTHESIA RESEARCH AS THE MONEY DECLINES: WHERE IS THE BEST CHANCE FOR NIH DOLLARS?

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Introduction: The declining success rates on NIH grant applications is of enormous concern to Anesthesia departments that seek to preserve serious academic activity. The best chance to preserve research, and to keep our specialty at the vanguard in anesthesia-related research is to encourage and support the success of committed junior faculty. However, few junior faculty will be competitive for RO1 grants. More senior faculty may have to seek alternate or more creative funding means in this era of decreasing NIH grant success. I reviewed the trends in NIH funding and here suggest strategies that are in particular directed toward junior faculty.
Methods: Data were obtained from the website of the Center for Scientific Research at the NIH (nih.gov). The website contains dollar funds for specific grant mechanisms and institutes of the NIH as of 2005. Training grant data were confined to mechanisms for which MDs and/or aspiring clinician-scientists would be eligible as determined by the "training grant wizard" at the CSR website.
Results: Discouraging is that, in Anesthesiology departments, success rates for RO1s declined from 39% in FY2002 to 19% in FY2005. This was despite an increase in applications during this time period from 198 to 259. However, other clinical departments have fared no better. The current overall success rates for new and competing RO1s were 18 and 37%, respectively, in FY2005. In the past, success rates were significantly higher for some NIH institutes vs others. Anesthesiologists typically are funded by NIGMS, therefore, orienting the application for review by Study Sections seeing few if any anesthesia grants, and for funding by other institutes was in some instances a successful strategy. In FY2005, there are few differences in success rates between NIGMS and others. The highest success rate was in NIAAA (30.5%). Training grants K23 and K08 (for no prior funding history), and K02 and K24 (prior funding) offer the best opportunity for junior faculty. The success rate for these awards in FY2005 was 33% for K23, 40% for K08, 38% for K02, and 52% for K24. The overall success rate for training grants has declined from 62% in FY2001 to 43% in FY2005. Among K08 and K24 applications, the best chances of success were at NEI (64%), NIDA (100%), NIDDK (56%), and NIGMS (70%). For K24, only 29% were successful at NIGMS, and 78% at NIAMS, 75% at NIDA, and 72% at NIDDK.
Discussion: Tightening of the NIH budget created enormous challenges for senior and junior investigators. Anesthesia departments should encourage K08 and K24 applications from junior faculty targeted to NIH institutes that do not traditionally fund anesthesia research but where there is a higher chance of successful application.
Acknowledgement: SR's research is supported by NIH grant EY10343

S-258.

PERINEURAL CATHETER REMOVAL IN PATIENTS RECEIVING WARFARIN FOR THROMBOPROPHYLAXIS

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Introduction: There is a scarcity of data regarding coagulation status associated with the removal of peripheral nerve block catheters in patients receiving warfarin for thromboprophylaxis. It is established that the safe removal of neuraxial catheters in patients receiving warfarin requires an INR <1.5.[1] In contrast, we frequently discontinue perineural catheters in patients receiving thromboprophylaxis without any consideration for the type of anticoagulant and/or the timing. This study was designed to determine the coagulation status at the time of the catheter removal in patients receiving warfarin after undergoing total hip or total knee replacement.

Methods: We retrospectively reviewed the charts of all patients over a 1-month period who benefited from continuous nerve blocks for postoperative analgesia while receiving warfarin following total hip or knee replacement. Warfarin treatment was initiated on the day of surgery at an average dose of 7.5mg. Subsequent doses were adjusted to maintain an INR in accordance with anti-coagulation guidelines for joint replacement. PT and INR values measured on the day of perineural catheter removal were recorded. The results for each catheter type are listed in Table 1. Normal PT values are 8.5-10.3.

Results: Forty patients were included in this study for a total of 59 perineural catheters (20 femoral, 19 sciatic and 20 lumbar plexus). All lumbar plexus and sciatic catheters were removed on post-operative day two except one sciatic catheter removed on day three. All femoral catheters were removed on post-operative day three. A significant number of the catheters were removed when the INR was ≥1.5 (40% of the femoral catheters, 60% lumbar plexus, 47% sciatic). Neither bleeding complications nor hematomas were reported.

Table 1. INR and PT prior to catheter removal

	INR (Mean ± SD)	PT (Mean ± SD)
Femoral	1.4 ± 0.6	13.3 ± 5.7
Lumbar Plexus	1.6 ± 0.6	15.2 ± 5.8
Sciatic	1.6 ± 0.7	14.8 ± 6.4

Discussion: These preliminary data demonstrate that in our clinical practice, perineural catheters are often removed with an INR ≥1.5. Additional data are required to confirm that in patients receiving warfarin for thromboprophylaxis it is safe to remove a perineural catheter in the absence of an INR measurement.

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S-259.

PREOPERATIVE GABAPENTIN PREVENTS INTRATHECAL MORPHINE-INDUCED PRURITUS AFTER ORTHOPEDIC SURGERY

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Introduction: Pruritus is the most common side effect associated with spinal or epidural morphine, and may be unpleasant and difficult to treat (1). Propofol and ondansetron have been used to prevent and treat pruritus, but with contradictory results (2, 3, 4, 5). The anticonvulsant gabapentin is reported to treat uremic pruritus (6, 7, 8), brachioradial pruritus (9), and pruritus of unknown origin (10). We thus tested the hypothesis that preventive gabapentin would decrease the incidence and severity of intrathecal morphine-induced pruritus in orthopedic surgery.

Methods: Following Institutional Review Board approval, thirty ASA I patients scheduled for arthroscopy-assisted anterior cruciate ligament reconstruction under spinal anesthesia were randomly allocated into two equal groups and received either gabapentin 1200 mg or placebo 2 hr before operation in a prospective, double-blinded manner. All patients received an intrathecal injection of 15 mg of 0.5% isobaric bupivacaine and 0.2 mg preservative free morphine. Postoperative pruritus was assessed, using a visual analogue scale (VAS), every 8 hr for 24 hr. Pruritus treatment was administered upon patient request and by a resident blinded to the treatment given.

Results: The incidence of pruritus was significantly more frequent in the placebo group compared with the gabapentin group (76% vs. 24%; $p < 0.0001$). The severity of pruritus score in the two groups was also significantly different. The patients in the placebo group had a higher VAS score than that in the gabapentin group (6.4 ± 1.2 vs. 3.2 ± 0.6, $p < 0.0001$).

Discussion: After prophylactic administration of 1200 mg of gabapentin, the incidence and severity of pruritus were decreased compared with placebo. Gabapentin prevents pruritus induced by intrathecal morphine in orthopedic patients after cruciate ligament reconstruction surgery.

References:
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(9) Br J Dermatol 2004;150:786-787.
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S-260.

PRACTICE AND PREFERENCE FOR REGIONAL ANESTHEISA/ ANLGESIA TECHNIQUES AMONG ANESTHETISTS

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Introduction: We conducted a survey on practice and preference for regional anesthesia/analgesia techniques among anesthetists.
Methods: Survey forms were mailed to 290 anesthetists in four different hospitals in the UK (one in England - 33, one in Northern Ireland (NI) - 97and two in Wales - 120 and 40 anesthetists). Four different clinical cases (hernia repair, lower limb orthopedic (LLO) case, major abdominal (MA) surgery and labor pain (LP) relief were proposed. Each clinical case had four options. First option was only preference for central regional anesthesia/analgesia and last option was the choice to avoid any nerve blockade (central or other) technique in preference to systemic analgesics. Second and third options offered various different choices including peripheral nerve blockade. Only one choice was allowed to make. For each case their choices for patient and for themselves (if they or their close relatives face the same clinical problem) were asked. Choices were considered 'opposite' when the first choice (central neuroxial blockade) was made for patient and the last choice (systemic analgesics only) was made for themselves for the same clinical scenario or vice versa. Choices were considered 'similar' when same choices were made for patients and themselves for the same clinical condition. We also asked their grades.
Results: 169 (58.28%) surveys were returned. Response rate was the highest in Wales (80% and 55%) followed by England (63.6%) and NI (51.6%). Overall only 44%, 51.5%, 66.7% and 53.3% anesthetists choose similar techniques for hernia repair, LLO case, MA surgery and LP relief respectively both for patients and themselves. Opposite choices were found mainly for hernia repair (12.4%) and LLO case (8.3%). 4.8% in case of MA surgery and 5.95% for LP relief had opposite preferences for themselves in compared to patients. In all these opposite choices tendency to avoid regional techniques for themselves was found. We have also noted differences among various grades of anesthetists. Consultants were more consistent for their choices in scenario of major abdominal surgery (only 2.2% had opposite choices). 11.9% specialist registrars would avoid central neuroxial blockade for hernia or LLO case for themselves but they would choose this technique for patients. No opposite choices (0%) were found for MA surgery and labor pain relief among anesthetists of NI.
Discussion: Though there are several limitations of this survey we have found that regional anesthetic /analgesic techniques are less preferred by anesthetists for themselves when compared to their choices for patients. This attitude may be due to fear of complications. Individual experience and responsibilities, pressure to get on with the cases and resources available in particular hospital might have played role in selection of choices for patients.

S-261.

WHAT IS THE RELATIONSHIP BETWEEN PRESSURE AND FLOW IN A PERIPHERAL NERVE BLOCK NEEDLE?

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Introduction:
Studies have examined injection pressures and its effect on peripheral nerve injury. Pressure was measured in pounds per square inch (psi) (1,2). We wished to determine the effect of the peripheral block needle on pressure and flow of injected saline.
Method:
A 20 cc syringe (Becton Dickinson, Luer-Lock, Becton-Dickenson, Franklin Lakes, NJ) of saline was connected to a peripheral block needle (Stimuplex A2250, BBraun, Bethlehem, PA). The syringe was placed into a syringe pump (PHD 2000, Harvard Apparatus, Holliston, MA) to supply a calibrated flow of saline. The pressure was measured between the syringe and the peripheral block needle. Flow was set from 8-50 cc/min, pressure was then measured.
Results:
Pressure was either linearly or exponentially related to pressure depending upon the flow rate. From 8-20 cc/min, flow was linearly related to pressure. Above 20 cc/min, flow became exponentially related to pressure.
Discussion:
If Ohm's Law (V= IR) is applied to fluids, pressure should be linearly related to flow times resistance (P= FR). Then, the pressure drop across the peripheral block needle, from syringe to air, divided by the calibrated flow, should yield the resistance of the peripheral needle. Relating this to a linear equation ($y = mx + b$), the needle resistance should be the slope of the line formed when graphing flow vs. pressure. We found that flow could be either linearly or exponentially related to pressure. Up to approximately 20 cc/min, flow was linearly related to pressure. Beyond this rate, flow became exponentially related to pressure.
Conclusions:
Clinically, most practitioners are likely to inject faster on 30 cc/min (1 cc every 2 sec); hence the pressure drop across the peripheral block needle will likely be significant. Therefore, the pressures felt by the practitioner when injecting anesthetics at high flow rates is not entirely due to obstruction of the needle, but may be due to the needle orifice, or any material beyond the needle, not necessarily indicating of an intraneural injection.
References:
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S-262.

NEEDLE COSTS FOR ULTRASOUND GUIDED VERSUS STIMULATOR GUIDED NERVE BLOCKS

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Introduction- US guidance for peripheral nerve blocks is effective (1), however, the equipment cost for this new technique is considerable. When US is used as an adjunct to nerve stimulator techniques, it becomes an added expense to the hospital and patient. However, if US guidance is used in lieu of nerve stimulation, it may offset the cost of nerve stimulating needles. In this study, we report the cost difference for needles when US is used as the sole method to guide needle placement for single injection and catheter techniques.
Methods- After IRB approval, we prospectively recorded the needle costs for single injection and indwelling catheter placement using only US guidance. Data were collected for 10 consecutive days and included the type of block, success rate, and the cost of each needle used. These blocks were then compared by cost to the corresponding needle that would have been used with a nerve stimulator technique. Needle costs were obtained from the manufacturer. Single US guided injections were performed using a 22G/ 4 cm regular bevel needle (cost 45 cents). Catheters were placed through a thin walled 18G/ 6.35cm introducer needle (cost $2.07). The cost for the corresponding stimulator guided single injection needle was $13.80 (22G/5cm stimulating needle). The cost for a stimulator guided needle for catheter placement was $16.70 (18G /10 cm stimulating needle). For purposes of this study, the success rate of nerve stimulator blocks was assumed to 100%.
Results- A total of 67 peripheral nerve blocks (41 single injections, 26 catheters) were placed during this 10-day period. Two blocks (1 single axillary, 1 interscalene catheter) were repeated for an overall success rate of 97%. The individual totals included;
Interscalene 11 single injections, 8 catheters
Axillary 16 single injections
Femoral 6 single injections, 8 catheters
Sciatic 8 single injections, 10 catheters
The cost difference for needles assuming a 100% success rate for stimulator blocks and an observed success rate of 97% for US guided blocks is:
$14.55 for catheter placement
$13.34 for single injection
Conclusions- The increased needle cost for stimulator guided blocks compared to US only guided blocks was calculated to be $13.34 for single injections and $14.55 for catheter placement. The needle costs at centers performing large numbers of nerve blocks could be considerable. For example, a center performing 5 single injections per day for 250 days per year could save $16,675.00/year. The cost savings for a similar number of catheters would be $18,188.00/year.
References
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S-263.

ACTUAL CLINICAL INFUSION RATE OF DISPOSABLE INFUSORS FOR POST OPERATIVE EPIDURAL ANALGESIA

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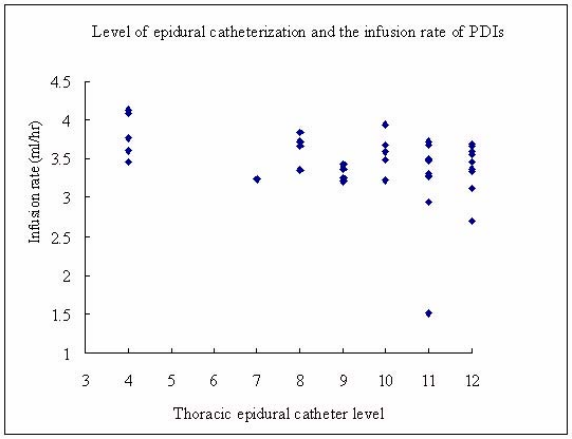
INTRODUCTION: A portable disposable infusor (PDI) is a convenient device for post-operative epidural analgesia. As each kind of PDIs incorporates various infusion mechanisms and materials, infusion pressure varies greatly among them. In addition, the infusion rate of these infusors is affected by other factors, such as temperature, height of PDI position, viscosity of drugs, kind of epidural catheters and filters used, and the nature of the epidural space. The purpose of this study was to measure the actual clinical infusion rate of PDI for epidural analgesia use.
METHODS: Twenty-five patients scheduled for elective abdominal or thoracic surgeries were recruited. They received thoracic epidural catheterization and the epidural catheter was connected to a PDI (Baxter infusor LVBB 4 x 4) filled with 0.2 % ropivacaine after measurement of its weight. A few days after surgery, the weight of PDI was measured again when the PDI was exchanged to a new additional PDI or when the epidural catheter was removed. Infusion rate was derived from the actual amount of the drug consumed and the infusion time by PDI. The frequency of the use of the patient controlled analgesia (PCA) device was also recorded and the amount used by PCA was taken account to the result.
RESULTS: The mean calculated infusion rate of 41 PDIs was 3.439 ml / hr. The relationship between the level of insertion of the epidural catheter and the infusion rate is shown in the figure. Infusion rate of epidural PDIs connected to lower epidural levels was smaller compared with those connected to upper levels(Y=3.993-0.57X). In 14 patients, additional new 16 PDIs were used. Infusion rate of additional PDIs tended to be lower compared with the original PDIs.
DISCUSSION: Actual clinical infusion rate of this type of PDIs was different from the indicated rate of these PDIs. Various factors might have affected the infusion rate of the PDI. Because the infusion rate of PDIs connected to upper epidural space was larger and the infusion rate of exchanged PDIs was smaller, the nature of the epidural space was the factor which most influences the infusion rate of PDIs. For exact control of epidural infusion for analgesia, it might be necessary to utilize a device under computer control.



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S-264.

PERCUTANEOUS INTERCOSTAL CATHETERIZATION FOR CATHETERIZATION OF THE PARAVERTEBRAL SPACE

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Background: Although continuous paravertebral infusion of local anesthetics is of growing interest, anesthesiologists often feel intimidated by the classic catheterization technique. Furthermore, the direct approach to the paravertebral space may be contraindicated in case of prior spinal surgery with instrumentation, spine trauma and/or deformity. An intercostal approach to the paravertebral space has been previously described[1]. However, this technique is used only for thoracotomy and requires the intraoperative placement of the catheter by the surgeon. We are describing an alternative technique to reach the paravertebral space by a percutaneous placement of an intercostal catheter that can be performed prior to surgery.
Methods: The block was performed in the sitting position. The skin was infiltrated with 1% lidocaine 8 cm lateral to the midline over the rib after appropriate preparation. At this point an 18-gauge Tuohy needle was introduced until the lower portion of the rib is contacted. The needle was then angled 30° inferior and 30° lateral to the perpendicular plane of the chest and walked off the inferior boarder of the rib and advanced 4-5 mm into the subcostal grove. Five ml of the local anesthetic was slowly injected. The distance from the midline is added to the depth of the needle to determine the length of catheter insertion through the needle. The catheter is secured with strerri-strips and covered with a transparent dressing. Patients received 1 mg midazolam and 50 mcg fentanyl for sedation. The paravertebral catheters were infused with 0.2% ropivicaine at 8 ml/hr post-operatively.
The effectiveness of the technique was assessed using pain scores and PCA consumption. Data are presented as mean (range).
Results: We performed 22 thoracic paravertebral catheterizations via an intercostal approach on eleven patients for postoperative analgesia for the following indications: ventral hernia repair, nephrectomy (the patient had posterior spinal fusion with interlaminar rods from T10-L5), bilateral partial nephrectomies, proctocystectomy, gastrectomy, total abdominal hysterectomy, mastectomy, colectomy, low anterior resection, resection of large retroperitoneal mass and adrenalectomy. The patients rated the percutaneous placement procedure as not uncomfortable. The paravertebral catheters were infused for 4 days (2-5 days). All patients indicated that they were very satisfied with their pain relief, rated their post-operative pain as mild 3 (0-5), and only had modest PCA usage 2.7 mg (0.4-6.6 mg) hydromorphone in the first 24 post-operative hours. None of the patients suffered an untoward event.
Conclusion: These preliminary results suggest that this intercostal approach to the placement of a catheter in the paravertebral space is well tolerated by the patient, easy to perform, reliable and effective in controlling postoperative pain and may be useful beyond patients undergoing a thoracotomy. However, larger series are required to confirm these results.
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S-265.

VERTICAL INFRACLAVICULAR BLOCK VERSUS DOUBLE STIMULATION AXILLARY BLOCK IN HAND AND FOREARM SURGERY.

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Regional anesthesia for upper extremity surgery is better than general anesthesia. The aim of this study is to compare the Vertical infraclavicular brachial plexus block (VIC) versus double stimulation Axillary block (AxB) in hand and forearm surgery. **Methods**: 40 patients received VIC block (40 ml levobupivacaine 0.5%)using the nerve stimulator, another 40 patients received AxB with double stimulation (40 ml levobupivacaine 0.5%). **Results**: The time of performance of block was significantly shorter in VIC vs AxB group (4.3±1.9 min vs 9.5±2.9 min respectively) $P<0.0001$. Sensory and motor block were more commonly achieved in the distribution of axillary, radial and ulnar nerves in VIC vs AxB ($P<0.05$). No significant side effects in both groups. **Conclusion**: the VIC brachial plexus block provides better efficacy, high success rate, less performance time and no significant side effects compared to AxB in hand and forearm surgery.

S-266.

POST-OPERATIVE PERIPHERAL NERVE BLOCKS DELAY PACU DISCHARGE

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INTRODUCTION: The use of peripheral nerve blocks (PNB) significantly decreases post-operative pain, improves function, and increases patient satisfaction following Total Knee Arthroplasty (TKA) (1). Maximum benefit occurs by placing the peripheral nerve block (PNB) pre-operatively, yet the increased time necessary for proper placement limits its use for fear of delaying the start of the operation. Increasing pressures at our institution forced us to place some of our peripheral nerve blocks post-operatively in the PACU. We therefore evaluated the effects of post-operative block placement on operating room start times, narcotic consumption, and PACU stay.
METHODS: We retrospectively studied 410 consecutive patients who underwent a TKA over a fourteen-month period and divided the patients into the following groups based on operative anesthetic: General Anesthesia (GA), Spinal Anesthesia (SAB), or Epidural Anesthesia (LEA). The groups were then sub-divided based on whether they received a peripheral nerve block, and if so, was it placed pre- or post-operatively. We compared OR start times, morphine usage, and time spent in the post-anesthesia care unit (PACU). We performed ANOVA tests between the groups to determine significant differences between groups.
RESULTS: There was no significant difference between any of the groups in regards to OR start time. Patients who received spinal or epidural anesthesia used significantly less narcotics in the operating room. Patients who received post-operative PNB following spinal anesthesia spent nearly forty-five minutes longer in the PACU ($P<0.001$) than all other groups.
DISCUSSION: Our data clearly demonstrates that delaying placement of PNB does not affect OR start time, but rather disproportionately increases PACU stay. Placement of PNB in the PACU following resolution of spinal anesthesia adds nearly an hour to the PACU stay. This delay negatively impacts patient satisfaction limits PACU bed availability, further disrupting OR discharge. Furthermore, our study demonstrates that OR start time was independent of operative anesthetic chosen. Thus, every effort should be made to place peripheral nerve blocks pre-operatively and choice of operative anesthetic should be tailored to exclusively to the best interests of the patient.
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S-267.

LOW ENTROPY OF RR INTERVAL PREDICTS HYPOTENSION AFTER SPINAL ANESTHESIA.

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Introduction:
Recently, some investigators have found that heart rate variability (HRV) predicts the incidence of hypotension caused by spinal anesthesia (SA) in pregnant (1) and non-pregnant patients (2). On the other hand, MemCalc method, which is a combination of the maximum entropy method for spectral analysis and the nonlinear least square method for fitting analysis (Tarawa, Suwa Trust, Japan), has recently been developed (3). This method enables us to estimate ultra short-term entropy (UsEn), as a non-linear index of HRV, from short series of RR interval. The objective of this study was therefore to determine whether preoperative UsEn estimated by newly developed MemCalc method predicts hypotension during SA.
Methods:
After IRB approval and written informed consent from all patients were obtained, 52 patients undergoing elective transurethral surgery were investigated in this study. Analysis of HRV was made before and during SA using MemCalc method (Tarawa, Suwa Trust, Japan). Patients were assigned to two groups (Group LO and HI) according to preoperative UsEn. In both groups, SA was performed by intrathecal injection of 17.5mg of isobaric bupivacaine via interlumbar space L3-4 or L4-5. Thereafter the block height of SA was evaluated by pinprick test every ten minutes. Hemodynamic fluctuations during SA were recorded and %decrease in systolic blood pressure (SBP) caused by SA was calculated and compared between the two groups.
Results:
As the mean of baseline UsEn was 43 this value was used as a discriminant dividing the cohort into two groups. There were no significant differences in patient demographic data and block height of SA between the two groups. %decrease in SBP after SA was 17.5±9.8% in Group HI, whereas it was 11.4±9.9% in Group LO ($p<0.05$). Furthermore, the number of patients who developed hypotension was significantly higher in Group LO.
Discussion:
It was concluded that decrease in blood pressure caused by SA was significantly greater in patients with low UsEn. Furthermore, the incidence of hypotension was higher in patients with low UsEn.
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S-268.

ADDING MEPERIDINE TO ROPIVACAINE FOR INTRAVENOUS REGIONAL ANESTHESIA

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Introduction: In a study of volunteers, ropivacaine 0.2% compared favourably with lidocaine 0.5% for IV regional anesthesia (IVRA)(1). However, ropivacaine did not prolong tourniquet tolerance compared with lidocaine. Addition of 100 mg meperidine for IVRA with prilocaine improved the quality of the sensory and motor block (2). The objective of this invetigation was to determine whether the addition of meperidine may improve the quality of IVRA with ropivacaine, especially tourniquet tolerance.
Method: The study was prospective, randomized and double blind. A number of 20 patients submitted for elective hand surgery in IVRA were divided in two equal groups to receive 10 ml of 0.2% ropivacaine (80 mg) and either 1 ml of isotonic saline (group R) or 1 ml of meperidine (25 mg)(group RM). A tourniquet was kept inflated until patients complained of pain, leading to release of the tourniquet cuff. The onset and duration of sensory and motor blockade, as the incidence of side effects and duration of postopertive analgesia were also recorded.
Results: The tolerance for the tourniquet was significantly longer in the ropivacaine-meperidine group (mean 40 vs 29 min., p=0.047). There were not significant differences in onset of sensory and motor block. Anesthesia quality was better in RM group in comparison with R group (4 patients needed supplementation of analgesia). Duration of postoperative analgesia was similar in both groups, and no side effects were registrated during the study.
Discussion: Ropivacaine in a dose of 80 mg was safe and efficient for IVRA for hand surgery. The addition of 25 mg of meperidine improved the quality of anesthesia and assured a better tolerance for tourniquet pain.
References: 1) Anesth Analg 1999; 88: 1327-30. 2) Anaesth 1993; 48: 382-6.

S-269.

ULTRASOUND-GUIDED INTERSCALENE BLOCK IMPROVES SURGICAL CONDITIONS IN ARTHROSCOPIC SHOULDER SURGERY UNDER GENERAL ANESTHESIA.

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Introduction:
Controlled hypotension is sometimes required for arthroscopic shoulder surgery in order to improve surgical condition. Attenuation of noxious stimuli to the shoulder with interscalene block (ISB) may also contribute to the dry surgical field via attenuation of sympathetic activation. Recently, it has been proposed that ultrasound-guided ISB may have a great advantage over conventional ISB in terms of accuracy and safety (1). The objective of this study was therefore to determine whether ultrasound-guided ISB improves surgical condition and decreases the need for the controlled hypotension.
Methods:
After institutional approval and informed consent from all patients were obtained, 30 patients undergoing arthroscopic shoulder surgery under general anesthesia were investigated in this study. They were randomly assigned to two groups, group G and group G+B. In both groups, general anesthesia was induced with propofol, fentanyl and vecuronium and maintained with sevoflurane (1-1.5%) and fentanyl. After induction of anesthesia the trachea was intubated and the lungs were mechanically ventilated with 50% oxygen in air. Fentanyl was titrated so that 1.5-2mcg/ml of effect site concentration was achieved during surgery.
In group G+B, ipsilateral interscalene block was performed with the assistance of ultrasound imaging of the brachial plexus after endotracheal intubation. 20ml of 0.375% ropivacaine was administered so that brachial plexus was surrounded by it. The same surgeon subjectively evaluated the surgical condition and decided whether induced hypotension is required. According to the surgeon's request for controlled hypotension, nicardipine or landiolol were administered. Hemodynamic fluctuation during surgery, the incidence of the surgeon's request and the amount of nicardipine and landiolol adiminstered were recorded and compared between the two groups.
Results:
There were no significant differences in patient demographic data, the duration of surgery, the doses of sevoflurane and fentanyl administered between the two groups. Hemodynamic parameters during surgery were also comparable between the two groups. In group G, the surgeon requested for controlled hypotension in 10 cases, whereas in group G+B they did only in 2 cases ($p<0.05$). The averaged dose of nicardipine was significantly smaller in group G+B (9.2±15.1 mg in group G vs 0.9±2 mg in group G+B). Fourteen out of 15 patients in group G+B were free from pain postoperatively, while 9 patients in group G were free from pain.
Discussions:
In spite of comparable hemodynamics between the two groups, the surgeon preferred to the ISB assisted anesthesia. Tissue perfusion may be greater in group G because of increased cardiac output via sympathetic activation. It was concluded that ultrasound-guided ISB contributes to the improvement of surgical condition in arthroscopic shoulder surgery under general anesthesia.
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S-270.

USE OF CLONIDINE AS AN ANALGESIC ADJUNCT IN PERIPHERAL NERVE BLOCKS.

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Introduction
Clonidine, an α2 adrenergic agonist has been used as an analgesic adjuvant for over 20 years. Its analgesic properties have been extensively studied in the last number of years and its ability to enhance both central and peripheral nerve blockade have been realized[1,2]. The aim of this review is to focus on the current evidence for the analgesic benefit of adding clonidine to peripheral nerve blocks. The evidence for perineuronal administration versus systemic administration of clonidine will be analysed in an effort to answer the question of whether the analgesic effect is local or systemic. In addition, meta-analyses will be performed in an attempt to obtain a quantitative review.
Method
Studies were identified in a search of PUBMED and EMBASE (between July 1991and July 2006) by using the MeSH terms: peripheral nerve block, nerve block, adjunct and clonidine. Inclusion criteria included double blind randomized controlled trials and adult patients (age > 18yrs) and English Language articles. We independently reviewed each article with regard to: regional anesthetic technique, type of local anesthetic, measurement of postoperative pain, adverse effects and inclusion of a systemic control. Studies were classified as supportive if the use of clonidine demonstrated either reduction in onset time, reduction in pain and/or total analgesia consumption, or prolonged sensory block time. Meta-analyses were performed with RevMan 4.2.8 (Cochrane collaboration 2005).
Results
Overall 23 studies were identified that reached the inclusion criteria. Only five studies included a systemic control group. Overall 62.5% of studies were supportive of adding clonidine to peripheral nerve blocks. Only two outcomes had sufficient data for meta-analyses: VAS score at 24hrs, and sensory block onset time. Due to the inadequate number of studies with a systemic control group, we were unable to determine if the effect of clonidine is local or systemic. No significant side effects were reported with doses up to 150µg. Cardiovascular and sedative effects may have some benefit in selected patient populations. In addition, meta-analyses were able to be performed on data from eleven studies. VAS at 24 hrs was not significantly different between clonidine and control with weighted mean differences centred along the zero line, (p= 0.67). Similarly, the effect of clonidine on sensory block onset time was not found to be signifcantly different (p = 0.39).
Conclusion
Due to the inconsistency of reported outcomes, only a limited number of studies could be included in the meta-analyses. As a result the meta-analyses did not provide much insight into the benefit of clonidine as an adjunct in peripheral nerve blocks. However, on qualitative analysis, clonidine appears to prolong analgesia primarily by increasing the duration of sensory block with no decrease in onset time.
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1. Acta Anaesthesiol Scand 2005;49:538-545.
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S-271.

PACU TIME SAVINGS RELATED TO PERIPHERAL NERVE BLOCKS

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Introduction: Potential savings would be gained by the addition of peripheral nerve blocks as an adjunct to general anesthesia. Previous studies addressing the use of peripheral nerve blocks focused mainly on better postoperative analgesia, less nausea and various other topics without specific regard to cost. Recent researchers have failed to identify how the use of peripheral nerve blocks effects PACU times, which in turn translate into cost savings. Recent researchers have failed to identify how the use of peripheral nerve blocks effects PACU times, which in turn translate into cost savings. This research will add a greater understanding of how peripheral nerve blocks can be cost effective for hospitals, patients and the general healthcare economy.
Methods: The method of this study **was a** quantitative design. The data collection tool included questions regarding age, gender, surgical procedure, receipt of peripheral nerve block, anesthesia and PACU time. The variables were either independent or dependant. The independent variable was the inclusion of peripheral nerve blocks. The dependent variable was total PACU time
Results: According to the descriptive statistics some conclusions can be made. A description of the age groups can be seen in the chart at right. Age groups were divided into four groups. There were 17.39% in the 25-35 and the 56-60 age groups, 26.09% in the 36-45 group, and 39.13% in the 46-55 age group. Of the 23 participants, 30.43% were male while 69.57% were female. The average mean of PACU times for patients having blocks and those without blocks were different. For those patients who received a block the average PACU time was 48.35 minutes. In contrast, those who did not receive a block stayed in the PACU for an average of 60.33 minutes. Though these numbers are different, upon further analysis with the Mann-Whitney U test, the difference was not statistically significant (p=.079). The hypothesis stated that there would be a significant difference in PACU stay times between patients receiving general anesthesia and those receiving general anesthesia and a peripheral nerve block.
Discussion: The data analysis leads to acceptance of the null hypothesis. The null hypothesis stated that there would not be a significant difference in PACU stay times between patients receiving general anesthesia and those receiving general anesthesia and a peripheral nerve block.

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