

Supplement to

& ANESTHESIA ANALGESIA[®]



Abstracts of Posters Presented at the
82nd Clinical and Scientific Congress of the
International Anesthesia Research Society
San Francisco, California
March 28–April 1, 2008

This Supplement will Appear Online Only

ANESTHESIA & ANALGESIA[®]

The official scientific 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, the Society for Technology in Anesthesia, the Anesthesia Patient Safety Foundation, the American Society of Critical Care Anesthesiologists, and the Society for Obstetric Anesthesia and Perinatology.

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Abstracts of Posters Presented at the International Anesthesia Research Society 82nd Clinical and Scientific Congress San Francisco, California March 28 -April 1, 2008

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IARS 82nd Clinical and Scientific Congress

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- (S-6) Berger, J.S., Saturday 8:00
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- (S-10) Chaney, M.A., Sunday 8:00
- (S-11) Jahr, J.S., Sunday 8:00
- (S-12) Gandhi, K., Sunday 8:00
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- (S-79) Cummisford, K., Monday 10:15
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Education and Patient Safety

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- (S-98) Gandhi, K., Saturday 1:00
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Liver / Transplantation

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- (S-137) Kamel, I.R., Saturday 10:15
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Ambulatory

S-1.

TITLE: REVIEW OF SPINAL ANESTHESIA USING BUPIVACAINE FOR ARTHROSCOPIC KNEE SURGERIES IN THE AMBULATORY SETTING

AUTHORS: G. Sudhakaran Nair, A. Abrishami, J. Lermitte, F. F. Chung;

AFFILIATION: Anesthesia Department, University Health Network-Toronto Western hospital, Toronto, ON, Canada.

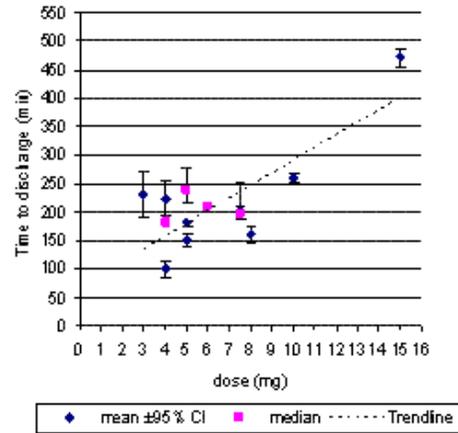
INTRODUCTION: The use of lidocaine in spinal anesthesia is associated with transient neurological syndrome (TNS)¹. Bupivacaine with lower incidence of TNS is a good alternative but has prolonged action. This study reviews the literature about the recovery profile of patients undergoing spinal anesthesia using bupivacaine for arthroscopic knee surgery.

METHODS: Systematic search was conducted through The Cochrane Library (Issue 2, 2007), MEDLINE (1966-April 2007), EMBASE (1980- April 2007) and reference lists of the retrieved articles to identify randomized controlled trials (RCTs) of bupivacaine in arthroscopic knee surgery irrespective of language. Trial inclusion, quality assessment and data extraction were carried out by the authors independently.

RESULTS: We identified twenty eligible RCTs (1499 patients). Five studies compared different doses of bupivacaine (range: 3-15 mg). Pooling of the data was not feasible due to significant heterogeneity, however; it was shown that large doses of bupivacaine (10 and 15 mg) were associated with delayed recovery (Figure-1). Whereas, low doses (3-5 mg) were associated with high incidence of failure ranging from 6% to 26%. Pooling of the data from six studies comparing bupivacaine with Ropivacaine showed no significant difference in recovery (Time to voiding (min); WMD: -2.3, 95%CI: -9.0 to -4.3). When bupivacaine was combined with Fentanyl in two studies, analysis showed delayed recovery (time to discharge (min); WMD: 14.1, 95%CI: 11.9 to 40.1). However, the use of Fentanyl resulted in improved postoperative analgesia at the cost of more complications. Bilateral and unilateral spinal anesthesia were assessed in two studies and the latter group was associated with early recovery and discharge (Time to discharge (min);

WMD: -41.6, 95%CI: -63.6 to -19.6). In quality assessment, the risk of bias was low in 13 trials and intermediate in 4 trials, however three trials could not be assessed due to insufficient data.

Figure -1: Recovery profile of different doses of bupivacaine



DISCUSSION: From our study, the recommended dose of bupivacaine is 6-8 mg, as the lower and higher doses resulted in failure and delayed recovery, respectively. This review also showed that the best recovery profile can be obtained with unilateral positioning. Ropivacaine or addition of adjuvants did not improve the recovery time. To draw definite clinical conclusion about optimum dose of bupivacaine, future quality RCTs with consistent design and more sample size are required.

REFERENCES: 1. Anesthesiology 1996;84:1361-7

S-2.

TITLE: FRANKLING MASK: REDUCES VOLATILE ANAESTHETICS PUNGENCY PERCEPTION DURING INHALATORY INDUCTION. COMPARISON BETWEEN ISOFLURANE AND SEVOFLURANE

AUTHORS: J. C. Kling, G. Franco;

AFFILIATION: Fundacion Cardioinfantil, Bogota, Colombia.

INTRODUCTION: Single breath inhalatory induction has become popular in ambulatory anesthesia but its use has been limited to sevoflurane, despite of the availability of other agents with better pharmacokinetic properties because it is the lowest pungent volatile anesthetic already available at the moment.^(1,2) The aim of this study was to try a prototype of FRANKLING MASK developed by authors, which was designed to reduce the pungency perception related to volatile anesthetics by avoiding its pass through the nasopharyngeal cavity thus limiting the contact of the anesthetic with the terminal branches of the trigeminal nerve; therefore making inhalatory induction more comfortable and allowing us to use other volatile anesthetics.

METHODS: Following IRB approval and signed informed consent, 103 ASA I - III patients undergoing surgery under general anesthesia, were enrolled in this randomized, double blind, prospective study. Study subjects were randomly divided into two groups, 4% Isoflurane induction with the FRANKLING MASK, and 8% sevoflurane induction with the FRANKLING MASK. Preoxygenation and induction time until the patient loses response to verbal commands were recorded, as well as the presence of adverse effects such as cough, bronchospasm, laryngospasm, and agitation, and also the pungency perception by the patient. At the end of the anesthetic recuperation phase, patients were asked about smell and flavor perception during the induction, qualify the anesthetic technique and if they would choose it again in case that they would have surgery again. Data were evaluated with ISTATA, t-test and Chi-square test. a P<0.05 was considered significant.

RESULTS: There were no demographic differences between both groups; the pungency incidence was not statistically significant (3 patients in isoflurane group and 1 in sevoflurane group). There also were not differences in cough, laryngospasm and bronchospasm

incidence. The anesthetic technique was qualified as good by 94% of the patients in both groups and 94% of them would choose it again.

DISCUSSION: The results in this study concludes that the use of FRANKLING MASK for inhalatory induction reduces the pungency perception of volatile anesthetics reported in the literature, making no difference in the pungency perception between sevoflurane and isoflurane, providing a better comfort during the inhalatory induction, therefore it could be use with more pungent anesthetics to profit their pharmacokinetic properties. In our current practice we had been used FRANKLING MASK with desflurane successfully. Future changes in the FRANKLING MASK design would be developed to make it more comfortable.

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S-3.

TITLE: EFFICACY AND SAFETY OF PERPHENAZINE IN THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING (PONV): A QUANTITATIVE SYSTEMATIC REVIEW

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INTRODUCTION: The antiemetic effect of perphenazine was first described in the literature in 1958 (1). Despite the introduction of newer molecules in the prevention of postoperative nausea and vomiting (PONV), perphenazine is still recommended in current guidelines (2). Therefore, the aim of this quantitative systematic review was to systematically assess the efficacy and safety of perphenazine in the prophylaxis of PONV in adults and children.

METHODS: All randomised controlled trials investigating the efficacy of perphenazine in the prevention of PONV in comparison to any other drug or placebo were systematically searched in Medline and the Cochrane Library. Relevant outcome data were extracted by three authors. Data were entered into RevMan 4.2®. Dichotomous data on efficacy and adverse effects of perphenazine were combined and relative risks (RR) as well as the corresponding 95% confidence intervals (CI) were calculated.

RESULTS: The systematic search identified 25 possibly relevant trials. Eleven trials published between 1965 and 1999 including a total of 2000 participants (805 patients received perphenazine and 1195 patients received a control) satisfied the inclusion criteria and were further analyzed. In children 0.07 mg/kg perphenazine was effective in preventing vomiting (RR: 0.71; 95%-CI: 0.56-0.91; P=0.07), while in adults a fixed dose of about 5 mg (5 to 7,77 mg) was effective for the prevention of PONV (RR: 0.65; 95%-CI: 0.49-0.86; P=0.006). There

was a trend for a better outcome when perphenazine (0.07 mg/kg in children and 5 mg in adults) was compared to ondansetron 4 mg in adults in one trial (RR: 0.82; 95%-CI: 0.49-1.39; P=1.0) and 0.15 mg/kg in children in another trial (RR: 0.89; 95%-CI: 0.62-1.55; P=0.94). The same holds true for one comparison versus dexamethason 0.15 mg/kg in children (RR: 0.72; 95%-CI: 0.52-1.01; P=0.06). In contrast to the latter results, perphenazine 5 mg was slightly less efficacious when compared to droperidol 1.25 mg in one trial (RR: 1.26; 95%-CI: 0.68-2.35; P=0.46). Only minor adverse effects (e.g. transient sedation) were noted in two eligible trials (RR: 0.42; 95%-CI: 0.08-2.34; P=0.32).

DISCUSSION: There is some evidence that perphenazine is effective in the prevention of PONV in children and adults without serious adverse effects. When compared to established newer drugs in the prevention of PONV, the administration of perphenazine appears to be comparably effective. In summary, perphenazine may favourably replenish the established antiemetic portfolio in the perioperative setting. However, data are sparse, so that the most promising timing and dose is far from being clear and it would necessitate further trials.

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S-4.

TITLE: DOES THE ADDITION OF INTRAVENOUS LIDOCAINE TO PROPOFOL BLUNT THE RESPONSE TO NOXIOUS STIMULI UPON INSERTION OF ENDOSCOPE FOR UPPER ENDOSCOPY?

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OBJECTIVE: Involuntary reflexes during upper gastrointestinal endoscopy (UGIE) is commonly encountered. IV lidocaine is effective in blunting the response to noxious stimuli. We determined whether the addition of IV lidocaine before administration of propofol for upper endoscopy can provide uninterrupted UGIE.

METHODS: Following IRB approval a randomized study of 71 (ASA I-II) patients scheduled for UGIE under general anesthesia. Standard monitoring of vital signs, telemetry and maintaining nasal O₂ was performed. Pts were randomized to one of two groups. Group I: control group (n=36) received IV propofol that was titrated to achieve deep sedation as required for the endoscopic procedure. Group II lidocaine group (n=35) received IV lidocaine 1 mg/kg immediately before intravenous induction with propofol 1.5 mg/kg. Data collected for comparison included: demographics, duration of the procedure, the total amount of propofol used, patient complaint of burning sensation upon IV propofol injection, patient movement, cough, or gag upon insertion of the endoscope and need for removal of the endoscope by the gastroenterologist. Data is expressed as mean ± SD or % incidence. P < 0.05 was considered significant.

There were no differences among the groups with respect to age, height,

	I:control (n=36)	II:Lidocaine (n=35)
Propofol total dose (mg)	475 ± 346	614 ± 405
Patient moved (n)	21(%)	7(%)*
Cough (n)	17(%)	7(%)
Gag	15(%)	10(%)
GI remove scope	12(%)	7(%)
Propofol burning sensation	8	0*
Duration (min)	28 ± 17	38 ± 24**

* p<0.001; **p<0.05

CONCLUSIONS: The injection of IV lidocaine prior to propofol for upper endoscopy reduced IV propofol burning sensation and patient movement upon insertion of the endoscope

S-5.

TITLE: SHOULD EPINEPHRINE BE INCLUDED IN THE IRRIGATION FLUID DURING ARTHROSCOPIC SHOULDER SURGERY?

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INTRODUCTION: Arthroscopic shoulder acromioplasty and subacromial decompressions induce bone bleeding which can obscure the arthroscopic field and make surgery difficult. Epinephrine is added to the irrigation solution to vasoconstrict blood vessels and reduce bone bleeding. However, the systemic absorption of epinephrine may exacerbate bleeding by causing an increase in blood pressure. This study examined the effect of adding epinephrine to the irrigation fluid on intraoperative bleeding and blood pressure.

METHODS: 20 patients for elective arthroscopic acromioplasty or subacromial decompressions were randomly assigned to have epinephrine included (E; 1mg/300cc 0.9% NaCl) or excluded (NE) from the arthroscopic solution. The anesthetic for all patients was an interscalene block with 1.5% mepivacaine and sedation with midazolam and propofol. The procedure was performed in the seated position. At four points during the procedure the surgeon who was blinded to the randomization was asked regarding the extent of bleeding (no bleeding, minimal, some bleeding obscuring the field, unable to visualize the field due to bleeding). Blood pressure was also recorded during this period, if the bleeding made arthroscopy difficult and the SBP exceeded 110 mmHg, it was lowered with labetalol to between 90 and 100.

RESULTS: 18 patients completed the analysis, 10 with epinephrine and 8 without, two were deleted because the procedure was changed intraoperatively. Systemic blood pressure decreased when patient was moved from the supine to the sitting position, but once arthroscopy started the addition of epinephrine to the irrigation did not have a significant effect on either heart rate or blood pressure during the surgical procedure (45 minutes). The addition of epinephrine did have an affect on visualization; in the E group in 7 of the 10 procedures there was no bleeding and in 3 procedures there was minimal bleeding;

while in the NE group bleeding was a problem for arthroscopy in 6 of the 8 procedures.

DISCUSSION: For short duration arthroscopic procedures the addition of epinephrine to the irrigation fluid did not have a significant effect on systemic blood pressure or heart rate. However, epinephrine in the irrigation reduced bone bleeding and improved visualization.

S-6.

TITLE: THE ADDITION OF APREPITANT TO A THREE-DRUG REGIME REDUCES THE LATE PONV RATE IN THE HIGH RISK PATIENT TO ONE WITH A LOWER RISK.

AUTHORS: J. S. Berger, S. S. Kee, R. N. Parris, J. R. Ruiz, F. Goravanchi, J. C. Frenzel;

AFFILIATION: M. D. Anderson Cancer Center, Houston, TX.

INTRODUCTION: Aprepitant is a neurokinin-1 receptor antagonist with antiemetic properties. Presently it is available in oral capsule formulation. Our standard antiemetic regime uses 3 agents to prophylactically treat patients with 3 PONV risk factors as defined by Apfel et al¹. Aprepitant was added as a 4th agent to treat patients identified with 4 risk factors.

METHODS: Computerized retrospective chart reviews and pharmacy dispensing data were analyzed to measure therapeutic outcome. Detailed data was collected on all patients who experienced postoperative nausea or vomiting. The nausea/vomiting rate was determined as well as time to first antiemetic rescue treatment. Early PONV was defined as PONV occurring between anesthesia end and 120 minutes following anesthesia end. Late PONV included all PONV after 120 minutes to the time of discharge. Risk factors were defined by criteria established by Apfel et al¹.

RESULTS: See Table

At Risk Population	Low Risk(3 or less factors)		High Risk(4 factors)	
Number of Cases	7732-209=7523		209	
Early PONV (≤120 min)	181-10 =171	2.27%	10*	4.83%* p=0.0313
Late PONV (>120min)	109-3 =106	1.41%	3	1.45% NS
Total PONV (at any time)	290-13 =277	3.68%	13	6.25% NS

*Fisher's exact test.

DISCUSSION: Since the ASC opened, there have been 290 cases that required rescue medication for PONV, indicating prophylaxis failure (out of 7732 cases, overall PONV rate 3.75%). Overall PONV rates showed no statistical difference between patients given the standard regime and those given aprepitant with the standard regime. The non-significance of the late PONV period demonstrates that aprepitant was effective in reducing the higher risk PONV patients to the same as those with lower risk. The early PONV rate was significant in the high risk population. Due to short surgery durations and our practice of giving aprepitant on patient arrival in the preoperative preparation area, this suggest that aprepitant was not administered early enough as peak blood levels occur 3 hours following ingestion². Adding aprepitant as a fourth agent to treat patients with four risk factors may have greater effect if the administration incorporates the delay in achieving peak blood levels. Therefore adding aprepitant effectively reduces the late PONV rate by one risk factor.

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S-7.

TITLE: INCREASED THROUGHPUT OF PEDIATRIC PATIENTS IN AN ADULT AMBULATORY SETTING: A WIN-WIN-WIN

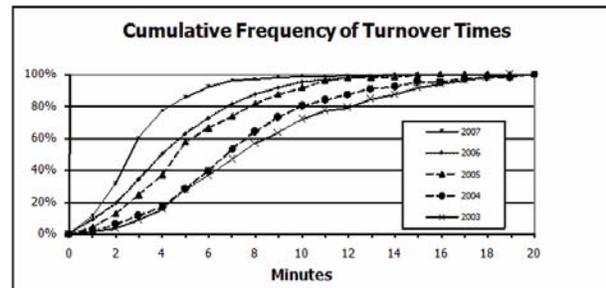
AUTHORS: M. M. Vigoda, J. Tutiven, S. Gayer, A. Müller, M. Murtha, L. I. Rodriguez;

AFFILIATION: University of Miami Miller School of Medicine, Miami, FL.

INTRODUCTION: Children with retinoblastoma (RB) require serial examinations under anesthesia (EUA) to prevent loss of vision and/or death. For these “frequent flyers” and their parents, NPO restrictions are difficult and repeated trips to the hospital and operating room (OR) can be stressful. Our facility is a referral center for children with RB. Following multiple small refinements to our perioperative care process, we studied turnover times for EUA, which were done in conjunction with photography and ultrasound. Laser treatment and/or chemotherapy injection were also performed when warranted.

METHODS: We analyzed our OR management system records spanning a period of 5 years. Data collected included age of patient, CPT codes, patient in-room and out-of-room time. OR cases included all patients <16 years of age who had or were at risk for RB.

RESULTS: Our case load on the designated day for children increased over a 5 year period (approximately 2003-338; 2004-387; 2005-359; 2006-535; 2007-576). Despite an increasing volume of patients, turnover times decreased over this 5 year period (2003- 8.65 ± 4.29 ; 2004- 7.98 ± 3.96 ; 2005- 5.84 ± 3.18 ; 2006- 5.09 ± 3.03 ; 2007- 3.56 ± 2.10).



DISCUSSION: Owing to the need for specialized equipment and/or personnel, children requiring anesthesia on an outpatient basis may be cared for in a setting other than a children’s hospital. While rapid turnover of short outpatient cases is common in children’s hospitals and ambulatory surgicenters, such OR efficiency is also possible in other settings.

Thinking outside the box combined with appropriate personnel can yield noticeable improvements on already highly functional systems. A major improvement involved having a pediatric anesthesiologist supervising 3 residents/CRNAs in 2 operating rooms. While each case was underway the third person was able to finish the documentation and prepare for the next patient. Teamwork between the transporters, recovery room nurses, surgeons, and the anesthesia team was also a key factor.

The improvements were seen as a “Win-Win-Win” not only for the patients and their parents, but also for all involved in their care.

Bleeding / Blood Product Conservation

S-8.

TITLE: CHANGE IN MEDICAL PRACTICE: REDUCING OPERATING ROOM BLOOD PRODUCT WASTAGE AND COST

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Medical practice is known for slow adoption of new clinical strategies. Herzberg's motivation-hygiene theory maintains implementation of change requires conducive work hygiene/structure and appropriate motivation.¹ Although outcome studies can reveal superior strategies, implementation is complicated by preference and uncontrolled variables. This study applies the Herzberg theory to blood wastage at a tertiary-care institution.

METHODS: After IRB approval, prospective data analyzing intraoperative blood product administration and wastage from 2002 to 2006 were reviewed. Motivational tools were identified and implemented in 2004 by analyzing transfusions administered by Anesthesiologists on a monthly basis. Number of wasted blood products, cause and cost were reported. Motivation for change required disseminating monthly operating room blood wastage data and detailing causes of wastage. A work environment was provided to facilitate efforts at decreasing blood wastage. Analysis of percent change in blood wastage was performed using chi-square test; a p-value of <0.05 defined statistical significance versus 2002 benchmark.

RESULTS: 1,140 units of blood were wasted over five years costing \$80,956. Prior to our intervention, blood wastage in 2002 and 2003 was 383 units and 358 units respectively; total cost \$50,191. This decreased nearly 50% in 2004 (blood wastage 199 units) saving \$14,532 versus 2003, despite the cost of blood products increasing over this same time period. Wastage fell another 48% in 2005. This reduction persisted in 2006 (Table 1). Overall, a decreased cost in annual blood wastage is demonstrated throughout the entire survey period despite the increased cost of blood products (\$86/unit March 2002 vs. \$168/unit March 2006).

Table 1: Blood Wastage 2002-2006

Year	2002	2003	2004	2005	2006
Units Wasted	383	358	199	96	104
Cost of Waste	\$21,592	\$28,599	\$14,067	\$7,871	\$8,827
Cost of Waste 2006 dollars	\$27,010	\$32,597	\$14,618	\$9,086	\$8,942
Total Transfused	43,677	46,896	48,896	49,143	37,131
% of total wasted per year	0.88	0.76*	0.41*	0.19*	0.28*
% Change (2002 base year)		13.63	53.41	78.41	68.18

DISCUSSION: Both Canada and England have examined individual hospital practices regarding use and wastage of blood, but no study, to our knowledge, has focused on individual departments or personnel.^{2,3} With medical knowledge constantly expanding, it is important not only to change the practice of providers but more importantly to motivate retention of these changes as practice evolves. Our application of educational theory and techniques helped implement and maintain best practice, accomplishing a sustained department wide decrease in blood wastage.

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S-9

WITHDRAWN

S-10.

TITLE: DECREASING APROTININ UTILIZATION MAY NOT LEAD TO INCREASED BLOOD PRODUCT UTILIZATION

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INTRODUCTION: Since publication of a pivotal study revealing potential problems associated with aprotinin use (1), much controversy has surrounded the drug. This retrospective analysis reviews this study's effects at a single institution by examining changes in aprotinin utilization and transfusion trends one year prior to and one year following its publication.

METHODS: Following IRB approval, the perfusion records of all adult patients at our institution undergoing surgery requiring use of cardiopulmonary bypass (CPB) over a two year period were reviewed. Group A patients underwent surgery the year prior to publication of the study (February 2005 - January 2006) and Group B patients underwent surgery the year after (February 2006 - January 2007). Patient demographics, aprotinin use/non-use ("full" versus "half" dose), blood product use while on CPB, and other variables were compared.

RESULTS: Patient demographic and clinical characteristics did not differ significantly between groups, nor did type of operation, length of surgery, or duration of CPB.

Aprotinin use decreased substantially, from 58% full-dose, 24% half-dose, 18% none in Group A to 17% full-dose, 36% half-dose, and 47% none in Group B ($p < 0.001$). Red blood cell (RBC) transfusion rate (percentage of patients receiving) remained stable (65% vs. 69%), but fresh frozen plasma (FFP) transfusion rates increased from 24% to 36% ($p = 0.004$). Since FFP was almost always given with RBC, rates of patients receiving both increased from 23% to 34%. Among patients receiving products, the mean number of units per patient did not differ significantly between years.

Both types of transfusion were also positively and significantly associated with duration of surgery and CPB. Females and older patients were significantly more likely to receive RBC transfusion; FFP transfusion did not differ by age or sex. RBC transfusion rates were lowest during heart transplant and CABG and highest during aortic arch

surgery. FFP transfusion was least likely during CABG and most likely for aortic arch and 'other' surgery.

DISCUSSION: The use of aprotinin remains controversial (1,2). Many studies have supported its efficacy in reducing blood loss and transfusion requirements in cardiac surgery. However, more supportive evidence of its risks is surfacing. Our retrospective study demonstrates the effect of a publication on its utilization. Aprotinin use significantly decreased, whereas RBC transfusion practices were similar between groups. Although more patients received FFP in the year with less aprotinin utilization, the amount transfused per patient was similar. Although our study has its limitations, this data suggests that perhaps our institution was overutilizing aprotinin in the years prior to the article and that blood product use may be more linked to factors other than the use or non-use of aprotinin.

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S-11.

TITLE: DOES HBOC-201 (HEMOPURE®) AFFECT PLATELET FUNCTION IN ORTHOPEDIC SURGERY: A SINGLE SITE ANALYSIS

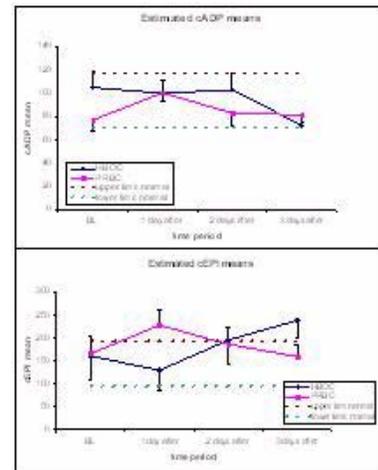
AUTHORS: J. S. Jahr¹, H. Liu², A. Gull², M. Moallempour¹, J. Lim³, R. Gosselin²;

AFFILIATION: ¹David Geffen School of Medicine at UCLA, Los Angeles, CA, ²UC Davis School of Medicine, Sacramento, CA, ³College of Letters and Science, UCLA, Los Angeles, CA.

INTRODUCTION: HBOC-201 (Hemopure®, Biopure Corp., Cambridge, MA) was studied in an international, multicenter, pivotal Phase III trial.¹ A subset analysis of blood products from all 688 subjects, indicated that the HBOC-201 group required no more transfusion than the packed red blood cell (PRBC) group and was limited to <6% in both treatment groups.² In a subset analysis from one site, platelet function using the PFA-100,³ was assessed before and after transfusion, and compared those receiving HBOC-201 versus PRBC.

METHODS: After IRB approval and patient consent for the Phase III trial and additional consent for blood draws, and IRB exemption for retrospective chart review, subjects at one site had additional blood drawn for PFA-100. cEPI and cADP means were compared at baseline, and 1, 2, or 3 or more days after transfusion,³ using ANOVA with $p < 0.05$ considered statistically significant. The units of PRBC or HBOC-201 used for each subject varied and platelet transfusions were not considered.

RESULTS: Twenty-seven (HBOC:n=12, PRBC:n=15) subjects were studied. For cADP means, HBOC-201 group remained the same over time and decreased at Day 3 compared to baseline ($p = 0.06$), Day 1 ($p = 0.08$), and Day 2 ($p = 0.06$), and PRBC group increased on Day 1 compared to baseline ($p = 0.06$) and decreased on Day 3 compared to Day 1 ($p = 0.06$). The marginal cADP mean at Day 3 was lower than Day 1 ($p = 0.0209$). For cEPI mean, HBOC-201 group increased at Day 3 compared to Day 1 ($p = 0.07$), and the PRBC group decreased at Day 3 compared to Day 1 ($p = 0.07$).



DISCUSSION: In PRBC group, cADP and cEPI means increased after transfusion and returned to baseline by Day 3. In HBOC-201 group, cADP mean did not change significantly after transfusion, while cEPI increased and did not return to baseline by Day 3 because HBOC-201 may require more than three days after transfusion to return to baseline. cEPI deviated from normal range more than cADP because of its higher sensitivity to drug-related effects.³ HBOC-201 and PRBC affected platelet function differently because of their differing effects on nitric oxide scavenging. HBOC-201 group also had lower hematocrits,¹ which are known to affect PFA-100.⁴ Based on these results, neither treatment significantly affected platelet function.

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S-12.

TITLE: TOTAL JOINT ARTHROPLASTY: BLOOD MANAGEMENT AND POSTOPERATIVE OUTCOME

AUTHORS: L. Pulido¹, K. Gandhi², J. Wei¹, I. Pawasarat¹, E. Viscusi², J. Parvizi¹;

AFFILIATION: ¹Rothman Institute at Thomas Jefferson University, Philadelphia, PA, ²Anesthesiology Department Thomas Jefferson University, Philadelphia, PA.

INTRODUCTION: Blood loss during total Joint arthroplasty (TJA) may result in a need for blood transfusion. The incidence of anemia following modern TJA, particularly symptomatic cases that necessitate blood transfusion, is not clearly known. Further, the effect of anemia and blood transfusion on the outcome of TJA is not delineated. This study intends to examine the correlation between postoperative anemia, transfusion therapy and patient outcome following TJA.

METHODS: Using our institutional database, a total of 10,995 patients undergoing elective TJA between 2001 and 2006 were identified. Detailed data related to blood parameters (Hb, Htc), surgical procedure, patient comorbidities, postoperative outcome, transfusion records, was available for 9,539 patients which constitute the cohort for this study. Anemia was defined as postoperative Hgb < 10 g/dL.

RESULTS: The mean preoperative Hgb for the patients was 13.3 g/dl. Postoperative anemia was present in 5,663 (59.4%) patients following TJA with a mean Hgb of 9.1 g/dL (range 4.0-9.9 g/dL). A total of 1,925 (20.2%) patients required at least one unit of allogenic blood transfusion. The use of preoperative autologous donation significantly decreased the need for allogenic transfusion. Allogenic transfusion was associated with a higher incidence of wound drainage, deep periprosthetic infection, and increased length of hospitalization.

DISCUSSION: Although significant blood loss during TJA can occur resulting in a high incidence of anemia, majority (two-thirds) of patients with low postoperative hemoglobin appear to do well following TJA without a need for transfusion. The lack of association between anemia and cardiovascular morbidity and mortality emphasizes the need for future studies that will establish a scientific and reasonable strategy for blood transfusion after TJA.

S-13.

TITLE: BLOOD CONSERVATION IN ELECTIVE ARTHROPLASTY: WHAT IS THE ROLE OF PREOPERATIVE AUTOLOGOUS DONATION?

AUTHORS: J. Parvizi¹, S. Chaudhry¹, L. Pulido¹, K. Gandhi², E. Viscusi²;

AFFILIATION: ¹Rothman Institute at Thomas Jefferson University, Philadelphia, PA, ²Anesthesiology Department at Thomas Jefferson University, Philadelphia, PA.

INTRODUCTION: Total joint arthroplasty is associated with blood loss and postoperative transfusion. Preoperative autologous donation (PAD) is a common blood conservation strategy proven to reduce allogenic transfusion in elective procedures. However, autologous donation and transfusion carry inherent risks, and blood is often wasted or unnecessarily transfused. This study intends to examine the role of autologous blood donation in elective joint surgery, define risk factors for allogenic transfusion and assess the relationship between preoperative and postoperative hemoglobin and transfusion practice.

METHODS: A retrospective comparative study was performed using the perioperative and transfusion history of 922 patients undergoing elective hip and knee arthroplasty performed between January and June of 2005. A total of 439 patients underwent primary hip arthroplasty, 373 primary knee arthroplasty, 74 revision hip arthroplasty, and 36 revision knee arthroplasty. All patients undergoing primary TJA were offered the opportunity to preoperatively donate blood. The number of autologous red blood cells, allogenic red blood cells, and platelets transfused were recorded.

RESULTS: During the study period 564 (61%) patients had donated autologous blood, with 402 donating one unit and 67 donating two units prior to surgery. Patients pre-donated blood at an average of 30 days before surgery. In primary TJA, 46 of the 509 donors (9%) did not receive their autologous blood. Allogenic blood was transfused to 24% of all patients. The allogenic transfusion rate among autologous donors was significantly lower than that of non-donors, 15% versus 33% in THA patients, and 20% versus 27% in TKA patients. Older patients with longer hospital stay and lower preoperative hemoglobin

were more likely to receive allogenic transfusion.

DISCUSSION: This study suggests that autologous predonation can effectively reduce the overall rate of allogenic transfusion. Based on our findings PAD should be considered as part of a blood conservation strategy for patients at high risk of postoperative allogenic transfusion which includes bilateral TJA, elderly, and those with low preoperative hemoglobin-if able to donate. Further studies are needed to clarify the exact indications of this blood conservation strategy.

S-14.

TITLE: IS BLOOD LACTATE LEVEL REASONABLE PARAMETER TO START RED BLOOD CELL TRANSFUSION?

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AFFILIATION: Department of anesthesiology, Tokai University School of medicine, Isehara, Japan.

INTRODUCTION: It is important to avoid the unnecessary blood transfusion and to evaluate the adequate timing of start. Therefore, the presence of the something convenient index to detect the timing of the start of red blood cell transfusion (rBT) is favorable. In this investigation, we tried to examine whether the measurement of blood lactate level (Lac) that is a tissue oxygen metabolism index is a reasonable and convenient method to become a standard to start rBT during operation.

METHOD: In elective surgery, ASA physical status I, II patients who were obtained the informed consent were investigated. Patients received standard general anesthesia that used sevoflurane or propofol with fentanyl. After induction of anesthesia, radial artery was cannulated with plastic needle used it for taking a blood sample. Blood sample was taken about 60 to 90 minutes interval in intraoperative period, and just before beginning of rBT. Lac, hemoglobin (Hb) and parameter of arterial blood gas analysis were measured. At the same time, blood pressure was recorded. Decision of rBT was referred to judge of each anesthesiologist.

RESULT: 28 patients (18 male and 10 female) were considered. Average age is 62 (range: 21-80) years old. There were 10 patients in blood transfusion group (BTG) and 18 patients in non-blood transfusion group (NBTG). Evaluating points were at the time of after beginning of operation, bottom value of Hb, and the end of operation. Lac (mM/l:mean±SD) values in NBTG were 1.0±0.4, 1.3±0.5, 1.4±0.5, and in BTG were 1.0±0.6, 1.9±0.8, 1.7±0.6. Hb (g/dl:mean±SD) values measured at the same time in NBTG were 12.1±0.9, 10.5±1.4, 10.8±1.4, and in BTG were 9.8±1.9, 7.8±1.6, 9.7±0.5. Lac value displayed 2.0±0.7 just before beginning of rBT in BTG.

DISCUSSION: As judgment materials of rBT during operation, some parameters have been used. From this investigation, Lac value in BTG

was higher than NBTG at the time of bottom value of Hb, and displayed abnormal high at the time of just before rBT. In other words, increasing of Lac will associate with the timing of the start of rBT. So, it was suggested that it might be possible to be a reasonable means for starting rBT likewise conventional blood transfusion start criteria. About the past investigation of measurement of Lac, the utility as a trigger of the blood transfusion in newborn babies was discussed in intensive care¹⁾. In conclusion, Lac measurement may be possible to be a reasonable and convenient means to start rBT.

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S-15.

TITLE: IMPAIRED PLATELET FUNCTION AND RISTOCETIN DEPENDENT AGGREGATION IN OUT-PATIENTS WITH LEFT VENTRICULAR ASSIST DEVICES (LVAD)

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INTRODUCTION: Anticoagulant management of patients with ventricular assist devices (LVAD) is not well established (1). We hypothesized that use of multiple monitoring devices for anticoagulation and platelet function, may help to better define the adequacy of combined therapy with oral anticoagulants and aspirin.

METHODS: In a cross-sectional design we compared blood from 12 out-patients with LVAD and 12 healthy age and sex matched controls by standard coagulation tests, thromboelastometry (ROTEM), the platelet function analyzer (PFA-100) (2) and a new whole blood aggregometer (Multiplate).

RESULTS: Oral anticoagulation produced an average INR of 3.5, and was associated with 50% lower levels of prothrombin fragment F1+2 (p<0.001) and a 2-fold prolongation in ROTEM clotting time (p<0.001). Despite that, D-dimer levels were 3-fold higher in patients than in controls (p<0.001). Platelet function under high shear was invariably and severely compromised: collagen adenosine diphosphate closure times (CADP-CT) were 2.5 fold longer in patients than in controls (p<0.001), and 50% of patients had maximal CADP-CT values of 300s. While von Willebrand Factor antigen levels were 80% higher in patients (p<0.001), vWF:RiCO was subnormal (<60%) in 5/12 patients. Thus, low vWF activity can only explain 50% of patients with long CADP-CT. Ristocetin induced aggregation was 3-fold higher in controls than patients (p<0.001), which indicates that this was not only a shear dependent phenomenon, but likely due a functional defect of platelets affecting the glycoprotein Ib/vWF axis.

DISCUSSION: There is an interesting dissociation between in vivo markers of high D-dimer but decreased prothrombin fragment in LVAD patients. LVAD patients have a marked impairment of platelet function under high shear rates and of ristocetin induced aggregation, which is only partly attributable to low vWF activity.

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S-16.

WITHDRAWN

Cardiothoracic & Vascular - Basic Science

S-17.

TITLE: CYTOSKELETAL REMODELING OF DESMIN IS A MORE ACCURATE MEASURE OF CARDIAC DYSFUNCTION THAN FIBROSIS OR MYOCYTE HYPERTROPHY IN OVINE HEART FAILURE

AUTHORS: G. Monreal¹, B. Han², M. S. Joshi², A. B. Phillips³, J. A. Bauer², M. A. Gerhardt¹;

AFFILIATION: ¹The Ohio State University, Columbus, OH, ²Columbus Children's Research Institute, Columbus, OH, ³The Heart Center, Columbus Children's Hospital, Columbus, OH.

INTRODUCTION: Fibrosis and myocyte hypertrophy are classical remodeling parameters in heart failure (HF); however, an intriguing possibility is that myocytes themselves undergo intracellular remodeling (intracellular 'fibrosis') which increases stiffness and contributes to diastolic dysfunction. The most obvious candidates are the cytoskeletal proteins. The cytoskeletal protein desmin reinforces the sarcomeres to enable force generation (1). We previously demonstrated desmin accumulation in HF (2). As a contributor to sarcomere performance, desmin content may therefore represent a better appraisal for cardiac dysfunction than fibrosis or myocyte hypertrophy. We established a sheep model of microinfarction-induced HF which recapitulates human HF and is appropriate for chronic and surgical interventions (3). We test the hypothesis that these key features of myocardial remodeling are temporally and spatially discrete during HF progression in this model.

METHODS: HF was induced via microembolization of the circumflex coronary artery (1). LV function and cardiac tissues were collected at 4 and 12 months post-embolization. LV EF and end-diastolic area (EDA) were measured via echocardiography at baseline and prior to sacrifice. Myocardium was collected from infarcted and noninfarcted LV regions. Spatial distribution of desmin content, fibrosis, and myocyte hypertrophy were measured in tissue microarray using histochemistry, immunohistochemistry, blotting, and automated digital image analysis techniques. Regional measurements and correlation analyses were used to assess the relationships among variables. *p<0.05 was considered significant.

RESULTS: EF decreased from 56% to 24%* in HF. Diastolic dysfunction (tau) was evident in HF. EDA increased 35%* and 135%* at months-4 and -12, respectively. Fibrosis increased only in infarcted LV (265%* and 717%* at months-4 and -12, respectively). Myocyte hypertrophy increased in both infarcted and noninfarcted LV but only at month-12 (65%*). Desmin content increased 121%* and 182%* at - and -12, respectively, in both infarcted and noninfarcted LV. Within infarcted myocardium of late HF sheep, the greatest desmin expression occurred in the endocardium (30% increase compared to epicardium). Endocardial desmin content in infarcted myocardium increased with HF progression (145%* and 259%* at months-4 and -12, respectively). Desmin inversely correlated to EF (r=-0.31*), and more strongly correlated to EDA in HF (r=0.41*) than fibrosis (r=0.32*) and myocyte hypertrophy (r=0.36*).

DISCUSSION: Our sheep microinfarction model of HF recapitulates clinical pathology and demonstrates that myocyte desmin content, myocardial fibrosis, and myocyte hypertrophy are temporally and spatially heterogeneous, providing evidence for the presence of multiple remodeling mechanisms. Desmin content more accurately correlated with worsening HF than fibrosis or myocyte hypertrophy, suggesting that intra-myocyte responses, which are likely related to mechanical stretch, are better predictors of LV function and disease progression. Differential remodeling pathways may represent novel targets for therapeutic interventions in chronic progressive HF.

REFERENCES: 1) Braz J Med Biol Res 2004;37:1819-30. 2) J Card Fail 2005;11:S97. 3) J Card Fail 2004;10:174-183.

S-18.

TITLE: SPATIAL HETEROGENEITY OF THE MAPK SIGNALING CASCADES IN AN OVINE MODEL OF HEART FAILURE

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INTRODUCTION: The mitogen-activated protein kinase (MAPK) signaling cascades are comprised of 3 main families: extracellular signal-related kinases (ERK), c-Jun N-terminal kinases (JNK), and p38 (1). Differential phosphorylation of MAPK pathways in infarcted versus noninfarcted myocardium may represent important mechanisms in heart failure (HF) pathogenesis (including both pro- and anti-apoptotic pathways) and reflect focal myocardial stressors and/or adrenergic stimulation; however, their spatial distribution/activation in HF is unclear (1). Using an ovine model of HF (2), we measure region-specific phosphorylation of ERK1/2, JNK1/2/3, and p38 to determine differential MAPK kinase activity between ventricles and in infarcted versus noninfarcted myocardium.

METHODS: HF was induced in sheep via microembolization of the circumflex coronary artery (2). Myocardium was harvested from 3 control and 3 HF sheep (12-24 months post-microembolization) from infarcted LV, noninfarcted LV, and RV. Protein microarray with densitometry was used to quantify p38, JNK, and ERK phosphorylation. *p<0.05 significant.

RESULTS: Our ovine model of HF recapitulated human cardiac remodeling events, with time and region-specific changes in LV function (LVEF 51 to 25%), chamber dilation, fibrosis, and myocyte hypertrophy. Within infarcted LV myocardium, there was no change in the phosphorylation of any MAPK except for JNK-3 which was decreased. In noninfarcted LV, there were no changes in ERK or JNK isoforms; however, p38 α , p38 β , and p38 δ phosphorylation were increased. In the RV, ERK-2 phosphorylation was reduced whereas JNK-1, JNK-2, and all p38 isoform phosphorylation increased.

% Change in Phosphorylation in HF					
	ERK-1	ERK-2	JNK-1	JNK-2	JNK-3
Infarcted LV	-11.5	-27.4	-6.8	-6.9	-49.3*
Noninfarcted LV	-0.005	-7.9	-7.9	-16.2	-24.4
RV	-41.3*	-13.6	80.6*	24.0*	-12.4

	p38 α	p38 β	p38 γ	p38 δ
Infarcted LV	-5.5	-16.1	4.5	24.1
Noninfarcted LV	13.0	25.7*	78.6*	101.0*
RV	37.3*	54.3*	60.8*	85.5*

DISCUSSION: ERK, JNK, and p38 kinases are heterogeneously phosphorylated in HF myocardium: ERK phosphorylation is globally reduced, JNK phosphorylation is differentially regulated between ventricles (decreased globally within the LV but increased in the RV), and p38 phosphorylation is decreased in infarcted LV only. It has been postulated that increased circulating catecholamines in HF stimulate β_2 adrenergic receptor (β_2 AR) activation resulting in a toggling from G α s to G α i-coupling; therefore, β_2 AR-G α i mediated MAPK activation may inhibit apoptosis and delay the transition from hypertrophy to failure (1). Importantly, region-specific phosphorylation patterns may reflect the influence and importance of local stressors during HF and represent novel therapeutic targets.

REFERENCES: 1) Circulation 2001;103:670-677. 2) J Card Fail 2004;10:174-183.

S-19.

TITLE: HELIUM-INDUCED EARLY PRECONDITIONING IS ABOLISHED IN OBESE ZUCKER RATS IN VIVO

AUTHORS: R. Huhn, A. Heinen, N. Weber, M. Hollmann, W. Schlack, B. Preckel;

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BACKGROUND AND GOAL: Ischemic cardiac preconditioning is abolished in Zucker obese rats with insulin resistance.[1] A recent study showed that the noble gas Helium induces pharmacological preconditioning in vivo by prevention of mitochondrial permeability transition pore (mPTP) opening.[2] The mPTP can be regulated by mitochondrial bioenergetics. In this study we aimed to investigate if Helium preconditions also the prediabetic heart and whether mitochondrial respiration is influenced.

MATERIALS AND METHODS: Animals were treated in compliance with institutional and national guidelines.

Chloralose-anesthetized Zucker rats were thoracotomized and, after pericardiotomy, a snare occluder was passed around a major left coronary artery. After surgical preparation, animals recovered for 20 minutes before starting the preconditioning protocol. Subsequently rats were exposed to 25 minutes ischemia followed by 120 minutes reperfusion. At the end of reperfusion, hearts were excised for infarct size measurement by TTC staining. Additional experiments were performed for Western blot analysis and mitochondrial respiration.

Animals were randomly assigned to one of four groups. Zucker lean (ZL) and Zucker obese (ZO) control animals were not further treated (ZL-Con and ZO-Con, each n=8). The preconditioning groups (ZL-He-PC and ZO-He-PC, each n=8) received 70% Helium for 3x5 minutes interspersed with 2x5 minutes and one final 10 minute washout period. For Western blotting and mitochondrial function measurements, hearts were excised 5 minutes after the third Helium application and cardiac mitochondria were isolated by differential centrifugation. Mitochondrial respiration was analyzed as parameter of mitochondrial function and the respiratory control index (RCI, parameter of the coupling between mitochondrial respiration and oxidative

phosphorylation) was calculated as state 3/state 4. Western blotting was performed for detection of phospho GSK3 β .

Statistical analysis: Student t-test followed by Bonferroni's correction for multiple comparisons. Data are expressed as Mean \pm SD.

RESULTS: There were no significant differences in heart rate (bpm) and mean aortic pressure (mmHg) between the experimental groups during baseline, ischemia and reperfusion. In ZL-CON, infarct size was 52 \pm 8% of the area at risk. Preconditioning by Helium reduced infarct size to 32 \pm 7% (P<0.05 vs. ZL-Con). In the ZO rats, Helium did not induce early preconditioning (ZO-He-PC; 56 \pm 8% vs. ZO-Con: 54 \pm 9%, P>0.05). Analysis of mitochondrial respiration showed that in ZL rats, Helium preconditioning reduced the RCI from 2.5 \pm 0.1 (ZL Con) to 2.3 \pm 0.1 (ZL He-PC) while in ZO rats, it had no effect on RCI (ZO He-PC: 2.5 \pm 0.1 vs. ZO Con: 2.5 \pm 0.1).

CONCLUSION: These data show for the first time that Helium-induced preconditioning is abolished in obese Zucker rats in vivo. The absence of cardioprotection may be at least partially explained by a diminished effect of Helium on mitochondrial function in order to prevent mPTP opening.

LITERATURE: [1] Am J Physiol Regul Integr Comp Physiol 2007; R920-R926 [2] Anesthesiology 2006; 105: A782

S-20.

TITLE: THE EFFECTS OF ENDOTHELIN-1 ON [Ca²⁺]_i IN RABBIT CARDIAC MYOCYTES DURING METABOLIC INHIBITION

AUTHORS: F. Li¹, Z. Su², W. H. Barry³;

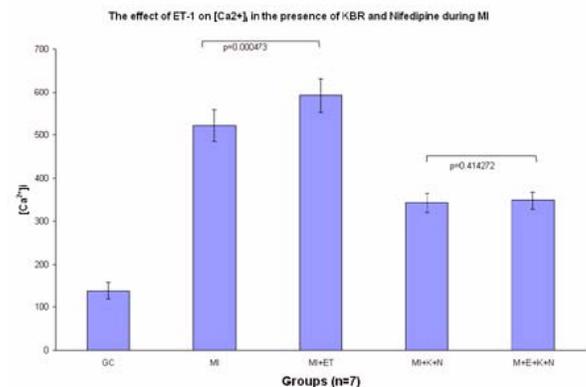
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INTRODUCTION: Endothelin-1 (ET-1) increases calcium transient in cardiac myocytes (1,2,3). ET-1 has also been shown to worsen cardiac ischemia injury (4,5,6)). Metabolic inhibition (MI) causes an increase in intracellular calcium concentration ([Ca²⁺]_i) which leads to calcium overload and cell injury (7, 8). The effect of ET-1 on [Ca²⁺]_i in cardiac myocytes during MI remains unknown. This study is to determine whether ET-1 further exacerbates [Ca²⁺]_i rise in rabbit cardiac myocytes during MI and possible mechanisms through which ET-1 induces [Ca²⁺]_i rise in myocytes during MI.

METHODS: Isolated rabbit left ventricle myocytes were loaded with 4 μ M fluo-3 for 30 min at 37.0°C. After washing, the myocytes were exposed to one of the following conditions: (1) Normal HEPES solution; (2) MI solution (2 mM NaCN, 20 mM 2-DG and 0-glucose); (3) MI+ET (50 nM); (4) MI+ET (50 nM) +Nifedipine (20 μ M) or MI+ET (50 nM)+KBR-9743 (10 μ M) or MI+ET+Nifedipine+KBR-9743 for 60 minutes. Flow cytometry was used to measure the [Ca²⁺]_i in myocytes (7,8). Reversal Na⁺-Ca²⁺ exchange current (I_{Na/Ca}) and L-type cardiac calcium current (I_{Ca,L}) in isolated rabbit left ventricle myocytes were recorded using whole cell patch-clamp technique. The effect of KBR on I_{Na/Ca} and effect of ET-1 on I_{Ca,L} were examined.

RESULTS: MI for 60-min caused a significant increase in [Ca²⁺]_i when compared to control; ET-1 further increased [Ca²⁺]_i significantly. ET-1 slightly but not significantly increased [Ca²⁺]_i in myocytes in the presence of NIF or KBR respectively. However, the increase in [Ca²⁺]_i was totally blocked by both NIF and KBR together (Figure 1). During patch-clamp studies, ET-1 (50 nM) increases I_{Ca,L} in rabbit ventricular myocytes by 15~33%; KBR-9743 (10 μ M) inhibited I_{Na/Ca} by 70% in

rabbit left ventricle myocytes.



DISCUSSION: This results suggest that ET-1 further increases [Ca²⁺]_i in rabbit cardiac myocytes during MI. The increase in [Ca²⁺]_i was mediated by both L-type cardiac calcium channel and reverse-mode Na⁺-Ca²⁺ exchanger.

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S-21.

TITLE: HELIUM INDUCES LATE PRECONDITIONING IN THE RAT HEART IN VIVO - IMPACT OF CONCENTRATION AND REPEATED ADMINISTRATION

AUTHORS: R. Huhn, A. Heinen, N. Weber, M. Hollmann, W. Schlack, B. Preckel;

AFFILIATION: Academic Medical Center (AMC), Amsterdam, The Netherlands.

BACKGROUND AND GOAL: Both, volatile anesthetics [1] and the noble gas Xenon induce cardioprotection by late preconditioning.[2] A recent study showed that the noble gas Helium induces early preconditioning of the heart in vivo.[3] We aimed to investigate if Helium induces late preconditioning and if so whether cardioprotection is concentration dependent. In a second part we investigated whether repeated administration on various days will result in an increased cardioprotection.

MATERIALS AND METHODS: Animals were treated in compliance with institutional and national guidelines.

Chloralose-anesthetized Wistar rats were thoracotomized and, after pericardiotomy, a snare occluder was passed around a major left coronary artery. After surgical preparation, animals recovered for 20 minutes and were subsequently exposed to 25 minutes ischemia followed by 120 minutes reperfusion. At the end of reperfusion, hearts were excised for infarct size measurement by TTC staining.

The study consisted of two parts. In part one, animals were randomly assigned to one of four groups. Control (Con, n=8) animals were not further treated. In the preconditioning groups animals received 70% Helium (He-LPC 70, n=12), 50% Helium (He-LPC 50, n=7) or 30% Helium (He-LPC 30, n=7) for 15 minutes 24 hours before I/R.

Based on findings from part one of the study, part two was performed with 30% Helium. Animals were randomly assigned to one of three groups. Helium administration was repeated on three days (He-LPC 3x30, n=5), two days (He-LPC 2x30, n=6) and on one day (He-LPC 1x30, n=6) before I/R.

Statistical analysis: Student t-test followed by Bonferroni's correction for multiple comparisons. Data are expressed as Mean±SD.

RESULTS: In both parts of the study, there were no significant differences in heart rate and mean aortic pressure between the experimental groups during baseline, ischemia and reperfusion. In the control group, infarct size was 55±8% of the area at risk. All three different Helium concentrations reduced infarct size (He-LPC 70: 37±13%, He-LPC 50: 34±16%, He-LPC 30: 40±9%; each P<0.05 vs. Con). Repeated administration of Helium more than one time did not further enhance cardioprotection (He-LPC 3x30: 39±9%, He-LPC 2x30: 38±10%; P>0.05 vs. He-LPC 1x30: 37±11%).

CONCLUSION: These data show for the first time that: 1) Helium induces late preconditioning in vivo 2) One-time 30% Helium induces maximal cardioprotection and 3) repeated administration of Helium can not further enhance cardioprotection.

LITERATURE: [1] Anesthesiology 2004;100: 547-54 [2] Eur J Anaesthesiol. 2006; 23; Suppl. 37: A2 [3] Anesthesiology 2006; 105: A782

S-22.

TITLE: EFFECTS OF PROPOFOL ON POTASSIUM CURRENTS IN ARTERY SMOOTH MUSCLES OF RATS

AUTHORS: Y. Jiang, L. Xu, H. Zhang;

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INTRODUCTION: The aim of the study was to investigate the effects of propofol on potassium currents in artery smooth muscle cells of rats.

METHODS: The effects of propofol on potassium currents in smooth muscle cells derived from rat arteries were observed by patch clamp technique (whole cell recording) after application of the drug in the bath.

RESULTS: The potassium current-voltage curves (I-V curves) of smooth muscle cells derived from normotensive rat pulmonary arteries were up-ward shifted by propofol (50 and 100 molL⁻¹). Within 5 minutes after application of the drug, the current amplitude could increase to (120.7 10.8)% (n = 7), (112.9 5.0)% (n = 8), (P<0.01) of initial current amplitude respectively. The potassium I-v curves of smooth muscle cells derived from pulmonary hypertensive rat pulmonary arteries were up-ward shifted after application of propofol (50 and 100 molL⁻¹) in extracellular solution. Within 5 minutes after application of the drug, the current amplitude changed to (125.5 5.2)% (n = 8), (122.2 7.6)% (n = 6) (P<0.01 vs control) of initial current amplitude.

DISCUSSION: The out-ward potassium currents in smooth muscle cells derived from normotensive, pulmonary hypertensive rats could be increased by propofol. This may be one of the mechanisms that propofol can decrease pulmonary vascular tension and dilate pulmonary vessel.

S-23.

TITLE: BRIEF SYSTEMIC HYPOTENSION RESULTS IN BEHAVIORAL DEFICITS AND PROGRESSIVE NEURONAL LOSS IN RATS

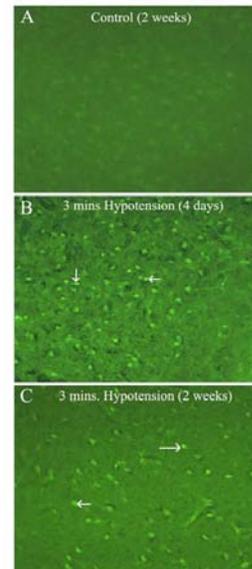
AUTHORS: E. R. Chaparro, R. A. Karlinski, A. Hansoti, L. Zhang, E. M. Camporesi, D. Mangar;

AFFILIATION: University of South Florida, Tampa, FL.

INTRODUCTION: Maintenance of adequate blood flow to the brain is necessary in the course of general anesthesia in order to assure safe recovery and normal brain function after surgical intervention. Brief episodes of hypotension have been shown to cause acute brain damage in several animal models^{1,2}. We used a rat hemorrhagic shock model to assess functional outcome and to measure the relative neuronal damage at 4 and 14 days post-injury.

METHODS: Sprague-Dawley rats were subjected to severe hypotension induced by withdrawal of arterial blood from the right femoral artery. The mean arterial blood pressure was maintained between 20-30 mm Hg with isoelectric EEG for one minute per hour, for a total of 2 or 3 times per rat. Shed blood was immediately return to venous circulation, returning systemic pressure to normal. The rats were separated into six groups as follows; groups 1 and 2 received 2 minutes of hypotension and were studied at 4 days and 14 days, respectively. Groups 3 and 4 received 3 minutes of hypotension and were studied at 4 days and 14 days, respectively. An additional group of rats, groups 5 and 6, received a sham operation. A neurological assessment was performed at 4 days or 14 days post-hypotensive insult. Brains were harvested and stained for fluorojade at 4 or 14 days. Image analysis of fluorojade-stained brain sections were used to qualitatively observe neuronal damage after the hypotensive insult.

RESULTS: Neurological assessment showed greater motor and behavioral deficits at 4 days versus 14 days. However, no significant differences in motor impairment were seen between 2 minutes of hypotension versus 3 minutes of hypotension at either survival point. Both hypotensive groups were associated with a pathological representation of numerous fluorojade-positive cortical neurons (Figure 1).



DISCUSSION: This observation suggests that in this hemorrhagic model, even brief hypotension results in cortical neuron damage which is reflected by motor impairment at the 4 day time point. Although functional outcome is recovering at the 2 week time point, ongoing neuronal damage can still be observed in the cortex.

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S-24.

TITLE: DEXMETETOMIDINE PROTECTS AGAINST RADIOCONTRAST NEPHROPATHY IN MICE

AUTHORS: F. T. Billings;

AFFILIATION: Columbia University College of Physicians and Surgeons, New York, NY.

INTRODUCTION: Radiocontrast nephropathy (RCN) is a clinical problem. Dexmedetomidine (DEX) is an anxiolytic with vasodilative and diuretic effects. We hypothesized that dexmedetomidine may protect against radiocontrast nephropathy.

METHODS: We performed in vivo studies using a murine model of RCN and in vitro studies using cultured human kidney cells. We induced RCN in DEX (4ug/kg/h) and control mice by injecting iohexol (1.5mg/kg SQ) after inhibiting cyclo-oxygenase (indomethacin, 10 mg/kg SQ) and nitric oxide synthase (levo-nitroargininemethylester, 10 mg/kg). Twenty-four hours later, plasma creatinine was determined, and kidneys were collected for histology. Proximal tubular necrosis, tubule vacuolization, and cellular apoptosis were quantified. For mechanism investigation we assessed changes in renal blood flow and direct cellular toxicity. We measured outer medullary renal blood flow using laser Doppler probes. Direct renal tubular toxicity was assessed using immortalized human proximal tubule cells pretreated with 10uM DEX or saline and then exposed to iohexol. Cellular viability was assessed using an MTT assay.

RESULTS: Dexmedetomidine protected mice from radiocontrast nephropathy as evidenced by reduced renal dysfunction.(DEX plasma creatinine: 0.8 +0.3 mg/dL, n=10 vs. Saline: 1.5 +0.3, n=7, p=0.011, mean +SEM). DEX treated mice also showed reduced proximal tubular necrosis, tubule vacuolization and cellular apoptosis (DEX: 0.50 +0.4 necrotic tubules/400x field, n=6 vs. Saline: 5.7 +1.6, n=6, p<0.01; DEX: 22.8 +8.2 vacuolized tubules/400x field, n=6 vs. Saline: 59.6 +7.0, n=6, p<0.007; DEX: 0.8+ 0.3 apoptotic cells/400x field, n=6 vs Saline: 8.8 +2.3, n=6, p<0.006)(Fig.1). DEX treated mice had significantly higher renal medullary blood flow after RCN injury (p<0.049, Fig.2A). DEX treatment failed to improve viability after iohexol exposure in cultured cells, n=12.(Fig.2B)

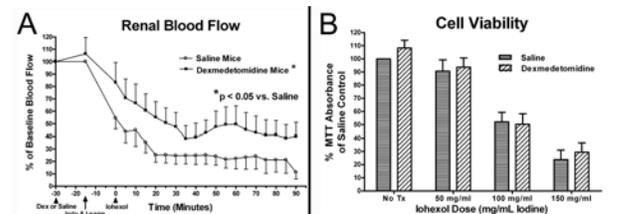


Figure 2: (A) Increased renal blood flow following radiocontrast injection in dexmedetomidine treated animals vs. saline. (B) Equivalent cell viability following radiocontrast exposure in DEX and saline treated human kidney cells.

CONCLUSION: Dexmedetomidine protects mice against radiocontrast nephropathy. Preserved renal blood flow may mediate this protection. Decreased direct tubular cytotoxicity does not appear to mediate RCN. Our findings may have significant clinical relevance to improving outcomes following radiocontrast exposure.

S-25.

TITLE: ACUTE METHADONE TREATMENT REDUCES INFARCT SIZE IN RATS DURING REPERFUSION AND IS RAT STRAIN SPECIFIC

AUTHORS: E. R. Gross¹, A. K. Hsu², G. J. Gross²;

AFFILIATION: ¹Medical College of Wisconsin and St Joseph's Medical Center, Milwaukee, WI, ²Medical College of Wisconsin, Milwaukee, WI.

INTRODUCTION: Previous studies in our laboratory suggest acute opioid administration prior to reperfusion is cardioprotective¹. However, it is unknown whether the opioid agonist methadone, an agent commonly prescribed to patient populations with chronic pain syndromes, sickle cell disease or heroin withdraw, can reduce infarct size. Additionally, reported in situ differences in infarct size for Sprague-Dawley (SD) and Brown-Norway (BN) male rat strains have not been studied in vivo or during acute opioid administration². Therefore, we determined whether methadone reduces infarct size in vivo and furthermore examined how methadone dose and timing, in addition to rat genetic strain alters methadone-induced infarct size reduction.

METHODS: Male SD rats (n=8/group) were acutely anesthetized and instrumented to measure hemodynamics (blood pressure, heart rate, rate pressure product). A silk suture was placed around the left anterior descending coronary artery (LAD). After surgical preparation and stabilization, rats were divided into a vehicle group (water) and groups receiving doses of methadone (0.01mg/kg-3mg/kg), that were administered intravenously 10 minutes prior to ischemia. After methadone or vehicle treatment, rats were subjected to 30 minutes ischemia, followed by 2 hrs of reperfusion, with infarct size determination by triphenyltetrazolium staining (expressed as a percentage of infarct size/area at risk). In separate groups, methadone (0.3mg/kg) was also administered 5 minutes prior to and 10 seconds after reperfusion in SD rats. Additionally, methadone (0.3mg/kg) was administered to BN rats.

RESULTS: No differences in hemodynamics existed between groups. Methadone administered 10 minutes prior to ischemia reduced infarct

size at 0.1mg/kg and 1mg/kg with maximal efficacy observed at 0.3mg/kg compared to vehicle (51±2*, 56±1*, 46±1* versus 61±1%, respectively, *P<0.01). Additionally, methadone (0.3mg/kg) reduced infarct size when administered 5 minutes prior to reperfusion, but not 10 seconds after reperfusion (46±1*, 60±1%, respectively). Methadone afforded no protection in BN rats compared to the BN control group (60±3, 66±2%, respectively).

DISCUSSION: These novel findings are the first to demonstrate methadone salvages the myocardium when administered prior to ischemia or reperfusion. Furthermore, there are genetic differences between the SD and BN rat strains that abrogate methadone-reduced infarct size reduction in the BN strain. These findings could have novel implications for using methadone for pain control in patients with high risk of myocardial infarction, in addition to the need for further studies to determine the mechanism involved in methadone-induced infarct size reduction.

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S-26.

TITLE: REMIFENTANIL PRECONDITIONING ATTENUATES MYOGLOBIN RELEASE EVOKED BY MYOCARDIAL ISCHEMIA AND REPERFUSION

AUTHORS: F. Komaki¹, H. Kitagawa², T. Yamazaki³, T. Akiyama³;

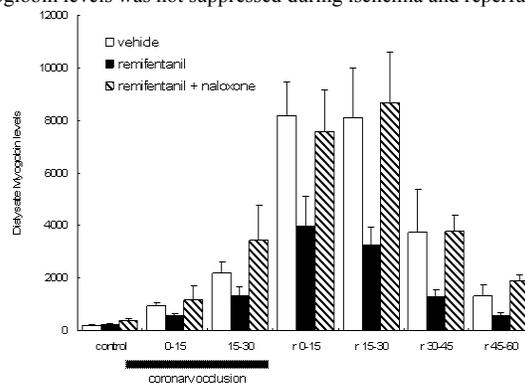
AFFILIATION: ¹Kohka Public Hospital, Koka, Japan, ²Shiga University of Medical Science, Otsu, Japan, ³National Cardiovascular Center Research Institute, Suita, Japan.

INTRODUCTION: In a fashion similar to ischemic preconditioning, opioids seem to trigger an acute cardioprotective memory effect. Remifentanil is a highly potent opioid, and its action is rapid and short due to rapid hydrolysis by esterase in blood and tissue. In the present study, we tested the hypothesis that cardioprotective memory effect of remifentanil lasts beyond the degradation. We applied microdialysis technique to the heart of rabbit and examined the effect of intravenous bolus injection of remifentanil on myocardial ischemia/reperfusion injuries.

METHODS: Rabbits were anesthetized with pentobarbital sodium and ventilated. After left thoracotomy, a dialysis probe was implanted into the region perfused by the left circumflex coronary artery (LCX) of the left ventricle and perfused with Ringer's solution at 5 µl/min. The main branch of LCX was occluded for 30 min. We monitored dialysate myoglobin levels as an index of myocardial membrane injury at 15 min-interval before, during and after coronary occlusion. Rabbits were randomly assigned into three groups: (1) vehicle group (n=6); without injection of remifentanil, (2) remifentanil group (n=6); with intravenous bolus injection of remifentanil (100 µg/kg) 30 min before coronary occlusion, (3) remifentanil + naloxone group (n=5); with local administration of naloxone hydrochloride (1 mM) through the dialysis probe in addition to intravenous bolus injection of remifentanil.

RESULTS: The results of dialysate myoglobin levels are summarized in figure. In vehicle group, dialysate myoglobin levels increased from 204 ± 34 ng/ml in control to 2172 ± 414 ng/ml at 15-30 min of coronary occlusion and then further increased to 8170 ± 1303 ng/ml at 0-15 min of reperfusion. In remifentanil group, the increase in dialysate myoglobin levels was suppressed during ischemia and reperfusion, and

the suppression during reperfusion 0-30 min was statistically significant. In remifentanil + naloxone group, the increase in dialysate myoglobin levels was not suppressed during ischemia and reperfusion.



DISCUSSION: Remifentanil preconditioning protected against myocardial ischemia/reperfusion injuries. Local administration of naloxone through the dialysis probe abolished the protection by remifentanil. These data suggested that cardiac opioid receptors play a role in myocardial protection against ischemia/reperfusion injuries. Intravenous bolus injection of remifentanil may preserve the cardioprotective memory effect after the degradation.

S-27.

TITLE: INHIBITION OF GLYCOGEN SYNTHASE KINASE LOWERS THE THRESHOLD FOR HELIUM-INDUCED CARDIOPROTECTION IN RABBITS

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INTRODUCTION: Brief, repetitive administration of helium (He), a noble gas without anesthetic properties, before prolonged coronary artery occlusion and reperfusion protects myocardium against infarction by activating prosurvival signal transduction and inhibiting the mitochondrial permeability transition pore (mPTP) (1). The beta isoform of glycogen synthase kinase-3 (GSK-3beta) is an important mediator of cellular function whose activation has been implicated in diabetes and Alzheimer's disease, whereas inhibition of GSK-3beta plays a critical role in protection against ischemia-reperfusion injury. Prosurvival signaling pathways converge on and regulate the activity of GSK-3beta, thereby favorably modulating mPTP and producing cardioprotection (2). We tested the hypothesis that inhibition of GSK-3beta lowers the threshold of He-induced cardioprotection 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 (FiO₂ = 0.30). All rabbits were subjected to a 30 min left anterior descending coronary artery occlusion followed by 3 h reperfusion. Rabbits (n=3 to 5 per group) were randomly assigned to receive 0.9% saline (control), one, three, or five cycles of 70% He-30% oxygen administered for 5 min interspersed with 5 min of the air-oxygen mixture before coronary artery occlusion, or the selective GSK-3beta inhibitor SB 216763 (SB21; 0.2 or 0.6 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 He with or without SB21 pretreatment. Body weight, LV mass, area at risk weight, and the ratio of area at risk to LV mass were similar between groups. Three and five cycles but not one cycle of He pretreatment significantly (P<0.05) reduced myocardial infarct size [25±4, 20±3, and 35±6%, respectively, of LV area at risk (mean±SD)] as compared to control (44±6%). SB21 alone (0.6 but not 0.2 mg/kg) also reduced myocardial necrosis (22±3 and 43±1%, respectively). Pretreatment with the combination of 0.2 mg/kg SB21 and one cycle of He decreased infarct size (25±4%) to an equivalent degree as three cycles of He pretreatment alone.

CONCLUSIONS: The results demonstrate that He-induced cardioprotection against myocardial infarction is dose-dependent and further indicate that inhibition of GSK-3beta lowers the threshold of He-induced preconditioning in vivo.

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S-28.

TITLE: TIMING AND DURATION OF EXPOSURE TO SEVOFLURANE EFFECTIVE IN PROTECTING CARDIAC ISCHEMIA-REPERFUSION INJURY IN RABBITS

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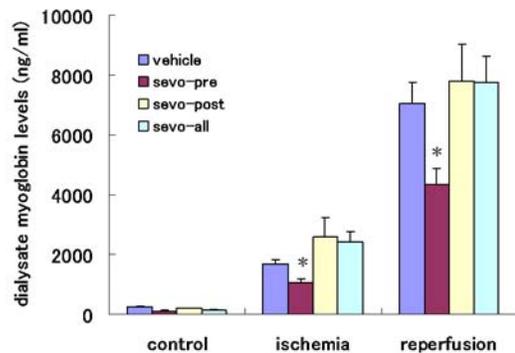
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INTRODUCTION: It has been reported that the exposure to volatile anesthetics protect against cardiac ischemia-reperfusion injury. But the timing and duration of exposure effective in protecting ischemia-reperfusion injury has not been fully elucidated. Recently we have developed cardiac microdialysis technique monitoring myocardial interstitial myoglobin levels as an index of myocardial cell injury. We tested three different timing and duration in the exposure to sevoflurane and evaluated the effects on myocardial interstitial myoglobin levels in the ischemic region during ischemia and reperfusion.

METHODS: Rabbits were anesthetized with pentobarbital sodium and ventilated. After left thoracotomy, a dialysis probe was implanted into the region perfused by the left circumflex coronary artery (LCX) of the left ventricle. The main branch of LCX was occluded for 30 min. We measured dialysate myoglobin levels as an index of myocardial interstitial myoglobin levels before, during and after coronary occlusion. Rabbits were randomly assigned into four groups: (1) vehicle group (n=6); without exposure to sevoflurane, (2) sevo-pre group (n=6); with twice exposure to sevoflurane (1 MAC) for 30 min followed by a 15-min washout period before coronary occlusion, (3) sevo-post group (n=6); with exposure to sevoflurane (1 MAC) during 60 min-reperfusion period, (4) sevo-all (n=6); with exposure to sevoflurane (1 MAC) from 30 min before coronary occlusion to the end of experiment.

RESULTS: The results of dialysate myoglobin levels are summarized in figure. In vehicle group, dialysate myoglobin levels were increased from 231 ± 63 in control to 1667 ± 170 ng/ml by coronary occlusion and then further increased to 7060 ± 710 ng/ml after reperfusion. In sevo-pre group, the increase in dialysate myoglobin levels was suppressed during both ischemia and reperfusion. In sevo-post and

sevo-all groups, the increase in dialysate myoglobin levels was not suppressed during ischemia and reperfusion.



DISCUSSION: The exposure to sevoflurane before ischemia was effective in protecting both ischemic and reperfusion injuries of myocardial cells in the ischemic region, but the exposure to sevoflurane during reperfusion and the exposure to sevoflurane during ischemia and reperfusion were not effective in protecting myocardial cell injury in the ischemic region. Monitoring myoglobin release by cardiac microdialysis technique is useful for evaluating the effects of volatile anesthetics against cardiac ischemia-reperfusion injury in the ischemic region.

S-29.

TITLE: PHAGOCYTTIC UROKINASE-RECEPTOR DRIVES LEUKOCYTE RECRUITMENT DEFECT IN U-PAR DEFICIENT MICE

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INTRODUCTION: Leukocytes are the immune systems most powerful tool to fight infections but also contribute to tissue damage. Molecular mechanisms of leukocyte trafficking have been investigated in great detail with the goal to gain therapeutic control over inflammation. The urokinase-receptor (u-PAR) functions as a β_2 -integrin partner molecule. Its lack results in a neutrophil and macrophage invasion defect in u-PAR^{-/-} mice^{1,2}, while it is unknown if leukocytic and endothelial u-PAR are equally important. We utilized 3-D-fluorescence mediated tomography (FMT, Visen) to non invasively image recruitment of cross-over adoptively transferred u-PAR^{-/-} and WT macrophages (M ϕ) to the inflamed peritoneum of mice to further detail the role of leukocytic versus endothelial u-PAR.

METHODS: u-PAR^{-/-} and WT mice underwent thioglycollate-peritonitis (TP). At day 3 after injection of 500 μ L thioglycollate M ϕ s recruited into the peritoneal cavity were quantified by lavage. For in vivo homing assays M ϕ s were harvested from peritoneal fluids, stained with NIRF dye DiR and used for IV injections as exogenous indicator cells. To understand the role of leukocytic versus endothelial u-PAR peritoneal M ϕ s were harvested from mice of each background, labeled with DiR and injected IV cross over into WT- or u-PAR^{-/-} recipients. M ϕ traffic into the peritoneum was assessed by FMT scans after injection of 10⁷ DiR labeled indicator M ϕ into the tail vein at baseline and on day 3 after induction of TP. FMT fluorescent signature was quantified as percentage of mean fluorescence measured in the

abdominal ROI on day 0. Mann-Whitney-U test was applied. ANOVA was used where required. Data are presented as mean \pm SEM.

RESULTS: In response to the inflammatory stimulus u-PAR^{-/-} mice recruit less M ϕ s into the peritoneum compared to WT (1.43 \pm 0.69 vs. 2.56 \pm 0.79 x10⁷ M ϕ , u-PAR^{-/-} vs. WT, n=8/9, p<0.02). FMT measured fluorescence increased by +235 \pm 40% in WT mice injected with WT indicator M ϕ s (d0 vs. d3, n=8, p<0.05). Injection of WT cells in u-PAR^{-/-} mice resulted in significantly less pronounced signal enhancement (92 \pm 18 vs. 235 \pm 40%, WT-M ϕ in u-PAR^{-/-}-mice vs. WT-M ϕ in WT-mice, n=6/8, p<0.05). Whereas the most pronounced effect was observed in WT mice receiving u-PAR^{-/-} M ϕ s (45 \pm 5 vs. 235 \pm 40%, u-PAR^{-/-}- M ϕ in WT-mice vs. WT-M ϕ in WT-mice, n=6/8, p<0.05).

DISCUSSION: We here report for the first time that the previously noted leukocyte adhesion defect in u-PAR deficient mice is due to both, endothelial and leukocytic expression of the protein. Leukocytic expression of u-PAR is however far more significant for macrophage recruitment to the inflamed peritoneum. This observation demonstrates that FMT is a very powerful tool to perform non-invasive in vivo-studies on the molecular mechanisms of leukocyte trafficking in mice.

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Cardiothoracic & Vascular - Clinical

S-30.

TITLE: CHANGE IN CARDIAC CONTRACTILITY WITH DYNAMIC SURGICAL POSITIONING USING TEE

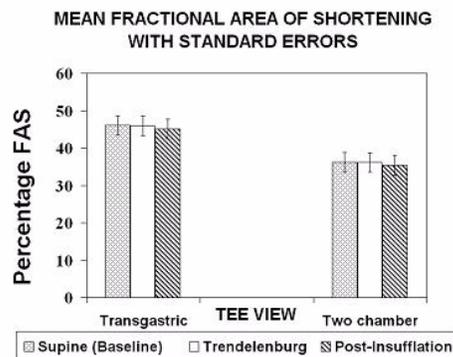
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BACKGROUND: Controversy exists regarding the extent cardiac contractility is affected by surgical positioning and pneumoperitoneum required for laparoscopic surgery. Previous studies^{1,2} have provided conflicting information regarding positioning, especially greater than twenty degrees of Trendelenburg. In this study, we sought to elucidate the effect of deep (>30 degrees) Trendelenburg and 15-20mmHg of abdominal insufflation on cardiac function by examining patients undergoing laparoscopic robotic prostatectomy. Using transesophageal echocardiography (TEE), we measured end diastolic area (EDA) and end systolic area (ESA) of the left ventricle and its fractional area of shortening (FAS), or [(EDA-ESA)/EDA x100] to verify left ventricular contractility. We hypothesized that FAS would significantly change after positioning and pneumoperitoneum, and thus affect contractility.

METHODS: After IRB approval and patient written informed consent, twenty two male ASA I-II patients with a mean BMI of 27.1 ± 3.52 and mean age of 61.1 ± 7.75 years underwent robotic prostatectomy. After standard anesthetic induction and pseudo-steady state anesthesia were achieved, TEE 2-D images were taken in mid-esophageal two chamber and transgastric short axis views during (1)supine, (2)thirty two degree Trendelenburg and (3)post-insufflation periods. During each view, three sets of EDA/ESA were recorded. The two most similar sets were averaged to calculate FAS as mean ± standard error.

RESULTS: In transgastric view, FAS was 46.01 ± 2.66% for supine, 45.89 ± 2.69% during Trendelenburg, and 45.04 ± 2.73% after insufflation. There was no statistically significant change in FAS both in transgastric and two chamber views. There was also less than ten percent concurrent increase in EDA (p<0.05 using mixed model analysis) and ESA between (1)supine (baseline), (2)Trendelenburg and (3)post-insufflation conditions as well.



DISCUSSION: Despite major postural changes and surgical pneumoperitoneum, left ventricular contractility was actually maintained and changed little in healthy patients, possibly compensated by increases in preload, release of vasoactive substances, and compression of splanchnic vasculature^{3,4}. Consequently, surgeries involving these parameters may be considered tolerable, even for patients with coexisting cardiopulmonary disease. However, based on these results, future studies may be warranted to directly determine whether contractility remains intact in patients with limited cardiac reserve.

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S-31.

TITLE: NEUROPROTECTION DURING INSERTION OF IMPLANTABLE CARDIOVERTER/DEFIBRILLATORS (ICD)

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INTRODUCTION: During insertion of ICDs threshold testing requires induction of repeated episodes of ventricular fibrillation. These short cardiac arrests (CA) are associated with neuronal damage (1) and neurocognitive dysfunction (2). Anesthesia can be provided either in the form of monitored anesthesia care or as general anesthesia. Sevoflurane reportedly has neuroprotective effects: through preconditioning it protects against ischemic neuronal damage; it also reduces cerebral O₂ consumption (3). We investigated, whether general anesthesia with sevoflurane mitigates the release of neuron-specific enolase (NSE), a marker of neuronal injury, compared to implantation performed under monitored anesthesia care.

METHODS: After approval by the IRB and obtaining written informed consent, we studied 18 patients in two centers (AKH Vienna and LKH Feldkirch) undergoing elective transvenous ICD insertion. Nine patients received general anesthesia (1 mg midazolam, 2 µg kg⁻¹ fentanyl and 0.1 mg kg⁻¹ etomidate IV for induction, laryngeal mask airway, 1 Vol% sevoflurane, FiO₂: 0.4) and in nine patients ICD insertion was performed under monitored anesthesia care (1 mg midazolam IV, 6 l min⁻¹ O₂ via face mask, 0.1 mg kg⁻¹ etomidate IV before induction of CA). Perioperative monitoring consisted of 5-lead ECG, invasive arterial blood pressure, pulse oximetry, etCO₂ and repeated blood gas analyses. We paid attention to maintain normal CO₂-values and avoided hemolysis during blood sampling. NSE was determined before, at the end of, and 2, 6 and 24 hrs after surgery. The Stat View 5.0 statistical package (SAS Institute, Cary, NC) was employed for data analysis. For in-between comparisons the Mann-Whitney-Test was used. Data are presented as mean ± SD and median (25/75 percentile). A P value of <0.05 was considered significant.

RESULTS: NSE levels before, at the end of, and 24 hrs after surgery were not different between groups. Significantly higher NSE values were

determined in the monitored anesthesia care group 2 and 6 hrs after surgery (11.8 ± 2.7 vs. 8.7 ± 3.2 and 14.5 ± 4.5 vs. 10.1 ± 3.9 µg L⁻¹ respectively; P < 0.05). This group, however, also showed a significantly longer cumulative duration of CA (28 (17/42) vs. 10 (9/12) s; P < 0.05).

DISCUSSION: These results may be explained by a neuroprotective effect of sevoflurane. Yet, further studies are necessary to demonstrate, that NSE release is also attenuated in patients undergoing general anesthesia with sevoflurane at comparable cumulative durations of CA.

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S-32.

TITLE: SUCCESS OF RADIAL ARTERIAL CANNULATION AFTER CARDIAC CATHETERIZATION VIA THE SAME VESSEL

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INTRODUCTION: Transradial cardiac catheterization (TRCC) is becoming more frequent in cardiology. Fewer significant complications, a good success rate, and earlier discharge of day patients are some of the advantages of using the radial vs the femoral approach. At the same time, full arterial revascularization is shown to improve long-term outcomes in CABG surgery and is also being increasingly utilized. Because the radial artery is a frequent conduit, the anesthesia team is left in patients after TRCC with the difficulty of placing a radial line in the same vessel that may have been catheterized, and perhaps recently.

Cardiology literature suggests the patency rate for radial arteries that have been cannulated at 85% within two weeks of catheterization. We postulated that our success rates for first-attempt cannulation with a 20 g catheter would be significantly lower than this.

METHODS: As part of our ongoing CQI, we prospectively record for all patients the number of attempts (a new catheter or skin penetration), number of sites (eg radial vs brachial vs femoral) and final position of our arterial lines for cardiac surgery. In accordance with our hospital's Human Research Ethics Board, we retrospectively reviewed two months of data, for patients with (group R) and without (group F) radial artery catheterization for their coronary study. Results were compared using a Student's T-test.

RESULTS: 130 patients underwent cardiac surgery during our time period. Two patients did not have catheterization at our hospital and have been removed from the study. Of the 128 remaining, 11 were in group R. Six of the 117 patients (5.1%) with femoral catheterization (group F) required more than one attempt at a radial line; 5 of the 11 group R patients (45%) required more than one attempt at a radial line with two requiring a brachial line, and one requiring a femoral line

insertion just after cardiopulmonary bypass (p<0.01).

CONCLUSION: Despite literature to suggest good patency rates following radial cannulation for cardiac catheterization, our data show that the initial failure rate for radial arterial line insertion is much higher. Not only patency, but a smooth and well-recannalized intima are likely required for a successful insertion and the continuation of accurate data from the line. A larger number of patients will help us resolve the time frame for the success rates to approach those of a never-used artery. Also, other non-invasive methods may help to distinguish the vessels that should not even be attempted.

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S-33.

TITLE: SHOULD PATIENTS UNDERGOING TOTAL JOINT ARTHROPLASTY HAVE TIGHT HEART RATE CONTROL?

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INTRODUCTION: Postoperative cardiovascular complications represent a significant source of morbidity and mortality for patients undergoing noncardiac procedures. Several prospective studies have shown that adequate beta-blockade reduces the incidence of postoperative cardiac complications in noncardiac surgery. More recent studies have suggested that the benefits are more significant in high-risk patients. Perhaps more important than the use of beta-blockers is the achievement of tight heart rate control in intermediate and high risk patients (1). The purpose of our study was to analyze adequate rate control and use of beta blockers preoperatively in patients who experienced cardiac complications after Total Joint Arthroplasty.

METHODS: Following IRB approval of this retrospective study, the sample (n=3929) consisted of all patients who underwent primary hip and knee surgeries during the years 2004 and 2005. Patient information was gathered from database and charts containing information on postoperative cardiac complications (angina/MI, tachycardia/arrhythmias, pulmonary edema/CHF, hypotension, and bradycardia). Patients were categorized according to Revised Cardiac Risk Index (RCRI) stratifications (low, intermediate, high risk) based on past medical history. Bivariate analysis was conducted on risk stratifications, tight preoperative heart rate control, and the use of beta blockers before surgery.

RESULTS: There were 181 patients who experienced cardiac complications after hip and knee surgeries. The mean age of these patients were 67.5 years. Majority of patients with cardiac complications were in low risk and intermediate risk groups (Table 1). Only 33.6% (n=44) of patients over the age of 60 had tight preoperative heart rate control of less than 65. In this age group (age over 60), only 36.6% (n=48 p<0.05) were on long term beta blockers and 35.90%

(n=47, p<0.05) took beta blockers on the day of surgery. When looking at all postoperative cardiac complications, less than 30% of these patients had adequate preoperative rate control before their joint surgery.

Table 1: Preoperative Risk Stratification vs. Postoperative Complications

	Low Risk	Intermediate Risk	High Risk
Age>60 (n=131)	84 (64.1%)*	44 (33.6%)*	3 (2.3%)
Angina/MI (n=49)	23 (46.9%)*	25 (51.0%)*	1 (2.0%)
Tachycardia/Arrhythmias(n=65)	47 (72.3%)	17 (26.2%)	1 (1.5%)
Pulmonary Edema/CHF (n=14)	8 (57.10%)	5 (35.7%)	1 (7.10%)
Hypotension (n=47)	40 (85.1%)*	7 (14.9%)*	0 (0%)
Bradycardia (n=13)	11 (84.6%)	2 (15.40%)	0 (0%)

n (%)

*P<0.05

DISCUSSION: These findings suggest the need for more aggressive beta-blockade in low and intermediate risk patients over the age 60 during elective hip and knee surgeries. These patients may benefit from tight heart rate control of less than 65 before Total Joint Arthroplasty.

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S-34.

TITLE: PROLONGATION OF QT INTERVAL INDUCED BY SEVOFLURANE IS NOT ATTENUATED BY LANDIOLOL

AUTHORS: Y. Fujiwara, M. Matsura, Y. Shibata, Y. Asakura, H. Ito, T. Komatsu;

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BACKGROUND Sevoflurane has been reported to prolong QT interval of the ECG (1). Torsades de pointes associated with sevoflurane inhalation was reported in a patient with long QT interval syndrome (LQTS) (2). On the other hand, the mainstay of treatment of congenital LQTS has been beta-blocker (3). The aim of this study was to investigate if an ultra short-acting beta1 adrenoceptor antagonist, landiolol, attenuates QT prolongation caused by sevoflurane.

METHOD After institutional approval and written informed consent was obtained, ten patients who are going to have elective orthopedic surgery under general anesthesia were enrolled in this study. Without any premedication, the patients walked into the operating theater. After 10 minutes rest on an operating table, the anesthesia was induced with propofol (TCI 3mcg/ml), remifentanyl (0.2mcg/kg/min) and vecuronium (0.1mg/kg). After tracheal intubation, the infusion of propofol was terminated and the inhalation of sevoflurane (2%) was initiated. Thirty minutes after end-tidal sevoflurane reached to 1.7%, continuous infusion of landiolol (30mcg/g/min) was started and continued for 30minutes. During the course of anesthesia, ECG signal (II lead) was continuously obtained from anesthesia monitor and stored on a personal computer at 1000Hz sampling rate. QT interval was determined by automated ECG analyzing software (Fluclet, Dainippon Pharmaceutical, Japan). The corrected QT interval (QTc) was obtained using Fridericia formula. QTc was compared between baseline, during sevoflurane and during landiolol administration.

RESULTS

The effect of landiolol on QTc during sevoflurane anesthesia			
	QT (msec)	QTc (msec)	Heart Rate (bpm)
baseline	395±31	408±22	64±7
sevoflurane	419±37*	426±23*	63±7
landiolol	424±31*	425±28*	59±5*

Data are shown as mean±SD. *:p<0.05 vs baseline.

CONCLUSION Sevoflurane significantly prolonged QTc interval. Landiolol did not attenuate the prolongation of QTc interval caused by sevoflurane.

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S-35.

TITLE: C-REACTIVE PROTEIN LEVEL IS A PREDICTOR OF SEVERE ATHEROMATOUS DISEASE IN PROXIMAL AORTA OF PATIENTS UNDERGOING OPCAB.

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INTRODUCTION: Neurologic complications constitute a major cause of morbidity and mortality after coronary artery bypass grafting (CABG). Although off-pump coronary artery bypass (OPCAB) has been reported to reduce the risk, neurologic complication remains a major concern during perioperative management. Several studies have identified severe atheromatous disease of proximal aorta (ascending aorta and aortic arch) as an independent risk factor for cerebrovascular accidents. Current evidence supports a central role for inflammation in all phases of the atherogenic process. C-reactive protein (CRP), a marker of inflammation has been established as an independent predictor of future cerebrovascular and cardiovascular events [1]. Therefore, we investigated preoperative CRP level can predict the presence of atheromatous lesions in proximal aorta of the patients undergoing OPCAB.

METHODS: Fifty consecutive patients undergoing OPCAB were examined prospectively after IRB approval and informed consent. The patients with inflammatory diseases, significant valvular diseases, and renal failure with hemodialysis were excluded. Preoperative high-sensitivity CRP (hs-CRP) level (mg/L) was measured the day before surgery. Proximal aorta was examined by transesophageal echocardiography intraoperatively, and the degree of atherosclerotic disease was graded according to the system developed by Katz and co-investigators [2]. Receiver operating characteristic (ROC) curves were used to test the predictive accuracy of CRP level for the atheromatous lesions, with an area under the curve (AUC) of 0.5 indicating no predictive power.

RESULTS: Overall mean±SD and median CRP values were 3.8±5.4 and 1.2 mg/L, respectively (interquartile range 0.46 and 5.6 mg/L). Significant atheromatous disease (grade 4, protruding atheroma >4 mm, and grade 5, mobile atheroma) of proximal aorta was found in 11

patients (22%). There was significant difference of CRP values of patients of severe atheromatous disease and non-significant atheromatous disease (median, 6.0 mg/L [IQR, 2.7 to 10.1 mg/L] versus median, 0.85mg/L [IQR, 0.39 to 2.5 mg/L]; P=0.004). ROC analysis revealed AUC was 0.787 (P=0.004). Optimal cut-off point of CRP value was 2.0 mg/L and corresponding sensitivity and specificity were 0.82 and 0.71 respectively. Incidence of neurologic complication was 0% both in the patients with and without severe atheromatous disease.

DISCUSSION: CRP is a good predictor of severe atheromatous disease in proximal aorta of patients undergoing OPCAB with high sensitivity. Because the specificity of CRP is relatively low, careful screening for inflammatory diseases such as connective tissue diseases and recent infection is necessary. Further investigation with larger number of patients is required to evaluate the predictive power of CRP of morbidity and mortality.

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S-36.

TITLE: “SUB-OPTIMAL” USE OF PREOPERATIVE B-BLOCKERS IS BETTER THAN NO B-BLOCKER USE

AUTHORS: L. I. Rodriguez, M. M. Vigoda, E. Wu, M. Murtha, D. A. Lubarsky;

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INTRODUCTION: Perioperative use of β -blockers can benefit some patients with coronary artery disease (CAD) [1]. Guidelines [2] recommend preoperative β -blockers to maintain a resting heart rate (HR) ≤ 60 beats per minute (bpm). We hypothesized that preoperative use of β -blockers would impact on intraoperative HR control even if the resting HR exceeded recommended guidelines.

METHODS: We reviewed electronic medical records of patients with documented CAD who had elective non-cardiac surgery between 1/04 and 6/06, analyzing preoperative and intraoperative β -blocker use on over 1,400 patients. We correlated patients resting preoperative HR when seen in the Pre-anesthesia Treatment (PAT) Clinic with the patients intraoperative HR. CAD was defined as s/p myocardial infarction, CABG, angioplasty/stenting or angina. A resting HR > 60 bpm was considered to be above the recommended guidelines [2] and adequate intraoperative (between surgery start and surgery end) HR control was defined as a HR < 75 bpm.

RESULTS: Of the 21,039 patients who had elective surgical procedures, 1,346 (6.4%) had documented CAD. Some patients (52 patients) were excluded from this retrospective review because their resting HR was either not documented or erroneously recorded (i.e. HR 150 bpm). Almost 60% (58.3% or 754) of patients with CAD were on chronic preoperative β -blockers.

Patients who were taking preoperative β -blockers even if “not β -blocked” (resting HR > 60) were more likely to maintain an intraoperative HR < 75 bpm than those patients not on preoperative β -blockers (24.6% vs. 13.1%; $p \leq 0.001$).

Patients with CAD seen at the PAT Clinic			
	Total	Intraoperative HR < 75	%
Patients on preoperative β -blocker	754	219	
HR > 60 in PAT Clinic	495	112	24.6
Patients not on preoperative β -blocker	540	98	
HR > 60 in PAT Clinic	442	58	13.1

DISCUSSION: For patients with a resting HR > 60 , those who were taking β -blockers preoperatively were more likely to have good intraoperative HR control than those who were not taking β -blockers. We recommend a larger study to determine if there are any clinical advantages to “sub-optimal” use of preoperative β -blockers.

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S-37.

TITLE: PREOPERATIVE ASSESSMENT OF THE CARDIAC PATIENT FOR DAY OF ADMISSION SURGERY

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INTRODUCTION: Day Admission Surgery (DAS) has become standard for elective procedures, including cardiac and major vascular operations (CMVO)^{1,2}. We report findings of a survey we conducted and reviewed concerning preoperative assessment of DAS patients for CMVO. We also report preliminary experiences of the first year of a pre-anesthetic clinic (PC) specifically designed for adult CMVO DAS patients.

METHODS: In October 2006, we conducted a survey about preoperative assessment of DAS patients for CMVO. Seventy-six directors of cardiothoracic and vascular anesthesia fellowship programs in the USA and Canada were requested to participate.

In April 2006, our institution opened a separate PC for DAS patients scheduled for CMVO. Patients visit the PC prior to DAS and are seen by staff consisting of a cardiac anesthesiologist, a nurse practitioner and nurses trained in cardiac intensive care. After a standard pre-anesthetic interview and examination, any additional examinations (dental, carotid duplex, hematological, urological, endocrinological, and possibly neuropsychological)³ are arranged and completed, usually on the same day. Patients and families also have the opportunity to visit the cardiac intensive care unit. The day prior to DAS, all aspects and requirements for surgery are again evaluated (blood bank, antibacterial prophylaxis, beta blockers⁴, blood conservation strategy, optimal monitoring plans) in preparation for a smooth admission and minimal precision time⁵. The patient returns to this PC on DAS, which maintains familiarity with personnel and location. After surgery, PC staff visit the patient in intensive care unit.

RESULTS: Of the 76 surveys, we received 55 responses (72.3%). In 15 programs, the patients were evaluated only on the DAS. In 40 programs, the patients were evaluated by: anesthesia fellow in 16 programs (P); anesthesia attending in 12 P; CRNA in 4 P, nurse practitioner in 4 P; and MD-not anesthesiologist in 4 P. A separate bill for consultation was

submitted from 11 P and service-consult was reimbursed in 9 P. During our first year experience, (April 2006 to May 2007) over 700 patients were seen in the PC. Advancements in communication with the anesthesia team, the surgeon, and perfusionist were made, which improved “harmony” in the operating room.

DISCUSSION: A well-organized PC can allay communication problems and enhance patient satisfaction. Financial burdens will be decreased by advanced retrieval of medical records from other facilities saving unnecessary laboratory tests, diagnostic studies or preoperative consultations. Decreases in DAS delays and cancellations, pre-incision time and duration of hospitalization may also be observed. And, of course, the immeasurable creation of a more “harmonious” operating room will contribute to optimal patient care.

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S-38.

TITLE: PREOPERATIVE STATIN THERAPY IS NOT ASSOCIATED WITH A REDUCED INCIDENCE OF POSTOPERATIVE RENAL DYSFUNCTION AFTER CARDIAC SURGERY

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INTRODUCTION: Postoperative renal dysfunction after cardiopulmonary bypass (CPB) occurs in 7 -13% of patients, with 1 - 1.5% of patients requiring dialysis therapy (1). Renal dysfunction after CPB is caused by renal ischemia reperfusion injury combined with the inflammatory response to CPB (2).

The inflammatory response may exacerbate renal hypoperfusion both indirectly as a result of hemodynamic instability, and directly via renal arteriolar vasoconstriction (3). Besides their lipid lowering effects, statins are proposed to have pleiotropic effects on the vasculature that might be protective against CPB induced renal dysfunction (4). Statins' anti-oxidant, antiinflammatory, antithrombotic effects and their tendency to reduce endothelin secretion may mediate these effects (5). The aim of our study was to evaluate the association between preoperative statin therapy and the incidence of postoperative renal dysfunction in patients undergoing CABG +/- valve surgery with CPB.

METHODS: A retrospective study of 10899 patients undergoing CABG +/- valve surgery between January 2002 and December 2006, utilizing our tertiary care center's cardiothoracic anesthesia patient registry. Patients were divided into 2 groups depending on whether or not they were taking preoperative statins. In the univariate analysis the two groups were compared on the binary variables using Chi-square or Fisher's exact test as appropriate and continuous variables using T-test or Wilcoxon rank sum test. In the multivariable analysis, logistics regression model with backward selection procedure was used to test the association between preoperative statin therapy and postoperative renal dysfunction (as defined by a postoperative serum creatinine \geq 1.5 times preoperative creatinine) after adjusting for the significant covariates.

RESULTS: Statin therapy was not associated with a reduced incidence of postoperative renal dysfunction (Table 1).

Table 1 :Backward Logistic Regression For Postoperative Renal Dysfunction

Factor	Odds Ratio Estimate	Odds Ratio(95%CI)	P Value
Statins	1.028	(0.889, 1.189)	0.7107
Chronic Obstructive Pulmonary Disease/Asthma	1.213	(1.003, 1.468)	0.0462
Congestive Heart Failure	1.532	(1.311, 1.791)	<.0001
Stroke	1.295	(1.046, 1.602)	0.0175
Diabetes	1.278	(1.084, 1.507)	0.0036
Ca channel blockers	1.574	(1.346, 1.84)	<.0001
Diuretics	1.375	(1.174, 1.611)	<.0001
Red Blood Cell	4.387	(3.66, 5.259)	<.0001
Fresh Frozen Plasma	1.093	(1.042, 1.146)	0.0003
Body Mass Index	1.033	(1.022, 1.044)	<.0001
Albumin	0.554	(0.491, 0.625)	<.0001
Cardiopulmonary Bypass Time	1.006	(1.004, 1.008)	<.0001
Emergency Surgery	2.275	(1.46, 3.545)	0.0003

DISCUSSION: A possible reduction in the serum concentration of statins on CPB may explain the lack of its renoprotective effect (6). Also, the magnitude of the inflammatory response to CPB may be too great for preoperative statin therapy to have any impact on (7). Lastly, CPB induced renal dysfunction may be influenced by hemodynamic mechanisms other than those prevented by statins (8).

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S-39.

TITLE: HYPERLACTACIDEMIA AND ABNORMALITY OF HEPATIC MITOCHONDRIAL REDOX STATE DURING CARDIOPULMONARY BYPASS IN ADULT HEART-VALVE REPLACEMENT: PROSPECTIVE CONTRASTIVE STUDY BETWEEN LACTATED RINGER'S SOLUTION AND BICARBONATED RINGER'S SOLUTION

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INTRODUCTION: Low hepatic perfusion, which inhibits the metabolism of lactate, plays an important role in hyperlactacidemia (HL) during cardiopulmonary bypass (CPB), although the exact mechanism is unknown.

We examined the extent to which exogenous lactate causes acid-base imbalance in during CPB by comparing perioperative differences in acid-base imbalance and arterial blood ketone body ratio (AKBR), an index of hepatic mitochondrial redox status for patients receiving lactate or bicarbonate CPB pump prime solution.

METHODS: Patients (n=28) who had undergone elective valvular surgery with CPB between January and December 2006 were included in this prospective study conducted with approval of our hospital's ethics committee. Patients were randomly and evenly allocated to two groups based on CPB pump prime solution received during surgery: the LR group received lactated Ringer's solution (Lactec®, Otsuka Pharmaceutical Factory, Inc., Tokushima, Japan) and the BR group received bicarbonated Ringer's solution (Bicarbon Injection®, Ajinomoto Pharmaceutical Co. Ltd., Tokyo, Japan). Patients with anesthesia time of \geq 420 min, CPB time of \geq 150 min, massive bleeding during surgery, and postoperative hemorrhage were excluded, and the final LR and BR groups had 11 and 9 patients, respectively. Arterial blood was collected at various time points from after the induction of anesthesia to 24 hr after ICU admission and analyzed.

RESULTS: In both groups, AKBR dropped to the critical level (0.4) or lower immediately after CPB initiation in all patients in both groups. It remained below the critical level 6 hr after the end of surgery in 7 of 11 patients in the LR group and 6 of 9 patients in the BR group but significantly increased 24 hr after ICU admission, remaining significantly elevated in the BR group at 24 hr after ICU admission.

Blood lactate levels in LR patients were significantly higher during and immediately after surgery than in BR patients, and for both groups, lactate levels increased after the start of CPB and continued to increase up to 24 hr after ICU admission, with the exception of a decrease at 24 hr in the LR group.

DISCUSSION: During CPB, the AKBR remained below the critical level in both LR and BR patients showing the following: these patients have low hepatic perfusion, inhibited lactate metabolism due to decreased LDH activity results in hyperlactacidemia, and LR further aggravates hyperlactacidemia. Significant hepatic metabolic disturbance may occur during CPB, even in patients with no serious hepatic dysfunction before surgery.

Exogenous lactate, which may induce continuous acidosis after surgery in patients with serious hepatic dysfunction, along with increased endogenous lactate caused by reduced hepatic energy formation are associated with HL during CPB. Our results suggest that using BR, instead of LR, might help lessen HL caused by exogenous lactate and reduced hepatic energy metabolism.

S-40.

TITLE: COMPRESSING THE NON-DEPENDENT LUNG DURING ONE-LUNG VENTILATION IMPROVES ARTERIAL OXYGENATION, BUT IMPAIRS SYSTEMIC OXYGEN DELIVERY BY DECREASING CARDIAC INDEX

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INTRODUCTION: Surgeons compress the non-dependent lung to improve the surgical field during one-lung ventilation (OLV) for esophagectomy. Compression of the non-dependent lung improves arterial oxygenation (I), but effects on hemodynamic indices have not been elucidated. If arterial oxygenation is improved without deterioration of hemodynamic indices, non-dependent lung compression may be an effective measure for treating hypoxemia during OLV.

METHODS: All study protocols were approved by the university ethics committee and written informed consent was obtained from all patients. Sixteen consecutive patients (ASA physical status I-II) who underwent esophagectomy with right thoracotomy were anesthetized using sevoflurane combined with epidural anesthesia. After general anesthesia was induced with intravenous propofol 2mg/kg, a left-sided double-lumen tube (Broncho-Cath) was placed for OLV with the aid of 0.2 mg/kg intravenous vecuronium. The dependent lung was mechanically ventilated with a tidal volume of 8 ml/kg and a fraction of inspiratory oxygen of 0.8 during OLV. After a 20-gauge intravascular catheter was inserted into the radial artery, cardiac index (CI) was monitored continuously using FloTrac™ sensor and Viogileo™ monitor (Edwards Lifesciences). The non-dependent lung was compressed using a retractor several times during surgery and data were obtained when the non-dependent lung was compressed for the first time in each case. Oxygen delivery index was roughly estimated as the product of CI and arterial oxygen saturation as monitored by pulse oxymetry (Sp_o), as changes in hemoglobin concentration and dissolved oxygen content during the course seemed very small.

RESULTS: Just before non-dependent lung compression (baseline), mean (+/- SD) CI and Sp_o were 2.6+/-0.6 L/min/m² and 95.0+/-3.9%, respectively. At 1 min after non-dependent lung compression, Sp_o increased significantly to 97.8+/-2.2% (P<0.05), but CI decreased significantly to 2.0+/-0.4 L/min/m² (P<0.05). The product of CI and Sp_o at 1 min was significantly lower (192.7+/-37.3) than baseline (250.5+/-66.3; P<0.05). Arterial blood pressure decreased after lung compression, and 5 mg of intravenous ephedrine was required to rescue 10 patients who developed low mean blood pressure (<60mmHg) within the observational period of 5 min.

DISCUSSION: Non-dependent lung compression during OLV improves arterial oxygenation but may impair both systemic oxygen delivery and CI. When the non-dependent lung was compressed, the heart may also have been compressed simultaneously. Although we previously considered non-dependent lung compression as a potentially effective measure to treat hypoxemia during OLV, the present results suggest that measures to increase CI (e.g., inotropic drugs) may be required to maintain systemic oxygen delivery and improve arterial oxygenation.

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S-41.

TITLE: FUNCTIONAL RIGHT-TO-LEFT INTRACARDIAC SHUNT CAUSED BY DELIBERATE SURGICAL CLOSURE OF THE CORONARY SINUS ORIFICE - A CASE REPORT AND DISCUSSION

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INTRODUCTION: Unroofed coronary sinus (URCS) is an uncommon congenital heart defect in which a communication exists between the coronary sinus and the left atrium due to partial or complete absence of the coronary sinus roof resulting in left-to-right shunt. We describe the transesophageal echocardiography (TEE) findings as well as the repair of this defect in a 64 year old patient.

CASE REPORT: One year prior to presentation this female had undergone tricuspid valve repair (TVR) for severe tricuspid regurgitation (TR). Despite excellent surgical results and initial functional improvement, her symptoms of heart failure returned. Repeat echocardiography exam revealed an URCS with predominant left-to-right shunting, right-sided cardiac enlargement, and mild TR. Contrast injection in the left arm vein showed no evidence of left superior vena cava (LSVC). In the operating room the diagnosis of URCS was confirmed by TEE. Reoperation was advised and it was elected to treat the lesion by closure of the coronary sinus entry into the right atrium. The postoperative course was unremarkable. She was discharged from the hospital with an arterial saturation of 95% breathing room air and marked improvement in her heart failure symptoms.

DISCUSSION: URCS is an uncommon cardiac anomaly often associated with a LSVC (1). The lesion results in bidirectional atrial shunting, increased pulmonary blood flow, and decreased arterial oxygen saturation. There is potential for cerebral embolism from right-to-left shunting.

URCS is usually discovered in childhood and may coexist with other congenital lesions. However, URCS has been reported as a cause of right heart failure in adults (3,4). In isolation, URCS may be difficult to diagnose as the clinical signs are non-specific and the

echocardiographic findings may not be readily apparent. In this patient the TR was likely secondary to right ventricular dilation and the intracardiac shunting was masked by the TR jet. With TVR and a reduction in the TR, shunting due to the URCS became apparent on color Doppler examination.

Two possibilities exist for repair of an URCS. In the presence of a LSVC, patch closure of the defect in the left atrium may be undertaken resulting in normal drainage of the coronary veins into the right atrium. Alternatively, the LSVC can be safely ligated when an innominate vein is present. Rerouting of the LSVC directly to the right atrium has also been described (1). In this case, no LSVC was present and it was elected to close the entrance of the CS into the right atrium resulting in coronary venous drainage into the left atrium. This results in a mild degree of arterial desaturation (~5% decrease).

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S-42.

TITLE: A PRELIMINARY STUDY OF THE INCIDENCE OF POST-THORACOTOMY SHOULDER PAIN

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INTRODUCTION: Patients undergoing thoracic surgery often benefit from aggressive post-operative pain management including thoracic epidural analgesia (1). A significant number of patients develop ipsilateral shoulder pain (ISP) refractory to epidural analgesia (2). The incidence and duration of this type of pain in patients undergoing thoracotomy or VATS is poorly defined. We undertook a prospective observational study of patients undergoing thoracotomy or VATS to determine the incidence of post-thoracotomy/VATS ISP, its duration, and potential etiologies.

METHODS: After obtaining Research Ethics Board approval and informed patient consent, 41 patients scheduled for thoracotomy or VATS were prospectively followed. Patients were assessed for the presence of ISP, intensity and duration of the pain, co-morbid conditions, intra-operative and peri-operative pain management. Pain was assessed on arrival to the PACU, at 1 hour every 24 hours until resolution or hospital discharge.

RESULTS: The overall incidence of post-operative ISP was 53.7%, with 64.5% of thoracotomy patients and 70% of VATS patients reporting post-operative ISP. However, 3 VATS patients and 5 thoracotomy patients reported atypical post-thoracotomy ISP. These atypical presentations included anterior chest pain, pain starting after a walk on post-operative day 3, pain over the proximal end of the incision, scapular pain and neck and trapezius pain. Atypical presentations after VATS included scapular pain, posterior shoulder pain and pain similar to previous arthritis. After accounting for atypical presentations, the incidence of post-operative ISP decreased to 36.6% overall, 48.4% after thoracotomy and 40% after VATS. The average duration of post-thoracotomy ISP was 4.1 days, 3.9 days after accounting for atypical presentations. The average duration of post-VATS ISP was 2.75 days, 2.8 after exclusion of atypical presentations.

S-43.

TITLE: CARDIAC ARREST IN-HOSPITAL AFTER CARDIAC TAMPONADE. THE ROLE OF THERAPEUTIC HYPOTHERMIA IN THE SUCCESSFUL RESUSCITATION

AUTHORS: R. Lopez, H. Elsayed-Awad;
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INTRODUCTION: More than 350,000 Americans die of sudden cardiac arrest every year. 10-30% of long-term survivors have permanent brain damage. Therapeutic hypothermia after cardiac arrest has been shown to improve neurological outcomes. In 2005, the International Liaison Committee on Resuscitation recommended therapeutic hypothermia after out-of-hospital cardiac arrest (1). The incidences of in-hospital cardiac arrest range between 1 and 5 events per 1,000 hospital admissions, and survival with good neurological outcome is rare (2).

METHODS AND RESULTS: A 68 year old male with a history of SVT. The patient underwent pulmonary vein isolation procedure for his SVT. A perforation occurred in the left atrium resulting in a pericardial effusion. A pericardiocentesis to drain the pericardial effusion resulted in a second perforation of the right ventricle. He went into cardiac arrest and CPR was performed for 41 minutes. He was transferred to the OR and placed on cardiopulmonary bypass for 43 minutes. Blood was cooled while on bypass and the holes repaired. He was transferred to the ICU. He remained in the moderate hypothermic range (32-34°C) post-operatively for 7 hours. He was discharged 10 days later with complete neurological recovery. The second case was a 43 year old female with viral myocarditis and hypothyroidism. She was presented on arrival with hypotension, tachycardia, and dyspnea. An echocardiogram showed pericardial and pleural effusion. A pericardiocentesis was attempted to drain the fluid. During the procedure, the wire went through RV and was removed which resulted in cardiac tamponade. She went to the OR for pericardial tamponade evacuation and repair of the hole. An awake fiber optic intubation was performed in the sitting position. Immediately after placing the patient in the supine position she arrested and ACLS protocol was initiated with open cardiac massage for a total time of 18 minutes. She was placed on cardiopulmonary

by-pass for a period of 36 minutes. The patient's blood was cooled, dropping her core temperature to 32°C. She remained in the mild hypothermic range (34-36°C) for 12 hours. She was discharged after 21 days with full neurological recovery.

DISCUSSION: We report two cases of in-hospital cardiac arrest secondary to cardiac tamponade that resulted in successful resuscitation and full neurological recovery following rapid institution of cardiopulmonary bypass and therapeutic hypothermia postoperatively. Our case report demonstrates the beneficial effect of therapeutic hypothermia after cardiac arrest in-hospital. Therapeutic hypothermia should be extended to the in-hospital cardiac arrest patients to prevent perioperative neurological insult after cardiac arrest.

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DISCUSSION: We report two cases of in-hospital cardiac arrest secondary to cardiac tamponade that resulted in successful resuscitation and full neurological recovery following rapid institution of cardiopulmonary bypass and therapeutic hypothermia postoperatively. Our case report demonstrates the beneficial effect of therapeutic hypothermia after cardiac arrest in-hospital. Therapeutic hypothermia should be extended to the in-hospital cardiac arrest patients to prevent perioperative neurological insult after cardiac arrest.

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S-44.

TITLE: PERSISTANT LEFT SUPERIOR VENA CAVA AND PLACEMENT OF SWAN-GANZ CATHETER IN THE CORONARY SINUS

AUTHORS: J. Wingate, H. Elsayed-Awad;
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INTRODUCTION: One estimate of use of Pulmonary Artery Catheter (PAC) monitoring in the USA showed that as of the year 2000 more than 1.2 million PACs were placed annually. Central catheters have long been regarded as dangerous by practitioners, manufacturers of central catheters, and the FDA. In the ASA, closed claims project database, claims related to central catheters had a high degree of severe patient injury with an increased proportion of death (47%) compared with other claims in the database (29%, $p < 0.01$). Persistent Left Superior Vena Cava Syndrome (PLSVC) occurs in approximately 0.4% of the general population and in 4% of people with congenital heart disease. We estimate that anesthesiologists and critical care providers face 4000 PAC insertions in patients with this anatomic anomaly annually.

METHODS AND RESULTS: A 48 year old man presented for open repair of an infrarenal abdominal aortic aneurysm [AAA]. A PAC was placed with some difficulty before his operation. There were two trials of cannulation by the resident of the right internal jugular vein and two attempts by the staff, one attempt which was successful, to cannulate the vein and insert the cords. The patient underwent open repair of his AAA without complication. Postoperatively, a chest x-ray was taken and the surgical fellow looking at the x-ray noticed the abnormal position of the catheter on it. A radiologist diagnosed the presence of a persistent left superior vena cava and the incorrect placement of the tip of the PAC in the coronary sinus. A postoperative CT scan documented the PLSVC, but the data was not relayed to the perioperative team in the final report before the surgery.

DISCUSSION: Our patient was not harmed as a result of incorrect PAC placement in this case, however, the complications of placing a PAC include arrhythmias, heart block, endobronchial hemorrhage, pulmonary infarction, catheter knotting, valvular damage, thrombocytopenia, and incorrect placement. Fortunately, this patient's

surgery involved his abdominal aorta and not his heart or the outcome may have been different. Despite the lack of clinical consequence in this patient, this mistake must be recognized and avoided to prevent morbidity and mortality in future patients with PACs. Any abnormal finding in the radiological study related to the vascular system in general and the PLSVC in specific needs to be communicated to the anesthesiologist before insertion of the PAC.

S-45.

TITLE: EVALUATION OF TRANSCUTANEOUS CO₂ EMPLOYING EAR SENSOR (TOSCA) AND CEREBRAL OXIMETRY DURING CARDIOPULMONARY BYPASS

AUTHORS: S. Vakharia, K. Gimenez, L. Estanol, H. J. Kim, B. Kavooosi, N. Shah;
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INTRODUCTION: The Cerebral Oximeter helps assess adequacy of brain oxygenation during cardiopulmonary bypass (CPB).^{1,2} Decrease in CO₂ will cause cerebral vasoconstriction with resultant decrease in brain oxygenation. TOSCA monitor (Radiometer Inc., Copenhagen) is a FDA approved, non-invasive device that provides continuous readings of P_{tc}CO₂ from a single heated ear sensor. Studies show that P_{tc}CO₂ from TOSCA is comparable to PaCO₂ obtained from ABG.^{3,4} We undertook the following study to evaluate the performance of TOSCA as an adjunct to cerebral oximetry during CPB.

METHODS: Following IRB approval and after obtaining written informed consent, 10 adult patients (2 females, 8 males, mean age of 59.9) were enrolled in the study. Standard monitors, arterial lines, and PA catheters were used to monitor the patients. The TOSCA ear sensor was placed randomly on either earlobe of the patients. Two sensors of cerebral oximetry were placed on either side of the forehead. Patients were monitored for the entire case. Data was collected every 5 minutes. In this study we present data while patients were on CPB. Patients were on CPB from 85 to 160 minutes. A univariate ANOVA was used for comparisons.

RESULTS: The results of the ANOVA showed that there is a positive correlation between pump flow and cerebral oximetry; and a negative correlation between pump flow and P_{tc}CO₂, and P_{tc}CO₂ and cerebral oximetry.

	Univariate ANOVA results	
	Mean	Standard Deviation
PtcCO2	52.68	12.90
Pump Flow	4.89	1.02
Cerebral Oximeter (Left)	56.57	8.96
Cerebral Oximeter (Right)	55.23	8.64

DISCUSSION: From this ongoing study, it appears that P_{tc}CO₂ should be further examined for its role during CPB.

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S-46.

TITLE: USE OF CONTINUOUS CENTRAL VENOUS OXYGEN SATURATION MONITORING IN PEDIATRIC PATIENTS UNDERGOING CARDIAC SURGERY

AUTHORS: N. Dhamija, J. K. Ho, E. Sanchez, C. Canales, K. J. Lee, R. Crowley, A. Mahajan;

AFFILIATION: Department of Anesthesiology, David Geffen School of Medicine, UCLA, Los Angeles, CA.

INTRODUCTION: Central venous oxygen saturation (ScvO₂) monitoring is an effective indicator of cardiac output and oxygen delivery (1). In high-risk adult patients, ScvO₂ has been shown to be a better indicator of global hypoxemia and tissue perfusion as compared to hemodynamic parameters (2). Despite the clinical usefulness, ScvO₂ has not been well studied in the pediatric population. Using a new pediatric venous catheter with integrated fiberoptic oximetry, we prospectively studied the accuracy and reliability of continuous ScvO₂ in pediatric patients undergoing corrective or palliative cardiac surgery in the operating room (OR) and intensive care unit (ICU). We compared its accuracy to blood co-oximetry values, and determined its correlation with hemodynamic parameters and blood biochemistry values.

METHODS: Following institutional review board approval and parent informed consent, twenty patients undergoing cardiac surgery and requiring central venous catheterization were enrolled. Catheter size was selected according to patient size and the position of catheter tip in superior vena cava (SVC) was confirmed using transesophageal echocardiography. Continuous ScvO₂, heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), arterial pulse-oximetry (SpO₂), and temperature (core and peripheral) were obtained intraoperatively and every 15 minutes in the ICU up to 24 hours post surgery. Venous blood gases and chemistry were obtained at pre-determined time points in the OR and ICU. Patients with cyanotic lesions and those undergoing CPB were placed in individual subgroups for analysis. Bland-Altman analysis was performed for determination of systemic error (bias) between ScvO₂-catheter and laboratory venous blood gas values. Pearson's correlation coefficient (Pr) was employed for correlation between ScvO₂-catheter, hemodynamics, and blood chemistry.

RESULTS: Mean age 41 months (0.4-116.4 months) and mean weight

15.3 kg (3.1-28 kg). Analysis of 146 pair data sets of ScvO₂-cath and laboratory venous blood gas showed difference of means (bias) was -0.04% with ±4.37% precision for cyanotic patients, +1.37% with ±3.07% for acyanotic patients, +0.47% with ±4.22% for patients who underwent CPB, +0.77% with ±2.47% for patients who did not undergo CPB. Correlations were found between ScvO₂ catheter measurements and HR (Pr=-0.51, p<0.4), lactate values (Pr=-0.71, p<0.02) in the ICU. ScvO₂ correlated weakly with core temperature in the ICU (Pr=0.49, p<0.04) and poorly with peripheral temperature in the ICU (Pr=-0.23, p>0.05).

DISCUSSION: Our results indicate that ScvO₂ is an accurate and reliable monitor in high-risk pediatric patients undergoing cardiac surgery in the OR and up to 24 hours in the ICU. Accuracy of ScvO₂ measurements were not affected by patient cyanotic lesions or CPB intervention suggesting a highly dependable tool in high risk pediatric patients.

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S-47.

TITLE: APROTININ AND PREOPERATIVE RISK FACTORS FOR THE DEVELOPMENT OF POSTOPERATIVE RENAL DYSFUNCTION FOLLOWING PEDIATRIC CONGENITAL CARDIAC SURGERY

AUTHORS: A. Manrique, B. A. Kuch, E. H. Jooste, S. E. Lichtenstein, V. Morrel, P. J. Davis;

AFFILIATION: Children's Hospital of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: Use of high dose aprotinin during cardiopulmonary bypass (CPB) in adult patients has been linked to postoperative renal dysfunction but the renal effect on the pediatric population undergoing complex congenital cardiac operations is unknown.^(1,2,3)

METHODS: We utilized a retrospective case-control design to evaluate children undergoing cardiac surgery requiring CPB between July 2004 and July 2006. Data collected included demographics, past medical history, preoperative status and medications. Surgical risk was quantified by Aristotle surgical complexity level. Renal dysfunction was defined as a 50% increase in the baseline serum creatinine during the first 5 days following surgery. Differences between groups were analyzed using nonparametric statistical tests. Continuous data are presented as median [interquartile range]. The propensity score was used to remove the significant differences found in observed covariates. The score was developed using a backward stepwise logistic regression with pre-treatment covariates associated with the administration of aprotinin. Covariates with a p value ≤ 0.25 via univariate analysis were included in the model. The score was then used as a single variable adjusting for the differences in covariates during regression modeling. A p value <0.05 is considered statistically significant.

RESULTS: Among 395 patients who underwent cardiac surgery 55% received aprotinin and 45% did not. Thirty one percent of the cohort had previous cardiac surgery, 1.8% were < 44 weeks gestation at the time of surgery and the overall postoperative renal dysfunction rate was 20%. Those receiving aprotinin had a higher preoperative incidence of (1) past cardiac surgery (54.1% vs. 3.4%; OR 33.63 [14.28 - 79.20]), (2) hospitalization (43.6% vs. 7.9%; OR 8.99 [4.89 - 16.51]), (3) sepsis

(6.9% vs.0.0%; p<0.001), (4) heart failure (24.8% vs. 13.0%; OR 2.21 [1.29 - 3.77]), (5) mechanical ventilation (25.2% vs. 2.8%; OR 11.61 [4.53 - 29.72]), (6) mechanical circulatory support (6.0% vs. 0.6%; OR 11.16 [1.45 - 86.17]), (7) a Aristotle level of 4 (26.6% vs. 2.8%; OR 12.47 [4.88 - 31.88]), (8) diuretics (63.8% vs. 26.6%; OR 4.87 [3.16 - 7.50]), (9) angiotensin converting enzyme inhibitors (21.1% vs. 7.9%; OR 3.11 [1.64 - 5.87]), (10) milrinone (25.7% vs. 4.5%; OR 7.30 [3.37-15.79]) and (11) vasoactive agents (18.8% vs. 2.8%; OR 7.97 [3.08 - 20.64]). There was a significant difference in the unadjusted risk of renal dysfunction (OR 1.99 [1.19 - 3.33]), however propensity score adjustment did not reveal an association between aprotinin and renal dysfunction (OR 0.80 [0.33 - 1.98]).

DISCUSSION: Patients who receive aprotinin are more likely to present with preoperative risk factors for the development of postoperative renal dysfunction. However, the use of Aprotinin is not associated with a higher risk of developing renal dysfunction in the immediate postoperative period when adjusting for associated risk factors.

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S-48.

TITLE: 3-D ULTRASOUND AND CENTRAL VENOUS CATHETER INSERTION

AUTHORS: B. A. Harrison, S. R. Clendenen, T. S. Shine, N. J. Clendenen, S. Aniskevich;

AFFILIATION: Mayo Clinic College of Medicine, Jacksonville, FL.

INTRODUCTION: Health care organizations advocate the use of ultrasound for the insertion of central venous catheters. Many anesthesiologists utilize ultrasound, but not in real time, using ultrasound to define the anatomy and then insert the catheter. With the introduction of 3-D ultrasound it is now possible to insert the catheter in real time and to know the exact location of the needle tip.

METHODS: Under anesthesia six patients requiring a right internal jugular catheter were studied using a 3-D ultrasound Philips IU 22(Andover, MA) with a X 7-2 probe. The catheter was placed with the head turned slightly to the left and the patient placed in 15-25 degrees of Trendelenberg. 3-D Images were recorded at baseline, finder needle insertion and 18-G angio needle insertion. At each image the diameter of the vein and artery was measured in cm, and the percentage overlap of the vein with respect to the artery was measured. The study is descriptive.

RESULTS. Table 1 depicts the diameters of the vein and table 2 the percentage overlap of the vein to artery with needle advancement. There were no complications and all catheters were successfully placed.

Table 1, Diameter of Vein

Baseline	22g Finder Needle	18g Angiocath	% change Baseline to Angiocath
1.6cm	1.28cm	0.73cm	55%
1.26cm	1.07cm	0.64cm	50%
1.27cm	0.85cm	0.46cm	64%
1.4cm	0.31cm	0.26cm	72%
1.1cm	0.6cm	0.3cm	73%
1.18cm	0.93cm	0.32cm	83%
		Mean Change	66%

Table 2, Percent Vein Wall Overlapping Carotid Artery

	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Overlap Mean
Baseline	25%	25%	25%	25%	0	25%	20.83%
22g Finder Needle	25%	50%	50%	50%	0	25%	33.33%
18g AngioCath	100%	50%	75%	50%	100%	25%	66.66%

DISCUSSION. Real time insertion of a right internal jugular venous catheter using a 3-D ultrasound shows that the vein is both compressed and distorted with respect to the artery with application of pressure with needle advancement.

S-49.

WITHDRAWN

S-50.

TITLE: WHAT'S IMPORTANT: PREOPERATIVE B-BLOCKADE OR A LOW RESTING HR?

AUTHORS: L. I. Rodriguez, M. M. Vigoda, E. Wu, M. Murtha, D. A. Lubarsky;

AFFILIATION: University of Miami Miller School of Medicine, Miami, FL.

INTRODUCTION: Perioperative use of β -blockers can benefit some patients with coronary artery disease (CAD) [1]. Guidelines [2] recommend preoperative β -blockers to maintain a resting heart rate (HR) ≤ 60 beats per minute (bpm). We hypothesized that a low resting HR (preoperative) was associated with good intraoperative HR control, regardless of the use of preoperative β -blockers.

METHODS: We reviewed electronic medical records of patients with documented CAD having elective non-cardiac surgery between 1/04 and 6/06. We analyzed preoperative and intraoperative β -blocker use in over 1,400 patients. We correlated patients resting HR when seen in the Pre-anesthesia Treatment (PAT) Clinic with their intraoperative HR. CAD was defined as s/p myocardial infarction, CABG, angioplasty/stenting or angina. Adequate preoperative HR control was defined as a resting HR ≤ 60 bpm [2]. Intraoperative (between surgery start and surgery end) HR < 75 bpm was considered to be adequate control.

RESULTS: Of the 21,039 patients who had elective surgical procedures, 1,346 (6.4%) had documented CAD. Some patients (52 patients) were excluded from this retrospective review because their resting HR was either not documented or erroneously recorded (i.e. HR 150 bpm). There were 58.3% (754) of patients with CAD taking preoperative β -blockers.

Patients with CAD taking β -blockers preoperatively were more likely to have resting HR ≤ 60 bpm than those not receiving this medication (34% vs. 18%, $p \leq 0.001$). However, for patients with resting HR ≤ 60 , there was no difference (41.3% vs. 40.8%, $p \leq 1$) in the percentage of patients with adequate intraoperative HR control.

	Patients with CAD seen at the PAT Clinic		
	Total Patients	Intraoperative HR < 75	%
Patients on preoperative β -blocker	754	219	
HR ≤ 60 in PAT Clinic	259	107	41.3
Patients not on preoperative β -blocker	540	98	
HR ≤ 60 in PAT Clinic	98	40	40.8

DISCUSSION: While preoperative β -blocker therapy has been recommended in selected subgroups of patients, we found that for patients with resting HR ≤ 60 there was no difference in the percentage with adequate intraoperative HR control. We recommend a larger study to determine if low resting HR (as opposed to preoperative β -blockade) is a factor in perioperative morbidity.

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- [1] Feringa HH, Bax JJ, Boersma E, et al. Circulation 2006;114: I-344 I-349.
- [2] Fleisher LA, Beckman JA, Brown KA, et al. Anesth Analg 2007;104:15-26.

S-51.

TITLE: PREOPERATIVE B-BLOCKERS, STATINS AND ASA: "ONE FOR ALL AND ALL FOR ONE"

AUTHORS: L. I. Rodriguez, M. M. Vigoda, E. Wu, M. Murtha, D. A. Lubarsky;

AFFILIATION: University of Miami Miller School of Medicine, Miami, FL.

INTRODUCTION: Perioperative use of β -blockers can benefit some patients with coronary artery disease (CAD) [1]. Guidelines [2, 3] recommend the use of β -blockers, statins, ASA or oral antiplatelets for secondary prevention in patients with coronary artery and other vascular diseases. We hypothesized that patients receiving β -blockers preoperatively were more likely to be receiving other risk reducing medications.

METHODS: We reviewed electronic medical records of patients with documented CAD coming to the pre-anesthesia clinic for non-cardiac surgery between 1/04 - 6/06. CAD was defined as s/p CABG, s/p angioplasty, s/p MI, angina or atypical angina with a positive stress test. We analyzed the preoperative (chronic) use of β -blockers and its association with the preoperative use of statins, aspirin and oral antiplatelets.

RESULTS: Of 21,039 patients who had elective surgery, 6.4% (1,346) had documented CAD. There were 57.9% (779) CAD patients with preoperative β -blocker use.

Patients with CAD taking β -blockers preoperatively were more likely to be taking Statins (59% vs. 38%, $p < 0.0001$), ASA (50% vs. 26%, $p < 0.0001$), and Oral antiplatelets (21% vs. 12%, $p < 0.0001$) than those patients not taking β -blockers.

DISCUSSION: Guidelines recommend the use of risk reducing medications in patients with CAD. We found that patients taking preoperative β -blockers were more likely to be taking other risk reducing medications than those patients not taking β -blockers. We recommend further studies to determine whether these differences are the result of access to care, physician education, side effects of medications, lack of financial resources or other factors.

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Association of <font face=

	Taking β -blocker %	Not Taking β -blocker %	
Total Patients with CAD	779	567	
Statins	460 59	215	38 $p < 0.0001$
ASA	386 50	148	26 $p < 0.0001$
Oral Antiplatelets	166 21	66	12 $p < 0.0001$

S-52.

TITLE: ADEQUACY OF TRANSTHORACIC ECHOCARDIOGRAM IN THE POST-OPERATIVE CARDIAC SURGICAL PATIENT.

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AFFILIATION: ¹Mt. Sinai Medical Center, New York, NY, ²Columbia Presbyterian Hospital, New York, NY.

INTRODUCTION: The purpose of our study was to evaluate the rate of adequacy of transthoracic echocardiograms (TTE) during the first week after cardiac surgery. Certain risk factors^{1,2} have been postulated to hinder adequacy of TTE in intensive care patients. To our knowledge, the adequacy of TTE in cardiac surgical patients has never been specifically analyzed during the postoperative period.

METHODS: We conducted a retrospective review of patients admitted to a tertiary care cardiac intensive care unit. Records of 919 consecutive patients were analyzed. The first 300 patients who received a TTE within the first seven days postoperatively were included for analysis. An attending cardiologist interpreted all echocardiograms. Results were recorded as adequate, inadequate, or partially adequate.

RESULTS: Of the 300 TTEs reviewed, 85 (28%) were adequate; 163 (54%) were partially adequate; and 52 (17%) were inadequate. Twenty-five (8%) of the TTE reports recommended a further study be done in the form of a transthoracic echocardiogram (TEE), a repeat TTE, or a contrast enhanced TTE. Of those, 19 (6%) specifically recommended a TEE be done. Twenty-one patients in our analysis received a TEE in addition to the TTE they received, regardless of recommendation.

DISCUSSION: Previous studies have reported risk factors for an inadequate TTE in the intensive care setting^{1,2,3}. In this specific population, echocardiography may provide data for care altering decisions including inotropic and vasopressor medication changes, volume resuscitation, chest opening and return trips to the operating room. Choosing the most effective and cost-efficient diagnostic study can decrease health care costs and prevent delays in treatment. We believe that TTE is often an inadequate diagnostic study in post-surgical cardiac patients during the postoperative period and that further

examination of patient and surgical risk factors is warranted to develop a protocol or algorithm for appropriate diagnostic testing.

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S-53.

TITLE: ASSESSMENT OF QT INTERVAL AND QT DISPERSION DURING ELECTROCONVULSIVE THERAPY USING COMPUTERIZED MEASUREMENTS.

AUTHORS: N. Tezuka, S. Yamaguchi, H. Egawa, S. Hamaguchi, T. Kitajima;

AFFILIATION: Dokkyo University School of Medicine, Mibu, Japan.

INDUCTION: Dispersion of the QT interval (QTD), which is defined as maximal QT interval minus minimal QT interval, on 12 leads of the surface ECG reflects regional heterogeneity of ventricular repolarization. Prolongation of the QTD has been considered about increased risk of ventricular arrhythmias and cardiovascular mortality. The purpose of this study was to investigate QT interval and QTD during electroconvulsive therapy (ECT) for patients with psychiatric disorders under general anesthesia using computerized measurements.

METHODS: After obtaining the approval of the hospital ethics committee and informed consent from patient's families, twenty psychiatric patients were enrolled in this study. All patients received propofol anesthesia for ECT. A 12-lead electrocardiogram (FDX-4521L, Fukuda Denshi Co. Ltd., Tokyo, Japan) was monitored to measure parameters. Muscle paralysis was achieved by succinylcholine 1mg/kg. The magnitude of the energy setting for ECT stimulus was predetermined by age, and the efficacy of ECT was determined by the tourniquet technique. The RR interval, QT interval, rate-corrected QT interval (QTc), QTD and rate-corrected QTD (QTcD) were determined by the use of newly developed software (QTD-1, Fukuda Denshi Co. Ltd., Tokyo, Japan).

RESULTS: The QTcD in patients with psychiatric disorders significantly increased, compared with healthy subjects. In psychiatric patients, anesthetic induction did not influence the RR interval, QT interval, QTc, QTD and QTcD. The RR interval significantly increased immediately after ECT. Although the QT interval significantly decreased immediately after ECT, the QTc was not influenced by ECT during the study. Increase of the QTD and QTcD was observed and lasted for several minutes after ECT, and spontaneously disappeared within ten minutes after ECT.

DISCUSSION: ECT used in the treatment of severe psychiatric disorders induces stimulation of the autonomic nervous system with initial parasympathetic outflow immediately followed by a sympathetic response. These responses may induce arrhythmias or cardiac events. Our results suggest that ECT increases the QTD, associated with risk of ventricular arrhythmias and cardiovascular mortality.

Critical Care Medicine & Trauma

S-54.

TITLE: INVOLVEMENT OF SENSORY NEURON TO ISCHEMIA/REPERFUSION-INDUCED ACUTE RENAL INJURY IN RATS

AUTHORS: S. Mizutani, A. Mizutani, K. Kudo, T. Uchino, T. Noguchi;

AFFILIATION: Oita University Faculty of Medicine, Oita, Japan.

[INTRODUCTION] We previously reported that promoting endothelial production of prostacyclin (PGI₂) improved ischemia/reperfusion (I/R)-induced acute renal injury in rats by reducing tumor necrosis factor (TNF)-alpha production. However, the mechanisms underlying this phenomenon remains to be fully elucidated. We also demonstrated that activation of capsaicin-sensitive sensory neurons increased endothelial production of PGI₂ by releasing calcitonin gene-related peptide (CGRP) in rats subjected to hepatic I/R and sepsis. In the present study, we investigated whether activation of capsaicin-sensitive sensory neurons contributes reduction of I/R-induced acute renal injury in rats by inhibiting TNF-alpha production via CGRP release.

[METHODS] Male Wistar rats were subjected to 45min of I/R.

[RESULTS] Renal tissue levels of CGRP and 6-keto-PGF1a, a stable metabolite of PGI₂, were promoted after renal I/R. I/R-induced increases in the levels of 6-keto-PGF1alpha were reduced by pretreatment with capsazepin (a vanilloid receptor antagonist), CGRP(8-37) (a CGRP receptor antagonist) and indomethacin (a cyclooxygenase inhibitor). Furthermore, the pretreatment exacerbated a series of I/R-induced responses, including increases in serum levels of blood urea nitrogen and creatinine, renal vascular permeability, renal tissue levels of myeloperoxidase activity, CINC and TNF-alpha, and decreasing in renal tissue blood flow.

[CONCLUSION] These findings strongly suggest that activation of sensory neurons contribute to improvement of I/R-induced acute renal injury in rats by releasing CGRP, which is capable of promoting endothelial production of PGI₂.

S-55.

TITLE: TRACHEAL INFLAMMATORY MARKERS ARE CORRELATED WITH TIME OF ENDOTRACHEAL INTUBATION

AUTHORS: C. A. Puyo, S. Tricomi, T. E. Dahms;

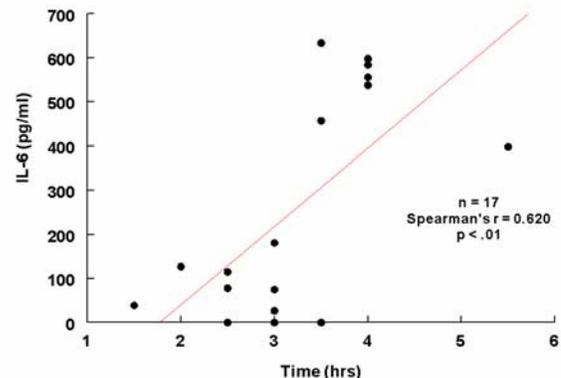
AFFILIATION: Saint Louis University, Saint Louis, MO.

INTRODUCTION: Although there are published reports of upper airway discomfort following routine endotracheal intubation for anesthesia¹, tracheal inflammatory response to this process has not been well studied. We hypothesized that inflammatory markers such as cytokines and polymorphonuclear cells (PMN) would increase in the trachea with intubation, and we began with a study of these markers following short-term (less than 6 hours) intubation.

METHODS: We obtained approval from the Saint Louis University Institutional Review Board to enroll 17 healthy non-smokers admitted for same-day elective surgery. After induction of general anesthesia an endotracheal tube (Mallinkrodt Hi-Lo Evac, size 7.0 ID for females and size 8.0 for males) was placed. Cuff pressure was maintained at 25cm H₂O, and peritracheal lavage above the cuff was performed using a single injection/aspiration technique with 5 ml of sterile saline before the start of surgery and just before extubation. The recovered lavage was analyzed immediately for PMN as percent of total cells, then centrifuged. The cell-free supernatant was frozen and later assayed by BCA for total protein and by ELISA for TNF- α , IL-1 β , IL-6 and IL-8.

RESULTS: Extubation occurred within 6 hours in all patients (mean time of intubation was 3.2 \pm 0.23 hours with a range of 1.5 to 5.5 hours). All measured parameters increased significantly from baseline to extubation, and levels at extubation significantly correlated with time of intubation in 3 of these: PMN (Spearman's r = 0.671, p < .01), IL-6 (Spearman's r = 0.620, p < .01) and TNF- α (Spearman's r = 0.519, p < .05).

IL-6 in Tracheal Lavage
Correlation with Duration of Intubation



DISCUSSION: In our study, inflammatory cells and cytokines increased even in routine, uncomplicated endotracheal intubation for short-term surgery. The correlation of the levels of PMN, IL-6 and TNF- α with time of intubation suggests that the presence of the tube exerts a cumulative inflammatory effect upon the upper airway. Further study of inflammation in the trachea is needed to assess the implications of this response for longer periods of intubation.

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S-56.

TITLE: INDUCTION OF HYPOTHERMIA IN RATS USING COOLED HELIOX VENTILATION.

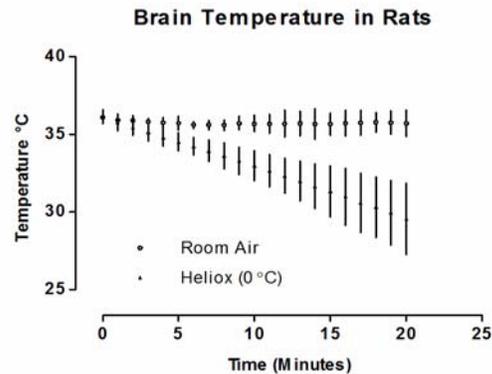
AUTHORS: M. M. Kumar¹, L. D. Johnson²;

AFFILIATION: ¹Mayo Clinic, Rochester, MN, ²MHTR, Red Wing, MN.

INTRODUCTION: Therapeutic hypothermia has become an important treatment option for myocardial and cerebral ischemia.¹ Yet current methods to induce hypothermia are ineffective.² The authors test the feasibility of achieving hypothermia using cooled heliox (80% helium + 20% oxygen) hyperventilation to extract heat from the lungs.

METHODS: Sixteen Sprague Dawley rats (440 ± 5 g) were equally divided into study and control groups. Both groups were anesthetized with halothane, followed by intraperitoneal injection of 50 mg/kg of ketamine and 25 µg/kg of fentanyl, and intubated through a tracheotomy. A thermistor probe was introduced percutaneously into the lateral ventricle of the brain and secured in place. Both groups were ventilated with a tidal volume of 5-6 ml/kg, with a pop-off valve set to open at 12 cm of water and at a respiratory rate of 60 breaths/minute. The study group was ventilated with heliox cooled to 0±2°C for 20 minutes with temperatures recorded every minute and arterial PaCO₂ measured at baseline and at the end of hyperventilation. Control animals were ventilated with room air (22°C). Rates of temperature decline were analyzed using simple linear regression. Differences between groups were analyzed using between-groups and repeated measures ANOVA.

RESULTS: Hyperventilation of rats with cooled heliox led to steady decline in brain temperature (figure). Simple linear regression analysis of the data showed a cooling rate of approximately 0.32°C/minute (R²=0.9992). The rate of cooling in control animals was insignificant (R²=0.1945). In both groups, the decreases in PaCO₂ were similar.



DISCUSSION: Hyperventilation with cooled heliox effectively extracts heat from the lungs. The large alveolar surface area, the temperature difference between alveolar gases and blood, and the thin alveolar membrane render the lungs an ideal heat exchanger. As per Fourier's law of heat conduction, all things being equal, heat transfer through the tracheobronchial tree depends on thermal conductivity of the gases. Thermal conductivity of helium (0.138 W/mK) is over six times that of oxygen (0.0238 W/mK) or nitrogen (0.0234 W/mK). Also, since helium is less dense, its thermal diffusivity is greater than other gases. Under normal circumstances, rapid diffusivity could retard convection. However, in the lungs, regardless of convection currents, the heated gases are expired through respiration.

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S-57.

TITLE: TRANSIENT RECEPTOR POTENTIAL VANILLOID 1 INHIBITION DECREASES SURVIVAL AND ALTERS CYTOKINE RESPONSE TO ENDOTOXIN CHALLENGES IN MICE

AUTHORS: J. Horowitz, V. Besch, L. Middleton, Y. Uehara, Z. Quezado;

AFFILIATION: National Institutes of Health, Bethesda, MD.

INTRODUCTION: Transient receptor potential vanilloid 1, subfamily V, member 1 (TRPV1), a sodium/calcium channel expressed in peripheral and central terminals of sensory neurons, plays a pivotal role in nociception. TRPV1 can be activated by capsaicin, decreases in pH, noxious heat, and inflammation. Agonists of TRPV1, such as resiniferatoxin and capsaicin, can reduce neurogenic inflammation and inhibit the release of inflammatory cytokines and transcription factors such as NF-κB by macrophages. Antagonists of TRPV1, such as capsaizepine (CZP), have also been shown inhibit expression of NF-κB.

METHODS: The purpose of this investigation was to define the role of TRPV1 in sepsis and in the host response to lipopolysaccharide (LPS, endotoxin). We studied TRPV1^{-/-} (TRPV1 knock out) and TRPV1^{+/-} (wild-type) mice and used CPZ to achieve pharmacologic inhibition of TRPV1 in wild type animals. We first investigated the role of genetic TRPV1 deficiency on survival after LPS challenge.

RESULTS: TRPV1^{-/-} (TRPV1 knock out) and TRPV1^{+/-} (wild-type) mice had similar survival (36% vs. 38%) after LPS injection. To determine the role of pharmacologic TRPV1 inhibition by CZP on survival after LPS challenge, TRPV1^{+/-} mice were injected (i.p.) with CZP or control and challenged with i.p. LPS. Pharmacologic inhibition of TRPV1 with CZP, compared with controls, significantly decreases survival after LPS challenge in wild type mice (10% vs. 42%, CPZ-treated vs. control, p<0.05). We then investigated the role of TRPV1 on cytokine and chemokine expression by LPS-challenged (16h) splenocytes. At baseline, TRPV1^{-/-} and TRPV1^{+/-} splenocytes had similar TNF-α and MIP1-α expression. In contrast, CZP decreased TNF-α and MIP1-α expressions in both TRPV1^{-/-} and TRPV1^{+/-} splenocytes after LPS challenge.

DISCUSSION: While the reason for increased mortality after pharmacologic TRPV1 inhibition is incompletely understood, our data shows that the addition of CZP alters expression of inflammatory cytokines and decreases survival after LPS challenge. Our results suggest that, by mechanisms incompletely understood, TRPV1 has a role in the immune response to LPS.

S-58.

TITLE: COAGULOPATHY IN SEVERE ISOLATED TRAUMATIC BRAIN INJURY (TBI) : A COMPARISON OF HAEMOSTATIC ACTIVATION MARKERS FROM JUGULAR BULB AND CENTRAL VENOUS SAMPLES

AUTHORS: R. Souissi, Z. Haddad, W. Trabelsi, K. Baccar, N. Baffoun, C. Kaddour;

AFFILIATION: National Institute of Neurology, La Rabta, Tunisia.

INTRODUCTION: Trauma patients develop various haemostatic disorders. The severity of post traumatic coagulopathy is considered to be major detrimental factor of outcome. This fact is discussed in critically ill severe isolated TBI.

Hypothesis: The aim of our study was to identify the coagulopathy disorders and its relation to outcome in severe isolated TBI.

METHODS: Prospective study, June 2003-March 2004. Included: critically ill severe isolated TBI, Collected data: Demographics, Management prior and during ICU hospitalization, CT-Scan, Daily worst GCS, admission SAPS II. A central venous catheter and an unilateral jugular bulb in front of the most damaged brain hemisphere were inserted. Jugular bulb thrombosis was prevented by continuous infusion of 2ml per hour isotonic serum without heparin. Blood samples were obtained simultaneously from the central venous line (K) and jugular bulb (B) at admission, 6th, 12th hour, and daily till 5th day. We measured platelet count, prothrombin time (PT), activated partial thromboplastin time (ACT), fibrinogen concentration (Fib), prothrombin fraction 1+2 (F) and thrombin anti-thrombin complex (TAT). Statistical analysis by Student's t test, paired t test for paired results and analysis of variance. Significance set as $p < 0,05$

RESULTS: Nineteen patients [9 survivors (S) and 10 deaths (NS)]. No differences between S and NS in demographics, management modalities, admission GCS (7±3), CT-scan, SAPS II (27±10 vs 30±17, $p=0,69$). B vs simultaneous K Platelet count was significantly lower in all drawn blood samples, with a trend to decrease overtime. S vs NS at Day2 and Day3: 191±60 vs 125±35 ($p=0,017$). Admission B thrombin fractions was higher in NS (1000±209 vs 460±294, $p=0,014$). B Day1 TAT was higher in NS: 45±20 vs 9,6±12 $p=0,02$. No difference for

other tests between B vs K and S vs NS for different paired tests

CONCLUSIONS: Pro-coagulant factors (F and TAT) are valuable prognostic factors at Day1 in isolated severe head trauma.

S-59.

TITLE: COMBINING VARIOUS SEVERITY OF ILLNESS SCORING SYSTEMS TO IMPROVE OUTCOME PREDICTION.

AUTHORS: Z. Haddad, R. Souissi, N. Baffoun, K. Baccar, C. Kaddour;

AFFILIATION: National Institute of Neurology, La Rabta, Tunisia.

INTRODUCTION No perfect severity score exists to predict ICU mortality, thus the search for new systems is still a preoccupation.

Hypothesis Use of much severity of illness scores simultaneously improves mortality prediction.

PATIENTS AND METHODS An open prospective observational study as part of the APRiMo project [1]. The study period was January 1996-September 2004. Inclusion criteria were critically ill obstetric patients and ICU length of stay >24 hours. Exclusion criteria were those of the used scores. The main outcome of interest was the survival status at ICU discharge. The database was divided into two samples: development and validation datasets. Development database patients were chosen randomly (n = 414) and the remaining patients composed the validation dataset (n = 229). A multivariable logistic regression model was developed to predict mortality associating the Acute Physiology and Chronic Health Evaluation II score [2], Simplified Acute Physiology Score II [3], Admission Mortality Prediction Model (MPM-H0) and Day 1 Mortality Prediction Model (MPM-H24) [4]. Discrimination and calibration were assessed by goodness-of-fit C-hat statistics and area under the ROC curve. The developed model was then tested in the validation dataset. Good discrimination was retained if C-hat statistics $P > 0.1$ and good calibration if area under the ROC curve > 0.8 .

RESULTS Six hundred and forty-three patients enrolled. The overall mortality rate was 11.51%. The new model predicted accurately 99% of survivors and more than 60% of nonsurvivors.

	development	validation
Hosmer-Lemeshow C-hat statistics test	0.868	0.42
ROC	0.936	0.945
Nonsurvivor prediction	28/46 (60.9%)	18/28 (64.3%)
Survivor prediction	364/368 (99%)	199/201 (99%)

CONCLUSION The 'multiscore' model seems to refine prognosis. This is partly due to mixing of new evaluated parameters. Testing the latest developed generations of scores and also organ dysfunction systems could be interesting.

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S-60.

WITHDRAWN

S-61.

TITLE: OXYGEN ADMINISTRATION PREVENTING TRANSMISSION OF RESPIRATORY DROPLET INFECTION WITH A MODIFIED N95 MASK

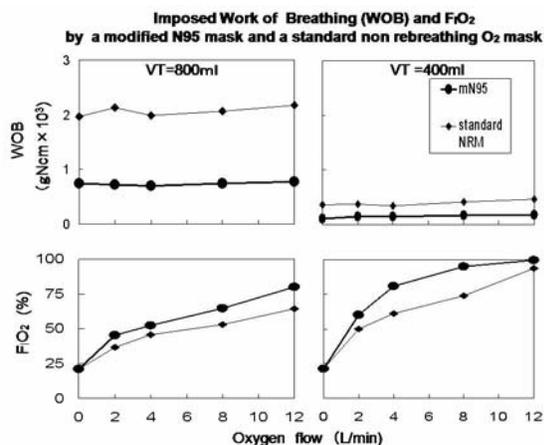
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In the event of a pandemic respiratory illness such as influenza, many patients will require oxygen therapy. Oxygen administration is a potential risk factor for transmission of droplet infection. N95 masks filter infectious particles but do not provide oxygen and may increase work of breathing. We compared the oxygen delivery and work of breathing (WOB) of a standard non-rebreathing oxygen mask (NRM) and a N95 mask modified by inserting a prototype plastic manifold (VIASYS Respiratory Care) consisting of a one-way inspiratory valve, an oxygen inlet and a gas reservoir (modified N95 mask: mN95).

METHODS: Each mask was sealed air-tight to the face of a resuscitation manikin attached to an adult lung simulator providing active inhalation and passive exhalation. Tidal volumes were set to either 400 mL or 800 mL and respiratory rate set to 15 per minute with I:E ratio of 1:2. We monitored airway pressure and oxygen concentrations and calculated inspired fractional concentration of oxygen (FiO₂) and work of breathing. The oxygen flow to the mask was increased from 0 to 12 L/min in 2 L increments.

RESULTS: At all oxygen flows and levels of ventilation, the FiO₂ provided by the mN95 mask was greater than that provided by NRM, while mN95 had lower WOB than NRM. (Fig.)



CONCLUSIONS: This modification of the N95 mask is effective in providing oxygen supplementation while the N95 material is used to filter infectious particles from exhaled breath. The major value of the mask will be to provide protection of frontline health care workers without jeopardizing patient care.

S-62.

TITLE: A CROSS-TALK BETWEEN ESTROGEN, A MEMBER OF THE NUCLEAR-RECEPTOR SUPER-FAMILY AND TOLL-LIKE RECEPTOR

AUTHORS: Y. Asakura, N. Kato, N. Kandatsu, Y. Fujiwara, T. Komatsu;

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OBJECTIVE: Cells of the innate immune system such as macrophages discriminate between “non-infectious self” and “infectious non-self” via pattern recognition receptors known as Toll-like receptors (TLRs). TLRs recruit the adaptor molecules such as myeloid differentiation marker 88 (MyD88) to initiate signaling cascades, which ultimately lead to the activation of NF- κ B, the major end-point of TLR signaling. We have previously observed that in patients aged between 20 and 45 years who were admitted to our hospital, the number who required mechanical ventilation for respiratory complications was significantly lower for women than for men. Additionally, the gender-related differences in the incidence of the development of respiratory complications were attributable to the anti-inflammatory properties of estrogen. 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 estrogen on the inflammatory responses mediated by TLR-signaling.

METHODS: RAW264.7 cells, a murine macrophage-lineage cell line, were transiently transfected with cis-reporting NF- κ B-dependent reporter plasmid and were stimulated with CpG ODN, a ligand for TLR9, in the presence or absence of estrogen. Following the stimulation with CpG ODN, the relative luciferase activities were measured. We then assessed the relative copy number of TLR9 mRNA transcripts by sensitive quantitative real-time reverse-transcription polymerase chain reaction in the presence or absence of estrogen. Additionally, the proximal promoter region was extracted for murine tlr9 gene using the murine genome assembly, and the motif discovery was performed using a comparative algorithm.

RESULTS: The presence of physiological concentration of 17 β -estradiol suppressed NF- κ B activation mediated by Toll-like receptor

signaling. However, the level of TLR9 mRNA transcripts was not altered in the presence of estrogen. In the promoter of murine tlr9, several putative cyclic AMP responsive elements, interferon- γ -responsive elements, as well as CAP sites and basic-helix-loop-helix were identified. However, we failed to identify neither the consensus IRF3/ISRE regulatory elements nor the estrogen-responsive elements.

DISCUSSION: The signals generated by the liganded Toll-like receptors are communicated to the changes in gene expression leading to enhanced expression of effector molecules such as cytokines and adhesion molecules. The process depends on the activation of various inducible transcription factors, among which NF- κ B plays an evolutionally conserved and critical role in the triggering of both the innate and adaptive immune responses. Here, we have shown that estrogen suppresses NF- κ B activation mediated by Toll-like receptor independently of its expression, acting as the specific NF- κ B inhibitor on the downstream target(s) of its signaling cascades. Recent reports suggest that LPS-, and CpG ODN-mediated transcriptional activation and nuclear-receptor mediated trans-repression are mediated via IRF3/ISRE regulatory elements. Our report suggests that estrogen appears to trans-repress TLR-mediated signaling cascades on its downstream targets independently of IRF3-MyD88-dependent signaling pathway.

S-63.

TITLE: PROGNOSTIC VALUE OF EARLY VS LATE ACUTE RENAL DYSFUNCTION IN THE CRITICALLY ILL OBSTETRIC PATIENT

AUTHORS: Z. Haddad, R. Souissi, K. Baccar, N. Baffoun, C. Kaddour;

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INTRODUCTION Acute renal dysfunction/failure (ARF) is newly considered as an independent mortality risk factor in the ICU [1]. The time of onset of ARF could have a prognostic impact.

OBJECTIVE To determine prognosis of acquired vs not acquired renal dysfunction.

METHODS Retrospective analysis of prospectively collected data as part of the APriMo study [2]. We defined ARF as serum creatinine level >100 μ mol/l. We defined the early ARF group (E) as renal dysfunction that occurred during maternity management (less than 24 hours before transfer to the ICU) or at day 1 of ICU admission. The late ARF group (L) was defined as renal dysfunction occurring from day 2 of ICU admission. Inclusion criteria: critically ill obstetric patients presenting with one or more of the presenting conditions: severe pre-eclampsia/eclampsia, postpartum haemorrhage, stroke, HELLP syndrome, hemolytic uremic syndrome, and so on. Exclusion criteria: length of stay in the ICU <2 calendar days, chronic renal failure. Setting: patients first managed in a tertiary referral maternity for high-risk pregnancies, then transferred to our independent multidisciplinary ICU. Collected data: demographic, obstetric management, daily SOFA score. Main outcome of interest: vital status at ICU discharge. Adequate statistical tests were used (t test, chi-square test, etc.). $P < 0.05$ was considered significant.

RESULTS Six hundred and forty patients, overall mortality 13.3%, included $n = 223$: 193 in group E and 30 in group L. There was no difference in demographic data, main admission diagnosis between E and L groups. Mean maximum creatinine level: group E = 270 μ mol/l, group L = 220 μ mol/l ($P = 0.15$). Renal replacement therapy: 30/193 and 7/30 ($P = 0.3$). Comparing group L vs group E: L had a higher mortality rate (73% vs 20.7%; $P < 0.001$), duration of mechanical

ventilation (5.8 ± 1 vs 3.5 ± 0.26 ; $P = 0.001$), rate of massive transfusion in the ICU (13/30 vs 34/193; $P = 0.003$) and length of stay (8.9 vs 6.2 , $P = 0.03$). Mean day 1 MOD score summing organ dysfunctions without renal dysfunction: 7.6 ± 3.3 vs 5.5 ± 4 ($P = 0.45$). Mean total maximum MOD score (TM_MODS): 11 ± 6 vs 6 ± 5 , $P = 0.001$. For group E, nonsurvivors (NS) showed significantly more unstable haemodynamic state with a lower diastolic arterial pressure ($P = 0.007$), uterine atonia ($P = 0.001$), transfusion rate in the labor ward/ operating room and ICU stay than survivors (S). For group L, NS vs S: mean MODS at day 1 ICU admission 8.1 ± 3.7 vs 6.2 ± 2.7 , $P = 0.15$), mean TM_MODS (16.2 ± 3.3 vs 7.8 ± 3.1 , $P < 0.001$). NS were paradoxically younger than the S (29 years vs 35 years, $P < 0.01$). Duration of mechanical ventilation was higher among NS ($P = 0.001$). The main diagnosis of admission was postpartum hemorrhage complicating HELLP syndrome or sepsis. Three organ failures lasting >2 days (renal failure not counted) is associated with 100% mortality ($n = 17$).

CONCLUSION Acquired ARF is an important prognostic factor. It is more serious than early ARF for the same level of serum creatinine.

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S-64.

TITLE: EVIDENCE THAT HYPERGLYCEMIA IS ASSOCIATED WITH DECREASED RENAL FUNCTION IN BRAIN DEAD KIDNEY DONORS

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BACKGROUND: The shortage of suitable organ donors has resulted in increased use of extended criteria donors. We evaluated the factors that were associated with elevated creatinine concentrations in brain dead (deceased) kidney donors to determine whether we could improve renal function in these donors.

METHODS: We analyzed medical records and more than 30 variables of the 458 brain dead organ donors in Northern California (January 2005-December 2006). Factors found to be significant on univariate analysis for elevated creatinines (>1.5 mg/dl, one criterion for extended donor) in these donors were then included in a multivariate analysis.

RESULTS: 198 women and 260 male were included in the analysis. The mean \pm standard deviation body mass index was 26 ± 6 . The final glucose concentrations in the donors were greater than 150mg/dl in 96.3% of all donors. The average glucose concentration was 211 ± 41 mg/dl, and the glucose concentration just before cross-clamping and removal of the kidney was 241 ± 68 mg/dl.

Using multivariate analysis to determine which factors were associated with a final creatinine concentration greater than 1.5 mg/dl. Independent factors were gender (OR=2.2, $p=0.008$) and race (OR= 10, $p=0.0007$) of having an creatinine greater than 1.5 mg/dl. Interestingly, DDAVP administration (in 48.6% of donors for treatment of Diabetes Insipidus) was associated with an Odds Ratio =0.2, $p<0.0001$

CONCLUSION: Therefore, it is possible that glucose control, with insulin infusions, might improve creatinine concentrations in these brain dead donors and improve the function of their transplanted kidneys. The protective role of DDAVP is somewhat surprising and warrants additional research.

S-65.

WITHDRAWN

S-66.

TITLE: INFLUENCE OF MUTATIONS IN THE MTHFR GENE ON HOMOCYSTEINE LEVELS AFTER NITROUS OXIDE ANESTHESIA

AUTHORS: P. Nagele¹, B. Zeugswetter², M. Huepfel², M. Mittelboeck², M. Foedinger²;

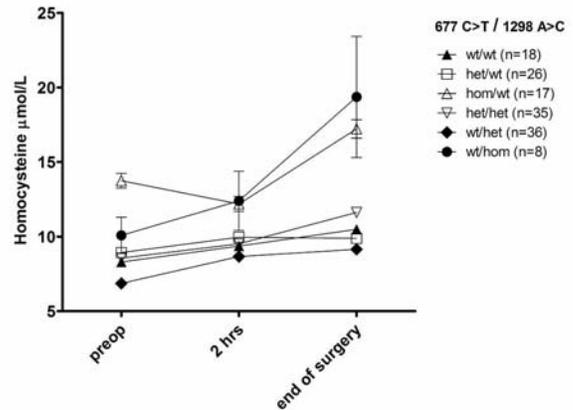
AFFILIATION: ¹Washington University School of Medicine, St. Louis, MO, ²Medical University of Vienna, Vienna, Austria.

INTRODUCTION: Exposure to nitrous oxide (N₂O) leads to a sustained increase in homocysteine levels and an inhibition of all Vit. B₁₂-dependent enzymes. Mutations in the MTHFR gene result in higher homocysteine levels due to inhibited enzyme activity. Based on several case reports that linked disastrous neurological outcomes after N₂O anesthesia with high levels of homocysteine, we hypothesized that patients carrying two common alleles in the MTHFR gene are at a high risk of developing abnormal homocysteine levels after N₂O anesthesia.

METHODS: We included 140 ASA I-II patients who gave written, informed consent and were scheduled for elective orthopedic surgery (based on a 12% prevalence of the most common homozygous MTHFR allele in the general population). All patients received a standardized anesthetic regimen including 66% N₂O. We collected the following blood samples before anesthesia, after 2 hrs and at the end of surgery: homocysteine, folate, Vit. B₁₂, holo-TC. Patients were subsequently tested for two mutations in the MTHFR gene: 677 C>T and 1298A>C (wildtype/ heterozygous/ homozygous). The study was approved by our IRB.

RESULTS: We identified 6 different combinations of the two alleles in the MTHFR gene in our patient population. In all 6 groups, anesthesia with N₂O led to an increase in homocysteine levels (figure). Patients who were homozygous for the 677 C>T (n=17) and 1298A>C (n=8) MTHFR mutation had the highest homocysteine levels after N₂O exposure, reaching potentially detrimental levels (>15 μmol/L). Being heterozygous for both alleles carried a slightly elevated risk of higher homocysteine levels after N₂O compared to patients who were wt/wt or het/wt. We did not observe patients with a double homozygous mutation or the combination hom/het. Baseline patient characteristics and

creatinine and albumin levels among the groups did not differ.



CONCLUSIONS: Our results show that patients carrying a homozygous mutation (677C>T and 1298A>C) in the MTHFR gene are at a higher risk of developing abnormal homocysteine levels after N₂O anesthesia.

S-67.

TITLE: THE IMPACT OF IL-1RN GENETIC POLYMORPHISM ON POSTOPERATIVE MORPHINE CONSUMPTION

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INTRODUCTION: IL-1β is involved in the mechanism of allodynia, and possibly in the development of postoperative neuropathic and chronic pain (1). Recently, it has been demonstrated that the IL-1Ra genotype is the principal determinant of IL-1β bioactivity within the IL-1 gene cluster (2). The present study was designed to understand the relationship between the genetic polymorphism of IL-1Ra (IL1RN) and morphine consumption during the first 24 h of the postoperative period.

METHODS: Morphine consumption and pain scores were evaluated for a 24 h postoperative period in 46 patients undergoing a nephrectomy. Morphine consumption was divided into two sub-groups: low morphine consumers (LMC) (≤ 20 mg/24 h, n = 21), and high morphine consumers (HMC) (>20 mg/4 h, n=25). A visual analogue scale (VAS) for pain was assessed at 2 h, 6 h, 12 h and 24 h postoperatively. DNA was extracted from blood in all patients and the IL-1Ra genotypes were determined by polymerase chain reaction amplification of the variable number of tandem repeats (VNTR) of 86 base pairs (bp) in intron 2 of IL-1Ra gene.

RESULTS: There is no significant difference in VAS at each time point between LMC and HMC groups. A significantly higher 24 h morphine consumption in individuals homozygous for allele IL1RN*1 was observed compared with individuals with IL1RN*2 carriage (genotype 1/2 + 2/2) (31.79 ± 4.128 mg vs. 20.06 ± 3.046 mg, P=0.0446). There was also a significantly higher incidence of homozygous allele IL1RN*1 in the HMC group than in the LMC group and conversely incidence of genotype 1/2 in the HMC group was reduced (table1).

Table 1. IL-Ra polymorphism in two sub-groups of morphine consumption

24 hrs Morphine	Alleles			Genotype				
	IL1RN*1	IL1RN*2	ILRN*3	1/1	1/2	2/2	1/3	3/3
Study group (n=46)	0.684(63)	0.217	0.097	0.52	0.239	0.086	0.065	0.065
)	(20)	(9)	(24)	(11)	(4)	(3)	(3)
≤ 20 mg n=21	0.595	0.261	0.142	0.333	0.428	0.047	0.095	0.095
	(25)	(11)	(6)	(7)	(9)	(1)	(2)	(2)
>20 mg n=25	0.760	0.180	0.060	0.68	0.12	0.120	0.040	0.040
	(38)	(9)	(3)	(17)*	(3)**	(3)	(1)	(1)

The results are expressed as relative values, with absolute numbers in parenthesis.

* p=0.019; **p=0.018 between two groups.

DISCUSSION: IL-1β plays a facilitatory role in pain sensitivity (3). Bessler et al (2) demonstrated that in healthy subjects allele 1 (IL1RN*1) homozygotes release more IL-1β than carriers of at least one IL1RN*2 allele and allele *2 of the IL-1Ra gene (IL1RN*2) is consistently associated with higher IL-1Ra release. These results are in accordance with our present findings that there was a significantly higher 24 h morphine consumption in individuals homozygous for allele IL1RN*1 when compared with individuals with IL1RN*2 carriage. This study shows that polymorphisms in the IL-Ra gene impacts on postoperative morphine consumption.

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S-68.

TITLE: MURINE STRAIN-SPECIFIC DIFFERENCES IN CARDIAC GENE EXPRESSION AND PHYSIOLOGY

AUTHORS: C. N. Chang, R. Agrawal, G. B. Walton, J. Wong, A. J. Patterson;

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INTRODUCTION: Clinically relevant differences exist between commonly used inbred mouse strains. For instance, FVB mice with overexpression of the TNF- α gene have a higher survival rate than mice of mixed FVB/C57Black6 background that overexpress this gene.¹ Strain-specific gene expression patterns are believed to significantly influence phenotype in both transgenic overexpression and knockout mice. We used pressure volume (PV) loop and microarray analyses to determine if significant hemodynamic and cardiac gene expression differences could be identified in three different wild type (WT) mouse strains.

METHODS: We studied C57, FVB and B6129SF WT mice (n=10 each). PV loops were used to compare cardiac performance and compliance. Heat maps were generated and principal components analyses were used to compare cardiac gene expression at baseline and after isoproterenol infusion. Gene expression profiles unique to each WT strain and treatment type were created using 2-way ANOVA and 2-fold filtering. Once gene lists unique to strain and treatment type were generated, we attempted to use class prediction with Fischer's exact test method to identify strain and treatment type of a separate test group of WT mice.

RESULTS: Left ventricle end diastolic volume (LVEDV) significantly increased in all groups following isoproterenol treatment (2 way ANOVA, $p < 0.0001$). Contractility (end systolic volume elastance) decreased in FVB and B6129SF mice after treatment, but did not change significantly for C57 animals (treatment effect $p < 0.0001$, interaction effect $p = 0.01$). In contrast, left ventricle compliance (gauged by the slope of the end diastolic pressure volume relationship) decreased for isoproterenol-treated C57 mice compared to untreated mice. Left ventricle compliance for the FVB and B6129SF mice did not change after isoproterenol administration. Using class prediction

analysis, we were able to correctly identify the strain of 14 out of 15 (93.3%) WT mice in a separate test group using gene expression analysis. We were able to predict whether animals had been treated with isoproterenol in 29 out of 30 (96.6%) study animals.

DISCUSSION: C57 mice developed diastolic dysfunction with isoproterenol treatment, in contrast to FVB and B6129SF mice that developed systolic dysfunction. All three strains experience cardiac remodeling as determined by increase in LVEDV. Each of the strains demonstrated unique cardiac gene expression profiles at baseline and after isoproterenol administration. These unique gene expression profiles allowed us to correctly identify strain and treatment type in a separate test group of WT mice. Based upon these results, we will explore whether cardiac gene expression profiling can be used to predict physiologic outcome after isoproterenol infusion. That is, we will attempt to predict whether other strains of mice will develop systolic or diastolic dysfunction in response to isoproterenol administration.

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Economics

S-69.

TITLE: DOES PAST PERFORMANCE GUARANTEE FUTURE RESULTS? ER VISITS, OUTPATIENT APPOINTMENTS, AND DAY OF SURGERY CANCELLATIONS

AUTHORS: N. Ray, A. Tung, D. B. Glick;

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INTRODUCTION: Case cancellations occurring on the day of surgery (DOS) can adversely impact Operating Room (OR) efficiency, disrupt schedules, and increase hospital costs. The ability to prospectively identify risk factors for cancellations may reduce the incidence of these cancellations. In previous work we demonstrated that patient-related variables account for more than 50% of DOS cancellations at an academic medical center¹. One interesting question is whether DOS cancelled patients differ from patients whose cases are not cancelled with respect to their past interaction with health care (non-operating room) providers. To test this hypothesis, we compared the number of appointments cancelled and ER visits within the past year in a group of patients cancelled on the DOS with a control group of randomly selected patients who were not cancelled.

METHODS: After IRB approval, we prospectively identified all patients from October 2005 to May 2006 who had been cancelled on the DOS. A DOS cancellation was defined as anyone that appeared on the OR schedule the morning of their surgery, but did not undergo surgery that day. Data collected included procedure, date, cancellation reason, and patients' demographic data. We also collected the number of health care provider interactions that were cancelled and visits to the ER during the year leading up to the scheduled surgery. Similar data were also obtained for an equal group of randomly selected patients who actually underwent surgery during the same period. Multivariate logistic regression was used to compare ER use and appointment cancellation data between the two groups. All data were analyzed using STATA (StataCorp LP, College Station, TX).

RESULTS: Over an 8-month period, 921 DOS cancellations were identified out of a total of 10,792 procedures scheduled, for a cancellation rate of 8.5%. We found that a patient was more likely to have a DOS cancellation if he or she cancelled an outpatient

appointment in the year prior to the surgical appointment (Odds ratio = 5.5, $p < 0.001$) or if they visited the ER at our hospital during that year (Odds ratio = 1.48, $p < 0.01$).

DISCUSSION: Identifying patients at risk for cancellations on the day of surgery and targeting interventions at these "high risk" patients may improve OR efficiency and reduce costs. We found that patients with health care provider interactions involving cancelled outpatient appointments and ER visits have an increased propensity for DOS cancellations. Further work is necessary to identify other patient characteristics that predict a DOS cancellation.

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S-70.

TITLE: RELATIONSHIP OF SYSTEM-SPECIFIC DISORDERS IN THE PRE-ANESTHESIA EVALUATION TO HOSPITAL LENGTH OF STAY

AUTHORS: B. Nath, D. G. Silverman, A. Mukherjee, R. G. Stout, N. Holt;

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INTRODUCTION: Anesthesiologists, epidemiologists, and colleagues from other medical fields have sought to assess the impact of preoperative comorbidities on outcome measures such as length of stay (LOS). However, assessment of comorbidities has been limited by traditional reliance on a nonspecific measure of patient illness (e.g., the ASA physical status); and outcome assessment has been impeded by the predominant impact of the varied risk/invasiveness among surgeries. The present study sought to evaluate the impact of attempts to address the aforementioned limitations. First, the nonspecific nature of the ASA physical status score was addressed by applying the newly introduced application of a comparable 1-5 assessment of systemic impact to each bodily system (1). Second, the LOS associated with the range of surgeries encountered at our tertiary care hospital was "normalized" by referencing to the arithmetic mean determined for each procedure by the Centers for Medicare and Medicare Services (2).

METHODS: With IRB approval, post-discharge records of 432 patients were reviewed for: case-by-case LOS; and for the arithmetic mean for LOS for the given surgery based upon Government data bases in the absence of a comorbid condition (2). The arithmetic mean then was subtracted from the actual LOS. Cases where arithmetic mean was more than 7 days and/or the actual LOS was more than 2 days briefer than the arithmetic mean were excluded from analysis. The LOS for the remaining 256 cases was compared to group assignment based upon the preanesthetic H&P in the Pre-Admission Center wherein each of 15 bodily systems (except for that associated with procedural diagnosis) was assigned a 1-5 system-specific comorbid disorder (SSCD) score. The number of systems with an SSCD ≥ 3 was determined. Patients were then grouped according to whether they had none, one, or at least two SSCD; the LOS associated with each grouping was determined.

Groups were compared using ANOVA and one-tailed unpaired t-test.

RESULTS: Patients with one or more SSCD based upon assessment of their pre-anesthetic H&P overall had a significantly greater LOS ($p=0.0008$ by ANOVA). The mean \pm SD LOS for patients with no ("0") SSCD, one ("1") SSCD and more than two (" ≥ 2 ") SSCD was 0.125 \pm 2.05, 0.63 \pm 2.8 and 2.27 \pm 5.2 days, respectively ($p=0.034$ for "0" vs "1"; $p=0.0001$ for "0" vs " ≥ 2 "; $p=0.037$ for "1" vs " ≥ 2 ").

DISCUSSION: Applying a system-specific score to the pre-anesthesia evaluation and referencing to arithmetic means for LOS has enabled documentation of the significant impact of a patient's comorbidities on an outcome such as LOS. The data support the application of system-specific scoring as a relatively simple method for consolidating information, not only for exchange of information among care-givers (1) but also for investigative and administrative purposes.

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S-71.

TITLE: WHO CARES IF I'M ON TIME?

AUTHORS: N. Ray, A. Tung, D. B. Glick;

AFFILIATION: University of Chicago, Chicago, IL.

INTRODUCTION: Improving operating room (OR) efficiency is a longstanding goal of hospitals. Many strategies have been suggested including reducing cancellations, perfecting block scheduling, and limiting surgical first case delays. Interventions such as "OR efficiency education programs" have been suggested to improve inefficiencies like delayed start times¹. However, a simpler intervention could also allow for more first cases to start on time. At our institution, prior to June 2007, operating rooms were not ready to receive the first case of the day until 7:30 AM. After 7:35 AM the case was considered delayed. Starting June 2007, nurses were asked to ready rooms at 7:15 AM, extending the time window for an "on time" start to 20 minutes. We hypothesized that having this greater window of time for arrival would allow more first cases to start on schedule and improve OR efficiency as determined by an earlier OR closure time.

METHODS: After obtaining IRB approval, we used the Optime computerized management system (Epic systems, Madison WI) to prospectively compare the percentage of cases that started "on time" pre- (June-July 2006) and post- (June-July 2007) intervention in both the outpatient (OPT) and general operating room (GOR) settings. All cases were defined as "on time" if arrival occurred on or before 7:35 AM. The final "room closure" time for each OR was also recorded. Only weekday surgeries were included. All times were translated to a 24-hour clock system and data analysis was performed using STATA (StataCorp LP, College Station, TX).

RESULTS: 847 weekday cases were performed before the intervention (OPT n = 310, GOR n = 531), while 841 occurred after (OPT n = 310, GOR n = 537). Post-intervention, a significantly greater percentage of cases started on time in both the OPT (69% VS 50%, p < 0.01) and GOR (75% VS 51%, p < 0.01), compared to pre-intervention. However, the average room closure times were not statistically different before or after the intervention in either the OPT (15:41 ± 1:51 VS 15:41 ± 1:53) or the GOR (16:17 ± 2:48 VS 16:08 ± 3:06) settings.

DISCUSSION: To improve OR efficiency, some interventions have

focused on improving on-time case starts at the beginning of the day. Our results suggest a simple intervention (larger window of arrival) can significantly improve the percentage of cases that start on time. However, simply increasing the number of cases that start "on time" does not lead to the ultimate goal of improving OR efficiency as measured by earlier OR room closure times. More research is needed to identify optimal strategies for maximizing efficient use of OR resources.

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S-72.

TITLE: THE MODIFIED STAGGERED START

AUTHORS: T. W. Cutter, N. Carli, M. O'Connor;

AFFILIATION: University of Chicago Medical Center, Chicago, IL.

INTRODUCTION At most institutions, the start time for the operating rooms is a single instant in time. The nurses and techs staffing the room stretch their preparation work out until the last possible second. Any delay encountered in routine preparation produces a delay in bringing the patient into the room. The net effect is to make it virtually impossible to bring a patient into the operating rooms 'on time.' It is politically problematic to bring a patient into the room 'early', and very easy to be 1 minute 'late'.

At our institution, failed solutions included education programs and reminders. Other solutions contemplated included scheduled staggered starts and rescinding the 'block time' of individual surgeons. In our discussions about our consistent failure, it became apparent that it is impossible to commence anesthesia and surgery in multiple locations simultaneously, and that a system that permitted some flexibility to start times would allow operating room teams to match individual patient starts with their degree of preparation.

METHODS Operating room staff revised their work shifts to start 30 minutes earlier and finish their day 30 minutes earlier. Surgeons committed to completing their paperwork at least 15 minutes prior to the earliest possible start of an operating room. The OR staff also agreed to allow the anesthesia team to bring the patient into the room after they had verified the presence and function of all critical equipment, but before they had completed their setup. When circumstances allowed, the anesthesia teams were allowed to bring the patient into the room as much as 15 minutes prior to the designated "start" time for the day.

RESULTS This intervention resulted in the average first case of the day on-time start increasing from 54% for the preceding twelve months to 80% for the first two months after implementation. There were no apparent incremental costs.

DISCUSSION Rule by decree can produce the appearance of success over the short term, but not over the long term. Changing workflow in a sustained way requires the allocation of resources and planning that is well fitted to the ordinary flow of work. In this instance, all participants

have sustained their commitment to the change in workflow, in part because they directly benefit. Most importantly, sanctions and the threat of sanctions have been unnecessary. Operational solutions that are well adapted to the real flow of work are more likely to be sustained without sanctions; plans that are a poor fit with work are doomed to failure and require strict sanctions to produce even the appearance of success.

S-73.

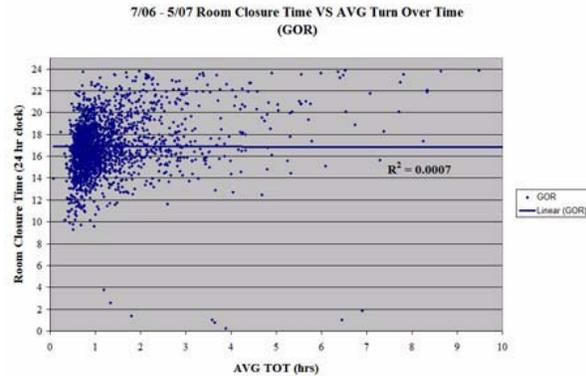
TITLE: WHY RUSH? YOU WON'T GET OUT ANY EARLIER!

AUTHORS: N. Ray, A. Tung, D. B. Glick;
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INTRODUCTION: Reducing turnover time (TOT) has been advocated to improve operating room (OR) utilization and employee satisfaction¹. Shorter TOT may also improve OR efficiency². One potential marker of efficiency is earlier OR closure times, which avoid costs associated with overtime for nurses and other OR personnel. We retrospectively investigated the relationship between surgery TOT and the final time the OR closed at a tertiary care medical center. We hypothesized that a shorter TOT would allow an OR to close earlier in the day.

METHODS: At our institution, the Optime computerized management system (Epic systems, Madison WI) is used to manage operating room utilization. After obtaining IRB approval, we used this system to study room times for all surgical procedures performed between June 2006 and May 2007 in the outpatient surgical facility (OPT) and general operating room (GOR) at a large academic, teaching hospital. Only weekday surgeries were included. TOT was defined as the time between the "room-out" time for one surgery and the "room-in" time for the next. The "room closure" time for each OR was also recorded. All times were translated to a 24-hour clock system and data analysis was performed using STATA (StataCorp LP, College Station, TX).

RESULTS: 12,426 weekday cases were performed during the study period. There was no correlation between daily TOTs and OR room closure times in either the OPT ($r^2 = 2E-05$) or the GOR ($r^2 = 0.0007$) (See figure for GOR data).



DISCUSSION: Previous studies suggested that shorter TOT allows hospitals to improve OR efficiency². One potential marker for increased efficiency is earlier OR closure times. However, our results suggest that shorter TOT does not change the time an OR closes on a given day. Therefore reducing TOT may not be an appropriate focus for hospitals when early OR closures are their goal. Hospitals may do better to examine other causes of inefficiency (e.g., case cancellations or intra-operative stumbling blocks) in their efforts to increase OR efficiency.

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¹Anesth Analg 97 (2003), 1119-1126.
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S-74.

TITLE: FACTORS ASSOCIATED WITH VARIABILITY IN TURNOVER TIMES BETWEEN SURGERIES: A SURVEY USING GENERAL LINEAR MODEL

AUTHORS: D. P. Strum¹, L. G. Vargas²;
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²University of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: Surgical scheduling is complicated by variability inherent in the duration of surgical turnover times (TT). We investigated factors associated with variability in 3 response variables: surgeon TT (STT), anesthesia TT (ATT), and white (idle) turnover time (WTT) between surgeries.

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 the trailing common procedural terminology (CPT) code. We modeled only TT occurring on regular scheduled workdays thus eliminating from analyses TT on weekends and holidays. To ensure the analyses were technically feasible, we divided the data into 20 categories based on main headers of the CPT classification and surveyed TT 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 CPTs with 2 or more surgeons each with a minimum of 10 surgeries. The resultant representative database consisted of 11,946 surgical turnovers, 41 CPTs, and 98 surgeons. A main effects general linear model (ANOVA) was used to investigate the association between TT 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 of STT, ATT, and WTT were analyzed because of prior indications of lognormality of the response variables (2).

RESULTS: Among turnovers associated with 41 CPTs surveyed, main effects ANOVAs for TT were found to be statistically significant at the 0.05 level or better for 27 of 30 main effect ANOVAs (see Table). As a guide to significance, 5% or less of main effects surveyed would be expected to be significant by chance alone.

TABLE: Tabular comparisons of main effect ANOVAs by level of significance for STT, ATT and WTT (n = 11,946 surgeries and 41 surgical procedures in the analytical database).

Tabular Summary of Results (procedure count, column% relative to number analyzed).										
P Value	Age	Anes	ASA	Deman	FODA	In_Hou	Same_su	Gende	Surgeo	TO S
				d	Y	r	e	r	n	U
Surgical Turnover Time (ATT)										
p <= 0.05	2(4.9)	6(22.2)	5(17.2)	8(19.5)	31(79.5)	37(94.9)	20(52.6)	2(6.3)	12(29.3)	20(64.5)
Anesthesia Turnover Time (ATT)										
p <= 0.05	3(7.3)	10(37.0)	7(24.1)	4(9.8)	31(79.5)	37(94.9)	22(57.9)	1(3.1)	9(21.9)	19(61.3)
White Turnover Time (WTT)										
p <= 0.05	3(9.1)	2(10.0)	2(9.1)	4(12.1)	0(0.0)	13(39.4)	18(54.5)	3(11.5)	5(15.1)	5(100)

CONCLUSIONS: Our results suggest that TT is associated with time of day, first of day, same surgeon, surgeon and type of anesthesia and knowledge of the sources of variability in TT are needed to improve modeling of turnovers and thus surgical scheduling. Poor scheduling may lead to sub-optimal utilization of costly **operating rooms**.

REFERENCES: 1. Anesthesia Analgesia 1985; 64:425-431.
2. www.crt.umontreal.ca/scrojopt2006/en/program, 2006.

S-75.

ARE POST-DISCHARGE CODERS FAILING TO CAPTURE DISORDERS IDENTIFIED BY SYSTEM-SPECIFIC SCORING OF THE PRE-ANESTHETIC NOTE?

AUTHORS: B. Nath, N. Holt, A. Mukherjee, R. G. Stout, F. Romberg, D. G. Silverman;

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INTRODUCTION: Administrators and insurers commonly rely on International Classification of Disease (ICD9) coding as the basis for determining a patient's primary diagnosis and complications and comorbidities (CC). These ICD codes, which primarily are determined by post-discharge chart review by specially trained coders, are consolidated into approximately 530 diagnostic-related groups (DRGs). Of these, 413 are based solely on the principal diagnosis; the remaining 117 constitute modifications based upon one or more of potential CC (1). A recent study at an academic medical center noted that information in the pre-anesthesia evaluation had the potential to increase DRG weight to a degree worth \$442,252 (mean \$6,804 per case where discrepancy was noted) over a 12 month period (2). The present study was undertaken to determine the degree to which clinically significant (and potentially financially significant) comorbidities that are identified in the Pre-Admission Clinic note at our institution are not subsequently identified by coders as CC. This was facilitated by a recently introduced system-specific ASA physical status score which applies a 1-5 systemic impact score on system-specific (e.g., cardiac, respiratory) basis (3) and thereby should facilitate identification of potential CC.

METHODS: With IRB approval, the records of 432 surgical patients were assessed for: preoperative system-specific scores and post-discharge ICD9 and DRG classifications. Each pre-anesthetic note was assessed for the number of systems with a system-specific comorbid disorder (SSCD) score ≥ 3 (on the 1-5 scale). Patients with at least one such SSCD then were assessed as to whether they subsequently were assigned a CC by the post-discharge coder. The incidence of such identification (vs. 100% identification) was analyzed using Chi-squared analysis.

RESULTS: 109 patients had one SSCD (in addition to the system

primarily associated with the procedure-related diagnosis); 31 (28.4)% of these were assigned a CC ($p < 0.001$ by Chi-squared). 41 patients had ≥ 2 SSCD; 18 (43.9)% of these had a CC ($p < 0.001$).

DISCUSSION: Although the primary purpose for introducing system-specific scoring of the pre-anesthetic H&P was to facilitate planning and communication among caregivers (3), the present study suggests that it also provides a unique opportunity for real-time recording of patient disorders for administrative purposes. It may help to identify clinically significant morbidities that otherwise might not be recorded.

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1. Diagnostic Related Groups; Definition Manual. Version 14.0. 3M 1996]
2. Anesthesiology 105:A192, 2006
3. Anesthesiology Clinics NA 24:427-459, 2006

S-76.

TITLE: POINT OF CARE HANDHELD ELECTRONIC CHARGE CAPTURE SYSTEM IMPROVES BUSINESS EFFICIENCY

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AFFILIATION: University of Kentucky, Chandler Medical Center, Lexington, KY.

INTRODUCTION: A handheld electronic billing system using a personal digital assistant (PDA) was implemented to allow at point of care and electronic billing. It was hypothesized this would result in faster billing for acute pain management services compared to previous manual charge entry.

METHODS: A one year prospective observational study was performed incorporating this electronic point of care handheld billing system utilizing a Palm T3 (Palm Inc. Sunnyvale, CA) and software from MDEverywhere (MDe) (MDEverywhere Inc. Long Island, NY). Approval was obtained from the University of Kentucky Institutional Review Board with written informed consent waived. All acute pain billing physicians were trained to use the PDA and billing software. After billing information was entered into the PDA, the charges were electronically encrypted and sent to a central billing center. Twelve months of data was examined pre-MDe and compared to a 12 month period post-MDe. Data were analyzed using a paired t-test pre and post MDe. A value of $p < 0.05$ was considered significant.

RESULTS: Total charges for each of the 12 month periods, represented 4051 charges pre-MDe and 5342 charges post-MDe. The number of days from date of service to date of billing for the provided services was 30.5 0.6 days pre-MDe and decreased to 6.7 0.3 days post-MDe which was significant ($p < 0.001$). In addition the average days in accounts receivable significantly decreased from 43.8 1.0 days pre-MDe to 39.4 0.8 days ($p < 0.001$) post-MDe. A net collection rate was calculated with gross cash revenues received during the 12 month periods divided by gross fees. The net collection rate increased from 37.5% pre-MDe to 40.3% post-MDe.

Table: Days to Post Bill

Pre-Electronic	≤ 30 days	31-59 days	60-89 days	> 90 days	Total Charges
01/01/03 - 12/31/03	3108	545	135	263	4051
% of All Charges	76.7%	13.5%	3.3%	6.5%	
Post-Electronic	≤ 30 days	31-59 days	60-89 days	> 90 days	Total Charges
07/01/04 - 06/30/05	5258	30	20	34	5342
% of All Charges	98.4%	0.6%	0.4%	0.6%	

DISCUSSION: Compared to the prior billing system the implementation of a point of care electronic billing using PDAs had a positive impact on net collection rate and significantly decreased the number of days to post charges and the number of days in accounts receivable. This technology was readily adopted by the providers due to ease of use.

S-77.

TITLE: WHAT MINOR ANESTHESIA COMPLICATIONS DO PACU NURSES CONSIDER MOST IMPORTANT?

AUTHORS: P. J. Tan, J. E. Tetzlaff, J. Na, J. Dalton, E. Mascha;
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INTRODUCTION: An article by Macario et al(1) addressed which minor anesthesia complications are most important to avoid based on the patient's perspective. Six of these complications are treated routinely in the post anesthesia care unit (PACU). They are: 1)Pain, 2)Nausea, 3)Vomiting, 4)Shivering, 5)Residual weakness, and 6)Somnolence. We anonymously surveyed our PACU nurses to determine how important they thought these complications were to patients and in what order they would address them. We also wanted to assess what complications were important in preventing a patient's readiness for discharge from the PACU.

METHODS: With IRB approval, we surveyed 81 PACU nurses at our institution in March 2007. A Likert scale from 1-10 was used to assess how important a nurse thought each complication was to patients and how frequently they thought each complication delayed a patients discharge from the PACU. Nurses were asked to rank-order how they would address the complications in a patient presenting with all six simultaneously.

RESULTS: 39 PACU nurses responded (48%). Table 1 shows the results of the survey. Nurses rated pain as most important to patients, however, they chose to address vomiting first. There was agreement on the importance of nausea, pain, and vomiting to patients, however, there was variability in the responses for the other complications. There was also a disparity in the order nurses chose to address somnolence. The four complications PACU nurses thought were most likely to delay a patient's readiness for PACU discharge were: 1) Pain, 2) Hypertension, 3) Hypotension, and 4) Vomiting.

How important are these anesthesia complications to patients and in what order would you treat them?

Complications	Number of Respondents	IMPORTANCE to patients(1=Unimportant and 10= Extremely important) Median [Quartiles]	ORDER to address Median [Quartiles]
Pain	39	10 [10, 10]	2 [2, 3]
Vomiting	39	9 [8, 10]	2 [1, 2]
Nausea	39	9 [8, 10]	4 [3, 5]
Residual weakness	39	6 [4, 8]	5 [4, 6]
Shivering	39	6 [5, 7]	4 [3, 4]
Somnolence	39	5 [4, 7]	5 [2, 6]

DISCUSSION: As no definition of the complications was given, much of the variability in the responses with regards to somnolence, shivering, and residual weakness appears to be related to each nurses' definition of the complication and perception of its severity. For example, on somnolence and residual weakness, write in comments included "depends if their breathing is ok." Nurses' opinions as to the importance of each complication were similar to those found by Macario et al when he surveyed patients. That nurses and patients agree on the importance of these complications should be reassuring in terms of patient satisfaction. Anesthesiologists should make efforts to improve pain control and hemodynamic stability to improve patients' readiness for PACU discharge.

REFERENCES: 1. Anesth Analg 1999;89:652-8

S-78.

TITLE: A NOVEL FORMULA TO DESCRIBE SURGICAL OPERATING LIST 'EFFICIENCY'

AUTHORS: J. J. Pandit¹, S. Westbury¹, M. Pandit²;
AFFILIATION: ¹John Radcliffe Hospital, Oxford, United Kingdom, ²Milton Keynes General Hospital, Milton Keynes, United Kingdom.

INTRODUCTION: Numerous reports have sought ways of improving the efficiency of surgical operating lists, but none has provided an explicit definition of 'efficiency' (1,2). We describe a formula that defines efficiency as incorporating three elements: maximising utilisation, minimising over-running and minimising cancellations on a list (3):

METHODS: We tested this formula in two ways: (A) by applying it to hypothetical (but realistic) scenarios; (B) applying it to data from 48 consecutive elective surgical lists from three gynaecology teams (two at a university hospital and one at a non-university hospital). The latter schedules cases according to predicted durations of operations; the former does not.

RESULTS: In (A), our formula yielded plausible descriptions of the scenarios. In (B), the formula confirmed that a team that schedules cases according to the predicted durations of the operations listed (ie, the non-university hospital team) suffered fewer cancellations (median 5% vs 8% and 13%), fewer list over-runs (6% vs 38% and 50%) and performed considerably more efficiently (90% vs 79% and 72%; p = 0.038; ANOVA) than teams that did not do so (ie, those from the university hospital; Fig. 1).

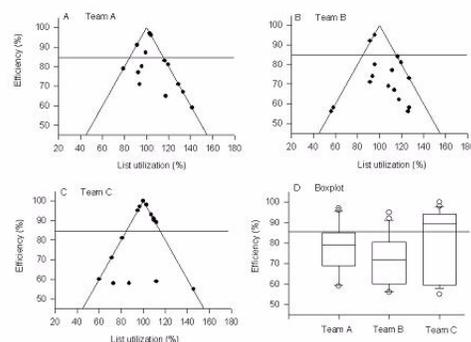


Fig. 1. Graphical representation of formula: efficiency vs list utilisation. The horizontal lines = 85% efficiency. The 'triangles' = lines where no patients are cancelled; any points within this triangle indicates a cancellation occurred. Each point = one list. The panels are for Teams A and B (university center) and Team C (non-university). The boxplot = data from other panels combined.

DISCUSSION: Our novel formula encapsulates much of what is intuitively felt about the planning of surgical operating lists (1-3). Since the factors 'utilisation', 'over-running' and 'cancellation' are also cardinal factors in minimising costs (4), our formula is adaptable to take costs into account: we have demonstrated the formula's ability to distinguish between the performance of different surgical centers.

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(3) Ann Roy Coll Surg (Suppl.) 1995; 77: 304-6.
(4) Br Med J 1994; 398: 138-9.

S-79.

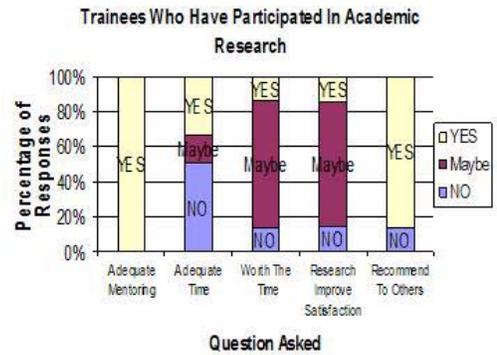
TITLE: RESEARCH DURING RESIDENCY? THE RESIDENT'S POINT OF VIEW

AUTHORS: K. Cummisford, R. Schumann, I. Ahmed;
AFFILIATION: Tufts/New England Medical Center, Boston, MA.

INTRODUCTION Recently, limited academic productivity in US anesthesia departments and declining research with its possible detrimental effects for our specialty has been recognized. Anesthesia residency review committees are critically appraising trainee's research involvement. A targeted effort over one year in our residency program encouraging trainees at all levels in academic project participation resulted in regional and national presentations. We conducted a survey at the end of this period to determine trainee attitudes and perceptions towards research and to elicit possible barriers to their participation.

METHODS Following IRB approval, an anonymous questionnaire was completed by all trainees (18 residents, 3 fellows). Descriptive data analysis and group comparison between trainees involved in research (RT) and those not involved (NRT) was performed using the Fisher exact test. A p-value < 0.05 was significant.

RESULTS Seven of 21 trainees (33%, CAI=1, CAII=4, CAIII=1, Fellow=1) participated in research. Of these, 100% felt adequately mentored and 33% perceived academic time as sufficient, while 50% did not. 86% of RT would recommend research participation to their peers. Few were certain that their time invested in research was worthwhile or improved their satisfaction with residency (Table 1), however, 85% of RT were satisfied with their residency overall versus 71% of NRT (p=0.8). In the NRT group, 33% respectively expected project involvement to improve, not change or decrease their residency satisfaction; 22% were interested in a project, and 64% were not. During training, the CAI year was considered the best to begin trainee research involvement by 71% of RT and 36% of NRT.



DISCUSSION Information on trainees' attitudes to, and needs for research participation during residency is limited. We present our data of trainees that participated in research, as well as their non-involved peers. Our small academic program achieved remarkable residents' research participation within 1 year. Research mentoring was perceived as unproblematic, while adequate time for research was an unmet need. Trainees with research participation would recommend such involvement to their peers, although they were uncertain that research improved their satisfaction with the residency. CAI is the recommended year to initiate academic projects. Although sufficient interest and motivation for research among residents exists, training programs are challenged to provide adequate research time and a culture that values trainee research to increase their participation.

S-80.

TITLE: THE ROYAL COLLEGE OF ANAESTHETISTS STRATEGY TO IMPROVE ACADEMIC ANESTHESIA IN THE UNITED KINGDOM

AUTHORS: J. J. Pandit;
AFFILIATION: John Radcliffe Hospital, Oxford, United Kingdom.

INTRODUCTION: Academic anaesthesia has been struggling in the UK in the past few years. While this is true of many other clinical specialties, not all the issues underlying the crisis are generic. Therefore, Royal College (RCA) Council agreed to a proposal (from Professors Hutton of Birmingham and Wildsmith of Dundee), that a review be undertaken, to make proposals for future development (1).

METHODS: A part-time 'strategy officer' post was appointed after competitive interview to lead the project and report to RCA. The views of key groups outside anaesthesia was sought via a panel of representatives from: the Wellcome Trust, the Vice-Chancellors of UK Universities, the Deans of UK Medical Schools, the Medical Research Council, the Postgraduate Medical Training Board, and from National Health Research and Development. This ensured that any conclusions were consistent with the collective national strategy of funding and training in biomedical research. Views from within the specialty were canvassed by structured questionnaire to heads of academic department, anesthesiologists in charge of training (Regional Advisers), and Specialist Society committees. A literature review informed the process.

RESULTS: The final report made 20 specific recommendations to improve academic anaesthesia (2). The main proposals include: (a) to identify anaesthetic research priorities that integrate with existing priorities identified nationally in other biomedical fields; (b) to make changes within the specialty that integrates academic anaesthetic training with new nationally-funded training programs for clinical academics (this includes an emphasis that future academic anesthesiologists undertake formal PhD training at an early stage in their career); (c) proposals for more integrated and targeted funding of anaesthetic research; (d) creation of an Academic Institute (located within RCA) to help achieve the recommendations.

CONCLUSIONS: In the US, specialties have flexibility to modify their training programs to influence the balance of applicants into the specialty. This is impossible in the UK, given the direct influence of government via the Postgraduate Medical Training Board (3). The RCA report is thus a pragmatic document. It proposals are achievable because (a) it identifies clear benefits for participants in the strategy; (b) it engages national non-anesthetic organizations that manage UK biomedical science; (c) its proposals are essentially cost-neutral, requiring only reorganization of current funding rather than injection of new capital. The early success of the strategy is indicated by representation of anesthesiology trainees on the new academic training programs; increased funding for anaesthesia; and steps towards creation of a national Institute for Academic Anaesthesia (4).

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- (2) At: www.rcoa.ac.uk/academic
- (3) Anesthesiology 2006; 105: 635-6.
- (4) Br J Anaesth 2006; 96: 411-414.

S-81.

TITLE: INCORPORATING A PERSONALITY ASSESSMENT TOOL INTO AN ACADEMIC ANESTHESIA DEPARTMENT TO MORE EFFECTIVELY INTERACT WITH AMBULATORY PATIENTS

AUTHORS: O. Gottlieb;

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INTRODUCTION: Anesthesiologists must often gain the trust of an ambulatory patient in a short period of time. "The Platinum Rule"(1) claims that rather than treating people the way you would want them to treat you, a more effective approach would be to treat people the way they want to be treated. Being able to quickly determine what a patient's personality style can be used to more quickly and effectively build trust.

METHODS: The DISC assessment method uses four styles (Dominant, Influential, Steady, and Conscientious) to help facilitate teamwork, strategy, negotiations, and interpersonal communications.(2,3) Whereas everyone's personality is composed of differing levels of all of the four major styles, most people are dominated by one. Every style has strengths and weaknesses and every style deals with coming to the hospital for a procedure differently.

The assessment survey contains 28 sets of 4 words. For each set, the subject is asked to mark the word that most describes him/herself and the word that least describes him/herself. This forced choice exam has been tested for reliability and validity and has been shown to score highly on both.

Taking this clinically, a more dominant anesthesiologist would benefit from being more empathetic when meeting a patient who is looking more for understanding and compassion than hard data. Some patients inquire as to every detail about the anesthetic plan and some just want to chat about the weather.(4)

RESULTS: While it is not appropriate to submit every patient to a personality style assessment exam, it is practical to educate residents (and attending) to 1) better understand themselves, and 2) pick up on certain cues from the patient and his/her chart, family, and nurse. Beyond a determination of the residents' styles, a basic appreciation of the four general styles must be taught. Identifying a patient's preferred

style can be tremendously helpful. Using both the knowledge about themselves and about the styles in general will save time in gaining trust and make the patient feel more comfortable with the anesthesia team and plan.

DISCUSSION: The time and place to begin incorporating the DISC assessment tool is in the academic anesthesia program early in the residency. Residents are learning everything there is to know about being a competent and skilled anesthesiologist. Learning about themselves and how to "read" patients' styles should be taught in conjunction with pharmacology and physiology. If that is accomplished, we will be moving closer to meeting our goal of graduating more effective anesthesia consultants.

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S-82.

TITLE: USING ESTIMATES OF OPERATING TIMES TO MATCH SURGICAL CAPACITY TO DEMAND

AUTHORS: J. J. Pandit¹, S. Westbury¹, M. Pandit²;

AFFILIATION: ¹John Radcliffe Hospital, Oxford, United Kingdom, ²Milton Keynes General Hospital, Milton Keynes, United Kingdom.

INTRODUCTION: We investigated whether demand for surgical services could be estimated in terms of the time required to undertake elective operations booked from clinic, then to match this with the capacity available (capacity also described in similarly as 'time available') (1).

METHODS: We studied the gynecology service in six steps: [A] time for 14 common procedures were estimated by combination of questionnaire to senior surgeons, anesthesiologists and nurses, and by data from OR logs. [B] uncommon operation data retrieved only from OR logs. [C] these time estimates were applied to bookings from gynecology clinics to yield demand (ie, min/week needed for surgery). [D] we estimated time consumed for emergencies scheduled onto elective lists. [E] we estimated the OR time available to gynecology. [F] we assessed 'efficiency' according to our new formula (2) to exclude the possibility that poor performance was influencing our data.

RESULTS: The mean demand (95% CI) was 1,980 (1,728 - 2,232) min/week (parts A-C). Emergency demand was an extra 591 (490 - 692) min/week (part D). Existing capacity of 1,680 min/week fell far short of these demands (part E) The efficiency of the service was acceptable making it unlikely that poor performance was an adverse influence (part F).

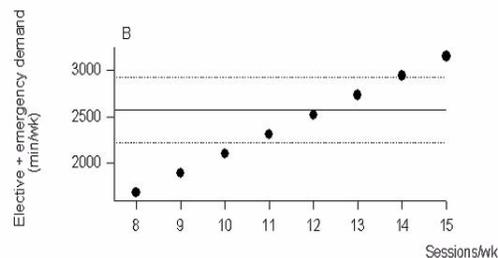


Fig. 1. Demand vs different levels of available capacity (in sessions/wk; a session = 3.5 hours = 210 min). The solid horizontal line is mean demand and dotted lines are the 95% confidence intervals. Solid circles = time available for each level of capacity.

DISCUSSION: Current capacity will inevitably lead to a rise in the waiting list for surgery. Our analysis provides a range of solutions that can be described in terms of a statistical probability that capacity almost certainly fails to match demand (at capacities of <2,470 min/week) to almost certainly absorbs demand (at >3,073 min/week) (Fig.1). This can guide strategic decisions (3). Our approach differs from traditional analyses based on 'queuing theory', where demand for the service is modeled in terms of discrete 'arrivals' (or numbers of patients) (4). In contrast, we place emphasis on the aggregate time demands created by the 'arrival'.

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- (1) Health Policy 2007; 1: 1-11.
- (2) Abstract presented to 2008 IARS Meeting.
- (3) J Healthcare Management 2003; 48: 82-98.
- (4) J Roy Stat Soc 1955; 118: 324-35.

Education and Patient Safety

S-83.

TITLE: INFLUENCE OF SEVOFLURANE FORMULATION WATER CONTENT ON DEGRADATION TO HYDROGEN FLUORIDE IN COMMERCIAL VAPORIZERS

AUTHORS: E. D. Kharasch¹, G. Subbarao², D. A. Stephens², K. R. Cromack², J. M. Meinhold², M. D. Saltarelli²;

AFFILIATION: ¹Washington University, St. Louis, MO, ²Abbott, Abbott Park, IL.

INTRODUCTION: Exposure of sevoflurane to Lewis acids (LAs) can produce the toxic degradant, hydrogen fluoride (HF). Water prevents such degradation and HF production. Sevoflurane (Ultane[®], Abbott) was reformulated in 1997 to contain >300 ppm water to ensure patient safety. New formulations of sevoflurane, without such water content, are being sold. Commercially marketed sevoflurane vaporizers potentially contain LAs that may interact with sevoflurane. The purpose of this investigation was to assess the relative stability of three sevoflurane products with different water contents, when stored in three commercial vaporizer models.

METHODS: Three sevoflurane products (two with low water content^{1,2} and one with high water content³) were placed in three vaporizer models (Draeger 2000, GE/Datex-Ohmeda Tec 7, and Penlon Sigma Delta). Vaporizers were stored for 3 weeks under accelerated stability conditions to model longer-term room temperature storage conditions. Aliquots of sevoflurane were removed from the vaporizers each week and analyzed for degradants (including fluoride ion, indicating HF), pH, and water content.

RESULTS: Both low-water sevoflurane products stored in Penlon Sigma Delta vaporizers degraded extensively, resulting in substantial increases in fluoride and reduced pH at all time points (maximum fluoride: Baxter = 444 ppm; Minrad = 600 ppm;). In contrast, the high-water sevoflurane product (Ultane[®]) remained stable (maximum fluoride = < 0.4 ppm). In addition, substantial degradation of the sight glass and metal filler shoe (reflecting HF-mediated glass etching and metal corrosion) occurred in the Penlon Sigma Delta vaporizers containing low-water but not high-water sevoflurane products. Concentrations of specific and total impurities (determined by gas

chromatography) were consistent with the fluoride and pH results. No degradation was seen with any sevoflurane formulation following storage in the other two vaporizers.

CONCLUSION: The data demonstrate that time-dependent, LA-mediated degradation of low-water sevoflurane products occurs following their storage in sevoflurane vaporizers, resulting in HF production, low pH, and degradation of vaporizer components. The increased water found in the high-water formulation fully inhibits HF production and vaporizer corrosion.

REFERENCES:

¹Baxter, Deerfield, IL, US (57 ppm water), ²Eraldin[®] (19 ppm water) Minrad/Richmond Laboratories, Buenos Aires, Argentina, and ³Ultane[®] (352 ppm water), Abbott Laboratories, Abbott Park, IL

S-84.

TITLE: INFLUENCE OF FORMULATION WATER CONTENT ON SEVOFLURANE DEGRADATION IN VITRO BY LEWIS ACIDS

AUTHORS: K. Cromack¹, E. D. Kharasch², D. A. Stephens¹, G. Subbarao¹, J. M. Meinhold¹, M. D. Saltarelli¹;

AFFILIATION: ¹Abbott, Abbott Park, IL, ²Washington University, St. Louis, MO.

INTRODUCTION: Sevoflurane exposure to Lewis acids such as metal oxides can cause sevoflurane degradation to hydrogen fluoride (HF) and other potential toxins. Water prevents such degradation and HF production. Sevoflurane (Abbott Ultane[®]) was reformulated in 1997 to contain >300 ppm water to ensure patient safety. New formulations of sevoflurane, without such water content, are being sold. The purpose of this investigation was to compare the influence of formulation water content on the degradation of sevoflurane in vitro by activated alumina, a Lewis acid.

METHODS: Two commercially available sevoflurane products (Sevones[®], Baxter, Japan, 14 ppm [low] water and Ultane[®], Abbott Laboratories, 345 ppm [high] water) were exposed to a range of alumina (source: Sigma-Aldrich) concentrations (0, 0.02, 0.04, 0.08, and 0.16 mg/mL) using an accelerated model of storage stability. Degradation products were quantified by gas chromatography after sevoflurane storage at 55°C for 24 hours, simulating one month storage at 20°C.

RESULTS: Increasing alumina concentrations caused progressively greater degradation of low-water, but not high-water sevoflurane (Table). Sevoflurane degradant concentrations were 40- to 90-fold greater in low-water vs high water sevoflurane formulations.

Table: 24 Hour Stability

Alumina (mg/mL)	0	0.02	0.04	0.08	0.16
Sevoflurane formulation	Mean total degradation products (ppm)				
Low-water					
(Sevones [®] , Baxter, Japan)	132	1979	2898	4163	6232
High-water					
(Ultane [®] , Abbott Laboratories)	51	52	59	63	67

CONCLUSIONS: Degradation of low-water sevoflurane occurs following exposure to Lewis acids. Higher water content is protective against this degradation.

S-85.

TITLE: LIVER TRANSPLANT ANESTHESIA: LOOKING FOR CONSENSUS OF PRACTICE

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INTRODUCTION: With over 100 medical centers in the United States performing liver transplantation, there are very few formal fellowship training programs that teach an evidence based curriculum focused on the multitude of dilemmas that arise during the anesthetic management for liver transplantation. Our pilot survey of several acknowledged centers of excellence in the field revealed that a wide variety of techniques are employed, and lead to a detailed query of practice.

METHODS: With IRB approval, the UNOS web site was examined and transplant anesthesia directors in programs performing more than 65 liver transplants per year were e-mailed a detailed survey to question the major components of anesthetic management ranging from line access, thromboelastography (TEG), veno-venous bypass, treatment of reperfusion syndrome, coagulation disorders, invasive monitoring and medication usage. There were 27 responders.

RESULTS: Among the responders there was no evident consensus of practice. TEG is used in 44% of centers. TEE and PA catheters are used by 50%, while 50% use only PA catheters. Only 15% use veno-venous bypass routinely, however 48% utilize it when necessary. Cell saver is used in 63% of centers with 50% exclusion for coexisting malignancy. There is a wide range of understanding of the pathophysiology of reperfusion syndrome and its treatment. For hepatorenal syndrome, 22% use dialysis during transplantation while 33% occasionally employ it for severe electrolyte disturbances. Platelet transfusions are routine, and 96% employ antifibrinolytics. For central venous access 52% use ultrasound guidance for placement and 74% use the Belmont rapid infuser. By post-op day (POD) 3 all patients are extubated while 59% are extubated on POD 1. Recombinant factor 7 is only used for uncontrollable bleeding.

DISCUSSION: Our data demonstrates a wide disparity of practice. Thromboelastography, which reveals information concerning the “dynamics” of clot formation and guides administration of blood

products and antifibrinolytics¹, is only used in less than half of the centers. The lack of consensus on the understanding of reperfusion syndrome and its treatment leaves a broad area of research that has not yet been addressed by our clinicians. On the other hand, the number of centers using ultrasound guidance for placement of central lines, and the increasing use of TEE, is indicative of practice improvement. The wide use of antifibrinolytics and platelets demonstrates a high level of confidence by both surgeons and anesthesiologists that the hepatic artery and portal vein anastomoses will not thrombose². The emergence of liver transplant panels at national and international meetings clearly reflects a growing interest in our pursuit to provide seamless anesthesia for our patients, and to generate a consensus for practice and improvement in this field.

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S-86.

TITLE: THE EFFECT OF GLYCOPYRROLATE AND NEOSTIGMINE ON BACTERIAL GROWTH

AUTHORS: I. Batai¹, M. Bauer¹, R. Batai², M. Kerenyi²;

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INTRODUCTION: Contaminated intravenous medications pose a serious infection risk if the drug supports bacterial growth (1). Neostigmine and glycopyrrolate may be prepared well before administration. In this study we investigated bacterial growth in the above mentioned preparation, in glycopyrrolate and in neostigmine. Not only the common microorganisms encountered during infectious complications but the recently arising extended spectrum β -lactamase (ESBL) and metallo- β -lactamase producing strains were also included in the paper.

METHODS: The growth of *Staphylococcus aureus* (ATCC 23923), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), clinical isolate of *Klebsiella pneumoniae* ESBL, MRSA, and metallo- β -lactamase producing *P. aeruginosa* in glycopyrrolate 200 $\mu\text{g mL}^{-1}$ (pH 2.4), in neostigmine 2,5 mg mL^{-1} , 0,5 mg mL^{-1} (pH 5,3) and in the mixture of neostigmine 2,5 mg mL^{-1} and glycopyrrolate 500 $\mu\text{g mL}^{-1}$ (pH 3,5) were investigated. Ten μL bacterial suspension was inoculated into the above medications and kept at room temperature. The initial bacterial count was 5×10^3 colony forming units (cfu) mL^{-1} . At 0, 1, 2, 3, 4, 6, and 24 hours 10 μL was plated on Mueller - Hinton (MH) agar. Having incubated for 24 hours at 37°C the cfu was counted. The method was described in details elsewhere (2). Saline 0.9% and MH broth controls were also applied. Two-way analysis of variance served as the statistical method.

RESULTS: Glycopyrrolate killed all Gram negative strains within 1 hour but staphylococci survived for 6 hours. The mixture of glycopyrrolate and neostigmine reduced the cfu only after 3 hours. Both neostigmine preparations were bacteriostatic for the examined strains.

CONCLUSIONS: All examined preparations are safe as far as infection control is concerned as none of them supported bacterial growth. The low

pH of glycopyrrolate may contribute to its antibacterial effects.

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S-87.

TITLE: REMOVABLE DENTAL APPLIANCES IN ANESTHESIA - RESIDENCY TRAINING PROGRAMS ROUTINELY VIOLATE JCAHO STANDARDS

AUTHORS: D. R. New, D. Hall, A. Kuppusamy, D. Mann;

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INTRODUCTION: The Joint Commission on Accreditation of Healthcare Organization (JCAHO) states in its guidelines that "Before going to the preoperative 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, "toothless surgeries" are not consistently performed in our institution, with removable dental appliances (RDA) remaining untouched. Therefore we wished to determine to what extent (if any), do other anesthesia residency training programs tolerate the presence of RDAs perioperatively.

METHODS:

- After IRB approval, we surveyed the 145 ACGME-approved anesthesia residency training programs regarding RDAs in the perioperative period.

- Surveys were mailed once and follow-up emails were sent twice to non responding programs.

- Survey questions included the presence of RDAs during various anesthetic techniques, timing of RDA removal/reinsertion, procedures/protocols for RDAs, and known complications related to these devices.

RESULTS: We mailed 145 surveys and received 46 responses (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.

DISCUSSION:

- This investigation was conceived after an incident in our institution during which orotracheal intubation proceeded in the presence of dentures secondary to surgeon and patient insistence.

- Over 17% of the surveyed institutions tolerated the presence of RDAs for oral intubation, over 60% during regional anesthesia, and over 80% for cases performed under local anesthesia. Reasons for this were not assessed.

- We postulate that political/economical realities may play a significant role as with the incident in our hospital. A Google internet search revealed that all 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.

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- (3) Niger Postgrad Med J 2005; 12:65-6
- (4) Health Serv Res 2001; 35:1347-55

S-88.

TITLE: THE HUMAN PATIENT SIMULATOR TO ENHANCE LEARNING AMONG MEDICAL STUDENTS IN THE MANAGEMENT OF CRITICALLY ILL PATIENTS

AUTHORS: Z. Hassan, T. McLarney, P. A. Sloan;

AFFILIATION: University of Kentucky, Lexington, KY.

INTRODUCTION: Human patient simulators (HPS) have demonstrated educational value for teaching critical care skills without exposing real patients to risk.^{1,2} Our department has created a program on the HPS which exposes final-year medical students to a simulated patient with a sudden and life-threatening illness. The purpose of this study was to develop and evaluate the efficacy of the HPS to enhance learning among medical students in the management of the critically ill patient.

METHODS: A 40-minute clinical scenario of a critically ill patient was presented to small groups (5 students) of final-year medical students using the HPS. Ninety-one students completed the short course. The content and objective criteria for the structured scenario were developed by a multidisciplinary group of experts.³ During the scenario, students evaluated and managed a floor patient with sudden hypoxia and hypotension, including airway management (intubation), blood pressure support, recognition of anaphylaxis, and recognition and treatment of myocardial ischemia. Students self-assessed their clinical skills before and after the course using a six-item questionnaire with a 5-point Likert scale (1=not competent; 5=very competent). All students completed a 10-item evaluation (1=strongly disagree; 5=strongly agree) of the HPS short course.

RESULTS: Students agreed [mean (S.D.)] very strongly that the HPS course was a valuable educational experience [4.9 (0.3)] and that the HPS helped improve clinical skills [4.8 (0.4)] for the management of the critically ill patient. Students showed significant improvement ($p < 0.01$) in all areas of clinical skills self-assessment (pre- to post-course) including [mean (S.D.)] competent to manage a critically ill patient [1.8 (0.7) to 2.8 (1.0)], competent to manage the airway [2.2 (0.7) to 3.0 (0.8)], and comfortable with independent judgment of the critically ill ward patient [2.4 (0.8) to 3.1 (0.7)]. All students agreed that

the HPS was realistic [4.8 (0.4)], the HPS provided opportunity to practice clinical skills in the care of the critically ill patient [4.9 (0.3)], and that the HPS should be used regularly in the training of medical students [4.9 (0.2)]. Students agreed that the small group format was beneficial to learning [4.9 (0.3)].

DISCUSSION: 1) The HPS is a valuable and novel instructional format to teach essential clinical skills in the assessment and management of the critically ill patient to medical students. 2) Medical students demonstrated learning clinical skills in the management of the airway. 3) The HPS short course was realistic and helped prepare final-year medical students for internship. 4) Use of the HPS should be encouraged in the training of medical students.

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S-89.

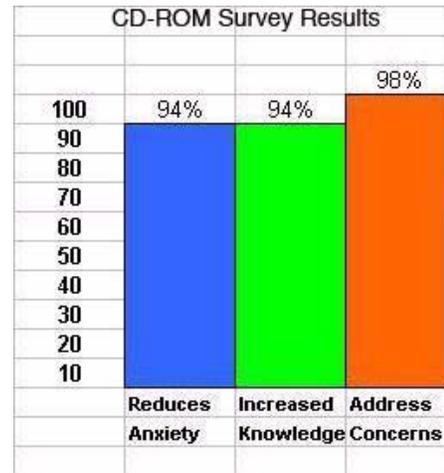
TITLE: EVALUATION OF GINNY AND ERNIE'S SURGICAL DAY: A GUIDE TO PEDIATRIC ANESTHESIA

AUTHORS: M. P. Carson¹, M. Wood², R. Kazim², L. Sun²;
AFFILIATION: ¹Columbia University, New York, NY, ²Columbia University College of Physicians and Surgeons, New York, NY.

INTRODUCTION: Preoperative care and anesthesia administration can be a source of anxiety for pediatric patients. Parents wanted information about anesthesia including risks and presurgical assessment (1). A previous study had shown that patients educated with video tapes prior to surgery were more relaxed and better informed. (2). We designed an interactive CD-ROM for home use by parents and children that is simple to operate, fun, informative, and easy to understand. It aims to inform children and their families about issues regarding anesthesia and improve their experience. To test the effectiveness of this CD-ROM, we designed a 9 question survey and distributed to the families who received the CD-ROM.

METHODS: After IRB approval, we approached all families receiving our CD-ROM to perform the following assessment: pre-CD-ROM knowledge of pediatric anesthesia, post CD-ROM knowledge of pediatric anesthesia and patient satisfaction in this group. The four areas we assessed were (a) perioperative anxiety (b) knowledge of pediatric anesthesia (c) addressing concerns (d) the overall quality of the content. In the first three areas, we requested a yes or no response, and applied a Likert scale from 1-10 (10=excellent) for the overall quality of the content.

RESULTS: A total of 250 CD-ROM were distributed over the past year: 59% were cardiac surgical patients and 41% were urological patients - the two services with the greatest volume. 100 questionnaires have been returned to date. An overwhelming positive results was solicited in all three areas: Perioperative anxiety (94%), knowledge of pediatric anesthesia (98%), and addressing concerns (98%). The overall quality of the contents was 8.75+/- 1.57.



DISCUSSION: Our results demonstrate that this CD-ROM is a useful adjunct in providing information. Our results demonstrate that this CD-ROM is an useful adjunct in providing information. Based on our survey response, the results were positive. Families are better prepared to provide histories of medical problems and the use of medications at home since the CD-ROM contains a section dealing with medical backgrounds including forms that can be filled out at home. Our goal is that the continued use of this helpful guide would significantly improve patient satisfaction.

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S-90.

TITLE: A MINITAB MACRO FOR NONPARAMETRIC POST HOC PAIR-WISE COMPARISONS AFTER FRIEDMAN'S TEST AND KRUSKAL-WALLIS TEST

AUTHORS: S. Mantha¹, M. F. Roizen², J. F. Foss²;
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INTRODUCTION: Nonparametric analysis of variance (ANOVA) of data between more than two groups requires the use of Friedman's test for repeated measures (comparison of data at different time periods in a particular group) and the use of the Kruskal-Wallis test for independent measures (comparison of data in different independent groups). Statistical significance, if obtained in the initial ANOVA, indicates that at least one of the conditions differs from at least one other condition. It does not tell the researcher which one is different, nor does it tell how many groups are different from each other. Such inference requires the use of post hoc pair-wise comparisons.¹ Although the computational scheme for post hoc pair-wise comparisons analysis is easy to comprehend, the algebraic calculations are tedious for repeated use.

METHODS: Minitab (Minitab Inc., State College, Pennsylvania) is statistical software widely used for medical applications. Although Minitab software does not provide facilities for post hoc pair-wise comparisons after Friedman's test or Kruskal-Wallis test, the software allows one to write macros. A macro is a set of commands, prepared in text file format and stored in a file, to automate various calculations. We describe Minitab macros (for Release 10 and above) to perform post hoc pair-wise comparisons after the Friedman's test and the Kruskal-Wallis test. The macro for pair-wise comparisons after Friedman's test uses input from two columns in the Minitab's worksheet: one column with sample size being located in its first row and rank sums in another column. The macro for pair-wise comparisons after the Kruskal-Wallis test also uses input from two columns in the Minitab's worksheet: one column with sample sizes and average ranks in another column. After the macro is invoked, the user is asked whether the all pair-wise comparisons are required or only comparisons with the baseline value are required. After the appropriate response from the user, the macro

performs the required calculations and yields an output. The macro was validated using several sets of data coupled with manual calculations and using illustrative data from textbooks.

RESULTS: Macro validation revealed satisfactory performance of the macro coupled with speed. For example, the analysis for 100 pairwise comparisons takes few seconds.

DISCUSSION: Commonly used statistical packages do not have built-in functions to do the pairwise comparisons, but there are macros available in SAS and S-plus (function) to do such pairwise comparisons after Kruskal-Wallis. In the case requiring comparisons after Friedman's, test statistical experts tend to program in SAS or other similar packages. Following the presentation of this abstract, the macro will be made available on the personal website of the first author.

- REFERENCE**
- Siegel S, Castellan NH. Nonparametric statistics for the behavioral sciences. 2nd ed. New York: McGraw-Hill, Inc, 1988.

S-91.

TITLE: EVALUATION OF THREE DIAGNOSTIC TESTS IN THE DIAGNOSIS OF ANAESTHETIC RELATED ANAPHYLAXIS USING LATENT CLASS MODELLING.

AUTHORS: P. McKinnon¹, M. M. Fisher²;

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INTRODUCTION: In the investigation of anaesthetic anaphylaxis, none of the three commonly used tests, mast cell tryptase (MCT), intradermal skin tests (IDT) and drug specific antibodies (radioimmunoassays) (RIA) performs adequately for one to be considered the gold standard. Latent class modelling, a statistical method that treats the disease state as an unknown or latent variable, can be used, where no gold standard exists, to provide estimates of diagnostic test performance. This study using both conventional methods and a latent class model will assess each test's performance in patients with suspected anaphylaxis during anaesthesia.

METHODS: One hundred and forty-two patients with clinical features suggestive of anaesthetic related anaphylaxis were investigated at an anaesthetic allergy clinic. All had blood sampled at an appropriate time for MCT and had specific RIAs measured and IDT performed for the relevant drugs. A separate ROC curve analysis was performed for the MCT assay to determine its diagnostic cutoff point. Positivity for the IDT and RIA was determined by reference to previously established criteria (1, 2). Estimates of sensitivity, specificity, and positive and negative predictive values were obtained by conventional means and by a latent class model (fitted using the LCAP software (3)).

RESULTS: Anaphylaxis was diagnosed in 81 patients (57%). The diagnostic cutoff point for the MCT assay was 4.06 ng l⁻¹ (86% sensitivity and 97% specificity). The traditional and latent class estimates are summarised in the table. The performance of MCT and IDT was not significantly different in the latent class model, however in this model, the sensitivity and specificity of the RIA improved.

	Conventional Statistical Analysis		Latent Class Analysis	
	Sensitivity	Specificity	Sensitivity	Specificity
Mast cell tryptase	86.4 (79 - 93.9)	96.7 (92.2 - 100)	85.2 (77.4 - 92.9)	96.7 (95.3 - 100)
Intradermal skin test	92.6 (86.9 - 98.3)	91.8 (85 - 98.7)	95.1 (90.3 - 99.8)	96.7 (92.3 - 100)
Radioimmunoassay	69.1 (59 - 79.2)	91.8 (84.9 - 98.7)	74 (64.5 - 83.6)	100 (100 - 100)

Values expressed as% (95% Confidence intervals)

DISCUSSION: Generally, the latent class model agrees with the results from the conventional statistical analysis and no test can be regarded as the gold standard. The "best" test (reference test), is the IDT with over 90% sensitivity and specificity. The RIA is the poorest performing test (70% sensitivity), but in the latent class model it's specificity increased to 100%. This result should be interpreted with some caution as biased estimates in a latent class model occur when the conditional independence assumption fails, as might have occurred here.

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S-92.

TITLE: TRENDS IN BILATERAL TOTAL KNEE REPLACEMENT: 153,259 HOSPITAL DISCHARGES IN THE UNITED STATES BETWEEN 1990 AND 2004

AUTHORS: S. C. Reid¹, L. K. Gaber², M. C. Besculides³, A. González Della Valle⁴, S. G. Memtsoudis¹;

AFFILIATION: ¹Department of Anesthesiology, Hospital for Special Surgery, Weil Medical College of Cornell University, New York, NY, ²LKG Consulting, Plainsboro, NJ, ³Mathematica Policy Research, Inc., Princeton, NJ, ⁴Department of Orthopaedics, Hospital for Special Surgery, Weil Medical College of Cornell University, New York, NY.

INTRODUCTION: The debate over the safety and practice of bilateral total knee arthroplasty continues to be a prevalent topic. This proves to be a concern for anesthesiologists as they seek to ensure the safety of the patient by familiarizing themselves with trends and any potential concerns related to the bilateral procedure. There has clearly been an increase in the amount of procedures being performed and the purpose of this study was to identify trends associated with the increase of patients undergoing bilateral total knee arthroplasties. We hypothesized that substantial changes have occurred over time.

METHODS: We analyzed information collected for the National Hospital Discharge Survey (NHDS) from 1990 to 2004, to elucidate temporal changes in the demographics (including comorbidity profiles), hospital stay, and in-hospital complications of patients undergoing primary bilateral total knee arthroplasties (BTKA) in the United States. Data collected for each year between 1990 and 2004 in the NHDS with discharges after BTKA (ICD-9-CM 81.54 code occurring twice) were included in the sample. Three five-year periods were created (1990-1994, 1995-1999, 2000-2004) to facilitate temporal analysis. Temporal changes in patient related and health care variables were analyzed. Trends in comorbidity profiles, procedure related complications, and length of stay were studied.

RESULTS: We identified a total of 153,259 hospital discharges. The number of BTKA's performed increased 153% over the 15 years studied. Length of stay decreased from an average of 9.17 days to 4.68

days. An increase in both, the proportion of discharges to long- and short-term care facilities and in the proportion of procedures performed in smaller hospitals was noted. Comorbidity burden increased, while procedure related complications decreased by more than half.

DISCUSSION: We identified significant changes in the majority of variables studied. The risks procedure related complications decreased. Further analysis and additional studies are necessary to identify causal relationships and define the impact of these changes on various aspects of the health care system.

S-93.

TITLE: PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN A COHORT OF PATIENTS WITH MAJOR DEPRESSIVE DISORDERS PRESENTING FOR ELECTROCONVULSIVE THERAPY

AUTHORS: K. W. Smith, P. Teman, M. Vukin;
AFFILIATION: University of Utah, Salt Lake City, UT.

INTRODUCTION: Recent reviews in the anesthesiology and surgical literature have emphasized the importance of recognizing patients with obstructive sleep apnea (OSA).^{1,2} A recent study has shown that the prevalence of OSA in a surgical population of 3.2% is in agreement with estimates of clinically significant OSA of 4% in men and 2% in women in the general population.³ The prevalence of breathing-related sleep disorders in subjects with major depressive disorders has recently been reported to be 18%.⁴ We have done a retrospective analysis to determine the prevalence of OSA in a cohort of patients presenting to our neuropsychiatric hospital for electroconvulsive therapy (ECT) over the past 5 years.

METHODS: All anesthetic records, including the pre- and post-anesthetic evaluation are available in coded electronic data tables for this patient population. Following exemption from our IRB, records were analyzed for all patients having ECT between 8/1/2002 and 7/31/2007. De-identified demographic data with patient problem lists were grouped into diagnostic categories using ICD9 codes. A diagnosis of OSA was recorded if the patient had previously undergone a sleep study and therapy had been prescribed. Analysis was done using JMP statistical software (SAS Corp.)

RESULTS: The prevalence of OSA was 18% for men and 9.7% for women in this cohort of 559 patients. Mean age was 49.8 years with a range of 15 to 96. Women comprised 66% of the population. The median BMI was 34.5 in patients with OSA and 25.8 for patients without. Associations with strong predictive values for OSA using Fisher's Exact Test are listed in the table (p<0.001 in all analyses).

Table:

Variable	Relative Risk	95% CI
Obesity	5.6	3.5-9.0
Hyperlipidemia	3.4	2.2-5.3
Diabetes Mellitus	2.5	1.5-4.0
Asthma	2.5	1.5-3.9
Hypertension	2.4	1.6-3.8
GERD	2.0	1.3-3.0
Osteoarthritis	1.9	1.3-3.0
Male Gender	1.8	1.2-2.9

DISCUSSION: The data show a prevalence of clinically significant OSA in patients with major depressive disorders that is more than four times the rate reported in the general population. This strong association between depression and OSA along with other factors shown in the table should be helpful when evaluating patients prior to anesthesia.

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S-94.

TITLE: TYPE OF INTERNSHIP AND ITE PERFORMANCE: DOES IT MATTER?

AUTHORS: M. Cobas, A. Varon, K. Arheart, M. A. De la Pena, N. Crescimone, D. Lubarsky;
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BACKGROUND: The Accreditation Council for Graduate Medical Education (ACGME) has requested that Anesthesiology programs incorporate the clinical base year (CBY) into a 4-year continuum of education, effective July, 2008. The reason for this change is to include more relevant rotations to the field and provide residents with a customized experience that will allow them to initiate their first year of clinical anesthesia training (CA-1) having knowledge relevant to the specialty. To improve the PGY-1 experience, our Department took control over the CBY in 2003 and redesigned it including rotations considered essential for an Anesthesiologist. In addition, some of the residents assigned to this CBY were offered a one-month clinical anesthesia rotation as an elective towards the end of the training period.

OBJECTIVE: The purpose of this study was to determine if differences exist in residents' In-Training Examination (ITE) scores at the end of the CBY amongst 3 different internship pathways: Anesthesiology with Anesthesia elective [AA], Anesthesiology without elective [A0] and non-Anesthesia internships like Internal Medicine or Surgery [NA].

METHODS: After obtaining IRB approval, residents' information regarding internship pathway, USMLE and ITE scores for the prior 3 years was obtained from departmental records. The ITE scaled scores at the beginning (ITE-Y1) and end (ITE-Y2) of the CBY were analyzed for each of the internship groups (AA, A0, and NA) using ANOVA. A p value <0.05 was considered significant.

RESULTS: Information from 88 residents was obtained. USMLE and Scaled scores (ITE-Y1) were comparable among the different groups at the beginning of their internship. As expected, each group had a statistically significant increase in the mean ITE scaled score from year one to year two. Analysis of ITE-Y2 among the different groups

demonstrated a significant difference between them. Group AA had an ITE-Y2 mean of 24.26 +/- 1.53; Group A0 had a mean of 18.39 +/- 1.20; and Group NA had a mean of 17.71 +/- 1.08. A significant difference was observed between AA and A0 (p=0.003) and between AA and NA (p=0.001), however, there was no difference between groups A0 and NA (p=0.676).

DISCUSSION: An Anesthesiology CBY that includes an Anesthesia elective is associated with higher ITE scores at the end of the first year of training. Whether this association is sustained throughout training remains to be determined and is currently under analysis as part of this prospective study.

Although we did not observe differences in ITE scores between those residents who enrolled in an anesthesiology internship without anesthesia elective, and those who completed traditional clinical base training in other specialty, the true impact of the ACGME proposed changes will likely be reflected in attributes that are cannot be assessed in standardized knowledge tests such as intern satisfaction, clinical performance and professional attitude.

S-95.

TITLE: DOCUMENTATION QUALITY OF PONV

AUTHORS: M. Franck, F. M. Radtke, R. Kuhly, A. Baumeyer, C. D. Spies;

AFFILIATION: Charité - Universitätsmedizin Berlin, Berlin, Germany.

INTRODUCTION: Postoperative nausea and vomiting (PONV) is used as a quality indicator and plays an important role for the patients. Aim of this study was to investigate the documentation quality in routine clinical care.

METHODS: This ethically approved observational trial included 504 adult patients with general anesthesia seen in the recovery room. A retrospective analysis of anesthesia record sheets was combined with data obtained by medical students (1). The documentation quality of PONV was checked. Only patients that were admitted to the recovery room during regular working hours between July 2006 and June 2007 were analyzed.

RESULTS: Of 131 patients (26%) with PONV, 34 (7%) patients were entered in the anesthesia record sheet by physician or nurses. 38 (8%) received antiemetic medication in the recovery room, so that a total of 59 (12%) of the patients with PONV were documented on the anesthesia record sheet. Combined with PONV that was observed by medical students, the total number of early PONV in the recovery room was 78 (16%). Including the information from the postoperative visit the following day our total rate of PONV was 131 (26%). The number of patients with early PONV documented on the anesthesia record sheet differs significantly from the number of patients with PONV in the recovery room ($p < 0.01$) and from patients with PONV in the first 24 hours ($p < 0.01$) with the chi-square test.

DISCUSSION: PONV documentation was poor. One quarter of the patients with early PONV in the recovery room were not documented in the anesthesia record. PONV in the first 24 hours postoperative added additional patients. Of 78 patients with early PONV in the recovery room, only 34 patients were documented by physician or nurses. In order to be able to use anesthesia record sheets as a tool for quality improvement one either has to be aware of the poor

documentation quality or should apply measures to improve documentation discipline.

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S-96.

TITLE: USMLE: PREDICTOR OF IN-TRAINING EXAMINATION PERFORMANCE IN ANESTHESIOLOGY?

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INTRODUCTION: Many authors have tried to demonstrate predictors for success within a residency program. Standardized knowledge tests, such as the USMLE, are commonly used as screening tools during the applicant selection process. They are important factors for resident selection in most programs, but their role in future resident performance is still unknown. In the Anesthesiology literature, the data is scant regarding the value of USMLE scores as predictors of performance in the Anesthesiology In-Training examination (ITE).

METHODS: The purpose of this study is to determine whether United States Medical Licensing Examination scores can predict In-Training examination results during their second year of training (CA-1). After obtaining IRB consent, residents' scores in USMLE Step 1 and Step 2 obtained from departmental records at our institution over the past 3 years were correlated to CA-1 ITE scores using Pearson's Product Moment Correlation Coefficient. A p value < 0.05 was considered significant.

RESULTS: A total of 172 residents' USMLE scores were analyzed. Step 1 (n=87) and Step 2 (n=85) were correlated with ITE results. We found that there is a moderate correlation between the performance in USMLE Step 1, Step 2 and results in the ITE with $r=0.56$ ($p < 0.001$) for Step 1 and $r=0.53$ ($p < 0.001$) for Step 2. (Table 1).Table 1

	ITE	P value
USMLE1 (n=87)	0.56	< 0.001
USMLE2 (n=85)	0.53	< 0.001

DISCUSSION: Even though other studies with smaller sample size, have found no correlation between USMLE Step 1, Step2, and the Anesthesiology In-Training examination scores the present data

indicates that a moderate correlation can be observed between these scores when a larger sample is analyzed. This study demonstrates statistically significant association between the three scores in the 87 residents available for the study. Even though USMLE Step 1 shows a slightly stronger correlation than USMLE Step 2, both tests were valuable tools in predicting ITE performance. While standardized tests and other measures of cognitive skills do not necessarily correlate with resident clinical performance, USMLE may help predict ITE performance. Programs struggling with accreditation issues based on written board achievement may find this information extremely useful to become more competitive, improve program performance, and to explain lower than hoped for board score performance as well.

1 Anesthesiology 2003; 99: A1323

S-97.

TITLE: DOCUMENTATION OF CRITICAL INCIDENTS USING AN ANESTHESIA INFORMATION MANAGEMENT SYSTEM

AUTHORS: D. T. Goulson;

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INTRODUCTION: Anesthesiologists' training provides both a general approach and specific knowledge intended to help diagnose and treat critical incidents. However, it has been shown that learned routines properly applied may significantly expedite the management of a crisis.¹

The Australian Patient Safety Foundation has applied learned routines to anesthesia critical incidents by constructing a series of algorithms to provide both a general framework and situation-specific methods for event management.²

Since existing incident-management algorithms communicated on paper have been shown to be effective³, a natural progression is to incorporate algorithms into computerized systems. This relieves the practitioner from the burden of memorizing the algorithms and provides key prompts at decision points in care during critical incidents.

METHODS: Within our anesthesia information management system CareSuite (Picis, Wakefield, MA), "events" are pre-defined phrases that are used in the descriptive documentation of points of care during an anesthetic. The system contains more than 1000 "events" (grouped into "event sets" for ease of organization) that can be chosen by the practitioner from a menu for inclusion in the record of an individual patient.

Algorithms for specific critical incidents have been developed and are published in the Crisis Management Manual.⁴ Critical incident event sets in CareSuite were based on these algorithms.

RESULTS: Event sets were created for several critical incidents that may arise during anesthesia, such as anaphylaxis, malignant hyperthermia, myocardial ischemia, cardiac arrest, and bronchospasm. As a prototype, the anaphylaxis event set is shown in the Table. Each statement can be added to the record with one mouse click.

Events in the Anaphylaxis Critical Incident Set

Anaphylaxis noted
Cardiovascular changes were associated sign
Bronchospasm was associated sign
Erythema or rash or pruritis was associated sign or symptom
Edema of face and lips was associated sign
Surgeon informed
Assistance requested
Administration of all drugs, blood products, and colloids halted
Volume expansion with crystalloid bolus given
Inspired oxygen concentration adjusted to 1.0
Epinephrine bolus as treatment
Epinephrine infusion as treatment
Histamine 1 antagonist as treatment
Histamine 2 antagonist as treatment
Corticosteroid as treatment
Bronchodilator as treatment
Blood specimen sent for tryptase measurement in 2 gold-top tubes

DISCUSSION: This preliminary report describes the use of previously-available algorithms¹ in electronic anesthesia records. The practitioner need not rely on memory, so that no management steps are missed. No separate resource must be consulted because the algorithm is contained in the documentation. Lastly, there is easy documentation of negative as well as positive findings, which produces a more complete record. As use of this system proceeds, critical incident data will be generated that will drive specific departmental patient safety and risk management efforts.

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S-98.

TITLE: IN HOSPITAL COMPLICATIONS AFTER TOTAL HIP AND KNEE ARTHROPLASTY

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INTRODUCTION: Total joint arthroplasty (TJA) is a safe and successful procedure. With the demographic tendency towards an elderly society and a relatively high prevalence of arthritis, the number of joint replacements in the US will increase dramatically in the upcoming years. The medical community needs to be aware of the various types of complications in the early hospital setting associated with elective TJA.

METHODS: This study prospectively collected data on systemic and local in hospital complications after 15,383 TJA, which included 8,230 total hip arthroplasties (6,795 primary, 224 conversions and 1,211 revisions) and 7,153 total knee replacements (6,500 primary and 653 revisions). The hospital course of every patient was followed closely. The circumstances leading to the complications and the details of the therapeutic intervention for each complication were recorded.

RESULTS: In general the incidence of complications was higher following knee arthroplasty and revision surgery. Bilateral arthroplasties also presented with higher rate of complications. There were 22 (0.16%) deaths, the majority of which occurred within 6 days after surgery. 486 systemic major complications occurred in the cohort that included pulmonary embolus (152), tachyarrhythmia (92), myocardial infarction (36), stroke (19), asystole (2), respiratory failure (14), aspiration pneumonitis (8), pneumothorax (2), systemic sepsis(7), gastrointestinal bleeding(3), small bowel obstruction (3), toxic megacolon (3) and acute renal failure (48). There were 109 major local complications, including 16 vascular injuries, 29 peripheral nerve injuries, 25 periprosthetic fractures and 18 dislocations. Most of the local complications occurred within 4 days of index surgery. There were 490 minor systemic complications and 364 minor local complications in

this cohort.

DISCUSSION: Total joint arthroplasty despite its success can be associated with serious and life threatening complications. This prospective study provides the baseline complications that can occur following elective joint arthroplasty

S-99.

TITLE: FASCIA ILIACA NERVE BLOCK SUCCESS RATES IN AN ANESTHESIOLOGY RESIDENCY TEACHING PROGRAM

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INTRODUCTION: Post-operative pain management in patients undergoing total knee arthroplasty (TKA) has become increasingly difficult due to the common use of anti-coagulants. At our teaching institution, epidural analgesia is often used and then discontinued after 36 hours post-operatively due to anti-coagulation. We continue multimodal pain management with fascia iliaca nerve blocks (FINB) in addition to oral and parenteral analgesics. New methods to improve performance by anesthesiology residents in regional anesthesia techniques are constantly being sought (Anesth Analg 2002;95:1423-7). We have evaluated the rate of achieving successful FINB in newly trained anesthesiology residents.

METHODS: As a teaching program, we are always looking to teach residents procedures that have a high degree of success and safety. We have found that the FINB is such a procedure; it is easy to learn and, in over 3000 procedures, we have had no complications. It is performed 1 cm below the inguinal ligament at the junction of the lateral 1/3 and medial 2/3 and anesthetizes the femoral and lateral femoral cutaneous nerves. A 22g B bevel needle is inserted perpendicularly until two "pops" are felt (fascia lata and fascia iliaca). After negative aspiration, 20 ml 0.25% bupivacaine with 200 µg epinephrine and 100 µg clonidine was injected. To learn how to perform the block, our residents are given a handout with a description of the block along with drawings of the anatomy involved. Afterward they accompany an attending on rounds and observe the attending performing one or two blocks and then they perform 2-3 blocks under direct supervision with an ongoing critique by the attending. Afterward the residents are allowed to perform the blocks at bedside on postoperative day 1 (after the epidural catheter has been removed). VAS scores pre- and post-block were compared with paired t-test.

RESULTS: Our results show a high degree of success with a significant reduction in pain scores after TKA. Newly-trained residents were able to perform a successful FINB 88.4% of the time (680/769 patients). The VAS pain scores were 6.26 ± 0.23 prior to block, and 3.35 ± 0.19 the next morning ($P < 0.001$).

DISCUSSION: The FINB is an easy to learn, exceptionally safe block with a high rate of success even in inexperienced hands. It provides significant analgesia for post-operative pain management in patients undergoing TKA. The 88.4% success rate of our residents with 2-3 'training' blocks compares favorably to the 70% success rate reported for axillary blocks after 20 'training' blocks (Anesth Analg 1998;86:635-9).

S-100.

TITLE: EDITORIAL REFERENCES IN ANAESTHESIA JOURNALS: CONTRIBUTIONS FROM OTHER JOURNALS.

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INTRODUCTION: Editorials are a time-honoured component of medical journals and provide an excellent area for transmitting important information to readers (1). Scientific journal needs to be accurate in references cited therein and an accurate reference lists provide useful information (2). Despite the well-established presence of editorials, little has been written about their reference citation (1). Therefore we analysed the references quoted by the editorials sections of the leading anaesthesia journals for the month of August 2007 to identify the influence of anaesthetic and non-anaesthetic specialities through reference citation distribution.

METHODS: Six leading English language anaesthesia journals published for the month of August 2007 were selected. These include journals published from USA: Anesthesiology and Anesthesia & Analgesia, United Kingdom: British Journal of Anaesthesia and Anaesthesia, Canada: Canadian journal of Anaesthesia, and Australia: Anaesthesia & Intensive care. The editorial section of each journal was analysed and the references cited by each editorial were assessed.

RESULTS: Fourteen editorials were published and a total of 236 references has been cited by these editorials. The table below shows the contribution of anaesthesia and non-anaesthesia specialities through reference citation in anaesthesia speciality journals. Only 38.56% of the citations are from anaesthesia journals and remaining 61.44% are from various medical, surgical and basic science specialities. Our study also showed that among anaesthesia journals citation Anesthesiology references has been cited most (43 times). Interestingly Anesthesiology journal has more self citation than any other journal (17 times). Among non-anaesthesia journals Circulation and The New England Journal of Medicine (NEJM) leads the list (15 and 7 citations). NEJM was quoted by maximum number of journals.

Journal Origin	Anesthesiology n	Anesthesia & Analgesia n	British Journal of Anaesthesia n	Anaesthesia n	Canadian Journal of Anaesthesia n	Anaesthesia and Intensive care n (%)	Total n (%)
USA	18	24	14	15	18	2	91 (38.56)
UK	9	22	41	7	3	5	87 (38.87)
Canada		26	6		3		35 (14.83)
Australia	5	1	3		3		12 (5.08)
Books, society and website	2	1	1		7		11 (4.66)

DISCUSSION: Anaesthesia is a multi talented speciality which uses knowledge from non-clinical and various clinical specialities. It is vital to link other specialities to anaesthesia for the future development of anaesthesia practice. One way to seal this link is to collect evidence and references from all specialities when anaesthesiologist are involved in research. Our study clearly showed the influence of non-anaesthetic speciality through reference citation in anaesthesia journals. Further study over a longer period is needed for in-depth analysis to identify individual speciality influence on anaesthesia publications.

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S-101.

TITLE: COMMERCIALY MARKETED SEVOFLURANE VAPORIZERS CONTAIN LEWIS ACID METAL OXIDES THAT CAN POTENTIALLY DEGRADE SEVOFLURANE CONTAINING INSUFFICIENT PROTECTIVE WATER CONTENT

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INTRODUCTION: Sevoflurane exposure to Lewis acids, such as metal oxides, can cause sevoflurane degradation to hydrogen fluoride (HF) and other potential toxins. Water prevents such degradation and HF production, and sevoflurane (Abbott Ultane[®]) was reformulated in 1997 to contain >300 ppm water. Commercially marketed sevoflurane vaporizers may contain Lewis acids that could contact and potentially degrade sevoflurane that does not contain protective amounts of water. The purpose of this investigation was to identify and quantify potential Lewis acids and their sites of location within three commercially marketed sevoflurane vaporizers.

METHODS: Three types of vaporizers (Draeger Vapor 2000, GE/Datex-Ohmeda Tec 7, and Penlon Sigma Elite), both new and old, were disassembled and examined by scanning electron microscopy, energy dispersive spectroscopy, and stereomicroscopy to determine which surfaces come into contact with sevoflurane (liquid or vapor) and which surfaces may contain potential Lewis acids. X-ray photoelectron spectroscopy and electron spectroscopy for chemical analysis was used to identify metal oxides, their oxidation state, and the surface depth of any oxides in contact with sevoflurane.

RESULTS AND DISCUSSION: Sevoflurane, both as liquid and vapor, is exposed to multiple potential Lewis acid contact sites within each vaporizer type. No substantial differences were observed between the new and used vaporizers.

Vaporizer	Surface area of potential LA exposed to liquid (cm ²)	Surface area of potential LA exposed to vapor (cm ²)
GE/Datex-Ohmeda Tec 7	183	189
Draeger Vapor 2000	917	481
Penlon Sigma Elite	400	429

CONCLUSIONS: Potential Lewis acids were identified in all brands of vaporizers analyzed. If chemically active, potential Lewis acids in vaporizer components could lead to degradation of low-water sevoflurane formulations.

S-102.

TITLE: A BRIEF EDUCATIONAL INTERVENTION IMPROVES ACCURACY OF INTRAOPERATIVE PRECORDIAL LEAD PLACEMENT

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INTRODUCTION: Intraoperative electrocardiographic (ECG) monitoring is used to detect of myocardial ischemia. The V3-V5 precordial leads provide most sensitivity^{1, 2}, and ischemia may be missed with inaccurate placement³. We previously demonstrated⁴ that, at our institution, the precordial lead was >3 cm from ideal in 61% of 101 patients [mean(SD) 5.8(4.8) cm, range 0-22 cm]. 1-3 weeks after a 10 min lecture to anesthesia providers, lead placement was significantly improved: 40% of 101 patients > 3 cm (p<0.003), mean (SD) 3.8(3.6) cm (p<0.0007), range 0-20 cm. BMI, type of surgery, surgical position and level of training were not significant contributors to accuracy. We performed a follow-up assessment 5 months after the initial training (and after a new group of residents started) to determine whether the impact of the brief educational intervention was durable.

METHODS: With IRB approval, we measured the accuracy of lead placement in 73 patients in the PACU. Patients having cardiothoracic surgery or surgery in the prone position were excluded. Anesthesia providers were unaware that the study was being conducted. PACU nurses were instructed not to move ECG electrodes until after data was collected. Distance (cm) of the actual precordial electrode from ideal (either V3 or V5 was accepted) was measured on arrival in the PACU. BMI, type of surgery, age, gender, and the level of training of the anesthesia provider were also recorded.

RESULTS: Mean (SD) distance from ideal was 2.7 (2.7) cm (range 0-11 cm) (p<0.001 vs. pre-education; p=0.032 vs. 1-3 weeks by t-test), with 28% > 3 cm (p<0.001 vs. pre and 1-3 weeks by chi-square analysis of contingency). As in the previous study, faculty did slightly better than CA-1 residents [1.9(2.1) vs. 2.6(2.8) cm] but this was not statistically significant. BMI, type of surgery, age, and gender again were not significant factors.

CONCLUSIONS: A brief (10 min) educational intervention

significantly improved the accuracy of intraoperative precordial lead placement 5 months after the intervention, even when compared to immediately after the intervention, despite the lack of further formal education and the inclusion of CA-1 residents who did not receive the training. Our results were presented at the Western Anesthesia Residents Conference (4/07), which likely contributed to continued awareness of the importance of ECG lead placement within our department. A brief educational intervention for a simple but important behavior may have long-term effects on performance. This may be related in part to increased departmental awareness of the issue.

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S-103.

TITLE: DELIRIUM IN THE RECOVERY ROOM PREDICTS DELIRIUM ON THE FIRST POSTOPERATIVE DAY

AUTHORS: F. M. Radtke, M. Franck, J. Bieler, A. Heymann, C. D. Spies;

AFFILIATION: Charité - Universitätsmedizin Berlin, Berlin, Germany. ³

INTRODUCTION: Delirium is reported to occur in the recovery room in a relevant proportion of up to 30% of the patients and is often in the postoperative period (1). Aim of this study was to determine the incidence of recovery room delirium and its association with delirium on the first postoperative day.

METHODS: This ethically approved observational trial included 376 adult patients seen in the recovery room and on the floor. Patients were seen in the recovery room by registered nurses during time of discharge and on the first postoperative day on the regular floor by trained research assistants. The presence of delirium was determined using the nursing delirium screening scale (Nu-DeSC (2)), a score ≥ 2 points was considered as delirium. Only patients that were admitted to the recovery room during regular working hours between July 2006 and June 2007 were analyzed.

RESULTS: Of 42 patients with delirium in the recovery room, 12 (29%) patients showed delirium on the first postoperative day. From 334 patients without delirium in the recovery room 7 (2%) patients were diagnosed with delirium on the following day. Delirium in the recovery room is highly associated with delirium on the first postoperative day ($p < 0.01$) with the chi-square test.

DISCUSSION: Delirium in the recovery correlates with delirium on the first postoperative day. Of 42 patients with delirium in the recovery room, 12 patients showed delirium as inpatient. Therapeutic and preventive measures should be considered in the recovery room to avoid prolongation to the postoperative ward period.

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S-104.

TITLE: “ANAESTHESIOLOGIES”: USING ANALOGIES TO TEACH ANESTHESIOLOGY PRINCIPLES TO NON-MEDICAL STUDENTS

AUTHORS: D. Miller¹, L. K. Hoke², M. J. Meyer², Y. F. Bryan²;

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INTRODUCTION: Exposing undergraduate students to anesthesia is important to pique their interest and attract them to medical careers. However, understanding clinical anesthesia can be quite difficult and frustrating due to the large amount of medical jargon used and can run the risk of the student becoming bored, confused and losing the big picture. By using analogies and metaphors, students are easily engaged which can make learning more entertaining by providing examples that are level with the student’s knowledge and ensure the student and the educator are on the same page (1,2). The goal for the educator is ensuring that the big picture is supported by specific examples and that the context is not misunderstood nor the details misinterpreted. We present a teaching template created for non-medical students and clinical research staff to assist in comprehending the goals of anesthesia through the use of analogies.

CASE PRESENTATION: A teaching template was created consisting of 5 basic questions which were subdivided into four separate categories; principle (educator’s goal or perspective), purpose (student’s expectation or perspective), concept (medical issues from the educator’s view), analogies (explanation of issue on the student’s level). See Table 1.

Table 1

Question	Principle or Educator’s goal	Purpose or Learner’s perspective	Concept	Analogies
What is anesthesia?	Distinguish between different medication types	Understand differences between anxiolytics, inhalation, intravenous agents and narcotics.	Treating with anxiolytics Inhalation agents Intravenous Pain meds	Being nervous before soccer game. Getting oxygen on the bench. Receiving IV fluids after the game. Taking meds after game.
What are some of the risks of anesthesia?	Explain oxygenation, ventilation and cardiac function	Understand oxygenation, ventilation and cardiac function.	Hypoxia (low O ₂) Hypocarbia (low CO ₂) Hypercarbia (High CO ₂) Cardiac arrest	Climbing high altitude. Hyperventilating from rapid breathing. Stuck on space capsule with no ventilation. Heart (motor) not pumping.
How medications are administered?	How to deliver medications to the body?	Understand advantages and disadvantages of different routes.	Routes Oral Rectum Intramuscular Intravenous Inhalation Subcutaneous	Giving common medicines. Headache (acetaminophen) Stool softener Vaccine Chemotherapy Inhaler for asthma TB test
What breathing devices are used and why?	How do we get oxygen in and carbon dioxide out of the body under anesthesia?	Understand the difference between supra- and infraglottic devices.	Bag-mask ventilation LMA ETT	Drilling for oil on the surface. Drilling for oil deep above the actual deposit. Drilling for oil directly into the deposit.
What do we observe on monitors and what does it mean?	Explain the monitors and what we are looking at during anesthesia.	Understand the different monitors and how we interpret the data.	Blood pressure EKG Temperature Capnography Pulse oximeter	Tire pressure. Speedometer of the heart. Engine temp. Exhaust. Oxide of gas.

DISCUSSION: Overall, it is quite challenging for the busy anesthesiologist to simplify anesthesia concepts to enhance the learning experience of non-medical students exposed to clinical practice. We found that our teaching template utilizing analogies provided the students with a fun, yet challenging experience and the ability to grasp significant details. The students were encouraged to develop their own analogies which best suited their own experiences.

REFERENCES: 1) Macrone M. Animalogies Doubleday 1st ed. 1995; 2) Science Education 2006;(75):649-672.

S-105.

TITLE: UNINTENTIONAL INTRACEREBROVENTRICULAR ADMINISTRATION OF ETOMIDATE AND ROCURONIUM

AUTHORS: S. M. Howell, R. Driver;

AFFILIATION: West Virginia University School of Medicine, Morgantown, WV.

INTRODUCTION: Medication errors continue to be a source of preventable morbidity and mortality. We describe the unintentional intracerebroventricular (ICV) injection of etomidate and rocuronium. The precipitating factors, clinical effects, clinical course, and strategies for prevention will be discussed.

METHODS: The patient described in this case report was a 61 year old male who presented with ruptured anterior communicating aneurysm, GCS 14. A ventriculostomy catheter was placed upon admission to the intensive care unit. The aneurysm was successfully clipped via right frontotemporal craniotomy and the patient was exubated post-operatively with a stable neurological exam. Cerebral vasospasm complicated his post-operative course. Endotracheal intubation was required for airway protection and hypoxemia. In preparation for rapid sequence induction the patient was preoxygenated. A verbal order was given for etomidate 20 mg and rocuronium 100 mg intravenously. The drugs were unintentionally injected into the ventriculostomy catheter, which was mistaken by nursing personnel for an intravenous line.

RESULTS: Within one minute, the patient lost consciousness and became apneic. Endotracheal intubation was immediately performed under direct laryngoscopy. During the endotracheal tube placement, vocal cords were abducted and neither coughing or movement occurred. Hemodynamic stability was maintained. After securing the airway, 20 mL of cerebrospinal fluid was aspirated from the ventriculostomy catheter and the catheter was left open to drain. Cerebrospinal fluid became progressively more blood tinged. The nature and severity of the medication error was discussed in detail with the patient’s family. After several hours the patient began to withdraw to pain briskly, but could not follow simple commands as he had done intermittently prior the drug error. The patient’s neurological exam never improved. The patient continued on standard therapy for cerebral vasospasm until transcranial

doppler exams were consistent with resolution. Without hope of meaningful neurological recovery, his family decided to withdraw supportive care. An autopsy was not performed.

DISCUSSION: It is critical to trace the course of any line prior to injection of medication. This simple step would have prevented this tragic error. However, a systems error was also identified. The tubing connected to the central venous catheter was very similar in appearance to the tubing connected to the ventriculostomy catheter. Moreover, the position of stop-cocks and injection ports was nearly identical. Ideally, the ventriculostomy catheter should be attached to tubing that has a unique appearance. Additionally, tubing attached to the ventriculostomy catheter should be devoid of injection ports that could facilitate unintentional ICV injection. The preventative strategy adopted by our institution was to place red “dead-end” caps on all ventriculostomy access ports. A superior solution may be possible at the manufacturing level. External ventricular drain systems could be redesigned to prevent the attachment of standard-sized syringes and stop-cocks.

S-106.

TITLE: TEMPLATE FOR A SENIOR RESIDENT RETREAT: WHAT WE ARE NOT TEACHING IN RESIDENCY TRAINING PROGRAMS

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AFFILIATION: Medical College of Wisconsin, Milwaukee, WI.

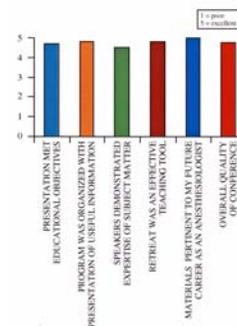
INTRODUCTION: Clinical anesthesiology residency training programs consist of 4 years of didactic and clinical instruction addressing the six core competencies. Residents emerge clinically competent to render patient care in an unsupervised environment, the majority of whom enter private practice. However, practical and business aspects of private practice are typically not addressed in a formal residency training program, leaving the resident potentially unprepared to meet these challenges.

METHODS: A three-day retreat was developed and conducted at an off-site facility. Professional speakers were utilized addressing the following topics:

1. Interviewing Skills -Presenting Oneself to a Prospective Employer: What to Say and Do
A professional recruiter provided insight, tips and practical interviewing advice.
3. Billing: The Business End of Practice
Practical billing information with exposure of common errors in coding is discussed.
2. Contracts: How to Negotiate an Effective Employment Agreement
A health-care contract attorney discussed contract negotiation techniques, law, and restrictive covenants.
4. Malpractice and the Patient Compensation Fund
Discussion of coverage of excessive damage awards, insurance and disability and the impact upon the practitioner provided by experts.
5. Money Management: Resourceful Financial Planning
Money management techniques and strategy is conveyed.
6. Social Events
Social events are planned with families as a complement to the conference schedule allowing for informal interaction between residents, faculty and speakers.

RESULTS: The conference was rated a 4.75 on a scale of 1 = poor to 5 = excellent. The following parameters were evaluated:

1. Presentation met educational objectives
2. Program was organized with presentation of useful information
3. Speakers demonstrated expertise of subject matter
4. Retreat was an effective teaching tool
5. Material pertinent to my future career as an anesthesiologist
6. Overall quality of conference



DISCUSSION: The advent of a senior resident retreat addressing non-core competency subject matter may empower graduating residents to significantly improve self-confidence and knowledge base while transitioning out of residency training into the private practice arena.

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Equipment / Monitoring

S-107.

TITLE: CLINICAL EVALUATION OF THE DIFFERENCES ON TRANSCUTANEOUS MEASUREMENTS OF CARBON DIOXIDE TENSION AT VARIOUS BODY SITES DURING GENERAL ANESTHESIA

AUTHORS: A. Mizushima, S. Katashima, Y. Kawauchi, M. Yamamoto, H. Iwata, Y. Kamiyama;

AFFILIATION: Juntendo University Urayasu Hospital, Urayasu, Japan.

INTRODUCTION: The measurement of transcutaneous carbon dioxide tension (PtcCO₂) allows useful estimation of PaCO₂. Very little has been published, however, about the differences of PtcCO₂ measurement at various body sites. The aim of this study was to evaluate the differences at the various body sites of PtcCO₂ measurements during general anesthesia in adult patients.

METHODS: With approval of ethical committee and informed consent from each subject, 34 (ASA 1 or 2) adult patients aged 20 to 72 years for elective abdominal surgery under sevoflurane anesthesia were studied. The heated (42 degrees centigrade) miniaturized PtcCO₂/SpO₂ single ear sensor (TOSCA monitor; Linde Medical Sensors, Switzerland) was applied at the ear lobe with a special low ear clip and at the chest with a special attachment ring. The heated (42 degrees centigrade) combined PtcCO₂/PtcO₂ sensor (9900MK2; Kohken Medical, Japan) was also applied on the chest, forearm or abdomen. Endotidal CO₂ tension (PetCO₂) measurements were compared with the values displayed by a standard capnometry (AS5; Datex-Ohmeda, Finland). PaCO₂ values were measured by a calibrate blood-gas analyzer (288Blood Gas System; Ciba-Corning, USA). The simultaneously obtained PtcCO₂, PetCO₂ and PaCO₂ values were compared by linear regression analysis and Bland-Altman bias analysis.

RESULTS: A total of 108 paired measurements were correlated. No skin lesions occurred. PtcCO₂ were highly correlated with PaCO₂ (PtcCO₂ TOSCA ear = 1.46 * PaCO₂ + 0.12, p < 0.01; PtcCO₂ TOSCA chest = 1.27 * PaCO₂ + 0.12, p < 0.01; PtcCO₂ 9900MK2 chest = 1.13 * PaCO₂ + 0.10, p < 0.01; PtcCO₂ 9900MK2 forearm = 1.08 * PaCO₂ + 0.12, p < 0.01; PtcCO₂ 9900MK2 abdomen = 1.18 * PaCO₂ + 0.15, p

< 0.01; PetCO₂ = 0.88 * PaCO₂ + 0.08, p < 0.01) in the PaCO₂ range of 2.9 to 8.7 kPa. The bias (mean difference between values) and precision (standard deviation of bias) are shown in the Table.

The bias (mean difference between values) and precision (standard deviation of bias)

	bias	precision
PtcCO ₂ (TOSCA ear) - PaCO ₂ ; (kPa)	0.82	0.76
PtcCO ₂ (TOSCA chest) - PaCO ₂ ; (kPa)	0.52	0.64
PtcCO ₂ (9900MK2 chest) - PaCO ₂ ; (kPa)	0.31	0.58
PtcCO ₂ (9900MK2 forearm) - PaCO ₂ ; (kPa)	0.29	0.53
PtcCO ₂ (9900MK2 abdomen) - PaCO ₂ ; (kPa)	0.37	0.68
PtcCO ₂ - PaCO ₂ ; (kPa)	-0.44	0.52

CONCLUSION: Although the blood gas analysis is a gold standard for evaluation of ventilation, PtcCO₂ monitor is a helpful add-on to non-invasive respiratory monitoring, even in adult patients. The PtcCO₂ measurements at the ear lobe showed relatively high values compared with those at the chest. The PtcCO₂ measurements by the PtcCO₂/SpO₂ sensor showed relatively high values compared with those by the PtcCO₂/PtcO₂ sensor.

S-108.

TITLE: EFFECTS OF DEEP TRENDLENBURG POSITIONING ON INTRAOCULAR PRESSURE DURING ROBOTIC RADICAL PROSTATECTOMY

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INTRODUCTION: Prostate Cancer is third leading cause of cancer death among American men. It is estimated that 1 in 6 men will be diagnosed with prostate cancer in their lifetime (1). There are many treatment options available for prostate cancer and Robot-assisted radical prostatectomy is the one of the newest and most technically advanced. This specific position is known to increase intraocular pressure. However, the amount of this increase is unknown, particularly during the long procedures and in combination with the carbon dioxide insufflations during laparoscopy. The aim of this study was to investigate the IOP changes in patients undergoing robotic radical prostatectomy at different time points and body positions through the procedure to determine if there is clinically significant elevation in IOP.

METHODS: In this cohort study, IOP was measured using a Tonopen® XL handled tonometer in 32 patients undergoing Robot-assisted Prostatectomy. The IOP was measured prior to anesthesia supine (baseline T1), anesthetized supine (T2), anesthetized after insufflations with CO₂ (T3), anesthetized in deep Trendelenburg (T4), anesthetized in the Trendelenburg at the end of the procedure (T5), anesthetized supine prior to awakening (T6), and 1 hour after awakening (T7).

RESULTS: IOP was significantly higher in deep Trendelenburg T5 IOP (29 +/- 6mmhg) compared to supine T2 (18.2556 units higher, SE=0.5596, P-value <.0001). A time dependent increase in IOP was also noted with T5 IOP (29 +/- 6mmhg). One hour following the conclusion of the procedure, IOP was on average significantly higher than baseline (T1) (1.2565 units higher, SE=0.5988, P-value=0.0362), despite return to supine position. A linear regression model and the measurements from T2 to T5 were used for analysis of this period and IOP increased on average 0.18 mmHg per minute between T2 and T5.

DISCUSSION: This study shows that IOP increases significantly

during robotic prostatectomy in a deep Trendelenburg position. This study quantifies the change in IOP and concludes that robotic prostatectomy patients reach IOP levels similar to those observed in glaucoma patients who have temporarily stopped their medication and are put in the deep Trendelenburg position (2). The magnitude of this increase in IOP was also confirmed in an animal model of α -chymotrypsin induced glaucoma in which a combination of CO₂ pneumoperitoneum and head down positioning were utilized (3). Significant elevation in IOP occurs when anesthetized patients are placed in the deep Trendelenburg position following insufflations of the abdomen with CO₂ and this elevation in IOP appears to increase with time.

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3. Anesth Analg 1998; 86: 1283-1288.

S-109.

TITLE: VOLUME VERSUS PRESSURE CONTROL VENTILATION DURING ROBOTIC ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMY

AUTHORS: A. Falabella, R. Nelson, M. W. Lew, W. Chang, M. J. Sullivan, L. Crocitto;

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INTRODUCTION: Robotic assisted surgery often requires pneumoperitoneum and trendelenburg positioning. This can lead to high airway pressures which have been associated with lung barotrauma¹. In order to limit barotrauma, the anesthesiologist can limit the peak airway pressure (PAP). Two common modes of intraoperative ventilation are volume control (VCV) and pressure control ventilation (PCV). This study measured the tidal volumes of patients on PCV and VCV in the supine, trendelenburg, and trendelenburg with pneumoperitoneum positions when PAPs were controlled.

METHODS: 50 male ASA 2 patients undergoing robotic assisted prostatectomy were prospectively studied. After a standard protocol induction and paralysis, patients were intubated with 8.0mm endotracheal tubes and ventilated with Drager Fabius GS ventilators (Telford PA). Spirometry data during VCV were recorded in the supine, trendelenburg, and trendelenburg with pneumoperitoneum positions after a period of stabilization. Tidal volumes for VCV were 10ml/kg, respiratory rate was 10 breaths per minute, PEEP was 5 cmH₂O, FiO₂ was 100% at 2L/min and I:E ratios were 1:2. Spirometry data for PVC was recorded after VCV data was obtained for each position and patients served as their own controls. The PAP for VCV was used to set the maximum inspiratory pressure during PCV. All other values remained the same. Inspiratory flow for PVC was 75L/min. Pneumoperitoneum was set at 15 cm H₂O.

Univariate analysis was performed using Student's t-test and data was presented using means and standard deviations with p-values <0.05 indicating statistical significance.

RESULTS:

	SUPINE		TRENDELENBURG		PNEUMOPERITONEUM	
	Mean	Std Dev p-value	Mean	Std Dev p-value	Mean	Std Dev p-value
Tidal volume:						
Volume control	919	151 <0.0001	921	152 <0.0001	923	147 <0.0001
Pressure control	1069	173	1074	166	1103	189
Plateau pressure:						
Volume control	17.2	3.9 0.05	20.4	5.1 0.1	31.4	6.7 0.33
Pressure control	18.7	4.1	22.4	5.4	32.7	6.5
Compliance:						
Volume control	78.1	19.1 0.27	65.9	15.8 0.36	34.5	6.7 0.33
Pressure control	82.1	16.5	86.7	15.1	36	8.9

DISCUSSION: Our data demonstrate that PCV allows for larger tidal volumes than VCV when PAPs are kept constant. This mode of ventilation may be beneficial in patients undergoing laparoscopic surgical procedures where intra-abdominal insufflation and trendelenburg positioning may affect respiratory mechanics.

ENDNOTES

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S-110.

TITLE: A NOVEL METHOD FOR CREATING ALERTS OF INTRAOPERATIVE GAPS IN PATIENT MONITORING DURING ANESTHESIA

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BACKGROUND: Much of the safety attending modern anesthesia can be attributed to improved physiologic monitoring, yet patients under anesthesia are not always appropriately monitored. One example occurs when a single blood pressure reading is obtained with a non-invasive cuff, without engaging the automatic cycling function. This kind of a gap in monitoring can degrade safety. Having previously reported on the incidence of this problem,¹ we have set out to develop a real-time intraoperative monitoring gap alert and detection system.

METHODS: We have developed software (ABE) that continuously examines physiologic data stored in our automated information management system (AIMS). The AIMS automatically records monitoring data every 60 seconds throughout each case. ABE searches each case between the initial administration of an anesthetic agent and either extubation or the end of surgery for gaps in the measurement of blood pressure greater than 10 minutes, oxygen saturation greater than 3 minutes and heart rate greater than 3 minutes. Our search includes blood pressure readings from both non-invasive cuffs as well as arterial lines and heart rate readings from ECG monitoring and pulse oximetry. Once a gap has been detected, ABE immediately sends an alert via the hospital paging system.

In order to determine the overall system performance, we have set out to measure the error detection and alert latency by examining the time between error detection and provider receipt of the alert. In order to measure this interval, we programmed ABE to send alert pages to a standard hospital text pager that had been assigned to a member of our research team. Using a digital clock synchronized with ABE, we then logged 50 alert messages noting the time of message receipt and the time of message initiation (provided in the actual message by ABE). The difference in times was then calculated using Microsoft Excel and the average system latency was determined.

RESULTS: We logged fifty alert pages generated by ABE. The average time between when an error was detected and when an alert was received was fifteen seconds with a standard deviation of three seconds. The shortest delay was ten seconds and the longest was twenty. The pages were generated at different times of the day (morning and afternoon) as well as on different days of the week (Monday, Tuesday and Friday) to account for variations in overall hospital paging traffic.

DISCUSSION: We have successfully employed our hospital text paging system to provide near-real time alerts of intraoperative events as a part of our larger effort to develop an intraoperative monitoring gap detection and alert system.

REFERENCES:

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S-111.

WITHDRAWN

S-112.

TITLE: DISTANCE FROM THE INCISOR TO THE LARYNX MEASURED BY USING THE AIRWAY SCOPE

AUTHORS: N. Sasano¹, H. Sasano²;

AFFILIATION: ¹Inabe General Hospital, Inabe, Japan, ²Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

INTRODUCTION: An AirWay Scope (AWS, Pentax Corporation, Tokyo, Japan) is a novel airway device for orotracheal intubation, which provides an excellent view of the glottis without requiring alignment of the oral, pharyngeal, and laryngeal axes. It consists of the following three components: an integrated fiberscope system, a 24-inch built-in liquid crystal device monitor, and an anatomically curved blade (INTLOCK) that holds and guides the tracheal tube (1). We have found this device useful for orotracheal intubation not only in daily anesthetic practice but also in patients with difficult airways (2). We, however, have encountered a patient whose trachea was failed to be intubated with AWS because INTLOCK could not reach the larynx (3). We prospectively investigated the length from the incisor to the larynx by using INTLOCK of the AWS.

METHODS: With ethical committee approval and written informed consent, adult patients who underwent general anesthesia for elective surgery at Inabe general hospital were enrolled in this study. After induction of anesthesia, the AWS was inserted into the oral cavity and advanced beneath the epiglottis. When the glottic opening was visualised on the monitor and was set on the target mark, we marked the position of the lower incisor on the INTLOCK. The tracheal tube was then advanced into the trachea. After removal of the AWS, we measured the length from the tip of the LNTLOCK to the mark, which represents the distance from the patient's incisor to the larynx. Data are shown as mean \pm SD (range).

RESULTS: There were 34 men and 42 women aged from 20 to 89. The tracheas of all patients were successfully intubated with the AWS. The distance from the incisor to the larynx was 10.5 ± 0.7 (9-11.8) cm, and 9.7 ± 0.8 (7.7-11.7) cm, in men and women, respectively. The distance from the incisor to the larynx correlates with the height, but not with the thyromental distance.

DISCUSSION: The present study demonstrated that the distance from the incisor to the larynx differs substantially among individuals, and that it correlates well with the heights. As the AWS has only one fixed-sized blade, it may fail to reach the larynx in tall patients or the tracheal tube tends to go downward, toward the esophagus, in small patients. We hope that different-sized INTLOCKS including ones sized for children will be available in the near future.

REFERENCES: (1) *Anaesthesia* 2007; 62: 19. (2) *Can J Anesth* 2007; 54: 160-161. (3) *Can J Anesth* 2007; in press

S-113.

TITLE: FUNCTIONAL NEAR INFRARED SPECTROSCOPY AS A MONITOR FOR DEPTH OF ANESTHESIA

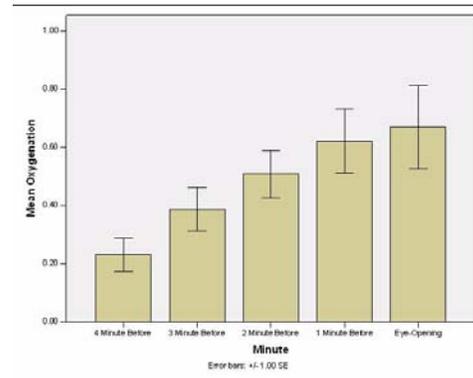
AUTHORS: C. Hoffman, J. Horrow, K. Izzetoglu, J. Levitt, Y. Hua, G. Goyal;

AFFILIATION: Drexel University, Philadelphia, PA.

BACKGROUND. Functional near infrared (fNIR) reflectance spectroscopy detects the hemodynamic response of brain cortex to cognitive activation.¹⁻³ Relative absorption and backscatter of oxy- and de-oxy hemoglobin reflect neural activity via neurovascular coupling. Awareness during general anesthesia occurs in approximately 0.13% of cases.⁴ This initial application of fNIR hypothesized that increases in blood oxygenation in the prefrontal cortex occur with emergence from anesthesia.

METHODS. The fNIR probe consists of a 3-wavelength light source and detector separated by 2.5 cm, providing for collection of photons scattered by capillary hemoglobin at 2 Hz. The 3rd wavelength and principal component analysis allowed capture of motion artifact; subtraction of the artifact from the signal preceded calculation of oxygenated and deoxygenated hemoglobin using a modified Beer-Lambert Law. With IRB approval and written, informed consent, 50 patients undergoing general anesthesia had the fNIR forehead probe applied prior to the induction of general anesthesia and recorded continuously through emergence, including initiation of verbal response, opening of the eyes, and extubation. Administration of medications and key procedures were recorded by embedding markers into the acquired signal. Cortex oxygenation data at 1-min intervals for 5-min prior to eye opening underwent repeated measures analysis of variance using p<0.05 for significance. Lack of prior data in this setting precluded sample size calculation.

RESULTS. 24 of 50 patients had signals amenable for analysis in the 5-min period preceding eye opening to command. Oxygenation increased with emergence from anesthesia (figure; F=3.13, p<0.05).



DISCUSSION. fNIR reflects cognitive load: attention, working memory, and problem solving.¹⁻³ Increases in cortical blood flow accompanying increased cortical activity increase the oxy-hemoglobin and decrease the deoxy-hemoglobin portions of the fNIR signal. Hemoglobin in small arterioles, capillaries, and venules participates most because blood in larger vessels absorbs its own reflected light. fNIR detects adverse ischemic neurological events in congenital cardiac surgery and improves clinical outcomes.⁵ Placental tissue oxygenation index changed in patients with intrauterine fetal growth retardation.⁶ This pilot study demonstrates that fNIR changes during emergence from anesthesia. Additional studies should assess the change of fNIR with specific anesthetic agents and to monitor depth of anesthesia.

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S-114.

TITLE: MEASUREMENT OF VO₂ AND VCO₂ DURING SPONTANEOUS BREATHING IS MORE ACCURATE WITH THE BYMIXER-FLOW SYSTEM COMPARED TO THE DATEX-OHMEDA S5 MONITOR

AUTHORS: K. Scherrer, C. Leung, A. Rosenbaum, P. H. Breen;

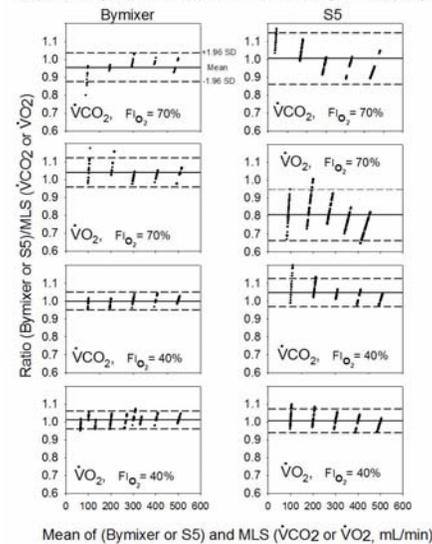
AFFILIATION: UCIMC, Orange, CA.

INTRODUCTION: The measurement of pulmonary O₂ uptake (VO₂) and CO₂ elimination (VCO₂) can detect critical events during anesthesia. Furthermore, in the spontaneously breathing patient, these measurements can be used for preoperative exercise testing for risk assessment. Spontaneous ventilation is characterized by variable FRC, tidal volume (VT) and respiratory frequency (f), which challenge measurements of VO₂ and VCO₂. We compared a commercial monitor (M-COVX, Datex Ohmeda S5) to our bymixer-flow system.¹ Both monitors use the Haldane transformation. To determine mixed gas fractions, the and integrates gas flow and gas concentrations. The bymixer-flow system hydraulically generates flow-averaged gas mixtures. We hypothesized that the bymixer-flow system provides higher accuracy and precision compared to the Datex S5 during spontaneous ventilation.

METHODS: The two monitors were tested with a previously described metabolic lung simulator (MLS).² A humidity sensor³ and a pneumotachometer cuvette were placed at the mouth piece. The inspiratory arm was attached to a reservoir bag, supplied with 40% or 70% O₂. We tested the 2 measurement systems over a range of 50.0-500.3 mL/min for VO₂ and 33.3-332.8 mL/min for VCO₂. To generate spontaneous ventilation, a second mechanical lung drove the ventilated lung by a coupling clip, over a wide range of VT and f.

RESULTS: The Figure represents the Bland/Altman ratio analysis for the bymixer-flow (left) and the Datex S5 (right), compared to the MLS. For both, the bias and precision were better for FiO₂ of 40% compared to 70%. The bymixer-flow accuracy and precision were significantly better (p<0.05) than the Datex S5, particularly at FiO₂ of 70% (p<0.01). At 70% Fi, the average (±SD) bymixer-flow percent errors for V and VC were 3.72±4.18% and -4.51±4.09%, respectively.

Comparison of Bymixer-Flow or Datex S5 vs. Metabolic Lung Simulator (MLS)



DISCUSSION: As expected, the measurements of VO₂ and VCO₂ for both the monitors were more accurate at FiO₂ of 40%, since the Haldane transformation is based on N₂ conservation. However, the bymixer provides better agreement, particularly at FiO₂ of 70%. We believe that the bymixer-flow measurements are superior because the bymixer more precisely generates mixed gas measurements than the digital determination from the Datex S5. Moreover, the humidity sensor augments the accuracy of the flow measurement.

REFERENCES: 1. Anesth Analg 2003; 97: 1414-20. 2. J Clin Monit and Comput 2007; 21:71-82. 3. U.S. Patent Number 6,014,890: 2000.

S-115.

TITLE: VIDEO ENDOTRACHEAL TUBE EXCHANGE CATHETER

AUTHORS: R. Glassenberg;

AFFILIATION: Northwestern University, Chicago, IL.

INTRODUCTION: Replacing an endotracheal tube in the ICU is a risky maneuver because : (1) the patient is apneic during the procedure allowing very little time to perform the switch; (2) airway edema is present after prolonged intubation distorting anatomy; (3) exchange catheters are frequently misplaced into the esophagus. What can be done to make this process less dangerous?

METHODS: The booming market for slimmer cellphones with video capability has created an economy of scale price reduction in disposable microchip video cameras. We have incorporated a CCD camera with 320 X 240 resolution into a Cook-Aintree catheter.

RESULTS: Despite its small size, the camera can easily be focused on the carina during tube changes (Figure).



DISCUSSION: While it is possible to railroad a new endotracheal tube down a fiberoptic bronchoscope, the bulky handle required for tip flexion precludes the possibility of sliding damaged endotracheal tubes over the top of the scope without removing the device from the trachea. A tube exchange catheter avoids this problem, because it can remain inside the trachea during the exchange process. A video enabled exchange catheter allows the user to verify at all times during the switch the presence of tracheal rings.

S-116.

TITLE: NON-INVASIVE ASSESSMENT OF CEREBRAL AUTOREGULATION USING NEAR INFRARED SPECTROSCOPY

AUTHORS: C. Pritchard¹, T. Leung², M. Tisdall¹, I. Tachtsidis², C. Elwell², M. Smith¹;

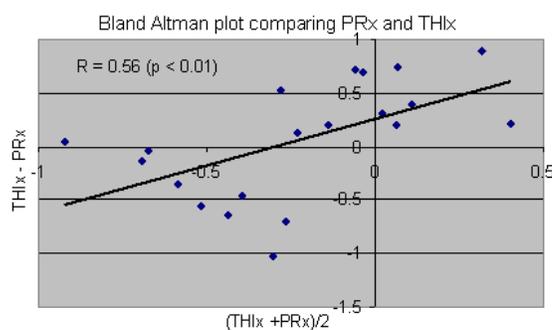
AFFILIATION: ¹Department of Neuroanaesthesia and Neurocritical Care, National Hospital for Neurology and Neurosurgery, University College London Hospitals, London, United Kingdom, ²Department of Medical Physics and Bioengineering, University College London, London, United Kingdom.

INTRODUCTION: Cerebrovascular autoregulation (CA) is frequently impaired after TBI and is associated with poor outcome [1]. Continuous monitoring of CA may predict patients at risk of secondary injury and help to define individual specific treatment targets. CA can be assessed continuously using a pressure reactivity index (PRx) derived from continuous monitoring and analysis of slow waves in arterial blood pressure (ABP) and intracranial pressure (ICP) by calculation of the correlation coefficient of consecutive time averaged data points of ICP and ABP [2]. Near infrared spatially resolved spectroscopy (SRS) systems are able to make real-time measurement of absolute tissue haemoglobin concentration (THI) that is related to cerebral blood volume [3]. In this study we derived a novel SRS assessment of CA (THIx) and compared it to simultaneous measurements of PRx.

METHODS: Five adult patients with severe TBI were included in this pilot study. ICP and invasive ABP data were measured continuously as part of standard care. THI was measured continuously using SRS (NIRO 300, Hamamatsu Photonics). The SRS optodes were placed 3.5 cm apart in a black plastic holder and fixed to the upper forehead in the midpupillary line ipsilateral to the invasive cerebral monitoring. Data was collected for 3 hours during the first 24 hours after injury and downloaded onto a PC for subsequent off-line analysis. THIx was calculated in a similar manner to PRx, using a moving correlation coefficient of consecutive time averaged data points of THI and ABP over 30 min periods. PRx and THIx were compared according to the

method described by Bland and Altman.

RESULTS: All patients had intact CA as assessed by PRx. The Bland Altman relationship between PRx and THIx is shown ($R = 0.56$, $p < 0.01$) (see figure).



DISCUSSION: This pilot study explores the feasibility of a novel SRS assessment of CA in patients with TBI. In this small number of patients there was only a weak correlation between PRx and THIx. Further studies are therefore required, in larger numbers of patients, to determine the validity of THIx as a measure of CA. SRS assessment of CA has the potential to be entirely non-invasive and applicable in patients in whom ICP monitoring is not indicated or practical.

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S-117.

TITLE: THE EFFECTS OF NEUROMUSCULAR BLOCKADE AND POSITIVE END-EXPIRATORY PRESSURE ON LUNG AND CHEST WALL MECHANICS DURING LAPAROSCOPIC SURGERY

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AFFILIATION: ¹UFRJ, Rio de Janeiro, Brazil, ²FIOCRUZ, Rio de Janeiro, Brazil.

INTRODUCTION: Videolaparoscopy procedures are carried out through insufflating carbon dioxide (CO₂) into the peritoneal cavity. During the pneumoperitoneum procedure, the elevation in intra-abdominal pressure (IAP) increases airways pressure and reduces ventilation with significant impact over the respiratory mechanics. The main objective of the present study was to evaluate the effects of neuromuscular blockers (NMB) and positive end-expiratory pressure (PEEP) in respiratory mechanics.

METHODS: Through least square fit method, we performed the dynamic analysis of the elastance and resistance of respiratory system in 22 patients submitted to videolaparoscopy cholecystectomy. Pulmonary elastance (Ep), chest wall elastance (E_{cw}), and respiratory system elastance (E_s) were measured after induction, during the pneumoperitoneum, after completely NMB (train of four = 0) with atracurium 0,5 mg/kg and after initiation of PEEP (8 cmH₂O).

RESULTS: The E_s raised 29,6% after the pneumoperitoneum (p < 0.001). This effect was related to a direct elevation of both components Ep and E_{cw}. The use of BNM did not induce any change in E_s. On the other hand, the utilization of PEEP significantly reduced E_s (9.96%), Ep (8,33%) and E_{cw} (15%) (p < 0.05).

DISCUSSION: These results showed beneficial effects of PEEP in respiratory mechanics during laparoscopic procedures. The advantage of using PEEP is evident and is useful to alleviate the changes in respiratory system induced by pneumoperitoneum in laparoscopy surgeries.

S-118.

TITLE: THE NEW VAMA® INTUBATING AIRWAY: A UNIQUE DESIGN FOR FIBEROPTIC INTUBATION

AUTHORS: P. Marzal¹, F. Llobell¹, J. Cardona¹, A. Madrid¹, V. Madrid¹, Y. Bryan²;

AFFILIATION: ¹Hospital G. U. Marina Alta, Denia (Alicante), Spain, ²Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

INTRODUCTION: Several available intubating airways facilitate performing fiberoptic intubation and placing an endotracheal tube (1,2). The new VAMA® intubating airway incorporates design features which address common problems encountered during fiberoptic intubation. A line with an arrow (lasermark) embedded on the distal part of the ventral surface of the posterior portion of the airway facilitates orientation (see Figure 1). A detachable piece on the proximal portion of the airway facilitates removing the VAMA® airway while the endotracheal tube (ETT) remains connected to the circuit; thus avoiding interruption in ventilation and inadvertent extubation. We describe our experience with the VAMA® intubating airway for fiberoptic intubation.

METHODS: After obtaining verbal consent, 19 patients undergoing surgery and requiring endotracheal (ETT) intubation were recruited. After general anesthesia or sedation and topical anesthesia, a 5.5 mm flexible fiberscope was loaded with an ETT and placed orally via the VAMA® airway. Using the lasermark on the VAMA® for guidance, the FFB was inserted until the glottic opening was visible. After advancing the FFB through the vocal chords, the ETT was railroaded into the trachea and the position was confirmed. The detachable piece of the VAMA® was first removed and while holding the ETT, the remaining part of the VAMA® airway was removed without disconnecting the ETT from circuit.

RESULTS: The mean and range of age and time to intubation were 57.5 years (31-86) and 42 seconds (25-70). In 13 patients, the glottic opening was visualized on first pass of the FFB placed in the VAMA® airway. In 6 patients, a chin lift exposed the glottic opening. All intubations occurred on first attempt, except one which required three attempts. Five patients had known difficult airways (DA), 7 intubations

were awake and in 7 patients, paralytic agents were used.

Figure 1



DISCUSSION: The lasermark of the VAMA® airway helps identify the anatomical landmarks necessary for fiberoptic intubation. Disconnecting the removable piece facilitates complete removal of the VAMA® airway. Further research is required comparing to other intubating airways in patients with known DA's who are both awake and anesthetized.

REFERENCES: 1) J Clin Anesth 2004 16:66-73; 2) Anaesth 2004 59: 173-176; 3) VAMA Canula Package Insert www.ajlsa.com

S-119.

TITLE: RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE VENTILATION DISTRIBUTION AND THE INFLUENCE OF A CO₂ PNEUMOPERITONEUM WHILE PEEP AND ZEEP VENTILATION DURING LAPAROSCOPIC CHOLECYSTECTOMY BY ELECTRICAL IMPEDANCE TOMOGRAPHY (EIT)

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INTRODUCTION: The induction of general anesthesia (1) and the application of a CO₂ pneumoperitoneum (PP) (2, 3) results in atelectasis of the dependent lung regions and is associated with an impairment of oxygenation. Application of positive end-expiratory pressure (PEEP) can maintain pulmonary gas exchange. To determine respiratory function during surgical operations, measurements of state of global oxygenation and the monitoring of common respiratory mechanics are used in standard clinical routine. EIT is a non-invasive monitoring method allowing a continuous functional visualization of ventilation distribution during surgery (4, 5). We investigate the effect of anaesthesia, mechanical ventilation and PP on regional ventilation distribution and arterial oxygenation monitored by EIT with and without PEEP.

METHODS: After the local ethics committee approval we prospectively randomised 32 consecutive patients (ASA physical status I/II) scheduled to undergo elective laparoscopic cholecystectomy. The patients were randomly assigned to PEEP (10 cm H₂O) or ZEEP group (0 cm H₂O). Anaesthesia and respiratory management was standardized and patients were ventilated volume controlled. EIT was performed before and after the induction of anaesthesia and tracheal intubation, after application of the PP and after exsufflation of the PP during a one minute time interval. We calculated the impedance ratio (IR) to

investigate the differences in distribution and homogeneity of pulmonary ventilation. EIT data and variables related to gas exchange and respiratory mechanics were compared between PEEP and ZEEP groups. T-test and variance analysis by Greenhouse-Geisser-methode was used for statistical analysis.

RESULTS: Both groups did not differ regarding demographic data, pre-operative spirometry data, length of surgery and anaesthesia. There was significant difference between both groups on PaO₂ (p=0.02), PF-ratio (p=0.04), AaDO₂ (p=0.04) and respiratory compliance (p=0.01). There was a significant difference in IR ratio between both groups over time of examination (p=0.04), but no significant difference in IR of right and left lung between both groups (p=0.12). The distribution of the pulmonary ventilation changed, and impedance was reduced in the dorsal parts of the lung especially in ZEEP group. The application of PEEP exhibited an elevation of ventilation in the dependent lung areas, which corresponded well to the significant higher respiratory compliance and improving arterial oxygenation in the PEEP group.

DISCUSSION: The effect of intraoperative PEEP application can be evaluated by dynamic EIT monitoring under clinical circumstances. The application of PEEP has been shown to reduce the inhomogeneity of ventilation distribution and the shift of ventilation in the dependent lung regions during general anesthesia.

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S-120.

TITLE: RELATIONSHIP OF CEREBRAL OXIMETRY-MEASURED HEMOGLOBIN PER VOLUME OF TISSUE TO ARTERIAL BLOOD HEMOGLOBIN

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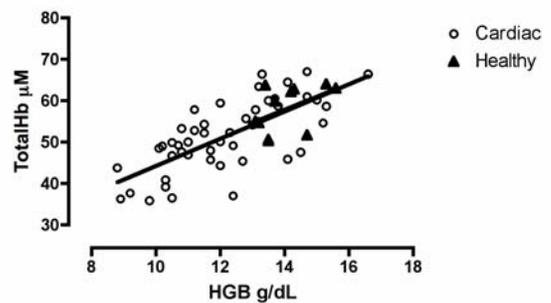
INTRODUCTION: In addition to measuring cerebral tissue oxygen saturation (SctO₂), the FORE-SIGHT cerebral oximeter (CASMED, Branford, CT) also measures the concentration of hemoglobin per volume of brain tissue (TotalHb) given as micromoles (μM) per liter of tissue. We hypothesized that TotalHb would correlate to arterial HGB (hemoglobin concentration in blood; units g/dL) and arterial carbon dioxide tension (PaCO₂) measured from arterial blood gas (ABG) analysis.

METHODS: With informed consent, the FORE-SIGHT cerebral oximeter was used to measure TotalHb. Simultaneous HGB and PaCO₂ were measured from ABGs. Data was taken from healthy subjects breathing room air (spontaneous ventilation) and from cardiac subjects prior to incision (controlled ventilation).

RESULTS: Data was collected from 57 subjects (36 males & 21 females; 11 healthy & 46 cardiac). Correlation by linear regression of TotalHb and HGB was R² = 0.53 (figure). Mean TotalHb (males) was 56.0 μM (CL 53.7 - 58.2); (females) was 46.9 μM (CL 43.1 - 50.7). Mean HGB (males) was 13.2 g/dL (CL 12.6 - 13.7); (females) was 11.4 g/dL (CL 10.7 - 12.1). Using t-tests, there was a significant difference between genders for both TotalHb and HGB.

Mean TotalHb (healthy subjects) was 58.0 μM (CL 54.2 - 61.7); (cardiac subjects) was 51.3 μM (CL 48.8 - 53.9). Mean HGB (healthy) was 14.0 g/dL (CL 13.5 - 14.6); (cardiac) was 12.1 g/dL (CL 11.6 - 12.7). Using t-tests, there was a significant difference between healthy and study subjects for both TotalHb and HGB.

PaCO₂ ranged from 24 - 56 mmHg. Correlations between PaCO₂/HGB: R² = 0.056 and PaCO₂/TotalHb: R² = 0.112.



DISCUSSION: TotalHb is an optically-derived estimate of hemoglobin within a given volume of brain tissue. This study has shown that it correlates with measured arterial hemoglobin. The sites from which the two measures are taken are dissimilar. HGB is derived from per unit volume of blood whereas TotalHb is derived from heterogeneous brain tissue, consisting mostly of brain cells and blood vessels.

In this data set TotalHb correlated predominantly to HGB as opposed to PaCO₂. In the clinical setting TotalHb could potentially be used to provide a non-invasive and continuous estimation of brain tissue hemoglobin levels.

REFERENCE: Anesthesia Analgesia 2006; 102(2S):S162

S-121.

TITLE: INTUBATION AT FLOOR LEVEL - EVALUATING THE AIRTRAQ LARYNGOSCOPE

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INTRODUCTION: Pre-hospital intubation is usually performed whilst the patient is on the floor. Achieving optimal alignment of the oral, pharyngeal and laryngeal axes with traditional laryngoscopes can be difficult at floor level and patients with normal airways may subsequently present as difficult intubation. The Airtraq laryngoscope has been used effectively during the management of both easy and difficult laryngoscopies^{1,2}. This study was designed to evaluate the Airtraq during intubation of manikins at floor level by pre-hospital practitioners.

METHODS: Following ethical approval and written informed consent, pre-hospital practitioners attending the 2007 International Trauma Care Conference, were invited to participate in the study. Each received a standardised demonstration³ and was allowed to practice the Airtraq intubation technique, on an airway training manikin. Five minutes later with the manikin positioned at floor level, mask ventilation with a self-inflating bag was commenced. Each subject intubated the manikin using both laryngoscopes in a randomised sequence. The total intubation time (from facemask removal to confirming ventilation of the lungs) for both laryngoscope groups, was recorded for each participant. Following successful intubation the difficulty of laryngoscopy and intubation for both groups was rated (from 0 = extremely easy to 10 extremely difficult) using a 100 mm visual analogue scale (VAS).

RESULTS: Thirty delegates, who had no previous experience using the Airtraq, were recruited. The intubation success rate was 100% in both groups. Data collected for each group is shown in table 1. All data were analysed using Wilcoxon signed rank test, which showed that the laryngoscopy and intubation using the Airtraq was significantly easier

($P < 0.001$). There was no statistically significant difference in the total intubation times between the two groups ($P = 0.13$).

Table 1. Intubation time and VAS. Data for both groups is presented as median, [inter-quartile range] and (range).

	Macintosh Group (n=30)	Airtraq Group (n=30)
Total Intubation Time (sec)	19.5 [15.6 - 34.5] (11.2 - 71.3)	23.5 [17.9 - 34.7] (9.2 - 117.3)
VAS (mm)	60 [50 - 70] (20 - 100)	30 [20 - 60] (0 - 100)

DISCUSSION: No significant difference was detected in total intubation time between the two laryngoscopes. In anatomically correct manikins, tracheal intubation performed by pre-hospital practitioners at floor level is easier with the Airtraq than with the Macintosh laryngoscope.

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3. Anaesthesia 2006; 61: 469-77.

S-122.

MAPLESON D VS AMBU BAG™ FOR ECT: WHICH WOULD YOU CHOOSE?

AUTHORS: M. Walter, C. G. Choukalas, D. Glick, M. O'Connor, A. Tung, M. E. Nunnally;

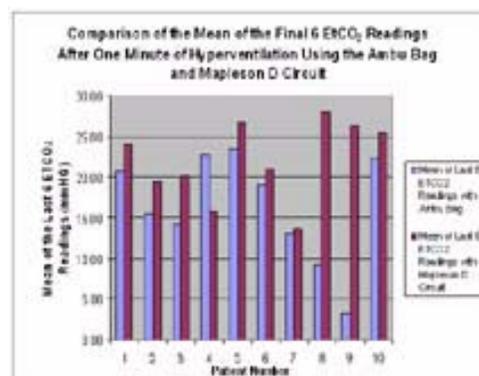
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INTRODUCTION: Short seizures limit the anti-depressive effects of electroconvulsive therapy (ECT).¹ Lowering arterial carbon dioxide (CO₂) levels increases seizure duration.² Consequently, anesthetists typically ventilate patients aggressively using a manual ventilation device. The effectiveness of these devices in inducing hypocapnia, however, is unclear. Although inexpensive, the Mapleson D circuit allows patients to rebreathe exhaled CO₂,³ and may not be as effective as other devices. We compared the Mapleson D circuit with the Ambu Bag™ with regards to their ability to induce hypocapnia during ECT using end-tidal CO₂ (EtCO₂) as a noninvasive measure of arterial CO₂.

METHODS: This study was approved by our Institutional Review Board. Eligible patients included inpatients and outpatients age ≥18 presenting to the University of Chicago Medical Center for ECT. Exclusion criteria included pregnancy and concurrent enrollment in another study. Patients were initially randomized to one of two devices by a coin flip, and crossed-over to the other device for the subsequent treatment. Each device was attached to an EtCO₂ monitor. Oxygen flow rates were 10 liters per minute for all patients.

Following muscle relaxation, the anesthetist was instructed to ventilate as efficiently as possible for one minute. The anesthesia team was blinded to the EtCO₂ readings. After this period, ECT proceeded as per standard of care. The last 6 EtCO₂ measurements were then averaged and compared for each device.

RESULTS: Ten patients have been enrolled in the study. Ventilation with the Mapleson D circuit produced an average mean EtCO₂ of 22 mmHg among the 10 patients while ventilation with the Ambu Bag™ produced an average mean EtCO₂ of 16 mmHg among the same patient group ($p = .07$). Among the 10 pairs, only one patient had a higher mean EtCO₂ with the Ambu Bag™ than with the Mapleson D circuit (Figure 1).



DISCUSSION: After hyperventilation, EtCO₂ was lower with the Ambu Bag™ than the Mapleson circuit in all but one subject. Our results suggest that manual ventilation with the Ambu Bag™ more effectively induces hypocapnia in patients receiving ECT than the Mapleson D.

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S-123.

TITLE: MEASUREMENT ERROR IN CENTRAL VENOUS PRESSURE MONITORING

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INTRODUCTION: The accurate and consistent placement of pressure transducers for invasive monitoring of central venous pressure (CVP) is critical important. Inaccurate or inconsistent placement between health care providers can result in significant measurement error. The variation in transducer placement between health care personnel has not been systematically evaluated. This information is important when interpreting data obtained by different healthcare providers. We hypothesize that there is significant variation in the placement of these transducers between healthcare personnel, which results in significant measurement error.

METHODS: A sample of 50 perioperative healthcare providers (24 anesthesia residents, 14 nurses, and 12 faculty members) familiar with the practice of invasive central venous pressure monitoring were asked to place a transducer at the appropriate level for a sample patient in three positions: flat supine, approximately 30° head up, and approximately 15° Trendelenburg. The position of the transducer was recorded after each placement.

RESULTS:

Position	Standard Deviation (cm)	Interquartile Range (cm)	Range (cm)
Flat Supine	4.3	5.8	17.5
30° Head up	6.5	5.7	40.3
15° Trendelenburg	4.3	6.0	21.6

DISCUSSION: CVP measurements either alone or as a trend are frequently used to monitor cardiac preload. Small changes in CVP may translate to large changes in physiologic status. Our data demonstrates that measurement error in CVP transducer placement may be equal to or even greater than the magnitude of a normal CVP value. These data suggest that careful consideration must also be taken when interpreting

CVP data obtained by different healthcare personnel or reported by different authors. Further, interventions to minimize the measurement error associated with transducer placement should be investigated.

S-124.

TITLE: PROPOFOL MUST BE EXPELLED FROM ANESTHESIA WITH MONITORING OF MOTOR-EVOKED POTENTIALS (MEPs) IN PATIENTS WHO HAVE SYMPTOMS IN UPPER AND LOWER EXTREMITIES AND MIDAZOLAM CAN SUBSTITUTE FOR PROPOFOL.

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INTRODUCTION: Monitoring of descending corticospinal pathways by using motor-evoked potentials (MEPs) has been proven to be useful in preventing neurological deficits during spinal procedures. We found out propofol effect-site concentration (PESC) at 1.0µg/ml markedly improved MEPs amplitude in patients whose MEPs facilitation was very poor at PESC 2.41µg/ml (average). (1) PESC 1.0µg/ml is very light sedation, so another sedative agent, such as ketamine must be concurrently-administered to maintain anesthesia. However ketamine affects bispectral-index (BIS) and it makes difficult to evaluate sedation-levels during anesthesia. This study aimed to explore 1) the possibility to give sufficient MEPs facilitation at PESC 1.0µg/ml in all patients, 2) the effect of midazolam in MEPs amplitudes, and 3) the possibility to substitute midazolam for propofol.

METHODS: This study protocol was approved by the local ethical committee. Seven patients undergoing cervical vertebrae surgeries with ASA I or II were included in this study. MEPs were recorded from deltoids and anal sphincters in all patients and MEPs from other two muscles of lower extremities were recorded in accordance with symptoms. Induction of anesthesia was performed with remifentanyl, propofol, and lidocaine and the patient trachea was intubated without using muscle relaxants. Anesthesia was maintained with remifentanyl and propofol. Propofol was administered in target-controlled infusion (TCI) fashion with Diprifusor and BIS was monitored in all patients.

After MEPs were recorded at PESC 2.0µg/ml (control), midazolam was administered as a bolus of 2-4mg followed by continuous infusion at 3-

5mg/h and PESC was lowered to 0.2-1.0µg/ml. MEPs at different PESC were compared with control measurement.

RESULTS: Four patients did not have any symptoms in upper and lower extremities. In these patients, MEPs were recorded at PESC 2.0µg/ml and the amplitudes of MEPs were not different from those at PESC 0.3µg/ml. Three patients had symptoms in upper extremities. Although in 2 of these 3 patients, MEPs were recorded only at deltoids at PESC 2.0µg/ml, MEPs were recorded at all muscles by lowering PESC. One of these 3 patients, MEPs were recorded from all muscles at control, however, MEP from left quadriceps was decreased at PESC 1.0µg/ml and it improved at PESC 0.3µg/ml.

Midazolam did not show any suppressive effect on MEPs in all patients.

CONCLUSIONS: Propofol suppressed facilitation of MEPs in patients who had symptoms. It suppressed MEPs facilitation even at PESC 1.0µg/ml in some patients. Midazolam did not show any suppressive effect on MEPs amplitude. Propofol must be expelled from anesthesia with monitoring of MEPs in patients who have symptoms in upper and lower extremities and midazolam can substitute for propofol.

REFERENCES: (1) Anesthesiology 2007; 107: A1500

S-125.

TITLE: HYPERVENTILATION AND SEIZURE LENGTH: A COMPARISON OF MAPLESON D AND AMBU BAG™.

AUTHORS: C. G. Choukalas, M. Walter, D. Glick, M. O'Connor, A. Tung, M. E. Nunnally;

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INTRODUCTION: Hypocapnia may lower the seizure threshold and increase seizure duration.^{1,2}, thus enhancing the anti-depressive effects of electroconvulsive therapy (ECT).^{3,4} The present study was designed to evaluate the effect of hyperventilation to induce hypocapnia using two different mask ventilation devices (Mapleson D and Ambu Bag™) on seizure duration in patients undergoing general anesthesia for ECT.

METHOD: After IRB approval, participants were recruited from patients undergoing ECT at an academic tertiary medical center. Subjects were ventilated with each device in a crossover design, with the initial device chosen by randomization. Aside from the airway device, clinical care was not altered by participation in the study. During treatment, the anesthetist was instructed to ventilate as effectively as possible for one minute following anesthetic induction. ECT was then initiated, and seizure duration assessed using single-channel EEG and gross motor EMG. Data were analyzed via paired t-test.

RESULTS: Ten participants completed the study. Eight received the same anesthetic agents and doses for both treatments. Gross motor EMG and EEG duration were recorded for eight and ten of the participants, respectively. Seizure duration as measured by EMG and EEG were not different between the two groups. For gross motor EMG, the mean and standard deviations for the Mapleson and Ambu Bag were 17.0s (12.2) and 18.6s (12.2), respectively ($p > 0.05$). For EEG, the mean and standard deviations for the Mapleson and Ambu Bag were 34.5 s (16.4) and 37.0s (16.8), respectively ($p > 0.05$).

DISCUSSION: Although not significant, we found a trend toward longer seizures when the Ambu Bag™ was used. One likely reason for a lack of significance is that, at present, the study remains underpowered. Our power analysis indicates that 50 subjects are required to detect a 25% difference in seizure duration. It is also

possible that hypocapnia makes no difference in seizure length. Finally, the degree of hypocapnia may not depend on device type.

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Liver / Transplantation

S-126.

TITLE: IDENTIFYING POTENTIAL PREOPERATIVE PREDICTORS OF ADVERSE POSTOPERATIVE OUTCOMES IN ORTHOTOPIC LIVER TRANSPLANTATION: A RETROSPECTIVE ANALYSIS

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INTRODUCTION: The purpose of this study was to identify preoperative characteristics that could predict adverse postoperative outcomes in orthotopic liver transplantation (OLT). Of particular interest was the ability of preoperative MELD scores to predict postoperative outcomes, as previous research has garnered mixed results (1, 2).

METHODS: We identified 182 adult patients who underwent OLT at the Medical University of South Carolina between 2003 and 2007. Univariate regression models were run for each predictor (age, hypertension, coronary artery disease, ejection fraction, QT, and diabetes mellitus) with continuous and categorical outcomes. Multiple regression models were fit to the data to adjust for possible confounders (sex, etiology of liver disease, preoperative MELD score). The distributions for the length of the ICU stay and the hospital stays were highly skewed, so they were log-transformed before analysis. A total of 10 patients died while in the hospital, 9 of which while in the ICU, so the length of stay up until time of death was used in the analysis.

RESULTS: The participants were mostly male (70.2%) with a mean (SD) age of 51.0 (10.74) years. Hypertension, coronary artery disease, and diabetes mellitus were present in 30.8%, 5.5%, and 30.2% of patients, respectively. The most common etiology was Hepatitis C (31.3%). The mean (SD) of the MELD score was 21.74 (8.57) [range: 11 to 65, median: 19]. The mean (SD) of length of ICU stay was 4.8 (5.6) days, and the mean (SD) length of hospital stay was 13.1 (15.0) days. MELD was a significant univariate predictor of length of stay in the ICU ($p=0.04$) and length of stay in the hospital ($p<0.01$) when both outcomes were log transformed. When adjusted for potential confounders, the MELD score was no longer significant in predicting

log ICU days ($p=0.38$), but was for length of hospital stay ($p=0.04$).

DISCUSSION: This study illustrates that MELD is a significant predictor of length of hospital stay. More importantly, it demonstrates two significant negative findings. First, it further illustrates that MELD scores are not predictive of postoperative adverse outcomes. Second, multiple preoperative characteristics that are often considered risk factors for perioperative morbidity, such as age, cardiac disease, and diabetes, were not associated with adverse events or prolonged hospital stays. The implication of this finding is that MELD scoring remains the most appropriate system for evaluating organ allocation in OLT and that the patient characteristics evaluated in this study should not affect liver transplant candidate selection. However, as MELD scoring best predicts mortality while on the waiting list, further studies are needed to develop a predictive model for adverse events in OLT, thus improving allocation of such a limited resource.

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S-127.

TITLE: ANESTHETIC COMPLICATIONS AND MORBIDITY IN LIVING LIVER DONOR SURGERY

AUTHORS: D. Beebe, J. Jochman, P. Luikart, H. Singh, R. Gruessner, K. Belani;

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INTRODUCTION: Living liver donation is becoming a more common means to treat patients with liver failure because of a shortage of cadaveric organs and tissues. There is a potential for morbidity and mortality, however, in patients who donate a portion of their liver. The purpose of this study is to identify anesthetic complications and morbidity resulting from living liver donor surgery.

METHODS: The anesthetic records of all patients who donated a segment of their liver between 01/1997 and 01/2006 at University of Minnesota Medical Center-Fairview were retrospectively reviewed. The surgical and anesthesia time, blood loss, hospitalization length, complications, morbidity and mortality were recorded. Data were reported as mean \pm SD.

RESULTS: 74 patients (34 male, 40 female, mean age=35.5 \pm 9.8 years) donated a portion of their liver and were reviewed in the study. Fifty-seven patients (77%) donated the right hepatic lobe, while 17 (23%) donated a left hepatic segment. The average surgical time for all patients was 7.8 \pm 1.5 hours, anesthesia time 9.0 \pm 1.3 hours and blood loss 423 \pm 238 ml. Forty-six patients (62.2%) autologous blood either from a cell saver or at the end of surgery following acute, normovolemic hemodilution, but none required an allogenic transfusion. Following the surgery, 40 patients (54%) were extubated in the operating room. However 1 patient had to be re-intubated in the operating room following extubation due to respiratory depression. The remainder were moved to the recovery room while intubated, and remained intubated for an average time of 40 \pm 37 minutes. There were a total of 2 patients admitted to the intensive care unit due to respiratory depression and a low respiratory rate. One remained intubated overnight. The other was extubated but required observation for a low respiratory rate. Twelve patients (16.2%) had complaints of nausea, and 2 reported nausea with vomiting during their hospital stay. There were 4

patients that developed complications related to positioning during the surgery: 2 patients complained of numbness and tingling in the hands which resolved within two days, 1 patient reported a blister on the hand, and 1 patient complained of right elbow pain that resolved quickly. Post-operative hospitalization averaged 7.4 \pm 1.5 days. There was no patient mortality.

DISCUSSION: Living liver donation operations can be performed with low morbidity. However, post-operative respiratory depression is a concern and is perhaps due to altered metabolism of administered narcotics. This complication has been noted in patients undergoing hepatic resection for other causes.¹ Further investigation is necessary to determine the magnitude of loss in metabolic activity of the liver and its impact on anesthetic agents following living liver donation.

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S-128.

TITLE: PATIENTS WITH HEPATOCELLULAR CARCINOMA WITH PREVIOUS TRANS ARTERIAL CATHETER EMBOLIZATION TREATMENT ARE NOT AT HIGHER RISK OF HYPERKALEMIA DURING HEPATECTOMY FOR LIVER TRANSPLANTATION

AUTHORS: S. Roy, G. Neelakanta, M. Braunfeld, V. Xia;

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INTRODUCTION: Patients with hepatocellular carcinoma (HCC) who meet certain criteria are accepted for orthotopic liver transplantation (OLT). We have encountered several patients with HCC with previous trans arterial catheter chemoembolization treatment develop rapid and potentially dangerous hyperkalemia during hepatectomy for OLT. The purpose of this study is to determine if serum potassium is likely to be greater in patients with HCC following TACE or radio frequency ablation (RFA) treatment during hepatectomy, possibly due to release of potassium from the liver.

METHODS: After institution review board approval, we reviewed medical records of adult patients with chronic hepatitis and primary hepatocellular carcinoma who underwent primary orthotopic liver transplant over a one-year period (March 2006-2007). A control group of patients with chronic hepatitis without HCC who underwent OLT during the same period were also studied. Data collection included demographics, trans arterial catheter chemoembolization or radio frequency ablation treatment for HCC prior to OLT, preoperative MELD score, preoperative hemoglobin, platelet count, INR, preoperative serum potassium, peak potassium during or immediately following hepatectomy and number of units of red cell transfusion during hepatectomy. Exclusion criteria was preoperative dialysis or serum creatinine > 1.3 mg/dl. Analysis of change in serum potassium during hepatectomy from preoperative level was done by two-tailed student t-test.

RESULTS: A total of 75 patients were included for analysis. Seven patients who had preoperatively diagnosed HCC but no TACE or RFA

treatment and 7 patients who had incidental HCC at the time of OLT were included in the control group. The results are shown in the table. There was no difference in the mean change in serum potassium from the preoperative level between the two groups (p=0.9).

Table: Change in serum potassium during hepatectomy

	Control patients	Patients with TACE or RFA	P value
n	27	48	
Age (yrs) Mean±SD	55±8	56.8±7.8	0.35
Gender			
MELD Score (Mean±SD)	22.8±4.2	20.1±6.9	0.06
Pre-operative hemoglobin (Mean±SD)	11.3±1.5	13±2	<0.001
Pre-operative platelet count (Mean±SD)	57±18	98±61	<0.001
Preoperative K ⁺ (Mean±SD)	3.9±0.4	4.1±0.4	0.2
Red cell transfusion during hepatectomy (units) (Mean±SD)	7.7±4.7	5.8±4.7	0.13
Change in K ⁺ during hepatectomy (Mean±SD)	0.6±0.5	0.5±0.6	0.9
No of patients with K ⁺ > 5.5 mmol/L during hepatectomy	0	3	

DISCUSSION: The results of this study does not support the view that patients with chronic hepatitis and primary HCC status post TACE or RFA treatment are more likely to develop greater change in serum potassium during hepatectomy for OLT. Further studies are warranted and alternative explanations may be sought in patients who develop rapid rise and potentially dangerous hyperkalemia during hepatectomy for OLT.

REFERENCE:

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S-129.

TITLE: HOW FARE CAN WE GO WITH PEEP IN LIVER TRANSPLANT PATIENTS?

AUTHORS: F. H. Saner¹, S. Oldedamink², G. Pavlakovic³, G. Sotiropoulos¹, A. Radtke⁴, C. E. Broelsch¹;

AFFILIATION: ¹University Essen, Essen, Germany, ²University Maastricht, Maastricht, Netherlands Antilles, ³University Goettingen, Goettingen, Germany, ⁴Universoty Essen, Essen, Germany.

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 liver transplantation (LT) we performed a clinical trial on patients following LT regarding to relationship between PEEP, hepatic performance, and systemic hemodynamics.

METHODS: 52 patients following LT were enrolled in this study. All patients were mechanical ventilated with biphasic positive airway pressure (BIPAP). The effects of three randomly chosen PEEP levels (5, 10, 15 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 at a PEEP of 5, 10 and 15 mbar did not reach statistical difference. There was no impact of increased PEEP of 10 mbar on mean arterial pressure (88 mmHg (5 mbar) vs 85 mmHg (10 mbar); however a PEEP of 15 mbar significantly decreased the MAP to 83 mmHg), mean pulmonary arterial pressure was not influenced at PEEP of 10 mbar (23 mmHg at PEEP 5 and 10 mbar), however a significant increase to 26 mmHg at a PEEP of 15 mbar was recorded. The cardiac index showed no statistical significance at any PEEP level (CI, 4.6 L/min⁻¹*m² (PEEP 5 mbar), 4.6 L/min⁻¹*m² (PEEP 10 mbar), and 4.4 L/min⁻¹*m² at PEEP 15 mbar). The central venous pressure increased from 8 mmHg to 9 mmHg (p=0.07) while increasing the PEEP from 5 to 10 mbar and showed a significant increase to 12 mmHg at a PEEP of 15 mbar. The

pulmonary capillary wedge pressure increased from 11 mmHg at 5 mbar to 12 mmHg at a PEEP of 10 mbar, but showed also a significant increase to 15 mmHg at a PEEP of 15 mbar.

DISCUSSION: The most striking feature of our study was that even a PEEP of 15 mbar does not impair the liver outflow. Moreover, the unchanged blood flow velocities for HA and PV and RHV with an unchanged CI even at a PEEP level of 15 mbar indicates that the blood flow throughout the liver is unaffected by this PEEP level. In conclusion, short term ventilation with PEEP up to 15 mbar in LT patients does not impair the liver outflow.

S-130.

TITLE: INTRAOPERATIVE ASSESSMENT OF TRANSPLANT PANCREAS ALLOGRAFT FUNCTION AS A MEASURE FOR TRANSPLANT OUTCOME

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INTRODUCTION: Pancreas transplant allografts have their highest risk of graft failure in the perioperative period. Predictors of pancreas graft failure have not been conclusively determined. This study uses a retrospective review of the intraoperative anesthesia records for all pancreas transplants performed over a 4 year period to determine if intraoperative and perioperative measures of allograft function are predictive of graft survival.

METHODS: The general medical and anesthesia records of all pancreas transplants performed between 2003 and 2006 at Indiana University hospital were reviewed. Recipient and donor transplant information and outcomes were extracted from the transplant center registry. Transplants included in the analysis were simultaneous kidney and pancreas transplants, pancreas alone transplants, and pancreas after kidney transplants with a minimum follow-up of 6 months. Intraoperative and perioperative measures of allograft function included blood glucose (BG) levels, serum amylase and lipase levels, as well as need for exogenous insulin administration. Insulin was withheld in the perioperative period for BG levels less than 200.

RESULTS: There were 179 of the aforementioned transplants performed with complete data available on 129. Overall one-year graft and patient survival were 89.4% and 97.5% respectively. Graft loss within 7 days of transplant was 3.9%. Sixty percent of patients required no insulin intraoperatively. At allograft reperfusion, 10% of the patients had blood glucose levels less than 120. Over time, this statistic improved to 27% at 1 hour, 51% at 2 hours, and 59% at 3 hours. The median rate of change in blood glucose levels in the first two hours post-reperfusion was a 32% decrease, with 21% of patients having a greater than 50% reduction. Kaplan-Meier graft survival analysis failed

to demonstrate a significant difference in graft survival based upon the factors of need for intraoperative insulin, post-reperfusion blood glucose levels, or initial rate of change of blood glucose levels post-reperfusion.

DISCUSSION: Most pancreas transplant patients experience immediate pancreas allograft function upon organ reperfusion as measured by changes in blood glucose levels and need for exogenous insulin. The majority of these patients require no exogenous insulin administration after allograft reperfusion. Changes in blood glucose levels in the first 3 hours post-transplant are not associated with perioperative and 1 year graft survival.

S-131.

TITLE: USE OF APROTININ IN INTESTINAL TRANSPLANTATION

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INTRODUCTIONS: Aprotinin is frequently utilized intraoperatively in liver transplantation to minimize blood loss. Our center has used aprotinin intraoperatively in multivisceral and isolated intestinal transplantation since 2003. Multivisceral transplantation is comprised of liver transplantation with simultaneous transplantation of the stomach, pancreaticoduodenal complex (including pancreas) and the small intestine. We report the outcomes and complications associated with the use of aprotinin in intestinal transplantation.

METHODS: The records of all adult patients undergoing multivisceral and isolated intestinal transplantation were reviewed. Data analysis included blood loss, hemodynamic instability, and peri-operative complications including myocardial infarction (MI), stroke, deep venous thrombosis (DVT) and vascular thrombosis of the transplanted allograft.

RESULTS: There were 35 adult intestinal and multivisceral transplants performed between 2003 and 2006. Twenty patients received intraoperative aprotinin (57%) including 18 of 23 undergoing MVT (78%) and 2 of 12 undergoing intestinal transplantation (17%). Seven patients received simultaneous kidney transplantation. No patients experienced graft thrombosis post-transplant. No patient developed DVT, MI, acute renal insufficiency, or stroke related to aprotinin use.

CONCLUSIONS: Aprotinin can be safely utilized in intestinal transplantation without an increased rate of perioperative complications, and use of this agent may be beneficial in minimizing intraoperative blood loss.

Neuroanesthesia

S-132.

TITLE: MULTIMODAL FUNCTIONAL IMAGING OF LOSS OF CONSCIOUSNESS UNDER PROPOFOL ANESTHESIA USING SIMULTANEOUS EEG/FMRI: FMRI CORRELATES OF THE 40-Hz ASSR AND LOSS OF CORTICAL-FUGAL INHIBITION

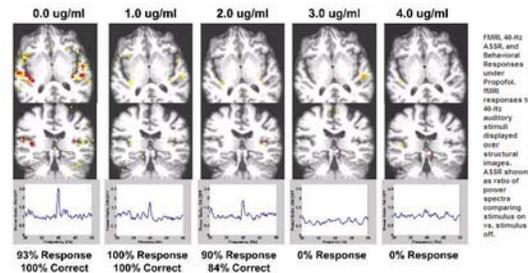
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INTRO: Loss of consciousness (LOC) under General Anesthesia (GA) is measured clinically by observing the loss of response to stimuli. However, auditory perception and memory are possible in patients who are clinically unconscious, which may result in post-operative recall. GA also results in respiratory depression and autonomic instability. The 40-Hz auditory steady-state response (ASSR) is an event-related potential that is abolished during LOC under anesthesia, but its neural basis is not well understood. In this study, we measured simultaneous fMRI and EEG, and calculated 40-Hz ASSR during gradual induction of GA with propofol to assess auditory processing in brainstem and cortex during GA.

METHODS: Healthy post-laryngectomy patient volunteers were recruited for this study. Subjects' airways were secured using cuffed tracheostomy tubes inserted prior to induction. Hospital standards for monitoring, air, oxygen, suction, backup power, and advanced cardiac life support (ACLS) were established for the MRI environment and strictly followed. At least 2 anesthesiologists, plus a third ACLS-certified person, were present at every study, with one anesthesiologist solely responsible for the medical management of the subject. Intravenous propofol was administered at effect-site concentrations of 0, 1, 2, 3, and 4 ug/ml using STANPUMP. At each effect-site concentration, study subjects were presented 40-Hz auditory stimuli. Clinical LOC was measured using a behavioral task where subjects identified a randomized low or high-pitched tone via button press, with loss of response indicating LOC. Blood samples for propofol assay

were taken every ~5 minutes. Arterial blood gas samples were taken to confirm constant arterial CO₂ during the study. Simultaneous EEG and fMRI were recorded at 3 Tesla throughout the experiment.

RESULTS AND DISCUSSION: At baseline, 40-Hz ASSR and robust fMRI activity in primary and secondary auditory cortex were observed. After LOC, response in 40-Hz ASSR and secondary auditory cortex were lost, though primary cortex remained active. At deep anesthesia, brainstem activity (inferior colliculus) increased dramatically. These results suggest that 40-Hz ASSR is correlated with activity in secondary auditory cortex, and that cortical-fugal inhibition is released under deep anesthesia, suggesting a possible mechanism for clinically-observed autonomic instability during GA



S-133.

TITLE: THE EFFECT OF DEXMEDETOMIDINE ON PERIOPERATIVE HEMODYNAMICS IN PATIENTS UNDERGOING CRANIOTOMY

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INTRODUCTION: The perioperative course of patients undergoing intracranial surgery is frequently complicated by hypertensive episodes.¹ Dexmedetomidine (DEX), an alpha-2 adrenoreceptor agonist, is gaining popularity in neuroanesthesia because its sympatholytic and antinociceptive properties may improve hemodynamic stability at critical moments of surgery.² We designed this study to assess efficacy of DEX in controlling hypertensive responses in patients undergoing intracranial surgery.

METHODS: Patients scheduled for elective craniotomy were randomly assigned to receive either sevoflurane-opioid-placebo or sevoflurane-opioid-DEX anesthesia. Bispectral index was used to maintain similar level of hypnosis in both groups (40-50). Opioids, sevoflurane, and vasoactive medications were titrated in a routine manner, at the discretion of the blinded anesthesiologist managing the case, to maintain systolic blood pressure (SBP) targeted within 90-130 mm Hg and heart rate (HR) between 50-90 beats/min. Hemodynamic variables were continuously recorded and stored on a computer for analysis. Efficacy of the anesthetic technique in controlling SBP or HR is inversely proportional to the AUC outside the targeted range. Areas under the curves above and below targeted ranges for SBP-time (AUC_{sbp} mmHg * min/hr) and HR-time (AUC_{hr} beats/min * min/hr) were compared. We assessed global hemodynamic stability using the coefficients of variation (CV) of SBP and HR. In addition, we compared amounts of perioperative anesthetic and vasoactive drugs administered.

RESULTS: Sixty-four patients were recruited for the study. Demographic data did not differ between groups. CV and AUC hemodynamic analysis was performed on computerized records for 48

of 62 patients studied. AUC_{sbp} for above the targeted range was significantly lower for patients in the DEX group (P = 0.048). The CV for SBP and HR did not differ between groups. Significantly lower proportion of patients in the DEX group required treatment with antihypertensive medications (13/31, 42% versus 26/31, 84%, P=0.0013). The DEX group required fewer opiates in the intraoperative period but there were no differences in the use of sevoflurane. In the post anesthesia care unit (PACU), patients in the DEX group had fewer hypertensive episodes (1.3±1.5 versus 3.1±2.4, P=0.0012) and were discharged earlier (92±17 versus 139±18 min, P=0.0001). There were no differences in the requirement for postoperative opioids or antiemetics.

CONCLUSION: By using indices which assess a global hemodynamic stability of the anesthetic, we determined that intraoperative DEX infusion was effective for blunting the increases in SBP perioperatively. The use of DEX did not increase the incidence of hypotension or bradycardia, common side effects of the drug.

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S-134.

TITLE: NITROGLYCERIN INDUCED HYPOTENSION CAUSES DELAYED TRANSIENT COGNITIVE DYSFUNCTION IN ADULT MICE

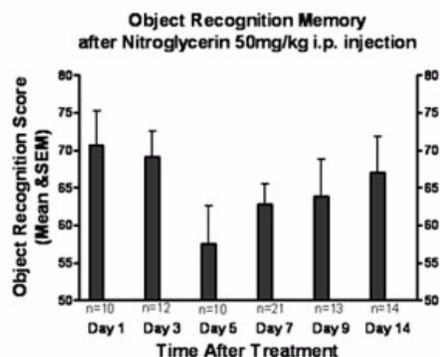
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INTRODUCTION: Decreased cerebral oxygen supply may lead to cognitive dysfunction. Moderate hypoxia causes a transient impairment of object recognition memory (ORM) in mice (1). We tested the hypothesis that nitroglycerin (NTG) induced hypotension would decrease cerebral blood flow (CBF) and would cause a similar impairment in ORM.

METHODS: Following IACUC approval, 80 Swiss-Webster, 30-35 g mice (6-8 wks) were assigned to 1 of 6 schedules. On Day 0 mice received 50mg/kg i.p. NTG in one cc of saline. Each mouse was only tested once during this study on either Day 1, 3, 5, 7, 9, or 14. ORM testing assesses memory exploiting the tendency of mice to explore novel objects where a familiar object is also present. Initially, the animals were allowed to explore the objects for 15 minutes. One hour later, a 3 minute testing trial was conducted with one of the objects replaced by a dissimilar novel object. Time spent exploring each object was recorded by a tracking system (San Diego Instruments). Mice with intact memory spend approximately 65-70% of the time exploring the novel object. Mice with impaired memory devote equal time to familiar and novel objects. A non invasive device (Kent Scientific) measured mean arterial pressures (MAP) in five mice. Data was analyzed with ANOVA (repeated measurements), and post-hoc comparisons using the Newman-Keuls test when appropriate. P-values < 0.05 were considered significant.

RESULTS: Mice subjected to 50mg/kg i.p. NTG exhibited normal ORM until Day 5. Performance improved after Day 7 and returned to normal by Day 14. MAP (data not shown) fell 38% during hypotension from 90 +/- 3.1mm Hg to 56 +/- 6.0mm Hg (SEM).



CONCLUSION: NTG induced hypotension transiently impairs the working memory of mice at MAP near the low range of CBF autoregulation in mice. Hypoxia / ischemia induced apoptotic injury may explain the delayed deterioration of cognitive function. Subsequent improvement in ORM scores may be attributed to “re-learning” of the behavior by healthy neurons. Further studies to explore this phenomenon and possible treatments appear warranted.

SUMMARY: Nitroglycerin induced hypotension causes delayed transient impairment of working memory in adult mice. Apoptosis and “re-learning” may explain the observed effect.

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S-135.

WITHDRAWN

S-136.

TITLE: A RETROSPECTIVE ANALYSIS OF RISK FACTORS FOR SSEP CHANGES INDICATING IMPENDING UPPER EXTREMITY PERIPHERAL NERVE INJURY DURING SPINE SURGERY

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INTRODUCTION Nerve injury is a major complication that can lead to significant patient disability, and is the second leading cause of malpractice claims against anesthesiologists (1). The prone (superman) position has been reported to have a higher potential for upper extremity nerve injury (2). We performed a retrospective analysis of potential risk factors for impending nerve injury, as measured by reversible SSEP changes, during spine surgery in the prone (superman) position.

METHODS After obtaining IRB approval, a retrospective case-control analysis of 107 spine surgeries performed in the prone (superman) position was executed. SSEP changes reversed by intervention were defined as impending nerve injury. A decrease of 50% or more in amplitude and/or an increase of 10% or more in latency were considered significant. Patients were assigned to group A (patients with impending nerve injury) or group B (patients without impending nerve injury). We compared the incidence of existing co-morbidities and American Society of Anesthesiologists physical status classification (ASA-PS) between the 2 groups. Cox-proportional hazards model was applied to look at the risk of impending nerve injury with various existing co-morbidities; $P \leq 0.05$ was considered significant.

RESULTS Thirty three patients had reversible intraoperative SSEP changes (Group A); 74 patients did not have SSEP changes (Group B). The mean ASA-PS classification for Group A was 2.7 (range 2-4); the mean ASA-PS for Group B was 2.7 (range 1-4). There was no significant difference between the groups ($P=0.48$). Data for co-morbidities are shown in Table 1.

Table 1: Incidence of co-existing medical conditions in patients with (Group A) and without (Group B) SSEP changes.

Co-Existing Condition	Group A		Group B		Total		p-Value
	N=3	Percentag e	N=7	Percentag e	N=10	Percentag e	
HTN	16	48.5%	26	35.1%	42	39%	0.1080
DM	5	15.2%	9	12.2%	14	13%	0.7026
Uremia	1	3%	3	4.1%	4	4%	0.8674
PVD	1	3%	5	6.8%	6	6%	0.5751
Anemia	1	3%	4	5.4%	5	5%	0.5579
EtOH	3	9.1%	3	4.1%	6	6%	0.0258

DISCUSSION ASA-PS classification, HTN, DM, uremia, peripheral vascular disease, and anemia were not significantly associated with impending upper extremity nerve injury. Heavy alcohol use was found to be significantly associated with impending upper extremity nerve injury during spine surgery in the prone (superman) position.

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- (1) Cheney FW, et al. Anesthesiology 1999; 90:4:1062-69.
- (2) Kamel IR, et al. Anesth Analg 2006; 102:1538-42.

S-137.

TITLE: THE USE OF SOMATOSENSORY EVOKED POTENTIALS (SSEP) TO DETERMINE THE INFLUENCE OF PATIENTS' AGE AND GENDER ON THE INCIDENCE OF IMPENDING UPPER EXTREMITY NERVE INJURY IN THE PRONE POSITION DURING SPINE SURGERY

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INTRODUCTION Peripheral nerve injury is a significant complication in anesthesiology practice accounting for 16% of malpractice claims (1). Upper extremity somatosensory evoked potential changes (SSEP) during spine surgery indicate impending upper extremity nerve injury (2). Patients positioned in the prone "surrender" position have a higher incidence of impending upper extremity nerve injury (2). We questioned whether the incidence of impending upper extremity nerve injury would be influenced by age and gender during spine surgery in the prone "surrender" position.

METHODS After obtaining IRB approval, we retrospectively reviewed 443 spine surgery surgeries in which patients were placed in the prone "surrender" position. Pediatric patients were defined as patients less than 18 years of age; adults as 18 years of age or greater. Impending upper extremity nerve injury was defined as a significant SSEP change in the prone position that was reversed by repositioning the arm, but not reversed by surgical intervention, decreasing anesthetic depth, increasing blood pressure, or increasing core body temperature; the cause-effect response establishes a relationship between the impending nerve injury and position. Significant SSEP changes were defined as a decrease of 50% or more in amplitude and/or increase of 10% or more in latency. Results were compared using two-sided fisher exact test. A P value less the 0.05 was considered significant.

RESULTS Of the 443 patients reviewed 226 were female; 217 were male. Fifty-three were pediatric patients; 390 were adult patients. The results of both comparisons are listed below in Table 1. There were no statistically significant differences in the incidence of impending upper extremity nerve injury due to difference in gender ($P<0.28$) or age ($P=1$).

Table (1)

Gender & Age	SSEP change	No SSEP change	Total
Female	9	217	226
Male	14	203	217
Total	23	420	443
Pediatric (<18 y/o)	2	51	53
Adults (≥18 y/o)	21	369	390
Total	23	420	443

DISCUSSION The patients' gender and age does not affect the incidence of impending upper extremity nerve injury in the prone "surrender" position during spine surgery. Impending upper extremity nerve injury is relatively common in the prone "surrender" position and is believed to be due to stretching of the brachial plexus.

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- (2) Kamel IR, et al. Anesth Analg 2006; 102:1538-42

S-138.

TITLE: CEREBROSPINAL FLUID AND PLASMA CONCENTRATIONS OF INTERLEUKIN (IL)-6, IL-1 β , IL-1RA, IL-8, AND TUMOR NECROSIS FACTOR (TNF)-ALPHA FOLLOWING INTRACRANIAL ANEURYSM CLIPPING.

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INTRODUCTION: The effect of surgical trauma on the immune system is not fully understood. Major surgery such as thoracoabdominal surgery induces a production of cytokines such as IL-1 β , TNF- α , IL-6, and IL-8 mainly in the operative field.

Recent studies have demonstrated increased cerebrospinal fluid (CSF) concentrations of cytokines after subarachnoid hemorrhage (SAH), suggesting that cytokines are induced in the brain after traumatic events. Although some reports have demonstrated about plasma concentrations of cytokines after neurosurgical procedure^{1,2}, few researches have been performed regarding the CSF and plasma concentrations of cytokines serially. The present study was carried out to investigate whether surgical trauma to the brain such as intracranial aneurysm clipping can induce a immediate production of cytokines intrathecally.

METHODS: After approval of Institutional Research Committee, informed consent was obtained from each patient's relatives. We studied 23 patients who underwent intracranial aneurysm clipping. Thirteen patients were with SAH and ten were without SAH. Anesthesia was induced with thiopental 5mg.kg⁻¹, fentanyl 2-4 μ g.kg⁻¹, and vecuronium 0.1mg.kg⁻¹ and maintained with isoflurane 1-2%, nitrous oxide 50%, and intermittent intravenous boluses of fentanyl and vecuronium. Plasma concentrations of IL-6, IL-1 β , IL-1ra, IL-8, and TNF- α were measured at the following times: after the induction of anesthesia, at the beginning of intracranial procedure, just after aneurysm clipping, at the end of surgery and on postoperative days (POD) 1 and 2. CSF concentrations of those cytokines were measured similarly after the beginning of intracranial procedure in patients with SAH.

RESULTS: Concentrations of IL-6, IL-1 β , IL-8, and TNF- α in CSF were significantly higher than those in plasma. CSF concentrations of

IL-6, IL-1 β , IL-1ra, and TNF- α were significantly increased on POD 1 compared to the beginning of intracranial procedure. CSF concentrations of IL-1 β increased after surgery in patients with Fisher Grade 3, but not in those with Fisher Grade 1 or 2. There was no significant difference in plasma concentrations of cytokines between the patients with and without SAH during the study period, except at the end of surgery when IL-6 concentration was higher in patients without SAH than in patients with SAH. There were significant correlations between plasma IL-1ra concentration after the induction of anesthesia and Fisher Grades ($r=0.67$, $p<0.05$), and between CSF IL-1ra concentration on POD2 and Glasgow Outcome Scale ($r=0.66$, $p<0.05$).

DISCUSSION: Intrathecal production of IL-6, IL-1 β , and TNF- α was induced following intracranial aneurysm clipping. Plasma concentrations of IL-6, IL-1 β , IL-1ra, IL-8, and TNF- α in patients with SAH were not higher than those in patients without SAH. There was a significant correlation between CSF IL-1ra concentration on POD2 and Glasgow Outcome Scale.

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S-139.

TITLE: DELAYED AWAKENING IN DYSTONIA PATIENTS FOR DEEP BRAIN STIMULATOR SURGERY

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INTRODUCTION: Dystonia is a clinical syndrome causing repetitive muscle contractions or abnormal postures^{1,2}. Deep brain stimulation (DBS) surgery provides an alternative in patients where medical treatment is unsuccessful. Anesthetic management during the DBS surgery includes a period of sedation followed by a period in which the patient should remain awake, able to perform simple tasks during micro-electrode recordings (MER) to ensure it's appropriate placement. Delayed emergence from anesthesia after neurosurgical procedures has been reported and can be due to several reasons: residual anesthetic effect, metabolic derangements or intracerebral events like hemorrhage or embolism. Present study identifies dystonia patients who had delayed emergence from anesthesia during DBS placement at our institution and determines the incidence and duration of delayed emergence.

METHODS: This is a retrospective study of 24 patients with different subtypes of dystonia who underwent DBS electrode placement between March 2002 and December 2006. The chart review included demographic data, anesthetic medications, dose, rate and duration of the infusions, time elapsed since the termination of the infusion and the time needed for emergence before MER ensued.

RESULTS: 24 patients underwent 33 DBS procedures for dystonia. The mean age was 44(SD \pm 15.7) years and 12 patients were male. Mean weight was 72.3(SD \pm 16)Kg. Propofol was used in 21/29 patients while Dexmedetomidine was used in 3/29 patients with an initial bolus dose followed by an infusion. The average loading dose for propofol was 0.7 mg/Kg, and infusion rate was 80-100 mcg/kg/min. for an average of 89 minutes. The average time of emergence was 36(SD \pm 16.5) minutes. 8/29 procedures where propofol was used time for emergence was longer than 40 minutes. In these patients the average dose of infusion was 77(SD \pm 30)mcg/kg/min. In 6 of these the infusion duration was less than 2 hours and only one had an infusion rate over 100 mcg/Kg/min. In

patients where Dexmedetomidine was used the mean infusion dose was 0.5 mg/kg/hr, for an average of 152 minutes. The average awakening time was 48 minutes. Time to emergence was longer than 40 minutes in 75% of the procedures.

DISCUSSION: In this study, we showed increased incidence of delayed emergence in 33% (11 out of 33 procedures) dystonia patients undergoing DBS surgery under propofol or dexmedetomidine sedation. The delay in emergence was not related to any specific agent, dose or rate of infusion. It was not specific to any specific type, duration or etiology of dystonia. The possible mechanisms could be excessive anesthetic potentiation of the low output pallidal state in dystonia depressing the pallido-thalamo-cortical circuitry. It could also be due to depression of already affected ventral-pallidal inputs to septo-hippocampal system that mediates general anesthesia and awareness or complex neurotransmitter disturbances.

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Obstetric

S-140.

TITLE: POST-PARTUM NEUROPATHY FOLLOWING EPIDURAL ANALGESIA: RESULTS OF A QUALITY ASSURANCE ANALYSIS

AUTHORS: R. P. Driver, A. L. Criser, C. D. Willoughby;
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INTRODUCTION: Post-partum neurological deficits are infrequent but serious complications, occurring in up to 1% of deliveries (1). Although regional anesthesia is commonly implicated, the mechanism of injury is four fold more likely to be mechanical (2). For quality assurance, we analyzed patients with post-partum neurologic deficits following epidural labor analgesia during a 7-month period.

METHODS: A retrospective chart analysis was initiated of patients with post-partum neuropathic symptoms following epidural analgesia during the period February to September 2006. Patients were identified during post-operative rounds and by retrospective analysis of CPT codes. Parameters analyzed included patient age, height, and weight, obstetric history, anesthetic management, labor duration, 2nd stage length, managing service, and delivery method.

RESULTS: Five patients were identified with post-partum neuropathy, summarized in the table below. All patients were less than 40 weeks gestation (mean 38.86). Three patients underwent SVD while two required operative delivery. Of these, both failed vacuum assistance; 1 delivered with forceps and 1 required cesarean delivery. The duration of 2nd stage labor averaged 183 minutes. Three patients received epidural infusions of 0.125% bupivacaine and 2 received 0.2% ropivacaine, all with 2 mcg/ml fentanyl; 1 had CSE with 10 mcg sufentanil. Three patients were managed by Obstetrics and 2 by Family Medicine. A single patient manifested prolonged sequelae requiring 8 weeks for return of +1 knee and ankle reflexes. This patient experienced a recrudescence of symptoms at four months and at six months electromyography continued to demonstrate a persistent, mild left femoral neuropathy.

#	Age Kg	Parity Gest.	Delivery Mode	Labor	Anesthetic Technique	Neurologic Exam	Resolution
1	34 81.8	G ₁ P ₀ 39 6/7 weeks	Failed vacuum forceps VD	12 hours 2 nd stage 3 hours	Epidural Bupiv 0.125% w/Fentanyl 2mcg/mL	Bilateral Femoral neuropathy	3 months Complete
2	28 104.5	G ₁ P ₁ 39 5/7 weeks	SVD	15 hours 2 nd stage 45 minutes	Epidural Bupiv 0.125% w/Fentanyl 2mcg/ml	Left LE numbness	2 Days Complete
3	23 74.1	G ₁ P ₀ 39 5/7 weeks	SVD	16 hours 2 nd stage 6 hours	Epidural Bupiv 0.125% w/Fentanyl 2 mcg/ml	Bilateral LE weakness	1 week Complete
4	25 65.9	G ₁ P ₂ 38 2/7 weeks	Failed vacuum C Section	27 hours 2 nd stage 4 hours	2 nd Epidural Ropiv 0.2% w/Fentanyl 2 mcg/ml	No deficit	
5	30 65.5	G ₁ P ₁ 36 5/7 weeks	SVD VBAC	12 hours 2 nd stage 90 minutes	Sufenta 10 mcg w/Ropiv 0.2% w/Fentanyl 2 mcg/ml	Left LE plexopathy	8 wks Partial Resolution 4 months Return of symptoms
	28 78.4	38 6/7		16.4 hr 183 min			Means Means

DISCUSSION: The etiology of post-partum neuropathy is often indeterminate. We identified five cases of neurological deficits in labor patients receiving epidural analgesia. No commonality could be identified with respect to the anesthetic care of these patients. The mean duration of 2nd stage labor was longer than 3 hours however 2 patients had 2nd stage durations of 90 minutes or less. There have been case reports of possible exacerbation of underlying neural disease by periaxial anesthesia (3-6). One patient's symptoms were recurrent and may have reflected an underlying mechanical or physiologic neurologic condition that was exacerbated by regional anesthesia.

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S-141.

TITLE: A COMPARISON BETWEEN COMBINED SPINAL-EPIDURAL ANESTHESIA (CSE) WITH OR WITHOUT EPIDURAL SALINE ADMINISTRATION FOR CESAREAN SECTION (C/S)

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INTRODUCTION: Epidural solution administration by gravity via the needle is associated with higher success rate than through the catheter. Objective: To determine whether administration of saline by gravity via the epidural needle into the epidural space after intrathecal injection of local anesthetic and before catheter insertion is associated with fewer adverse effects, we conducted, with IRB approval, randomized, study of 128 consenting pt's who received CSE for elective C/S.

METHODS: In all pt's the epidural space was located at L4-5 or L3-4 interspace in lateral decubitus position. Group I (n=64) the catheter was inserted immediately following administration of spinal solution via PENCAN 25g needle. Group II (n=64) 10 ml saline was administered by gravity into the epidural space following spinal solution injection. B. Braun catheter was then inserted 5 cm epidurally. All pt's received 10mg ropivacaine with 100mcg epinephrine and 25mcg fentanyl intrathecally. Increment epidural doses of 5-20ml of 0.75% ropivacaine with 5mcg/ml epinephrine & 5mcg fentanyl were administered when spinal anesthesia was unsatisfactory. Twenty minutes later, the investigator recorded: demographic data, the distance of the epidural space from the skin, the ability of the anesthesiologist to pass the catheter on the first attempt without manipulation, the appearance of frank blood or CSF. The catheter was observed for blood return; sensory level; degree of motor blockade. Additional epidural solution was injected via the epidural catheter to achieve a satisfactory block. Values are mean ± SD.

RESULTS: Groups did not differ in demographics, duration of surgery, and incidence of itching, sedation, hypotension or APGAR scores. There were 13 pt's in GI & 19 pt's in GII for whom S/A block was

unsuccessful (due to failure to pierce the dura). Time to incision was 34.1 ± 8.5 & 34.4 ± 8.6 for GI & GII, respectively. Time to T6 sensory level was 9.9 ± 5.9 & 7.0 ± 5.1, (p<0.001) for GI & GII respectively. Incidence of epidural catheter blood vessel puncture was 10 for GI & 3 for GII. More pt's in GI had catheter paresthesia (36 vs. 23, p<0.04) and required additional epidural local anesthetic to achieve satisfaction (14 vs. 2, p<0.003). Sensory was T1 ± 2.6 & C8 ± 3.1 for groups I & II respectively. No pt's complained of shortness of breath. 10 of 51 pt's in GI & 1 of 45 pt's in GII required additional N2O or IV fentanyl to achieve satisfactory analgesia, (p< 0.009).

CONCLUSIONS: Epidural administration of 10ml saline by gravity before insertion of epidural catheter for CSE for C/S has a higher success rate, better quality of anesthesia, fewer epidural vessel puncture & fewer paresthesia than CSE without epidural saline administration.

S-142.

TITLE: INCIDENCE OF FELLOWSHIP ANAESTHETISTS ON MATERNAL ANESTHESIA RELATED MORBIDITY AND MORTALITY

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INTRODUCTION: Recent recommendations stated that experienced anaesthetists are required to lower anesthesia related deaths in obstetrics. We focused on eventual detrimental role of young anesthetist colleagues on incidence of anaesthetic complications that required hospitalization in intensive care, and subsequent mortality.

PATIENTS AND METHODS: Retrospective chart analysis of critically obstetric patients from January 1996 till September 2004. Study period was divided into almost three equal periods: 1995-1998(B) where only experienced anesthetist were in charge of the labor ward, 1999-2001(A1) where inexperienced young fellowship residents helped in the management and 2002-2004(A2) where more experienced fellowships participated. Data collected: Demographics, obstetric and anesthetic management (cesarean section, anesthetic technique, transfusion, emergency surgery...), complications of anesthetic management (aspiration, difficult intubation, failure of spinal or epidural anesthesia...), main diagnosis at ICU admission, LOD score at admission.

RESULTS: 644 charts reviewed, anesthetic complications in 6% (n=38). Patients ASA2 or more (15%). Overall mortality 11%. Main characteristics of patients with anesthetic complications: [Table1]. Almost all the patients were ASA1. Failure of regional anesthetic techniques seen in 25 patients (5%) among 490 when resident fellowships were in charge of the patient, and in 3% of the cases (5/154) when senior anesthetist was the boss. This failure resulted in serious condition that motivated ICU admission in 12% of cases when fellowships were involved, but it hasn't resulted in any serious morbidity when senior anesthetists were the first to deal with patients. [Table2]; (Note that we can have one or more admission diagnosis which explains why the sum of percentages of diagnosis is superior to 100%).

ICU admission diagnosis was also influenced by experience of anesthetists. In fact, the more anesthetist is experienced (respectively period B then A2 then A1), the less we see severe pre-eclampsia/eclampsia that need intensive care management (respectively 51%, 62% and 62%); pulmonary edema (respectively 16%, 21%, 24%) and hemorrhagic complications (25%, 28%, 32%). Preventable morbidity and mortality were respectively: 3/7 and 0/2 during period B, 7/14 and 1/3 during period A2, 10/17 and 2/4 during period A1.

Anesthetic complications and related mortality through periods			
	1995-1998	1998-2001	2002-2004
n=	154	238	252
Anesthetic complications n=	7	17	14
Overall mortality	10%	7%	12%
Anesthetic mortality	2/7 (29%)	4/17 (24%)	3/14 (21%)

Comparing periods of senior vs fellowship anesthetists			
	1995-1998 (n=154)	1999-2004 (n=490)	significance
Emergency surgery	71%	83%	0.004
Failure spinal/epidural anesthesia	3%	5%	0.23
Difficult Intubation	1%	3%	0.027
Aspiration pneumoniae	3%	3%	0.95
Cesarean section	70%	78%	0.065
General anesthesia	73%	82%	0.027
Admission APACHE III	34.4 vs 25	28 vs 28.8	0.01
Admission LOD score	2.3 vs 3	2 vs 3	0.23

CONCLUSION: Major anaesthetic mortality and morbidity is related to difficult airway management during general anaesthesia, and inadequate supervision of trainees (50% and 33% preventable morbidity and mortality in case of adequate fellowship supervision). Supervision of trainees, especially the youngest could lower morbidity and mortality.

S-143.

TITLE: EFFICACY OF EPIDURAL ANALGESIA AT LOWER THORACIC LEVEL WITH ROPIVACAINE FOR POST-CAESAREAN ANALGESIA

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INTRODUCTION: Early postoperative ambulation is necessary for post-caesarean section (post-CS) mothers for their need to take care of their infants. High quality analgesia is essential for quick recovery, and intravenous administration of opioids is commonly used after post-CS analgesia. However it is well known that opioids alone do not achieve satisfactory analgesia. Continuous epidural analgesia with local anesthetic is a possible approach to achieve better results, diminishing side effects of opioids. In this study, we evaluated the efficacy of epidural infusion with 0.1% ropivacaine at lower thoracic level for post-CS analgesia.

METHODS: From January through October 2006, patients who underwent CS were retrospectively analyzed for post-CS pain. Anesthetic methods were determined by each anesthesiologist's decision. Patients were divided into combined spinal-epidural anesthesia (CSEA) group and spinal anesthesia (SP) group and were analyzed for post-CS pain. For post-operative analgesia, all patients received continuous injection of intravenous fentanyl (15mcg/hr). Patients with epidural catheterization, additionally received 5ml/hr of 0.1% ropivacaine for 24 hours. When analgesia was insufficient, a bolus dose of fentanyl (15mcg) was given. Suppository diclofenac was administered when bolus injection was ineffective. Visceral and somatic pain was scored by numerical rating scale (NRS 0-3) at 6 and 12 hours after the surgery. NRS and requested amount of bolus fentanyl and oral diclofenac were analyzed by nonparametric test.

RESULTS: Among 136 patients who underwent CS, 86 patients received CSEA, and 38 patients received spinal anesthesia. Among the CSEA group 16 patients who received lumbar epidural catheterization were excluded from the study. There was no significant demographic difference between the two groups. The SP group received larger amount of bupivacaine (SP 11.3mg+1.6mg, CSEA 9.9mg+2.3mg) for

spinal anesthesia. In the CSEA group, epidural catheterization was performed at lower thoracic level (Th10/11 15.7%, Th11/12 37.1%, and Th12/L1 45.7%). More patients in the SP group requested bolus injection of fentanyl than in the CSEA group (the median; SP 30mcg, CSEA 7.5mcg, p<0.01). In the SP group, 50% of patients required diclofenac, whereas 18% of patients in the CSEA required diclofenac (p<0.05). NRS for both somatic and visceral post operative pain was significantly lower in the CSEA group than in the SP group (somatic; median; CSEA 0, SP 1 (p<0.01), visceral; CSEA 0, SP 1(p<0.05)). No significant side effects of epidural analgesia were seen.

DISCUSSION: In this study, by using continuous epidural infusion of low dose ropivacaine at lower thoracic level, with intravenous fentanyl, provided better analgesia for post-CS analgesia, without side effects, such as leg numbness, that could inhibit early ambulation.

REFERENCES: 1)Anesth Analg 2005;101:S62-69, 2) Am J Obstet Gynecol 2006; 194, 961-71, 3) Curr Opin Anaesthesiol 2006;19:244-248.

S-144.**TITLE: CARDIAC ARREST DUE TO ABDOMINAL COMPARTMENT SYNDROME AFTER PACKING REMOVAL IN HEMORRHAGIC DELIVERY SURGEY**

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INTRODUCTION: Abdominal packing is a lifesaving technique used in damage control surgery schedule. Bleeding from abdominal cavity can generally be achieved by applying pressure with several large abdominal packs leading in multi-organ dysfunction syndrome due to excessive intra-abdominal pressure (over packing) or to an Abdominal Compartment Syndrome [1].

CASE: A 41years-old woman was admitted in our ICU because of massive obstetric hemorrhage due to placenta accrete with prior caesarean section for subintra-aneurysmal eclamptic seizures. After emergency hysterectomy and because of not reliable hemorrhage, in presence of metabolic failure (hypothermia < 35 degrees C, acidosis > 7.2, coagulopathy) abdominal packing with five surgical compresses was the treatment of choice. The patient developed oliguria and trends toward worsening of renal function (thought due to hemorrhagic shock). During re-operation (24 hours later), when the compresses were removed she suffered a cardiac arrest reversed rapidly by cardiopulmonary resuscitation, adrenaline and volume loading. After successful surgical hemostasis there was a prompt improvement in hemodynamic, respiratory and urinary flow. Because of Intra-abdominal pressure (IAP) monitoring in ICU was not effective, a CT thoracic scan was performed to eliminate massive pulmonary embolism (not found). She was discharged from hospital after a 2 month stay severely disabled because of ischemic damage due to eclampsia.

CONCLUSION: This case is a rare scenario where brutal abdominal decompression without IAP monitoring leads to cardiac arrest. We must emphasize that all the individuals responsible for the care of patients in the ICU should be familiar with the concepts and techniques of measurements of IAP (urinary bladder pressure).

REFERENCE:[1] Chang M. J Trauma 1998; Robotham J.L. Crit Care Med 1985.

Pain-Basic Science

S-145.

TITLE: DIFFERENTIAL UPREGULATION OF SPINAL PERK IN RAT SURGICAL PAIN MODELS

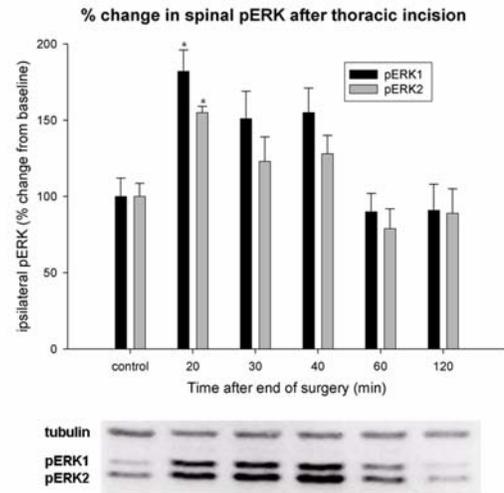
AUTHORS: J. S. Kroin, J. Li, A. Buvanendran, K. J. Tuman;
AFFILIATION: Rush Medical College, Chicago, IL.

INTRODUCTION: Activation of intracellular kinases are important because they can phosphorylate ion channels and receptors that result in increased pain sensitivity (Anesthesiology 2007;106:864). Extracellular signal regulated kinases 1 and 2 (ERK1/2) are rapidly phosphorylated (pERK1/2) and upregulated in the rat spinal cord following formalin injection in the hind paw (FEBS Letters 2006;580:6629). ERK1/2 are also phosphorylated and upregulated in a neuropathic pain model (Pain 2005; 114:149). This study examines the hypothesis that spinal pERK1/2 will also be upregulated in surgical pain models, and compares the response between models.

METHODS: Thoracic incision pain model: Following IACUC approval male Sprague-Dawley rats (300 g) were anesthetized with isoflurane and under sterile conditions a skin incision made over the left lateral thoracic region. Both superficial and deep muscles were incised by creating 3 cm long lateral cuts over the 3rd, 5th, and 7th ribs. The intercostal muscles were spared. The muscle wounds were closed with silk sutures and the skin incision closed with nylon sutures. This model produces pain-related behavior (Anesth Analg 2006; 103:334). Plantar foot incision pain model: Under isoflurane anesthesia, a left plantar foot incision (Brennan model) was performed (Pain 1996;64:493). Formalin foot injection model: Under isoflurane anesthesia, 2.5% formalin was injected into the left dorsal hindpaw (FEBS Letters 2006;580:6629). Animals were sacrificed at 20-120 min after surgery or injection, spinal cord rapidly removed, and appropriate section homogenized for Western blot analysis using pERK1/2 antibody. Control rats were anesthetized, with no surgery. Changes in pERK over different time points and control were compared with ANOVA and Tukey-B post hoc test.

RESULTS: Following thoracic muscle surgery, there is a moderate increase in both pERK1 and pERK2 in the ipsilateral thoracic spinal cord, with peak value at 20 min after surgery, and return to baseline by

about 60 min (fig). However, after plantar foot incision, ERK1/2 levels do not increase in the lumbar spinal cord over 120 min. By comparison, after injecting formalin in the hind paw we saw about a 300% increase in both pERK's at 30 min.



DISCUSSION: Spinal pERK1/2 is upregulated in a deep thoracic wound model but not in a plantar foot incision model, although both models produce postoperative pain-related behavior. The acute stage of activation of signal-regulated kinases may differ among surgical pain models.

S-146.

TITLE: SYNERGISTIC EFFECT OF INTRATHECAL NEOSTIGMINE AND PREGABALIN IN A RAT POSTOPERATIVE INCISIONAL PAIN MODEL

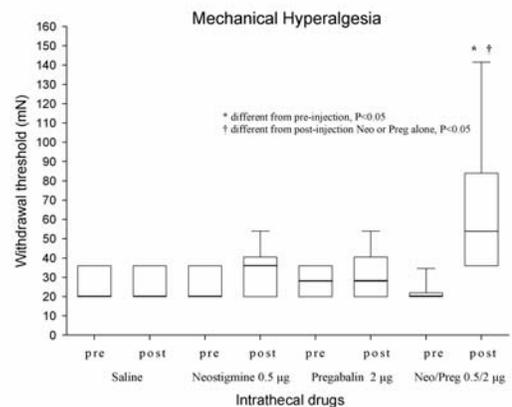
AUTHORS: J. S. Kroin, A. Buvanendran, M. Kari, K. J. Tuman;
AFFILIATION: Rush Medical College, Chicago, IL.

INTRODUCTION: In rats with peripheral neuropathy, the combination of oral gabapentin (a $\alpha_2\delta$ calcium channel antagonist) and the oral cholinesterase inhibitor donepezil produced a synergistic anti-hyperalgesic effect (Anesthesiology 106:1213, 2007). It was suggested that oral gabapentin acts supraspinally to activate the descending bulbospinal pathway leading to spinal cholinergic activation. Intrathecal gabapentin or intrathecal neostigmine (cholinesterase inhibitor) each reduces mechanical hypersensitivity following plantar foot incision (Can J Anesth 2003;50:904). The hypothesis of our study is that spinal pregabalin (a potent $\alpha_2\delta$ calcium channel antagonist) and spinal neostigmine, at doses that are ineffective alone, act synergistically to reduce postoperative pain.

METHODS: Following IACUC approval, male Sprague-Dawley rats (300 g) were implanted with chronic intrathecal catheters (Physiol Behav 1976;17:1031). After waiting 7 days for full neurological recovery, baseline mechanical sensitivity was evaluated with calibrated von Frey filaments (280 mN cutoff), and a left plantar foot incision made (Pain 1996;64:493). After waiting 24 h for mechanical hyperalgesia to develop (reduced withdrawal force from pre-injection level), animals were given an intrathecal injection (8 μ L) of saline vehicle, pregabalin 2 μ g, neostigmine 0.5 μ g or the combination of the 2 drug doses (n=10/group). Mechanical sensitivity was re-evaluated 60 min post-injection. Sedation was also evaluated based on the animal's ability to remain on a 10 rpm rotating rod for 180 sec. Withdrawal force thresholds were compared post-injection and pre-injection with the Wilcoxon signed rank test. Thresholds were compared among the 4 groups with the Kruskal-Wallis Test.

RESULTS: Prior to incision, the median withdrawal force was 288 mN, and 24 h later it dropped below 30 mN (fig). Saline, pregabalin 2 μ g alone, or neostigmine 0.5 μ g alone did not elevate the force

threshold post-injection. However, the pregabalin 2 μ g/neostigmine 0.5 μ g combination did increase the withdrawal force threshold. None of the doses caused sedation.



DISCUSSION: This study shows that at the spinal level alone, a $\alpha_2\delta$ calcium channel antagonist and a cholinesterase inhibitor can act synergistically to reduce incisional pain. Since it is unlikely that a very low dose of intrathecal pregabalin has any supraspinal effect, the mechanism by which pregabalin potentiates cholinergic activity at the spinal level remains to be determined.

S-147.

TITLE: LOCAL INJECTION OF RESINIFERATOXIN REDUCES HYPERALGESIA AT A NON-ANTINOCICEPTIVE DOSE IN A RAT INCISION MODEL OF POSTOPERATIVE PAIN

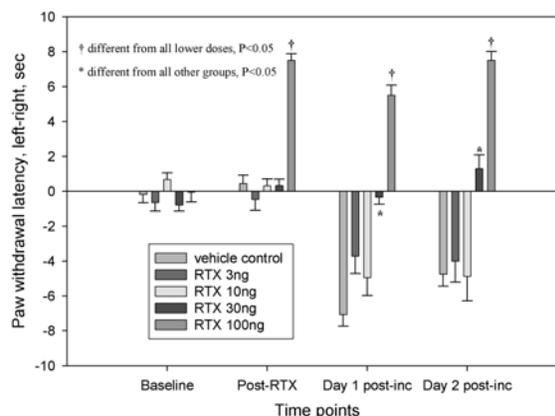
AUTHORS: J. S. Kroin, A. Buvanendran, K. J. Tuman;
AFFILIATION: Rush Medical College, Chicago, IL.

INTRODUCTION: Resiniferatoxin (RTX) is a potent capsaicin analog acting on the vanilloid-1 receptor. Behavioral studies indicate that unmyelinated C fiber and possibly A-delta nerve endings are targets of RTX. Peripherally injected RTX has been shown to block thermal hyperalgesia in carrageenan-inflamed rat hindpaw (Pain 2003; 104:219). The present study examines if peripherally injected RTX, at a dose that does not produce antinociception, is anti-hyperalgesic in a rat model of postoperative pain.

METHODS: Following IACUC approval, experiments were performed on male Sprague-Dawley rats (300 g). In the first set of experiments, rats received a 100 μ L left intraplantar tissue injection of 0 (vehicle control), 3, 10, 30, or 100 ng RTX (n=6/group) and 24 h later all animals received a left plantar foot incision using the method of Brennan et al (Pain 1996;64:493). Thermal hyperalgesia was monitored in both feet using a radiant heat foot withdrawal device (Pain 1998;32:77). Left latency-right latency was used as the primary measure of change in thermal sensitivity. In a second group of experiments, rats received the same doses of RTX as in the 1st experiment but did not have a subsequent foot incision, and thermal sensitivity (nociception) was followed for 14 days. RTX and vehicle groups were compared with repeated measures analysis of variance, with post hoc Tukey-B test.

RESULTS: At 24 h after RTX injection (pre-incision), thermal withdrawal latencies were not elevated, except for the 100 ng dose (fig). At 24 h after foot incision, withdrawal latencies decreased in the 10 and 3 ng RTX, and vehicle injection groups compared to pre-surgery, but not in the 30 ng group. On either day 1 or day 2 post-surgery, the latency of the 30 ng RTX group was different from all other groups. In the 2nd experiment with animals injected with RTX without subsequent

incision, thermal latencies were elevated in the 100 ng group for 14 days, but not in other groups, at any time point.



DISCUSSION: RTX at the 30 ng dose did not increase thermal withdrawal latency above the initial baseline, but prevented the post-incision decrease in thermal withdrawal latency. These results indicate that local RTX injection at an intermediate dose does not affect normal thermal pain sensitivity, but does prevent post-incision hyperalgesia.

S-148.

TITLE: UPREGULATION OF P2X₃ RECEPTOR IN DORSAL ROOT GANGLIA OF A RAT CANCER PAIN MODEL

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INTRODUCTION P2X₃ purinergic receptors are predominantly expressed in dorsal root ganglion (DRG) neurons and play an important role in pain sensation. Changes of P2X₃ receptor in DRG of cancer pain remains unclear. The aim of this investigation was to induce bone cancer pain in rats, and to observe the expression of P2X₃ receptor in cancer pain models.

METHODS Female SD rats received intra-tibial injection of 5×10^3 , 5×10^4 or 5×10^5 syngeneic Walker256 mammary gland carcinoma cells. Mechanical allodynia and thermal hyperalgesia were tested at 1d, 3ds, 5ds, 7ds, 10ds, and 14ds after cell injection. The development of the bone tumour and metastasis was monitored by histology. The L5-6 DRG were obtained from cancer pain rats. Expression of P2X₃ receptor was investigated by RT-PCR and Western-blot.

RESULTS Intra-tibial injections of walker256 cells produced a rapidly expanding tumor within the boundaries of the tibia, causing severe remodeling of the bone. No tumor was observed in the contralateral tibia. But rats receiving 5×10^5 walker256 cells showed significant body weight loss. One rat from this group developed lymph nodes and lung metastasis. Rats receiving intra-tibial injections of walker256 cells displayed gradual development of mechanical allodynia and thermal hyperalgesia, beginning from day 7-14 following injection of cells. These symptoms were not observed in rats receiving normal saline. The mRNA and protein expression of P2X₃ receptor in DRG were upregulated in cancer-induced nociception. The increases were seen ipsilaterally.

DISCUSSION The induction of bone cancer in rats by the syngeneic walker256 mammary tumour cell line provided a valid pre-clinical model for pain associated with bone metastases. Bone cancer pain resulted in an upregulation in the expression of P2X₃ receptor in DRG, suggesting that P2X₃ receptor may contribute to cancer pain.

S-149.

TITLE: EFFECT OF GABAPENTIN ON THE EXPRESSION OF PSD95 AND CAMKII IN SPINAL CORD OF CCI RATS

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INTRODUCTION: Gabapentin (GBP) has recently been widely and successfully used in clinic for many neuropathic pain syndromes, such as postherpetic neuralgia, diabetic neuropathy, trigeminal neuralgia and so on. Although designed as an analogue of γ -aminobutyric acid(GABA), gabapentin does not bind to GABA receptors and has no effect on GABA release in central nervous system. Many studies have been done trying to explore its analgesic mechanism from molecular and electrophysiologic levels. However its action still remains elusive. The aim of this study is to investigate the possible mechanism of gabapentin by CCI models.

METHODS: SD male rats were randomly divided into 6 groups: 1) naïve control rats with saline treatment, 2) naïve rats treated with gabapentin, 3)sham surgery rats with saline treatment, 4) sham surgery rats treated with gabapentin, 5) CCI surgery rats with saline treatment, 6) CCI surgery rats treated with gabapentin. Gabapentin (2%, 100mg/kg) or saline (0.5ml/100g) was injected intraperitoneally (i.p) 15min prior to surgery and then every 12h from postoperative (PO) day 0-4. Mechanical allodynia and thermal hyperalgesia were measured with VonFrey filament and hot plate to evaluate the success of the model and the analgesic effect of gabapentin. On PO day 8, all rats were sacrificed and lumbar spinal cords were collected for further RT-PCR and Western-blot analysis of PSD95 and CaMKII.

RESULTS: The analgesic effect of gabapentin on mechanical allodynia and thermal hyperalgesia in CCI model was significant (Figure 1), with maximal reduction reached on PO day 8. Gabapentin could normalize the up-regulation of CaMKII β mRNA in spinal cord of CCI rats. And expressional level of total CaMKII (tCaMKII) and phosphorylated CaMKII (pCaMKII) of CCI model decreased to baseline after intervention of gabapentin(Figure 2), while the phosphorylation ratio

remained unchanged. At the same time, expression of PSD95 was unchanged.

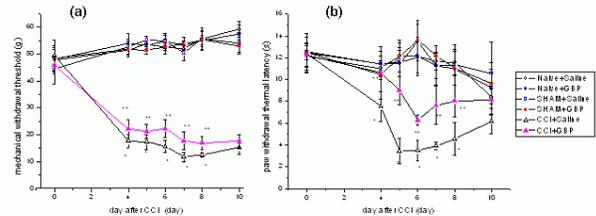


Figure 1: Analgesic effect of gabapentin in CCI rats. (a) mechanical allodynia; (b) thermal hypergesia. *; P<0.01, compared with Sham and Naive group; **; P<0.01, compared with CCI rats treated with saline.

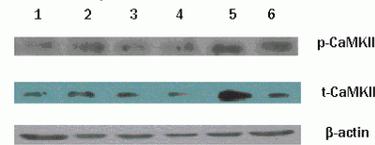


Figure 2: Western blot: Gabapentin attenuates expressional and activational level of CaMKII induced by CCI in spinal cord. 1.Naive+saline, 2. Naive+gabapentin, 3. Sham+saline, 4. Sham+gabapentin, 5.CCI+saline, 6. CCI+gabapentin

CONCLUSION: The present results indicate that analgesic effect of gabapentin on CCI rats may be related to the expressional normalization of CaMKII (especially CaMKII β subtype) in spinal cord, phorsphorylation may contribute less in this process and gapapentin has no effect on the expression of PSD95.

S-150.

TITLE: ALLEVIATE ALLODYNIA AND HYPERALGESIA BY SILENCING OF NAV1.8 WITH SIRNA IN BONE CANCER PAIN RATS

AUTHORS: L. Xu, Y. Jiang, H. Zhang;
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INTRODUCTION Nav1.8 is a tetrodotoxin resistant sodium channel and its restricted expression to the peripheral sensory neurons suggest that blocking this channel might have therapeutic potential in various pain states and may offer improved tolerability compared with existing sodium channel blockers.The aim of the study was to evaluate the in vivo gene silencing effect of Nav1.8 in dorsal root anglia(DRG) by intrathecal administration of chemically synthesized siRNA with 3' terminal methyl modification, and to investigate the antinociceptive effect of siRNA targeting Nav1.8 in a rat model of bone cancer pain.

METHODS (1).Female SD rats recieved intra-tibial injection of 5×10^4 syngenic Walker256 mammary gland carcinoma cells. Mechanical allodynia and thermal hyperalgesia were tested after cell injection. The development of the bone tumour and metastasis was monitored by histology.(2).Based on the general roles of siRNA design, three pairs of siRNA targeting Nav1.8 by in vitro transcription with T7 RNA polymerase were synthesized. A mismatched duple-strand RNA was choosed as negative control RNA. siRNA were transfected into primary cultured dorsal root ganglion neurons with cationic lipid based reagent Lipofectamine 2000. mRNA expression of Nav1.8 was determined with RT-PCR and Q-PCR 48h after the transfection.(3).We synthesized siRNA chemically according to the sequence that can most effectively attenuation of Nav1.8 mRNA in vitro and 3' terminal of siRNA was methyl modified(M-siRNA).M-siRNA, negative control RNA and normal saline were delivered as repeated daily bolus doses(25-100ug, for 7 days) via implanted intrathecal catheter to the lumbar spinal cord of bone cancer rats. Mechanical allodynia and thermal hyperalgesia were tested every day after intrathecal injection. (4).L4-6 DRG of the rats was obtained twenty-four hours after the last siRNA injection. Nav1.8 expression in the DRG was evaluated by using of RT-PCR and Q-PCR methods.

RESULTS Rats receiving intra-tibial injections of walker256 cells displayed gradual development of mechanical allodynia and thermal hyperalgesia, beginning from day 7 following injection of cells. Two siRNAs were identified that were capable of a highly-selective attenuation of Nav1.8 message in cultured DRG cells. Intrathecal injection of M-siRNA, but not the negative control RNA or vehicle alone, attenuated mechanical allodynia and themal hyperalgesia of bone cancer pain. Intrathecal administration of M-siRNA was concomitant with a reduction in the Nav1.8 transcripts in the lumbar DRG. Negative control RNA injection did not alter expression of Nav1.8 in lumbar DRG, and had no effect on the baseline threshold of nociception. The antinociception effect of M-siRNA continued to 72h after the last RNA injection.

DISCUSSION We conclude that silencing of Nav1.8 channel using a siRNA approach is capable of producing allodynia and hyperalgesia relief in the bone cance model.

S-151.

TITLE: FETAL PAIN CAN BE SUPPRESSED WITH INTRA AMNIOTIC SUFENTANIL IN THE CHRONICALLY INSTRUMENTED SHEEP MODEL

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INTRODUCTION: Fetal surgery has been introduced in the early 1980s in order to improve the prognosis of human fetuses with severe congenital malformations that progress in severity over the course of gestation and may destroy entire organ systems of the unborn. This advance is pooled by the ethical and controversial question whether the fetus has pain perception and awareness during these invasive procedures. First pain treatment was no issue but after reports of decreased morbidity and mortality in neonates after pain treatment for invasive procedures a debate about fetal pain treatment was initiated. In view of this debate we developed a chronically instrumented pregnant sheep model to measure fetal responses after a pain stimulus. The aim of this study was to investigate the fetal response to a pain stimulus with and without administration of opioids.

METHODS: Pregnant sheep were anesthetized and mechanically ventilated. A maternal carotid artery and jugular vein catheter were inserted. Subsequently a laparotomy was performed and the uterus was incised. Catheters were advanced into the fetal carotid artery and jugular vein. Electrocardiogram and electromyogram electrodes were placed on the head and in the neck of the fetus respectively. Subsequently the fetal hind paw was exteriorized and an electromyogram electrode was placed in the musculus biceps femoris. After placing of stimulation electrodes in the skin innervated by the nervus suralis, a catheter was inserted into the amnion cavity, lost amniotic fluid was replaced and the uterotomy closed. Fetal catheters and leads were tunneled subcutaneously and exteriorized through an incision in the maternal flank. After closure of the laparotomy, anesthesia was discontinued and animals were allowed to stabilize for 48 hours.

Two different experiments were performed on different days. All

animals were given an electrical stimulus which was considered a pain stimulus. In the first experiment animals were given the stimulus without medication. In the second experiment animals received 50µg sufentanil intra amniotically. Cortisol levels were measured before and after stimulation. Hemodynamic parameters, EMG and ECoG were monitored continuously. Blood gas samples were drawn at baseline and 60 minutes after stimulation.

RESULTS: During the stimulus a significant increase in heart rate was shown in the first experiment. Cortisol levels increased 15 minutes after stimulation in the same experiment. Contrasting with the other experiment in the experiment where sufentanil was given no increase in heart rate or cortisol was visible.

DISCUSSION: The chronically instrumented sheep model enabled us to administer electrical stimuli as well as medication to a fetus several days post operative. Results show that increased heart rate and cortisol levels following an electrical stimulus can be diminished with 50µg sufentanil intra amniotically.

S-152.

TITLE: CEPHARANTHINE REDUCES CARRAGEENIN-INDUCED INFLAMMATORY HYPERALGESIA IN RATS BY INHIBITING NEUTROPHIL ACTIVATION

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INTRODUCTION: Cepharanthine is a biscoclaurine alkaloid extracted from *Stephania cepharantha* Hayata, and this agent is used to treat postradiation leukocytopenia, snake bite, bronchial asthma. Cepharanthine also inhibits leukocyte activation. Activated neutrophils are important pathological mechanisms in the development of inflammatory hyperalgesia. These observations strongly suggested that cepharanthine might reduce carrageenin-induced hyperalgesia by inhibiting leukocyte activation. In this study we examined whether cepharanthine might reduce carrageenin-induced inflammatory hyperalgesia by inhibiting leukocyte activation in rats.

METHODS: After approval of the institutional Animal Care and Use Committee, male Wistar rats were subjected to hyperalgesia induced by intraplantar injection of carrageenin (2 mg/kg) into the hind paws. The animals were divided into four experimental groups: 1) sham (without injection of carrageenin) group, 2) vehicle (saline) group, 3) cepharanthine (1 mg/kg, iv) group, 4) nitrogen mustard (1 mg/kg, iv, 2 days before operation)-induced leukocytopenia group. Various agents were administered 30 min after injection of carrageenin. Hyperalgesia was evaluated by plantar test, and leukocyte activation was assessed by measuring of MPO activity, CINC and TNF-alpha. Data were analyzed using ANOVA and Scheffe's post hoc test. A $p < 0.05$ was considered statistically significant.

RESULTS: Cepharanthine and leukocytopenia reduced carrageenin-induced hyperalgesia and increase in MPO activity, CINC and TNF-alpha.

CONCLUSIONS: Cepharanthine could reduce carrageenin-induced hyperalgesia by inhibiting leukocyte activation in rats.

S-153.

TITLE: FETAL PAIN CAN NOT BE SUPPRESSED WITH MATERNAL INTRAVENOUS DIPIDOLOR IN THE CHRONICALLY INSTRUMENTED SHEEP MODEL

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INTRODUCTION: Fetal surgery has been introduced in the early 1980s in order to improve the prognosis of human fetuses with severe congenital malformations that progress in severity over the course of gestation and may destroy entire organ systems of the unborn. This advance is pooled by the ethical and controversial question whether the fetus has pain perception and awareness during these invasive procedures. First pain treatment was no issue but after reports of decreased morbidity and mortality in neonates after pain treatment for invasive procedures a debate about fetal pain treatment was initiated. In view of this debate we developed a chronically instrumented pregnant sheep model to measure fetal responses after a pain stimulus. The aim of this study was to investigate the fetal response to a pain stimulus with and without administration of opioids.

METHODS: Pregnant sheep were anesthetized and mechanically ventilated. A maternal carotid artery and jugular vein catheter were inserted. Subsequently a laparotomy was performed and the uterus was incised. Catheters were advanced into the fetal carotid artery and jugular vein. Electrocardiogram and electromyogram electrodes were placed on the head and in the neck of the fetus respectively. Subsequently the fetal hind paw was exteriorized and an electromyogram electrode was placed in the musculus biceps femoris. After placing of stimulation electrodes in the skin innervated by the nervus suralis, a catheter was inserted into the amnion cavity, lost amniotic fluid was replaced and the uterotomy closed. Fetal catheters and leads were tunneled subcutaneously and exteriorized through an incision in the maternal flank. After closure of the laparotomy, anesthesia was discontinued and animals were allowed to stabilize for 48 hours.

Two different experiments were performed on different days. All

animals were given an electrical stimulus which was considered a pain stimulus. In the first experiment animals were given the stimulus without medication. In the second experiment the mother received 20mg dipidolor intravenously. Cortisol levels were measured before and after stimulation. Hemodynamic parameters, EMG and ECoG were monitored continuously. Blood gas samples were drawn at baseline and 60 minutes after stimulation.

RESULTS: During the stimulus a significant increase in heart rate was shown in the first experiment. Cortisol levels increased 15 minutes after stimulation in the same experiment. In the second experiment where dipidolor was given to the mother an increase in heart rate and cortisol was also visible.

DISCUSSION: The chronically instrumented sheep model enabled us to administer electrical stimuli as well as medication to a fetus several days post operative. Results show that increased heart rate and cortisol levels following an electrical stimulus can not be diminished with the administration of 20mg dipidolor intravenously to the mother.

S-154.

TITLE: ALTERED THERMAL NOCICEPTIVE RESPONSES IN GLUTAMIC ACID DECARBOXYLASE (GAD) 65 DEFICIENT MICE

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INTRODUCTION: γ -amino butyric acid (GABA) is thought to inhibit both pre- and post-synaptically the transfer of nociceptive signals from primary afferent fibers to the central nervous system. However, the role of presynaptic GABA release in thermal nociception is less clear. GABA is synthesized by two isoforms of glutamic acid decarboxylase (GAD), GAD65 and GAD67. GAD67 is found mainly in the cell body, whereas GAD65 is localized to the nerve terminal. Therefore, GAD65 is thought to play an important role in the control of GABA release in times of high GABA demand. The aim of the present study was to evaluate the role of GABA release in acute antinociceptive responses by using mice lacking GAD 65.

METHODS: The study was approved by the Committee for the Guidelines on Animal Experimentation of Gunma University. All procedures were performed on adult (12-16 weeks of age) male wild-type (WT) and GAD65 knockout mice (GAD65^{-/-}).

Hotplate test: An animal was placed on an aluminum plate (25 × 20 cm) maintained at 53 ± 0.5°C and a Plexiglas cage (24 cm in height) was used to restrict the movements of the animal (Hot plate analgesia meter MK-350C, Muromachi Kikai Co., Ltd, Tokyo, Japan). The latency to responses, hind paw licking or jumping, was measured. The cut-off latency was set at 60 s.

Tail-immersion test: The spinally-mediated nociceptive thresholds were determined using a thermo regulated water circulating pump (NTT-20S, Tokyo Rikakikai Co., Ltd, Tokyo, Japan). The mouse was maintained in a mouse holder and its tail was immersed in the heated water bath (48 ± 0.5°C). The tail was rapidly immersed in the water and the latency to a rapid flick of the tail was measured. The maximum latency allowed was 20 s.

RESULTS: Supra-spinal mechanisms are involved in responses to

thermal nociception and these are classically assessed using the hotplate test. We measured latencies to licking or jumping from the hotplate set at 53°C. A significant alteration of the response was found in male GAD65^{-/-} ($P < 0.01$) mice (18.2 ± 4.0 s, $n = 20$) compared to their wild-type controls (22.1 ± 5.2 s, $n = 28$), indicative of increased nociceptive perception. However, there was no significant difference in the latency of the tail-immersion test (WT 6.93 ± 1.55 s, GAD65^{-/-} 6.78 ± 1.60 s, $n = 14$ each), which was known to spinally-mediated nociceptive thresholds.

DISCUSSION: Hot plate test is thought to evaluate the antinociceptive action via supra-spinal function. On the other hand, tail-immersion test evaluate the antinociceptive reflex through the spinal reflex arc. Therefore, our results suggest that modified GABA release from presynaptic terminals may play an important role in thermal nociception at the supra-spinal level.

S-155.

TITLE: ERK INHIBITION INCREASES THERMAL WITHDRAWAL LATENCY AND MECHANICAL WITHDRAWAL THRESHOLD IN A RAT POSTOPERATIVE PAIN MODEL

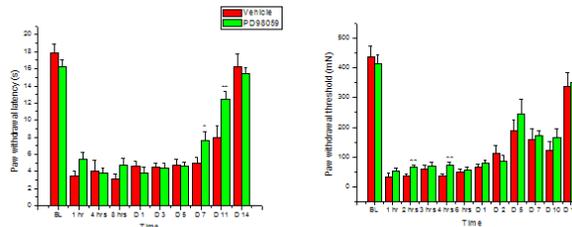
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INTRODUCTION: ERK (Extracellular signal Regulated Kinase) is activated by nociceptive input, growth factors and inflammatory mediators in primary sensory and dorsal horn neurons. (1,2) ERK has not been investigated in postoperative pain. We determined ERK's involvement in thermal and mechanical allodynia and hyperalgesia in a rodent postoperative pain model.

METHODS: Experiments are performed on 300 gram adult male wistar rats. A 1 cm plantar hindpaw incision is performed according to Brennan.(3) After a week of habituation and baselining, an intrathecal injection of PD 98059 (inhibitor of ERK activation via its upstream regulator, MEK) (n=8) or vehicle (20% DMSO in 10 mM Hepes pH 7.4) (n=7) is administered. 30 minutes later, a plantar hindpaw incision is performed. Rats are tested on a Hargreaves hotplate for thermal allodynia and hyperalgesia. A sham control group consists in injecting the animals without performing an incision. For mechanical sensitivity testing von Frey hairs ranging from 12 to 574 mN are used. Lower vFH's are used for testing allodynia, while higher ones test mechanical hyperalgesia (compared to baseline).

RESULTS: A 1.5-fold increase in paw withdrawal latency and a 2-fold increase in paw withdrawal threshold is observed when the ERK inhibitor is injected intrathecally 30 minutes before the incision.



DISCUSSION: The difference in mechanical hyperalgesia is apparent in the first postoperative day, whereas thermal testing reveals differences at postoperative days 7 and 11. It has been stated previously that thermal and mechanical hyperalgesia occur through different mechanisms. (4,5) This late onset of action for thermal hyperalgesia of ERK's inhibition could be due to an upregulation of a downstream regulator, which needs further examination.

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Pain-Clinical

S-156.

TITLE: FEMORAL NERVE CATHETER INFUSION VS. IV PCA OF FENTANYL IN KNEE REPLACEMENT SURGERY: A LOCAL ANALGESIC PHENOMENON.

AUTHORS: J. Dreier¹, J. Hamelin², N. Hubbard², K. Dunphy², D. Mangar²;

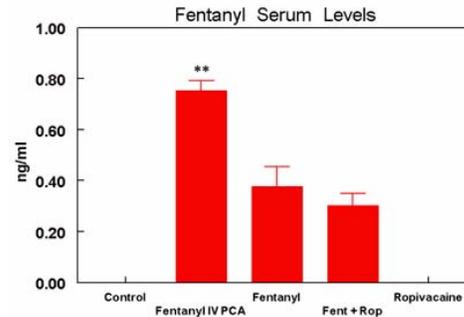
AFFILIATION: ¹University of South Florida, Tampa, FL, ²Florida Gulf-to-Bay Anesthesiology Associates, Tampa, FL.

INTRODUCTION: Postoperative pain after total-knee replacement (TKR) is a major concern. We designed the present study to compare efficacy of pain management with IV administered fentanyl and three femoral nerve sheath (FNS) catheter infusates: fentanyl alone, ropivacaine alone and fentanyl and ropivacaine in combination. Secondary aims were to identify a difference in muscle strength among the groups and to determine whether plasma fentanyl levels contributed significantly to pain relief.

METHODS: Seventy patients who underwent TKR under standardized general anesthesia participated in this prospective, double-blinded, randomized, placebo-controlled study. A FNS catheter was placed preoperatively. Post-operatively, a randomly assigned infusion of fentanyl (3µg/ml), ropivacaine (0.1%), a combination of fentanyl and ropivacaine (3µg/ml + 0.1%), or saline was initiated through the catheter. In addition, a group of patients were placed on an intravenous fentanyl patient controlled analgesia (PCA) pump to correlate serum fentanyl levels with level of analgesia. Pain was assessed postoperatively using the Visual Acuity Scores (VAS). Bilateral knee strength was determined using hand-held dynamometry post-operatively and preoperatively. Plasma fentanyl levels were measured and an evaluation of morphine use and side effects were also obtained.

RESULTS: Serum fentanyl levels were significantly lower when infused via the FNS catheter compared to the IV PCA group. Post-operative analgesia using the FNS catheter infused with fentanyl was comparable to that of ropivacaine and fentanyl plus ropivacaine, all requiring significantly less morphine than the control saline infusion. VAS scores were not different between the groups. The ratio of postoperative to preoperative extension and flexion was significantly

greater in the fentanyl only group compared to the other treatment groups.



DISCUSSION: This study revealed significantly better strength retention in subjects treated with fentanyl alone opposed to those receiving ropivacaine containing solutions, in spite of equivalent morphine consumption in all treatment arms. In order to determine whether the analgesia effects of fentanyl were local or peripheral, we compared catheter administration of fentanyl to IV infused fentanyl and found significantly lower serum fentanyl levels in the catheter administered group. This finding suggests that the analgesic effect reported is a local phenomenon occurring via a novel receptor in the FNS rather than an overall systemic effect. The benefit achieved from catheter administration of fentanyl shows promise in providing analgesia while facilitating greater recovery and muscle strength.

S-157.

TITLE: FEMORAL NERVE BLOCK FOR TOTAL KNEE ARTHROPLASTY; ULTRASOUND VS NERVE STIMULATOR

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INTRODUCTION: Femoral nerve blocks (FNB) provide effective analgesia after total knee arthroplasty (TKA). (1,2) Duration of analgesia varies from 6 to 24 hours. Prior studies have shown that FNB performed under ultrasound guidance (US) has faster onset and less risk of vascular puncture compared to nerve stimulator (NS) technique (3). We hypothesized that US FNB would provide more consistent duration of analgesia because circumferential spread of local anesthetic around the nerve is possible. We compared the duration of FNBs using either NS or US in each side of patients undergoing simultaneous bilateral TKA (BTKA).

METHODS: With IRB approval, 32 patients for BTKA received bilateral FNBs using a NS on one side and an US technique on the contralateral side. All patients received a combined spinal-epidural anesthetic and an epidural infusion of bupivacaine 0.06% and hydromorphone 10 mcg/ml for postoperative analgesia. A 22 gauge 2" insulated needle was used for FNBs. For NS, a quadriceps femoris twitch between 0.2 and 0.5 mA was accepted. For US, the femoral nerve was visualized in a short-axis view 2cm below the inguinal ligament using Sonosite Titan ultrasound and a C11/8-5MHz probe. The needle was inserted lateral to the probe and advanced in plane with the ultrasound beam. Local anesthetic was injected once the operator was satisfied with the final needle position. Anesthetic spread was evaluated by the operator, who repositioned needle tip to insure circumferential spread. 30ml of bupivacaine 0.375% with epinephrine were delivered for each FNBs. Efficacy of FNBs was assessed at 8, 12, 16, 18 and 24 hours after block placement in the femoral, lateral femoral cutaneous, and obturator nerve distributions.

RESULTS: The mean time to completion of the block was 5.5 minutes for the NS group and 5.9 minutes for the US group. The average number of passes was 2.5 for the NS group and 2.4 for the US group.

There was no significant difference in VAS between the two groups except at 12hr, mean VAS was 3.0 for US and 2.3 for NS, (p=0.05). There was no difference in sensation to pinprick between the 2 groups.

DISCUSSION: Our study did not demonstrate a statistically significant difference between the nerve stimulator technique and the ultrasound-guided technique in terms of rapidity of placement or duration of analgesia for all but one of the parameters measured. Variability existed between and within the two groups, but there was no meaningful correlative trend. Our findings suggest that the US technique is superior in neither the time to placement nor the duration of analgesia when compared the NS technique.

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S-158.

TITLE: EPIDURAL DEPODUR® 7.5MG AND 10MG A DOSE COMPARISON STUDY IN THE ELDERLY.

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AFFILIATION: Maimonides Medical Center, Brooklyn, NY.

DepoDur® is a single dose epidural injection that provides steady state release of morphine into the epidural space. The use of reduced dosing of epidural DepoDur® is suggested in elderly patients. Currently there are no studies to show what is an effective dose reduction.

OBJECTIVES: To assess the clinical efficacy and safety of single shot Depodur® 7.5mg compared to 10mg in the elderly patient after total knee replacement surgery.

METHODS: A single center retrospective chart review of patients undergoing total knee replacement with postoperative epidural Depodur® was conducted. Each patient received an epidural preoperatively. The first 24 hours postoperatively each patient received an epidural infusion of 0.1% bupivacaine with 4 mcg of fentanyl per mL at 8 mL per hour. The infusion was stopped on the morning of postoperative day one and 45 minutes later either 10mg or 7.5mg of Depodur® was injected via the epidural catheter. Patients were monitored for adverse opioid effects, and pain scores (0-10, 0=no pain, 10= worst pain) recorded at 24, 48, 72 hours postoperatively. Patients were evaluated on the use of supplemental opioids, antiemetic therapy, and opioid antagonist reversal of respiratory depression. The incidence of side effects and pain scores from the chart review was compared between the two doses given as well as to the results of the Viscusi et al study involving epidural depodur® 15mg alone.

Statistical analysis was performed using an unpaired t test to determine the significance of any difference in the reported pain score, and a Chi-square analysis of the differences in the reported incidences of side effects

RESULTS: In Viscusi's study the mean pain score at 24 hours was 3.6 and at 48 hours 3.4, compared to pain scores of 1.9 and 3.9 at 24 and 48 hours post 7.5 mg and 3.5 and 4.1 at 24 and 48 hours 10mg respectively. Pain scores in the 7.5mg group were lower or statistically similar to the other groups. The incidence of opioid related side effects was equal to

or less than the incidence reported by Viscusi. The greatest difference was in the incidence of nausea/vomiting 35% in the chart review compared to 72.9% in Viscusi's group (P =0.01).

CONCLUSIONS: Depodur® 7.5mg can be used effectively for post operative analgesia in the elderly. This dose reduction provides a safer and equally as effective method of postoperative analgesia that the standard dosing of DepoDur® 10mg-20mg. However large randomized clinical trials would be needed to determine the overall impact of this method of post-operative pain control in the elderly.

S-159.

TITLE: RETROSPECTIVE STUDY OF POSTOPERATIVE PAIN AND COMPLICATIONS ASSOCIATED WITH BARIATRIC SURGERY IN MORBIDLY OBESE AND SUPER OBESE PATIENTS

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INTRODUCTION: Anesthetic implications for severely obese patients undergoing weight loss operations are considerable ^{1,2}. At present, management of super obese (SO) patients (BMI ≥50 kg/m²) is based upon experience from morbidly obese (MO) patients (BMI 40-49.9 kg/ m²). With consideration of the type of bariatric surgery performed, we compared the perioperative and postoperative data of MO and SO patients.

METHODS: After IRB approval, we performed a retrospective analysis of data from 98 patients admitted to our medical center for bariatric surgery between January 2006 and January 2007. The cases selected were: high gastric bypass, laparoscopic gastroenterostomy, and laparoscopic gastric restrictive procedures, all performed by the same surgeon. Inclusion criterion was a BMI greater than 35 kg/m² with significant co-morbidities. Patients were classified into two groups based upon their BMI. Fifty-seven patients were classified as MO and 41 patients were SO. Both groups of patients received the same post-operative analgesic protocol. The following parameters were evaluated between MO and SO patients, length of stay, time to ambulate, postoperative complications, and pain assessment. The pain assessment was based upon the visual analogical pain scale (VAS), and was averaged each day to generate a daily VAS score. The average of each parameter was compared via one-way ANOVA followed by Fischer's LSD means comparisons using Statview® Version 5.0.1. All data are presented as group mean ± SEM.

RESULTS: Pain assessment recorded as mean daily VAS scores were significantly higher for super obese patients in the first three postoperative days compared to morbidly obese patients (Table 1). The

average length of stay was significantly higher for super obese patients who underwent high gastric bypass procedures. However, the average time to ambulate did not differ between the MO and SO groups. Super obese patients had significantly greater postoperative respiratory complications compared to morbidly obese patients. The most significant complications involved shortness of breath and relative hypoxia.

Table 1. Average VAS Scores

Procedure	VAS Day 1		VAS Day 2		VAS Day 3	
	Morbidly Obese	Super Obese	Morbidly Obese	Super Obese	Morbidly Obese	Super Obese
High Gastric Bypass	7.0 ± 0.1	8.1 ± 0.4	7.0 ± 0.1	7.7 ± 0.4	6.0 ± 0.1	6.7 ± 0.5
Laparoscopic Procedures	5.0 ± 0.1	7.0 ± 0.2**	4.5 ± 0.5	7.0 ± 0.2*	2.5 ± 0.5	5.0 ± 0.2*
Laparoscopic Gastroenterostomy	7.5 ± 0.2	8.2 ± 0.2*	6.8 ± 0.3	7.4 ± 0.3	5.6 ± 0.3	6.6 ± 0.4*

Mean VAS Score ± SEM * represents p<0.05 ** represents p<0.01

DISCUSSION: Weight loss surgery for SO patients presents a great challenge for the physician. Fear of overdosing pain medications may lead to poor pain management, greater incidence of pain, and longer hospital stays. A more effective anesthetic protocol should be created to obtain proper pain management in super obese patients.

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S-160.

TITLE: THE RELATIONSHIP BETWEEN OPTIMAL INITIAL IV. PCA BASAL DOSE AND PRE- AND INTRAOPERATIVE CLINICAL DATA IN SURGICAL PATIENTS

AUTHORS: Y. Shiga, H. Yamaguchi, K. Motokawa, D. Aya, K. Yoshimuta;

AFFILIATION: Tsukuba Medical Center Hospital, Tsukuba, Japan.

INTRODUCTION: Postoperative pain management is one of the key issues for anesthesiologists, and recently can be provided using a patient-controlled analgesic (PCA) method in an acute pain service (APS) setting (1,2). Postoperative pain status as well as its accompanying adverse effects should be closely monitored and a basal dose should be optimized during the service period (3), but it has been based on experience. In this study we examined the relationship between an optimal initial intravenous (iv.) PCA basal dose and perioperative patients' data.

METHODS: The complete 169 sets of perioperative data consisting of patient's demographics, surgical and anesthetic data, and postoperative pain management data in surgical patients received iv. PCA were collected from the database in our hospital after an approval of the study protocol by the local ethical committee. An analgesic used in iv. PCA was fentanyl, 10 ug/ml in saline solution. Fentanyl 0.6 ug/kg was given as a loading dose at the end of surgery, and rescue dose and lockout time were set at 0.3 ug/kg/time and 10 minutes, respectively. After surgery patients were asked their surgical pain status measured by Prince Henry score (PHS) and incidences of adverse effects every 12 hours. Iv. PCA basal dose was adjusted according to PHS and the numbers of the previous 12 hours' rescue dose requests and the rescue dose given. The optimized iv. PCA basal dose was defined as a dose with PHS of 0 or 1 and without incidence of adverse effects 24 hours after the end of surgery. The relationship between an optimal initial iv. PCA basal dose for postoperative pain relief and the patients' demographics, anesthetic and surgical data was analyzed using a multiple regression analysis. P value less than 0.01 was considered significant.

RESULTS: The relationship between an initial optimal iv. PCA basal dose and the perioperative data was analyzed as shown in Table, and its

correlation coefficient was 0.839, $p < 0.001$.

The significant parameters and coefficients related to an optimal initial iv. PCA basal dose (ml/h)		
Parameter	Coefficient	P value
(Intercept)	-8.112	0.003
ln(Age(yr))	-0.618	0.010
male	0.318	0.027
BMI	0.115	0.002
Endoscopic surgery	-1.857	0.000
ln(Surgical Time(min))	0.959	0.000
General Anesthesia	1.571	0.000
Opioid Use	-3.249	0.004
Height(cm)	0.0542	0.016

DISCUSSION: The results of this study show that an optimal initial iv. PCA basal dose could be calculated using preoperative patient's demographics and surgical and anesthetic data. But the evaluation of the relationship should be followed in the future.

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S-161.

TITLE: THE PREDICTION OF EPIDURAL PCA DURATION FOR POSTOPERATIVE PAIN RELIEF USING PERIOPERATIVE CLINICAL DATA IN SURGICAL PATIENTS

AUTHORS: K. Yoshimuta, H. Yamaguchi, K. Motokawa, D. Aya, Y. Shiga;

AFFILIATION: Tsukuba Medical Center Hospital, Tsukuba, Japan.

INTRODUCTION: Postoperative pain management using a patient-controlled analgesic (PCA) device has been widely used (1,2). Epidural PCA is superior to intravenous PCA in terms of the pain relief quality (3), but its adverse effects may be more often and its duration may depend on an individual patient. In this study we examined the relationship between the duration of epidural PCA and perioperative patients' data in surgical patients.

METHODS: The complete 176 sets of perioperative data consisting of patient's demographics, surgical and anesthetic data, and postoperative pain management data in surgical patients received epidural PCA for more than 2 days were collected from the database in our hospital after an approval of the study protocol by the local ethical committee. An analgesic used in epidural PCA was fentanyl, 2.5 ug/ml in 0.2% ropivacaine solution. The solution 5ml was given as a loading dose at the end of surgery, and rescue dose and lockout time were set at 3ml/time and 20 minutes, respectively. After surgery patients were asked their surgical pain status measured by Prince Henry score (PHS) and incidences of adverse effects every 12 hours. Epidural PCA basal dose was adjusted according to patient's PHS and the numbers of the previous 12 hours' rescue dose requests and the rescue dose given. Epidural PCA was continued until PHS got 0 or 1 12 hours after the cessation of basal epidural PCA dose. The relationship between the duration of epidural PCA for postoperative pain relief and the patients' demographics, anesthetic, surgical and postoperative PCA data was analyzed using a multiple regression analysis. P value less than 0.01 was considered significant.

RESULTS: The relationship between the duration of epidural PCA and the perioperative data was analyzed as shown in Table, and its correlation coefficient was 0.828, $p < 0.001$.

The relationship between epidural PCA duration and perioperative data.		
Parameter	Coefficient	P value
(intercept)	3.248	0.000
Male	0.453	0.022
Extremities Surgery	1.220	0.006
PCA dose (ml/h) at 48 hours	3.021	0.001
PCA dose (ml/h) at 72 hours	-2.330	0.009
PCA dose change (ml/h) at 48 hours	-2.891	0.001
PCA dose change (ml/h) at 72 hours	2.964	0.001
#Request - #Given at 48 hours	0.041	0.001

DISCUSSION: The results of this study show that epidural PCA duration could be predicted on the 3rd postoperative day based on patient's demographics, surgical data, and PCA data. But the evaluation of the relationship should be followed in the future.

REFERENCES: 1. Anesthesiology 2004;100:1573-81. 2. Drugs 2006;66:2321-37. 3. Cochrane Database Syst Rev. 2005;25:CD004088.

S-162.

TITLE: PREEMPTIVE ANALGESIA WITH FLURBIPROFEN AXETIL MICROSPHERE INJECTION IN PATIENTS UNDERGOING GYNECOLOGICAL LAPAROSCOPIC SURGERY

AUTHORS: X. Wang, H. Zhang;

AFFILIATION: The Dept of Anesthesiology 301 PLA General Hospital, Beijing, China.

OBJECTIVE To study analgesic effects of preemptive analgesia with non-steroidal anti-inflammatory drugs (NSAIDs).

METHODS Sixty-six patients (ASA I-II) scheduled to take gynecological laparoscopic surgery were randomly allocated into three groups. Before induction of anesthesia, flurbiprofen axetil microsphere injection 50mg was given intravenously (IV) in Group A (n=22) lornoxicam 8 mg was administered IV in Group B (n=22) and in Group C (n=22), equivalent dose of 0.9% NaCl was injected as control. The pain score with visual analogue scale (VAS), incidence of adverse events were recorded at the emergence from anesthesia, 0.5, 1, 2, 8 and 24 hour after emergence.

RESULTS At each observed point during 8h after emergence, the VAS of group A was significantly lower than those of group B or group C ($P < 0.05$). The VAS of group B was markedly less than those of group C during 2 h after emergence ($P < 0.05$). Furthermore, no important difference was found for side effects in three groups.

Tab 1 postoperative VAS of patients

postoperative time (h)	T0	T0.5	T1	T2	T8	T24
Group A (n=22)	0.41±0.34*	2.09±1.52**	2±1.53**	1.94±1.33**	2.57±1.39**	1.18±0.79
Group B (n=22)	2.14±1.47*	4.25±1.55*	3.93±1.41*	3.51±1.23*	3.06±1.03	1.3±0.8
Group C (n=22)	2.91±1.51	6.20±1.45	5.95±1.44	5.30±1.39	3.77±1.17	1.46±1.09

Compared with Group C * $P < 0.05$

Compared with Group B ** $P < 0.05$

CONCLUSION Before induction of anesthesia, the administration of flurbiprofen axetil microsphere injection or lornoxicam IV in patients undergoing gynecological laparoscopic surgery provided adequate preemptive analgesic effect, and flurbiprofen axetil microsphere may be a better choice.

S-163.

TITLE: PERIOPERATIVE PREGABALIN REDUCES NEUROPATHIC PAIN AT 3 MONTHS AFTER TOTAL KNEE ARTHROPLASTY (TKA)

AUTHORS: A. Buvanendran¹, S. S. Reuben², M. Kari¹, J. S. Kroin¹, C. Della Valle¹;

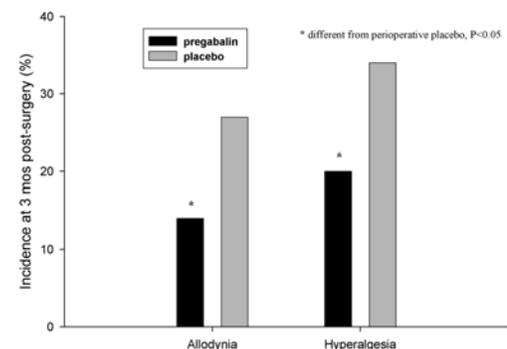
AFFILIATION: ¹Rush Medical College, Chicago, IL, ²Baystate Medical Center, Springfield, MA.

INTRODUCTION: Pregabalin has been shown to be effective for the treatment of chronic neuropathic pain (Pain Res Manag 2006; 11:16A-29A). Pregabalin administered before and after surgery reduced opioid use following spinal fusion surgery (Anesth Analg 2006;103:1271). This study examines the hypothesis that pregabalin administered perioperatively for patients' undergoing total knee arthroplasty (TKA) can reduce chronic long-term pain syndromes.

METHODS: Following IRB approval, a total of 146 patients having primary TKA were enrolled in this randomized, placebo-controlled, double-blind study. Patients were randomly assigned to 2 drug groups. Half of the patients received pregabalin 300 mg orally 2 hours prior to surgery, and the other half received matching placebo, at the same time point. In the operating room, patients were sedated with midazolam and a combined spinal-epidural procedure performed. At completion of surgery, epidural infusion of fentanyl/bupivacaine was initiated using continuous basal infusion with superimposed patient-controlled bolus. Patients subsequently received repeated doses of pregabalin 150 mg b.i.d. or placebo starting the day after surgery, with drug dosing continued up until day 14 post-surgery. The incidence of neuropathic pain was assessed 3 months post-surgery using the S-LANSS score, a valid diagnostic tool to assess neuropathic pain, with patients scoring ≥ 12 considered to have neuropathic pain (J Pain 2005;6:149). The incidence of mechanical allodynia (stroking) or hyperalgesia (pressure) was also recorded. Comparison between the 2 groups was by chi-squared test.

RESULTS: There was no difference in demographics (age, weight, etc.) between the 2 groups. At 3 months post-TKA, the incidence of patients with neuropathic pain post-TKA was lower in the pregabalin (1.49%)

group compared to the placebo (11.39%) ($P=0.018$). The incidence of allodynia in the operated leg (fig) was also lower ($P=0.0337$) at 3 months for the pregabalin group (14%) than the placebo group (37%). The incidence of hyperalgesia in the operated leg was lower ($P=0.0346$) for the pregabalin group (20%) than the placebo group (34%). Patients who received pregabalin also had lower VAS pain scores in the operated leg at 3 months post-TKA compared to placebo ($P=0.047$).



DISCUSSION: Perioperative administration of pregabalin decreased the incidence of neuropathic pain from 11.39% to 1.49% at 3 months after TKA. This suggests that pregabalin may be a useful perioperative medication for decreasing the incidence of chronic pain for patients undergoing this surgical procedure.

S-164.

TITLE: PRELIMINARY RESULTS FROM SINGLE-SHOT INTRATHECAL ZICONOTIDE TRIAL TO PREDICT ITS EFFECTS WITH PUMP INFUSION

AUTHORS: D. R. Okano, H. Akbik, M. Khan, R. Zollett, M. Munir;
AFFILIATION: University of Cincinnati, Cincinnati, OH.

INTRODUCTION: Ziconotide (PRIALT™, Elan Pharmaceuticals, Inc.) is a synthetic conopeptide, an N-type calcium channel blocker, with non-opioid analgesic property. It is indicated for the management of severe chronic pain in patients for whom intrathecal (IT) therapy is warranted, however are intolerant of or refractory to other treatment, such as IT morphine, systemic analgesics or other adjunctive therapies. Trials for Ziconotide in established IT pump patients have been usually performed by removing existing pump medications and adding Ziconotide to IT pump. We report our experience with single shot intrathecal Ziconotide for trial to predict its effects with continuous infusion.

METHODS: After informed consent, 11 established IT pump patients underwent a single shot trial with Ziconotide. All patients had a single shot spinal performed by a 22-G spinal needle placed at L2-3 or L3-4 (above the level of IT catheter) under fluoroscopic guidance. Fluoroscopic guidance was utilized to locate the exact site of entry and to avoid any damage to the IT catheter. Two patients had 5-µg dose, 5 patients had 2.4-µg dose and 4- patients had 1.2-µg dose. After the procedure, patients were monitored for 2 hours in the recovery room and discharged to home in stable condition. Patients were followed up within 24-48 hours via a telephone call and then seen in clinic within 2 weeks for follow up. The patient who had significant pain relief had Ziconotide added to their IT pump

RESULTS: Eight out of 11 patients had significant pain relief (more than 50% from preprocedure level) with single shot IT trial. Serious side effects included urinary retention requiring intermittent catheterization for three days, hallucinations which resolved in a few hours and one case of motor weakness that resolved in 2 days without intervention. Urinary retention and motor weakness was seen in patients receiving 5-µg dose. Seven out of 8 patients continue to get satisfactory

pain relief 6 months after the addition of Ziconotide to the IT pump infusion.

CONCLUSION: These preliminary results show that single shot intrathecal trial may be performed to predict response to IT infusion. There are multiple implications of this finding. Single shot IT trial may reduce the patient inconvenience (withdrawals, wait time), improve cost effectiveness (scheduling multiple patients on the same day for trial), and provide an easy alternate to continuous trial especially for patient without IT pump. However, further controlled trials are needed to establish safety and efficacy of single shot intrathecal Ziconotide injection.

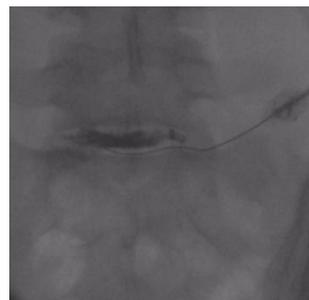
S-165.

TITLE: A NOVEL INTERLAMINAR APPROACH FOR DISCOGRAPHY AT L5-S1 DISC

AUTHORS: M. A. Khan, D. R. Okano, R. Zollett, M. A. Munir;
AFFILIATION: University of Cincinnati, Cincinnati, OH.

INTRODUCTION: Discography is the gold standard for identifying symptomatic disc degeneration and discogenic pain. The L5-S1 disc has been the most difficult for discography due to the iliac crest overlying the anterior portion of the L5-S1 disc space. Traditionally a posterior-lateral approach is used to gain access to L5-S1 disc; however, significant number of patients may not have optimal access to L5-S1 disc. We describe a novel interlaminar technique for L5-S1 disc access in such difficult patients.

TECHNIQUE REPORT: Patient is positioned prone on the fluoroscopy table with positioning rolls under lower abdomen to reduce lumbar lordosis. Patient is prepped and draped in usual sterile fashion. Fluoroscope is tilted in cranial-caudad angulation to align with superior endplate of sacrum. Fluoroscope is also moved in oblique projection to align the most lateral part of interlaminar space with the L5-S1 disc. After a skin wheal is raised with 1% lidocaine, a 22-gauge, 5- or 7-inch spinal needle bent at the tip is introduced and advanced under fluoroscopic guidance to the ligamentum flavum. Needle trajectory is confirmed in lateral projection. At this time the needle is introduced into the L5-S1 disc. The needle tip is positioned close to the center of disc in both anterior-posterior and lateral projections. A non-ionic contrast is then injected through a manometric syringe in the usual manner. A CT scan is obtained after the procedure to view axial anatomy of the disc.



CONCLUSION: Interlaminar discography may provide an alternate approach for patients with high iliac crest obscuring the entrance into the L5-S1 disc. Interlaminar approach from lateral aspect may be performed without dural puncture. However, the risk of dural puncture and post-dural puncture headache may be higher with interlaminar approach. The risks and potential benefits should be weighed before proceeding with interlaminar approach for discography.

S-166.

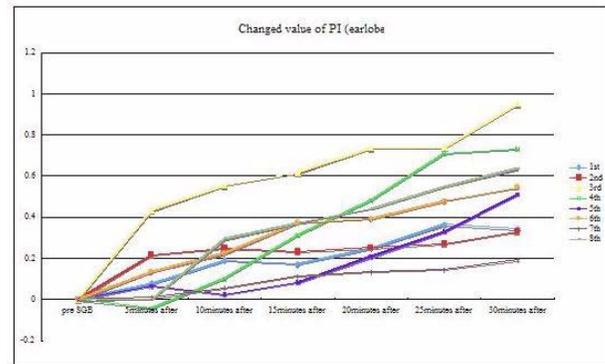
TITLE: USEFULNESS OF PI MEASUREMENT TO DETECT THE EFFECT OF SGB IN A SYRINGOMYELIA PATIENT

AUTHORS: K. Mizusawa, T. Kaneda, H. Yamazaki, T. Suzuki;
AFFILIATION: Department of Anesthesiology, Tokai University School of Medicine, Kanagawa, Japan.

INTRODUCTION: There have been various methods to detect the effect of Stellate Ganglion Block (SGB). Among them, we have been studying the usefulness of the Perfusion Index (PI) that is one of the measurement items on the Masimo SET Pulse Oximeter. This time, we measured PI in a Syringomyelia patient and compared the reading with the effect of SGB.

METHOD: The patient, who is 29 years old female had a left occipital headache, and a pain and palsy in the right upper extremity caused by syringomyelia with Chiari malformation. She is now undergoing treatment with SGB as an outpatient. In order to evaluate the effect of SGB, we put probes for pulse oximetry (Radical, Masimo Corporation) on both earlobes and index fingers of the patient. We also put probes for skin temperature nearby. For SGB, 6ml of 1% mepivacaine was injected in the base of the 6th transverse process. After the SGB, symptoms, objective signs such as Horner's syndrome, PI and temperature were observed.

RESULT: SGB was performed 8 times, in which Horner's syndrome was observed. The PI of the fingers and earlobes were reviewed every 5 minutes by comparing the changes baseline. The PI of the finger on the SGB side demonstrated an upward trend. And more, the PI of the earlobe on the SGB side showed an upward trend as well. The PI value of the earlobe were displayed in Fig. 1.



DISCUSSION: SGB is one of the treatments for Syringomyelia patient who takes on a sensory disturbance. But it is difficult to evaluate the effect of SGB. In this situation, effects of SGB can be observed by an increase of blood perfusion, and it can be detected by increasing of PI. So it is thought that increasing of PI is equal with appearing the effect of SGB. Furthermore, the temperature of the finger and earlobe on the SGB side showed an upward trend. These facts mean the effect of SGB for her. In this time, we find the increase of PI and it is in reproducibility. In conclusion, this case demonstrates the utility of the PI measurement as a useful method to detect the effect of SGB noninvasively in a syringomyelia patient.

REFERENCE: Anesthesiology, 2003; 99: A593

S-167.

TITLE: RADIOFREQUENCY ABLATION OF MEDIAL BRANCHES IN THE PRESENCE OF SACRAL NERVE STIMULATOR AND PACEMAKER.

AUTHORS: R. Zollett, M. A. Khan, D. R. Okano, M. A. Munir;
AFFILIATION: University of Cincinnati, Cincinnati, OH.

INTRODUCTION: Radiofrequency ablation of medial branches of dorsal rami has been successfully utilized for long term pain relief from zygapophyseal joint pain. The procedure utilizes uni-polar radiofrequency heat to produce a neurolytic lesion. Radiofrequency waves may interfere with implanted pacemakers or spinal cord/peripheral nerve stimulators. The safety of radiofrequency ablation has not been established with the concurrent presence of pacemakers and spinal cord or peripheral stimulators. This is the first report of utilization of bipolar radiofrequency in presence of pacemaker and sacral nerve stimulator in our patient.

METHODS: After informed consent, our patient with a permanent pacemaker and implanted sacral nerve stimulator, diagnosed with postlaminectomy pain syndrome, was scheduled for radiofrequency ablation of right L4 to S1 medial branches. Prior to the radiofrequency ablation, the patient's pacemaker was interrogated to assure settings. The patient was brought to the procedure room and placed on the fluoroscope table in prone position. After sterile prep and drape, a 21-G, 10cm radiofrequency cannula with 10mm active tip was placed into position under fluoroscopic guidance. A second radiofrequency cannula of same size was placed 4-5 mm adjacent to the first cannula. A similar procedure was repeated at all involved levels.

RESULTS: Sensory and motor stimulation was performed at each level. Bipolar stimulation did not alter the monitoring of the EKG and there were also no signs of abnormal discharge from the sacral nerve stimulator. Ablation was performed at each level with radiofrequency lesion mode at a temperature of 65-70 degree Celsius for 3 minutes. The patient tolerated the procedure well without any complications. There were no problems with pacemaker and the sacral nerve stimulator afterwards. Pacemaker was interrogated again after the procedure to assure proper functioning.



CONCLUSION: This is the first report of use of bipolar radiofrequency ablation in the presence of a sacral nerve stimulator and pacemaker without any immediate complications. Increasing number of patients are requiring advanced neuromodulation such as spinal cord stimulators and peripheral nerve stimulators for control of intractable pain. Some of these patients may also require use of radiofrequency ablation for facet related pain or for treatment of certain tumors (liver, bone etc). This report provides grounds for further investigations to elucidate the safety of radiofrequency ablation in presence of spinal or peripheral nerve stimulators and pacemakers.

S-168.

TITLE: COMPARATIVE EVALUATION OF GABAPENTIN, PREGABALIN AND A COMBINATION OF BOTH IN THE TREATMENT OF CHRONIC INTRACTABLE NEUROPATHIC PAIN DISORDER

AUTHORS: S. P. Ambesh, N. Verma, P. K. Singh;

AFFILIATION: Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow (India), Lucknow, India.

INTRODUCTION: Neuropathic pain is caused by functional abnormalities or structural lesions in the peripheral or central nervous systems and occurs without peripheral nociceptor stimulation. The treatment of neuropathic pain is difficult and done in variety of ways. This clinical study investigates the efficacy and safety of gabapentin, pregabalin and gabapentin plus pregabalin in the treatment of chronic intractable neuropathic pain, in patients who are resistant to current analgesic treatment regimens or conventional pain therapies.

METHODS: Eighty-six consented patients suffering with intractable neuropathic pain were included in this study. Patients in Group I (n=28) received gabapentin (300mg) thrice a day, Group II (n=28) pregabalin (150 mg) twice a day and Group III (n=30) gabapentin (150 mg) and pregabalin (75 mg) twice a day. All patients, irrespective of their groups, also received amitriptyline (25 mg) once a day in the evening. The duration of follow-up of our study was 2 to 18 months. Efficacy was evaluated using four verbal ranking scales, 0-10 of pain intensity, 0-3 for mood profile, 0-3 for quality of sleep, and 0-4 for activity. Measurements were taken before and after each treatment. Pain quality was assessed with the McGill pain questionnaire. Adverse effects and satisfaction (0-4 level scale) were also recorded. Data were analyzed by paired student's t-test with $p < 0.05$ considered statistically significant.

RESULTS: The 86 enrolled patients (49 male and 37 female) had a mean age of 52.4 years (range 29-78) and a history of neuropathic pain unresponsive to conventional medication. Previous duration of pain was three months to seven years (mean 21.6 ± 11.9 months). Significant improvement ($p < 0.001$) was found in initial versus final estimation of pain in all three groups however the combination therapy group performed better than gabapentin or pregabalin in initial vs. final

estimation of pain (9.15 ± 0.80 vs. 2.25 ± 1.45), interference of mood (2.50 ± 0.75 vs. 0.45 ± 0.55), quality of sleep (2.38 ± 0.95 vs. 0.35 ± 0.45), daily activity (1.56 ± 1.15 vs. 0.45 ± 0.67) and overall satisfaction with results (2.47 ± 0.65). The most frequent adverse effects were seen in gabapentin group and that were dizziness (28.6%), somnolence (25%), dry mouth (14%) and ataxia (10.7%).

DISCUSSION: The results of our study clearly show that low dose combination therapy of gabapentin plus pregabalin along with amitriptyline provide satisfactory pain relief in patients with intractable neuropathic pain disorders. Average daily pain score was used together with several quality of life measures, such as mood interference, sleep quality and reduction in daily activity. All parameters were significantly improved with combination therapy of gabapentin and pregabalin. There were fewer side effects in patients receiving low dose combination therapy in comparison to patients receiving gabapentin or pregabalin alone.

Pediatric

S-169.

TITLE: EFFECT OF DEXMEDETOMIDINE ON NEUROPHYSIOLOGIC MONITORING DURING SPINAL SURGERY (EEG, TIBIAL SOMATOSENSORY AND LOWER EXTREMITY TRANSCRANIAL ELECTRICAL MOTOR EVOKED POTENTIALS, F-RESPONSES AND H-REFLEXES).

AUTHORS: G. M. Cramolini, R. E. Leppanen, L. G. Smithson;
AFFILIATION: East Tennessee Children's Hosp., Knoxville, TN.

INTRODUCTION: Dexmedetomidine, an α_2 agonist with sedative, analgesic and sympatholytic/vasodilatory properties, yet lacking respiratory depressant effects, demonstrates neuroprotection in focal cerebral ischemia.⁽¹⁾ Approved for adult ICU sedation, many pediatric off label uses have arisen, such as being used as a component of total intravenous anesthesia (TIVA) for spinal surgery.^(2, 3, 4, 5, 6) Several reports show no interference with somatosensory nor auditory evoked potentials.^(6, 7, 8, 9) Concerned that dexmedetomidine might interfere with neurophysiologic monitoring during posterior spinal fusion, we examined its effects on brainstem and cortical tibial somatosensory evoked potentials (SEPs), transcranial motor evoked potentials (TCMEPs), EEG, F-responses, and H-reflexes using each subject as their own control. (A case report showing loss of TCMEPs with dexmedetomidine during 2 pediatric spinal surgeries was published recently.⁽¹⁰⁾)

METHODS: IRB approval and informed consent were obtained. Eleven idiopathic scoliosis patients (14 to 19yrs) received the same evoked potential benign anesthetic and intra-operative monitoring as usual. After final distraction and fixation of the spine, at which time neurophysiologic monitoring is normally discontinued, a loading dose of dexmedetomidine at 1 mcg/kg over 10 minutes, followed by a continuous infusion of dexmedetomidine at 0.5 mcg/kg/hour were added during wound closure. Since neurophysiologic monitoring was no longer required for patient safety, no changes were made to the dexmedetomidine infusion regardless of evoked potential findings. Fentanyl and propofol infusions were weaned based on clinical parameters in anticipation of extubation.

RESULTS: Dexmedetomidine caused no changes in SEPs or EEG.

Dexmedetomidine did markedly affect the TCMEPs, F-responses and H-reflexes in all patients. Lower extremity TCMEP amplitudes were decreased (0-100, mean: -86±16.6% decrement), F-response amplitudes were decreased (0-100, mean: -58±12.5% decrement) and H-reflex amplitudes were decreased (0-100, mean: -71±13.9% decrement).

DISCUSSION: TCMEPs, F-responses and H-reflexes activate different populations of motor neurons. Dexmedetomidine appears to affect each of these differently.

Dexmedetomidine, at doses recommended for adult ICU sedation, interfered significantly with lower extremity TCMEPs, F-responses and H-reflexes. These changes could not have been distinguished from those associated with spinal cord ischemia and/or distraction injury.

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S-170.

TITLE: ANESTHESIA FOR PET IMAGING OF GABA RECEPTORS

AUTHORS: J. K. Labovsky, W. Theodore, I. Dustin, N. Miao, Z. Quezado;

AFFILIATION: National Institutes of Health, Bethesda, MD.

INTRODUCTION: SSADH (succinic semialdehyde dehydrogenase) deficiency is a rare autosomal recessive disorder in which transamination of GABA (gamma-aminobutyric acid) to succinic semialdehyde is followed by its conversion to 4-hydroxybutyric acid (gamma-hydroxybutyric acid or GHB). In turn, there is accumulation of GABA and GHB in the CNS. Clinical manifestations of the disease include developmental delay, hypotonia, ataxia, seizure, hyperkinetic behavior, aggression, self-injurious behaviors, and hallucinations.

At a clinical research center, patients with SSADH deficiency were enrolled in a study aimed at examining binding and distribution of brain GABA(A) receptors and GABA levels. To that end, 11C-flumazenil positron emission tomography (PET), MRI, and NMRS were planned. The requirement that participants stay motionless for several hours to complete the PET scan and other imaging studies was anticipated to be problematic given the clinical manifestations of SSADH deficiency. As most agents used for sedation and anesthesia, including propofol, isoflurane and sevoflurane, have been shown to alter 11C-flumazenil binding to GABA(A) receptors, it was imperative to select an anesthetic agent with a mechanism of action not expected to involve GABA receptors. Possible alternatives included chloral hydrate or ketamine.

METHODS: Seven patients (age 10-27) with SSADH deficiency underwent MRI and 11C-flumazenil PET scans. ASA standard monitors were placed, as well as oxygen via nasal cannula (2-3 L/min). Given the possibility of mood alterations and hallucinations with ketamine and the unpredictable effect and time of onset of chloral hydrate in our patient population, we chose to administer dexmedetomidine for all 11C-flumazenil PET scans.

RESULTS: A bolus dose of 1mg/kg of dexmedetomidine, infused over 10 minutes, was followed by a continuous infusion, titrated to desired effect, ranging from 0.7- 2 mcg/kg/hr. Sedation with dexmedetomidine

allowed for successful PET scans in all seven patients. Hemodynamics remained stable, though bradycardia occurred frequently, with heart rate between 30 - 102. While bradycardia was not associated with hypotension, it was treated with glycopyrrolate in all but one patient.

DISCUSSION: We were presented with the challenge of sedating patients with severe developmental delay without using agents that would interfere with GABA receptors. Unlike the alternatives chloral hydrate or ketamine, dexmedetomidine, an alpha-2-agonist, appeared to be an ideal candidate to meet this goal. We found that infusion of dexmedetomidine allowed patients with SSADH deficiency to cooperate with the procedure and adequate PET images were obtained in all patients. All patients tolerated the infusion of dexmedetomidine, though isolated bradycardia was a frequent occurrence. Dexmedetomidine was successfully implemented as an anesthetic agent for PET scan imaging of GABA receptors in patients with succinic semialdehyde dehydrogenase (SSADH) deficiency.

S-171.

TITLE: A REVISED PEDIATRIC EMERGENCE DELIRIUM SCALE FOR INFANTS AND CHILDREN

AUTHORS: C. R. Galiza, A. Kakavouli, S. S. Lo, J. B. Sobol, M. P. Carson, L. S. Sun;

AFFILIATION: Columbia University, New York, NY.

INTRODUCTION: Emergence agitation/delirium (EAD) complicates postoperative patient care. A uniform definition and tool for its assessment is needed. The Pediatric Anesthesia Emergence Delirium (PAED) scale is validated in children 18 months to 6 years of age.¹ We previously developed the Pediatric Emergence Delirium Scale (PEDS) to also evaluate infants and young children. To improve the sensitivity of our scale, we have revised our scale and adopted the gold standard (GS) as assessment by three experienced pediatric anesthesiologists. The present study aimed to validate our revised scale and to compare the sensitivities and specificities of 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. Five and 30 minutes after PACU arrival, two observers scored each patient on the PEDS and PAED scales while three experienced pediatric anesthesiologists screened the patient for pain using the FLACC and determined whether the patient was experiencing EAD. All observers were blinded. Data were pooled from all awake points.

RESULTS: 115 patients were enrolled as a new study group (230 points). 107 awake points were used for scale validation (60 patients, average age 32.6±19.6 months). After screening for pain, EAD occurrence per the GS was 12/107 (11.2%). The average scores for patients with EAD were 17.9±1.5 using the PEDS and 16.1±2.9 using the PAED scale. Each scale was validated against the GS. For the PEDS, ≥16 was found to be the optimal cutoff for EAD diagnosis with sensitivity=1 and specificity=0.96. This corresponded to EAD in 16/107, 15.0%. A cutoff of ≥10 was defined previously for the PAED based on the need for pharmacologic treatment¹ Using this definition, we found sensitivity=0.92 and specificity=0.64 with incidence of 45/107, 42.1%.

S-172.

TITLE: ASSESSING THE FEASIBILITY AND SAFETY OF PERCUTANEOUS NEEDLE CRICOTHYROTOMY FOR INFANTS AND TODDLERS USING A PIGLET MODEL

AUTHORS: K. D. Matlock;

AFFILIATION: Scott & White Memorial Hospital, Temple, TX.

INTRODUCTION: Emergency cricothyrotomy is not recommended for emergency airway management in infants and toddlers. Dimensions of the cricothyroid membrane preclude the use of available cannulae and inadvertent division of the cricoid cartilage is associated with long-term airway complications (1). Percutaneous needle cricothyrotomy (PC) is recommended for children 8 years and older when ventilation and intubation prove impossible and has been recommended in life-threatening situations for younger children (2-6). No outcome based studies evaluate the safety or effectiveness of PC in toddlers. We hypothesized that it would be associated with an excessive risk of traumatic complications. Piglets were used to model the toddler airway.

METHODS: After IACUC approval, 27 piglets weighing 10-15 kg were induced with Telazol/Xylazine i.m. and maintained spontaneously ventilating via mask with isoflurane in oxygen and air at FiO2 of 24-28% during line placement. Monitors included four oximeter probes placed on the tongue, electrocardiogram and invasive blood pressure. Following preparation, animals were given a 15 minute recovery period. An arterial blood gas was drawn prior to administration of an anesthetizing dose of pentobarbital 10mg/kg and 0.1 mg/kg pancuronium intravenously. One of the three operators attempted PC using a randomly selected 14, 16 or 20 gauge catheter 30 seconds following cessation of breathing utilizing Pediatric Advanced Life Support protocol (7). Two attempts were permitted. After catheter insertion, ventilation was attempted using an infant self-inflating bag with 10 L/min oxygen flowing. Indicators for successful ventilation included chest wall movement, auscultation of air exchange and end tidal carbon dioxide. Arterial blood gases were drawn at 1 minute intervals for the first 5 minutes then at 5 minute intervals for 30 minutes after which the animals were sacrificed and neck dissections performed.

RESULTS: The first four experiments were complicated by

Table 1. Postoperative Emergence Delirium Scales (PEDS)

Score	1	2	3	4	Total Score
State	Sleepy; unarousable	Quiet/alert; arousable with stimulation	Alert/awake; responsive	Combative	
Vocalization/ Speech	None or clearly understood	Minimal; understand with effort	Whimpering; incoherent	Crying; shouting	
Orientation	Quiet	Easily consolable	Consolable with attention	Inconsolable; does not recognize parents	
Activity/ Movement	Minimal	Purposeful	Nonpurposeful movement of extremities; restless	Uncontrolled thrashing that requires restraints	
Facial Expression	Calm; eyes closed	Calm; visual tracking	Grimace; occasional eye contact	Contorted; does not maintain eye contact	

DISCUSSION: The revised PEDS is a valid tool for EAD assessment in children 6 months to 6 years in age with high sensitivity and specificity. We have improved our sensitivity and specificity as previously reported (0.62 and 0.89, respectively). Actual EAD incidence might be overestimated as sleeping time points were excluded. Further refinement to better differentiate pain and EAD may allow accurate recognition of EAD, improving postoperative care in children after anesthesia.

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unanticipated technical difficulties although the cricothyroid membrane was easily palpated. Each operator successfully cannulated the airway after an initial failed attempt with minimal or no trauma to surrounding structures except one attempt resulted in inadvertent division of the cricoid ring. Failed attempts and dislodged catheters resulted in diffuse subcutaneous air and/or minimal hemorrhage. Aberrant insertion sites were common but of minimal consequence. Effective oxygenation was achieved using catheters of all sizes; however, severe hypercarbia was associated with the use of the 20g angiocatheter. Short catheters were significantly more likely to dislodge or kink.

DISCUSSION: Percutaneous cricothyrotomy with Teflon-coated catheters warrants consideration as a bridging technique when infants and toddlers cannot be ventilated or intubated.

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S-173.

TITLE: VARIATIONS IN BODY TEMPERATURE AFTER BRAIN AND CARDIAC MAGNETIC RESONANCE IMAGING (MRI) IN CHILDREN SEDATED WITH PROPOFOL.

AUTHORS: C. Abdallah;

AFFILIATION: Children's National Medical Centre, Washington, DC.

INTRODUCTION: Temperature variations have important physiological, pharmacological and hemodynamic consequences in pediatric patients. We aimed to analyze body temperature changes in children, undergoing elective cardiac or brain MRI exam (1.5 Tesla (T) magnets GE Signa), and sedated with propofol.

METHODS: With IRB approval, the chart of 140 unpremedicated children aged 0 to 18 years, American Society of Anesthesiologists Physical Status I or II, were reviewed. Two groups were studied depending on the type of the elective MRI scan: Brain MRI or cardiac MRI exam. Anesthesia was induced with O₂/N₂O/Sevoflurane and maintained with a propofol infusion at a rate of 220 mcg/kg/min in both groups.

RESULTS: Pre and post MRI scan temperatures values were recorded. During an average cardiac MRI scan duration of 98.14 ± 32.29 min, mean axillary temperatures decreased from 36.12 ± 0.61° C to 35.5 ± 0.65° C (p < 0.001). The duration of brain MRI scan was 57.06 ± 29.64 min, and mean axillary temperatures decreased from 36.15 ± 0.54° C to 35.43 ± 0.46° C (p < 0.001). There was no significant correlation between the temperature gradient and the duration of the procedure or the weight of the patient in both groups.

DISCUSSION: Monitoring and controlling temperature in MRI is challenging secondary to magnetic field compatibility. As measured by axillary temperature (1), a significant decrease in body temperature is to be expected in pediatric patients, sedated with propofol, regardless of the type of the procedure.

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S-174.

TITLE: THE EFFECT OF ONDANSETRON ON THE EMERGENCE AGITATION AFTER SEVOFLURANE ANESTHESIA IN PEDIATRIC PATIENTS UNDERGOING TONSILLECTOMY.

AUTHORS: K. Lee, S. Cheong, S. Lim, Y. Kim, J. Lee, S. Lee;

AFFILIATION: InJe University Busan Paik Hospital, Busan, Republic of Korea.

INTRODUCTION: Emergence agitation is a common problem after sevoflurane anesthesia in children. 5-HT₃ antagonist, tropisetron significantly reduced the incidence of emergence agitation after sevoflurane anesthesia. We evaluated the effect of ondansetron on emergence agitation after sevoflurane anesthesia in children undergoing tonsillectomy.

METHODS: Eighty children, aged 3-9 years (ASA physical status I) undergoing tonsillectomy were randomly enrolled in this study. Group S received 0.1 ml/kg of saline and group O received 0.1 mg/kg of ondansetron during operation. Anesthesia was induced 5 vol% of sevoflurane and maintained with 2-2.5 vol% sevoflurane. Agitation score was recorded when they arrived at the postanesthesia care unit and 10 min after that.

RESULTS: The incidences of emergence agitation were 30% in group O and 27.5% in group S at arrival (P = 1.00). Ten minutes after arrival, the incidences were 12.5% in group O and 25% in group S (P = 0.25).

DISCUSSION: Ondansetron 0.1 mg/kg does not reduced the incidence of emergence agitation after sevoflurane in children.

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S-175.

TITLE: PERCEPTIONS OF PAIN MANAGEMENT IN A CHILDREN'S HOSPITAL

AUTHORS: C. C. Menser, T. Lockett, G. C. Marcou, J. K. Deshpande;
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INTRODUCTION: Pain in hospitalized children may often be inadequately assessed and treated, because patients cannot effectively communicate the degree of pain or healthcare providers are concerned about opiate side-effects or dependency. Recently national healthcare organizations such as JCAHO have increased efforts to improve pain management in hospitalized patients. Whether this focus has produced the desired results remains unclear.

The objective of this study was to evaluate the pain management practices in a children's hospital which has had a staff education program on pain management for several years. We hypothesized that healthcare providers would be satisfied with their practices while patients and families would report need for improvement.

METHODS: After receiving approval from the Institutional Review Board, questionnaires and a chart review were used to evaluate perceptions of hospitalized patients, their parents, and healthcare staff about pain management. Questions included frequency of pain assessment, adequacy of treatment, and reassessment after treatment. The study was conducted 7/3/2005-7/30/2005 at a children's hospital. Patients age 6 and up admitted to two floors, one surgical and one medical, were eligible for participation. We also recruited patients' parents/guardians, and attending physicians, residents, and nurses caring for these patients. A chart audit of participating patients was performed to collect data regarding frequency of pain assessment in the first 48 hours of care, method of pain treatment, and reassessment after treatment.

RESULTS: 105 of 114 eligible patients consented to participate. Study patients ranged from 6-20 years old. 99 of 105 parents/guardians participated. 59 staff (44 nurses, 15 physicians) participated. Overall, 97% of patients were happy with their pain management. 93.7% of parents were very satisfied or satisfied with treatment of their child's pain. On average, staff reported they believed the patients and

parents were very satisfied or satisfied with the treatment of pain 92.5% of the time. Parents reported that pain was assessed on average 9.48 times per 24 hour period, while nurses reported 6.14 assessments per 24 hours. The chart review indicated 4.64 pain assessments per 24 hours. Study participants identified barriers to pain management including family's perception of pain management, patient-staff communication difficulties, insufficient pain medication ordered, and interpretation of pain correctly for each patient.

DISCUSSION: Our results suggest that pain management in the study hospital is satisfactory to patients and parents. The parental impression of pain assessment frequency is consistent with that reported by the staff. Combining these results with the chart review suggests that pain is assessed more often than it is recorded. The results also showed that more patients and parents were satisfied with the pain management process than staff thought. While the data support high satisfaction, important barriers to pain management were identified and present opportunities for improvement.

S-176.

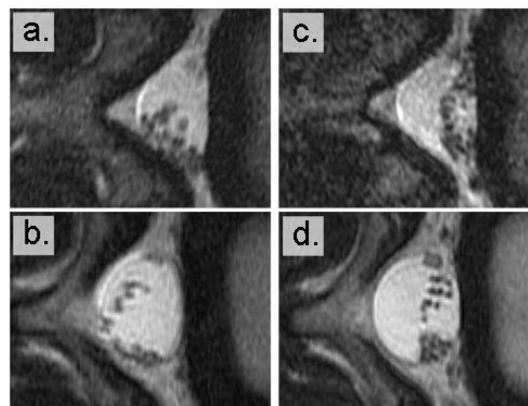
TITLE: MOVEMENT OF THE CAUDA EQUINA IN THE SUBARACHNOID SPACE DURING THE LATERAL DECUBITUS POSITION WITH OR FULLY FLEXED LEGS IN CHILDREN

AUTHORS: S. Yamaguchi, T. Takiguchi, N. Tezuka, T. Kitajima;
AFFILIATION: Dokkyo University School of Medicine, Mibu, Japan.

INTRODUCTION: It is very important for spinal puncture, to know detailed information how changing positions influence the movement of the cauda equina in the spinal canal. In our previous studies using adult volunteers (1,2), we demonstrated that the nerve roots of the cauda equina moved to the gravity-dependent side by changing positions, and shifted to the ventral side by fully flexed legs (the knees drawn up to the stomach, the fully flexed legs, and the neck flexed to curve the back outward). In this study, we studied how the nerve roots of the cauda equina moved in the subarachnoid space during the lateral decubitus position with or without fully flexed legs in children.

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. Magnetic resonance images of the nerve roots of the cauda equina were obtained in the supine position, and lateral decubitus position without and with fully flexed legs.

RESULTS: In both children and adults, the nerve roots of the cauda equina laid symmetrically and aligned in the subarachnoid space during the supine position. The nerve roots of the cauda equina shifted to the gravity dependent side during the lateral decubitus position without fully flexed legs in adults (fig. a). However, it was not obvious in children (fig. b). The nerve roots of the cauda equina moved to the ventral side of the subarachnoid space in the lateral decubitus position with fully flexed legs in both adults (fig. c) and children (fig. d). Furthermore, the free space of the dorsal side in the subarachnoid space was created by the lateral decubitus position with fully flexed legs in both of them.



DISCUSSION: Although the shift of the nerve roots of the cauda equina to the gravity-dependent side by changing positions was not obvious in children, those in children dynamically moved to ventral side in the subarachnoid space by the position with fully flexed legs, similar to those in adults. Our results suggested that the accurate lateral decubitus position with fully flexed legs should be required during the spinal puncture, to prevent nerve injuries.

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S-177.

TITLE: ANESTHETIC MANAGEMENT OF PATIENTS WITH NIEMANN-PICK TYPE C DISEASE (NPC)

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Niemann-Pick type C disease (NPC) is an inherited autosomal recessive disorder associated with mutations of the NPC1 or HE1/NPC2 gene and is characterized by intracellular accumulation of gangliosides and cholesterol. The clinical manifestations of NPC have variable age of onset and include a spectrum of neurologic deficits including seizure, vertical gaze palsy, dystonia, dysphagia, and progressive dementia as well as hepatosplenomegaly. The disease is lethal and at present, effective therapy is sorely lacking. In a study of the natural history of NPC seeking to identify biomarkers of disease that could serve as endpoints for a later clinical trial, children and adults with NPC required anesthesia for imaging studies in a 3 Tesla magnet, auditory brainstem response, and LPs. However, little is known about the anesthetic implications of NPC. The aim of this study was to describe the anesthetic management, course and implications in children and adults with NPC.

METHODS: All patients were enrolled in IRB approved research protocol. The authors performed and analyzed the perianesthetic records of patients with NPC who required anesthesia for diagnostic interventions from August 2006 to August 2007.

RESULTS: Fifteen patients with NPC who underwent 24 anesthetics for MRI/MRS in a 3 Tesla magnet, lumbar puncture and ABR. Among 15 patients, 14 were children. Fourteen patients were diagnosed with NPC at ages ranging between 3 months to 8 years and one at the age of 21. The age at the time of first anesthetic ranged from 3-32 years. All patients have mild to moderate hepatosplenomegaly and half of the patients have dysphagia. The majority of patients had some degree of motor impairment, vertical gaze palsy and cognitive impairment. After induction, anesthesia was maintained with propofol in all patients. After completion of MRI in the 3 Tesla magnets, 5 patients presented profuse sweating without significant elevation of temperature. In one patient, a

short-lasting seizure was observed during induction of anesthesia with sevoflurane. In the adult patient and the one with severe neurologic impairment, mild hypothermia and bradycardia was observed perioperatively.

CONCLUSION: NPC is a rare genetic disorder presenting with a spectrum of severe neurological deficits. We describe a series of anesthetics in children and one adult with NPC and observed events that warranted intervention including mild hypothermia and bradycardia and one episode of seizure in a patient with known history. However, despite the possible severe manifestations of NPC, no serious adverse events were observed and for the most part the anesthetics were uncomplicated.

S-178.

TITLE: EPIDEMIOLOGIC ASPECTS OF OFFSITE AND ONSITE ANESTHESIA IN CHILDREN

AUTHORS: A. Kakavouli¹, J. Sobol¹, C. Lin¹, G. Li², S. Ohkawa¹, L. Sun³;

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INTRODUCTIONS. Anesthesia for procedures performed at "outside-of-the-OR" ("Offsite") locations comprise a significant part of all pediatric anesthetic practice and safety can be challenging due to differences in equipment; staffing; and protocols. At our institution, we standardize the way we provide anesthesia care for children irrespective of location. We previously reported that our pediatric complications were comparable between Offsite and "in-the-OR" ("Onsite") locations. In this study, we assess the incidence and epidemiologic patterns of complications for both locations, using Patient-Specific-Quality-Assurance Forms (QAs).

METHODS. Following IRB approval, we collected QAs for all patients, under 21 years of age, receiving anesthesia in our institution, from May 1st 2006 to June 30th 2007. The resident/ fellow assigned to the case completed the QA at the end of each case. Data collected are: date and location of the anesthesia; patient age and ASA status; and complication type, when present. The complication types were characterized as respiratory, cardiovascular or neither. We excluded QAs with missing data. We analyzed the data using unpaired t-tests and chi-square tests; p<0.05 was considered significant.

RESULTS. We included 1375 Offsite QAs and 5330 Onsite QAs. Offsite patients were younger (average age±SD: Offsite=77±60.6 versus Onsite=82.9±69.5 months) and sicker (≥ASAIII: Offsite=58% versus Onsite=29.7%) compared to Onsite. But, there were relatively more patients whose ages were <6, 6-12 and 12-24 months Onsite compared to Offsite (Onsite: <6m=9.3%, 6-12m= 6.6%, 12-24m=10.1% vs Offsite: <6m=6.8%, 6-12m=4.6%, 12-24m=8.5%). There were fewer complications Offsite (2.6%), compared to Onsite (3.9%). Respiratory complications were fewer Offsite (1.09%) compared to Onsite (2.31%). They represented 41.7% of all offsite complications, and 59.6% of all Onsite ones. Incidences for

cardiovascular and non-respiratory/non-cardiovascular complications were comparable for both locations. For all three complication types, average age and ASA status were similar between the two locations.

		Offsite	Onsite	Offsite & Onsite
All QAs	QAs with ASA status≥ III	58%*	29.7%	35.5%
	Average Age ±SD (months of age)	77 ±60.6*	82.9 ±69.5	81.7 ±67.8
Respiratory complications	Incidence	1.09%*	2.31%	2.06%
	% of total complications	41.7%	59.6%	57.02%
	% of patients with ASA status≥ III	60%	38.2%	40.6%
	Average Age ±SD (months of age)	33 ±41.4	46.1 ±52.9	44.7 ±51.8
Cardiovascular complications	Incidence	0.65%	0.54%	0.57%
	% of total complications	25%	14.1%	15.7%
	% of patients with ASA status≥ III	100%	82.8%	86.8%
	Average Age ±SD (months of age)	74.2±65.8	70.78±81.7	71.6±77.4
Non-respiratory/ non cardiovascular complications	Incidence	0.87%	1.01%	0.98%
	% of total complications	33.33%	26.21%	27.27%
	% of patients with ASA status≥ III	41.7%	33.3%	34.8%
	Average Age ±SD (months of age)	100.3±69.3	88.88±71.2	90.9±70.5

* P<0.05

DISCUSSION. Despite being younger and of higher ASA status, Offsite pediatric patients were less likely to experience complications, particularly respiratory ones. This might be related to having more patients of the younger age groups Onsite. We didn't specifically analyze for gender, airway management protocols and procedure duration. Future studies will evaluate these variables to determine their contribution to the epidemiology of complications.

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S-179.

TITLE: THE INCIDENCE OF DIFFICULT AIRWAY IN CHILDREN: IS IT REALLY RARE OR DOES IT NEED TO BE WELL DONE?

AUTHORS: N. Yareni¹, N. Gomez¹, L. K. Hoke², Y. F. Bryan²;
AFFILIATION: ¹Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico, ²Cincinnati Children's Hospital, Cincinnati, OH.

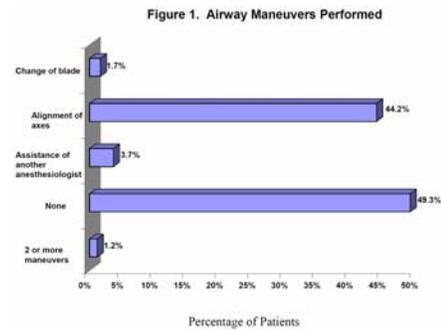
INTRODUCTION: The difficult airway (DA) in children may be defined using several criteria; experiencing difficulty with laryngoscopy, not visualizing the glottic opening or having difficulty placing the endotracheal tube. In addition, multiple intubation attempts leading to problems with oxygenation and ventilation may also occur during airway management. The incidence of the DA in children with craniofacial syndromes is suspected to be high, but the incidence of DA in normal children is unknown (1,2). We sought to determine the incidence of DA in normal children.

METHODS: After research study board approval, consent was obtained from parents of 600 patients ages 3-16 years old scheduled under anesthesia. Children with craniofacial syndromes, known difficult airways or intubations were excluded. Direct laryngoscopy and intubations were performed by pediatric anesthesiologists. Airway data collected included a pre-anesthetic airway exam, the Cormack Lehane (CL) grade view obtained, the number of intubation attempts, additional airway maneuvers performed, number of different personnel attempting intubation and any complications.

RESULTS: The mean and standard deviation for age and weight were 8.9 ± 4.1 years, 30. ±15 kg, respectively. Seventeen patients (3.5%) had a grade 3 or 4 CL glottic view (see Table 1). Seventy-seven patients (12.2%) required more than 2 intubation attempts while 33 patients (5.2%) required attempts by more than one person (see Figure 1).

Table 1. Frequency Distribution of grade view of glottis (Cormack and Lehane)

Grade view	Number (n)	Percentage %
1	467	78
2	111	18.5
3	16	2.7
4	5	0.8
Total	599	100



DISCUSSION: Our study found the incidence of DA in normal children may be similar to adults (3). A broader definition used to define the DA may have been the reason for the higher incidence. Our results suggest that a broader and more fine-tuned definition of DA in normal children may suggest a higher incidence of DA in children with craniofacial abnormalities.

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- 2) Paediatr Anaesth. 2001;11: 409-13;
- 3) Hagberg C. Benumof's Airway Management 2 ed. 2007: 215-220.

S-180.

TITLE: ENVIRONMENTAL TOBACCO SMOKE AS A RISK FACTOR FOR PEDIATRIC AIRWAY COMPLICATIONS IN THE PERIOPERATIVE SETTING

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INTRODUCTION: Environmental tobacco smoke (ETS) has been linked to several disease states in the pediatric population. Pediatric morbidity and mortality may not be limited to the medical population. Anesthetic/Surgical complications appear also to be increased secondary to passive smoking (1,2). However, a clear link has yet to be established as only a small number of studies have been performed to date. In order to assess a possible link between these two variables, we performed a retrospective chart review and gave a brief environmental exposure questionnaire modified from the American Thoracic Society including parental smoking history to the parent (s) of children who had prior surgery at our institution.

METHODS: Chart reviews of pediatric patients aged between one and eighteen years who underwent surgery under general anesthesia were performed. Additionally, parents of the patients were asked to fill out a brief environmental exposure questionnaire. Airway complications in both the operating room and PACU were recorded. These included: laryngospasm, bronchospasm, hypersecretion, oxygen desaturation (SaO₂ < 95%), and severe coughing. Statistical analyses of the data were performed using JMP Statistical Software to assess the relationship between ETS and perioperative airway complications.

RESULTS: To date data from 100 patients have been analyzed. Thus far no relationship between ETS and perioperative airway complications has been established.

DISCUSSION: A limited number of prior studies examining the association between ETS and pediatric airway complications have been performed up to this time. These studies have reached conclusions both supporting (1) and denying (3) a relationship between ETS and pediatric airway complications. Initial data from our institution indicate that there is no association between ETS and airway complications. These data are unique in that they assess not only intraoperative airway

complications but also assess any complications that may occur in the Post Anesthesia Care Unit (PACU).

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S-181.

TITLE: PERFORMING THE MALLAMPATI AIRWAY EXAM IN CHILDREN: DOES COOPERATION MEAN CORRELATION IN PREDICTING THE DIFFICULT AIRWAY?

AUTHORS: N. Yareni¹, L. K. Hoke², Y. F. Bryan², N. Gomez¹;

AFFILIATION: ¹Hospital Infantil de Mexico Federico Gomez, Mexico City, Mexico, ²Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

INTRODUCTION: The Mallampati airway exam helps identify adult patients with difficult airways. In infants and young children, the Mallampati airway exam may be difficult to perform due to a lack of cooperation (1). In addition, the Mallampati airway exam is thought to not be a good predictor of the difficult airway in children. We sought to determine the correlation between the Mallampati airway exam and the Cormack Lehane grade view in children.

METHODS: After obtaining approval from the research board of the Hospital Infantil Mexico Federico Gomez, consent was obtained from parents of 600 children ages 3-16 years old scheduled for surgery requiring general anesthesia and endotracheal intubation. Children with previous history of difficult laryngoscopy, intubation or those with craniofacial syndromes were excluded. Direct laryngoscopy and intubations were performed by trained pediatric anesthesiologists. Airway data collected included a pre-anesthetic Mallampati airway exam and the Cormack Lehane (CL) grade view of the glottis.

RESULTS: Thirteen patients (2.2%) with a Mallampati I or II classification had a grade III or IV view. Of the 51 patients (8.7%) with a Mallampati III or IV airway classification, 8 of the patients (16%) had a grade III or IV view and 43 (84%) had a grade I or II view (see Table 1). The sensitivity and positive predictive value were 38% and 16%, respectively. The airway exam could not be performed in 12 (2%) patients.

Table 1. Correlation between Mallampati Class and Cormack Lehane grade view

		Grade view (Cormack Lehane)				
		I	II	III	IV	Total
Mallampati Class	I	286	39	3	0	328
	II	147	52	8	2	209
	III	25	18	5	2	50
	IV	0	0	0	1	1
	Total	458	109	16	5	588

DISCUSSION: Our study found a lower sensitivity and positive predictive value (PPV) using the Mallampati airway classification in children than reported in adults (2,3). This difference between children and adults may have been due to several factors, such as the anatomical differences between children and adults. Further research is required regarding airway exams in infants and children.

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S-182.

TITLE: THE USE OF THE PROSEAL® LMA IN PRESCHOOL CHILDREN WITH CYSTIC FIBROSIS UNDERGOING HIGH RESOLUTION CHEST CT SCANS

AUTHORS: S. Sullivan, L. K. Hoke, S. Powers, A. Brody, Y. Bryan;

AFFILIATION: Cincinnati Children's Hospital, Cincinnati, OH.

INTRODUCTION: High-resolution computed tomography (HRCT) is more sensitive than pulmonary function tests (PFT's) in evaluating structural lung changes in cystic fibrosis (CF) (1). Young children with CF who can not lie still and perform the respiratory maneuvers required during HRCT (such as inspiratory hold and expiratory release) need sedation and control of ventilation to provide the necessary inspiratory and expiratory images without patient motion (2). The use of the Proseal® LMA under general anesthesia (GA) allows for higher inspiratory pressures during assisted ventilation (3). We are reporting our experience using the Proseal® in preschool children with CF who were undergoing HRCT chest scans as part of a clinical trial sub-study.

METHODS: After IRB approval, a retrospective study was performed in 9 children with CF that had HRCT chest with GA. Children were induced with sevoflurane and an age-appropriate Proseal® LMA was placed. Prior to obtaining the inspiratory scout film and inspiratory pause for imaging, the patients were assisted by ventilating with frequent breaths at pressures between 20-25 cm H₂O pressure. For expiration, the Proseal® was disconnected from the circuit and elastic recoil of the lungs provided expiratory images. The Proseal® was removed deep after scan completion. Patients were treated with oxygen blowby or facemask in PACU. Anesthesia personnel did not remain in the CT scan room during the scan and thus were not exposed to radiation.

RESULTS: Please see Table 1. There were no complications, cancellations or admissions. One patient experienced a decrease in SPO₂ to 93% and another required a brief period of positive pressure via facemask in PACU.

Table 1

Patient #	Age (months)	Weight (kg)	ASA	Proseal® LMA	Induction	Maintenance	Anesthesia time*	PACU time†	Total time‡
1	47	18.4	3	2	Sevo/N ₂ O	Sevo	35	46	81
2	38	13	2	2	Sevo/N ₂ O	Sevo	27	29	56
3	29	11	2	2	Sevo	Sevo	42	28	70
4	41	14	2	2	Sevo/N ₂ O	Sevo	21	39	60
5	45	18	2	2	Sevo/N ₂ O	Propofol††	32	28	60
6	52	18	2	2	Sevo/N ₂ O	Sevo	20	45	65
7	24	11	2	1.5	Sevo/N ₂ O	Sevo	24	65	89
8	52	14	3	2	Sevo	Sevo	19	25	44
9	28	13.4	2	2	Sevo/N ₂ O	Sevo	33	46	79
Mean	39.4	14.6					28.1	38.1	66
SD	7.1	2.2					8	6.6	7

* Propofol maintenance was 200 mcg/kg/min

† Anesthesia time (min) = anesthesia start time to PACU arrival

‡ PACU time (min) = PACU arrival to PACU discharge

§ Total time (min) = Anesthesia start time to PACU discharge

DISCUSSION: By allowing for assisted ventilation at higher pressures, the Proseal® provided high-quality inspiratory and expiratory images in CF patients undergoing HRCT. The Proseal® provided a better seal in the posterior pharynx with the ability to suction out the stomach via the drain tube and served as a safe and alternative technique to endotracheal intubation.

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Pharmacology - Basic Science

S-183.

TITLE: REGULATION OF $\alpha 2C$ ADRENERGIC RECEPTOR CELL SURFACE EXPRESSION BY ITS AMINO TERMINAL DOMAIN

AUTHORS: C. Hurt, B. Kobilka, T. Angelotti;

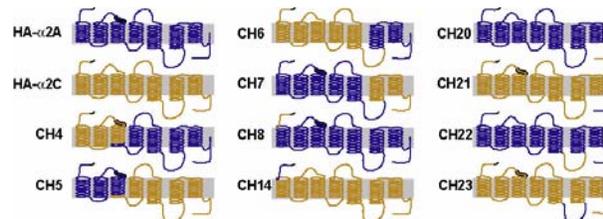
AFFILIATION: Stanford University, Stanford, CA.

INTRODUCTION: $\alpha 2A$ & $\alpha 2C$ adrenergic receptors (AR) have overlapping but unique physiological roles in neuronal signaling, possibly due to differences in cellular localization (1,2). Heterologous expression has revealed that $\alpha 2A$ & $\alpha 2C$ ARs traffic differently, depending on cell type. In non-neuronal cell lines, $\alpha 2A$ ARs target readily to the plasma membrane, however, $\alpha 2C$ ARs are predominantly found in an intracellular compartment. However, expression of $\alpha 2C$ ARs in neuronal cell lines results in plasma membrane expression. We sought to determine the specific amino acid motifs responsible for this differential trafficking.

METHODS: Epitope-tagged (HA) cDNA vectors encoding $\alpha 2A$ & $\alpha 2C$ ARs, along with ten chimeric swaps (e.g. amino terminal, 3rd intracellular loop) were constructed. Adenovirus vectors encoding the twelve wild-type and chimeras were also produced. Membrane binding to the $\alpha 2$ AR antagonist [³H]RX-821002 was performed for all twelve constructs following expression in HEK cells. Effects of the chimeric swaps on cellular localization were determined by immunofluorescent microscopy following expression in Rat 1 cells. In addition, quantification of cell surface expression was done by ELISA assay.

RESULTS: All twelve constructs (wild-type and chimeric) bound antagonist with similar affinity, suggesting that they still retained biochemical activity and membrane expression. Systematic immunofluorescence analysis of cell surface expression of the twelve constructs revealed that swapping the amino terminal extracellular domains of $\alpha 2A$ & $\alpha 2C$ ARs altered trafficking. Specifically, replacement of the amino terminal domain of $\alpha 2A$ AR with that of $\alpha 2C$ caused it to be retained in an intracellular compartment, whereas the reciprocal construct was readily targeted to the membrane. Further analysis of the $\alpha 2C$ amino terminus revealed that a nine amino acid alpha helix was necessary for this retention. Using a FACS-based assay, it was

demonstrated that removal or mutational disruption of this helix led to high level surface expression of $\alpha 2C$ ARs in non-neuronal cell lines.



DISCUSSION: The amino termini of $\alpha 2A$ & $\alpha 2C$ ARs are the most divergent part of these receptors and also appear to be important regulators of surface vs. intracellular trafficking. We have identified a previously known motif in that regulates differential expression of $\alpha 2C$ ARs in neuronal vs. non-neuronal cells.

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

S-184.

TITLE: CONVENTIONAL O_2 LEVELS USED FOR RAT HIPPOCAMPAL SLICES MAY BE NEUROTOXIC

AUTHORS: C. Quiroga del Rio, M. Matott, D. P. D'Agostino, E. M. Camporesi, J. B. Dean;

AFFILIATION: University of South Florida, Tampa, FL.

INTRODUCTION: Hippocampal slice cultures are an excellent model to study cellular and molecular neuronal mechanisms, and to evaluate pharmacological tools for neuroprotection. Nearly all experiments using in vitro hippocampal slice cultures create an environment equilibrated with 95% O_2 - 5% CO_2 . We have previously shown that, under these hyperoxic conditions, the rate of superoxide anion ($\cdot O_2^-$) production is time-dependently increased compared to lower levels of oxygen¹. These findings suggest that brain slices incubated in 95% O_2 undergo oxidative stress^{2,3}. In this study, we compare the conventional incubation environment to one with the addition of MnTMPyP, an antioxidant used to quench $\cdot O_2^-$ production, and characterize cellular viability in hippocampal slices in a time dependent manner.

METHODS: Rat sagittal, cortico-hippocampal slices, 400 μm thickness, were maintained in artificial cerebral spinal fluid (ACSF) with 25 μM MnTMPyP equilibrated with 95% O_2 + 5% CO_2 at 37° C. Control hippocampal slices were subjected to the same conditions except without the anti-oxidant. The relative level of hippocampal cell viability from 1 hr (t=0) to 4 hours post slicing were measured using Ethidium Homodimer -1 (EH-1), a fluorogenic probe that binds to DNA of dead cells⁴. At each time point a slice was incubated for 20 min with 2 μM EH-1 and then maintained on the microscope stage in a slice chamber using one sided superfusion.

RESULTS: Under conventional conditions, we found that the CA1 region of the hippocampus is most susceptible to hyperoxia and resulted in a time-dependent decrease in neuron viability, while the CA3 region was less affected. The addition of anti-oxidant prevented the neuronal death caused by the hyperoxic state. We found a significant decrease in cell death in the CA1 and CA3 regions (p<0.0001) when the antioxidant MnTMPyP was added.

DISCUSSION: Under normobaric hyperoxia (95% O_2), cell death in

hippocampal slices increases in a time dependent manner. The addition of antioxidants reduces cell death presumably by decreasing the production of $\cdot O_2^-$ and its byproducts. These findings suggest that lower levels of control oxygen or supplemental antioxidants should be considered for use with brain slices.

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S-185.

TITLE: ESTIMATION OF ED50 OF NEUROMUSCULAR BLOCKING DRUGS: COMPARISON OF LOG DOSE REGRESSION ANALYSIS WITH THE ESTIMATES OF POTENCY FROM A SINGLE OBSERVATION IN A SUBJECT

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INTRODUCTION: Traditionally, the estimates of potency of neuromuscular blocking agents (MRs), ieED50, are obtained by performing regression analysis of the log dose-neuromuscular block (NMB) relationship with data gathered from many subjects. An alternative method has been suggested for estimating the ED50 in individual subjects using a single dose of a MR, and assuming a parallel log dose-response relationship (1). We have conducted the current study to determine whether the estimates of ED50 obtained using a single dose of a MR in a single subject agrees with the ED50 estimate obtained by regression analysis.

METHOD: After approval by the local IRB, 30 adult non-obese subjects scheduled for elective surgery consented to participate. Following iv administration of 1-2 mg midazolam and fentanyl 3-5 µg·kg⁻¹, anesthesia was induced with propofol 2-3 mg·kg⁻¹ and maintained with propofol infusion (100-150 µg·kg⁻¹·min⁻¹) and 66% N₂O in oxygen. Orotracheal intubation was performed after tracheal application of lidocaine (4%, 3 ml). Ventilation was controlled to maintain normocapnia. The thumb of one hand was abducted (preload 250-300 g) and connected to a force transducer. Trains of four supramaximal stimuli at 2 Hz were applied to the ulnar nerve at the wrist and repeated every 12 s. Elicited contractions were recorded for subsequent analysis. Following a stabilization period, vecuronium was injected (10 to 60 µg·kg⁻¹), the doses were chosen to produce from minimal to almost complete NMB. ED50 was estimated by regression analysis of the log dose-NMB data from all subjects. Alternatively, NMB observed in each subject was used to estimate ED50 by using the Hill equation and assuming γ in the to be 4.0, 4.75, or 5.8 (1).

RESULTS: ED50 for vecuronium estimated by regression analysis was

16.9 µg·kg⁻¹ (95%CI 15.6 to 18.3 µg·kg⁻¹). Using the same data, but estimating the ED50 from NMB observed in individual subjects, we found that the mean ED50 was not significantly different from the ED50 obtained by regression analysis (Figure 1). Within the range studied, the value of γ appeared not to significantly alter the estimate of ED50.

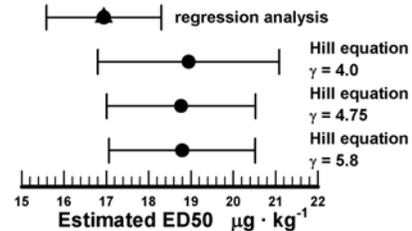


Figure 1. Estimates of ED50 (95% confidence intervals) of vecuronium obtained from regression of the NMB-versus-dose relationship or using the same data but estimating ED50 from NMB observed in each subject using the Hill equation.

DISCUSSION: The estimates of ED50 using the single observed NMB are similar to the ED50 estimate obtained by regression analysis.

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S-186.

TITLE: HALOTHANE AND SEVOFLURANE EXERT DIFFERENT DEGREES OF INHIBITION ON CAROTID BODY GLOMUS CELL HYPOXIC RESPONSE

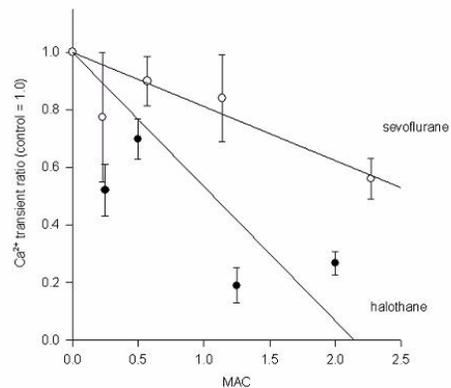
AUTHORS: J. J. Pandit¹, K. Buckler²;
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INTRODUCTION: We investigated the effects of halothane and sevoflurane on the rise in intracellular calcium ([Ca²⁺]_i) with hypoxia in carotid body glomus cells to assess if their effects paralleled their known effects on the human hypoxic ventilatory response, where halothane depresses this response more than does sevoflurane (1,2).

METHODS: Glomus cells were enzymatically isolated from 9-12 day old rat pups and plated onto coverslips coated with poly-D-lysine. Intracellular Ca²⁺ transient responses (measured using fluorescence of indo-1 dye) to hypoxia (P_{O₂} ~2 mmHg) were measured with and without halothane or sevoflurane (dose range 0.23 - 2.27 MAC), all gases and agents equilibrated to standard Tyrode solution perfusing the coverslips. Intracellular Ca²⁺ transient responses to hyperkalaemia (Tyrode with external K⁺ 100mM) were also measured, with and without halothane or sevoflurane.

RESULTS: Halothane depressed the magnitude of Ca²⁺ transient with hypoxia more so than did sevoflurane (p = 0.036) and did so at all doses tested (sevoflurane depressed the Ca²⁺ transient only at 2.27 MAC; Fig. 1). Both agents also depressed the Ca²⁺ transient response to hyperkalaemia - halothane more so than sevoflurane (p = 0.004).

Figure 1. Ca²⁺ transient effect of anesthetics (ratio of anesthetic:control magnitude) for halothane (#) and sevoflurane (○). Total of 80 experimental periods. Error bars represent ± SEM. Lines of best fit are drawn for each agent.



DISCUSSION: These effects in single cells parallels their known effects on human hypoxic ventilatory response, indicating that the cellular effect underlies the whole-body effect (1-3). Hyperkalaemia depolarises the cell membrane and inactivates the TASK-like potassium channel (putatively the mediator of the hypoxic and anesthetic response): the depression by both agents indicates that other mechanisms (possibly a voltage-activated calcium channel) may also be involved in the anesthetic effect (3). To understand how volatile anesthetics depress hypoxic responses, further studies should focus on the molecular effects of agents at cellular level, especially potential effects on TASK-like K⁺ or voltage-gated Ca²⁺ channels.

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S-187.

TITLE: EFFECT OF COCAINE ON SOS1 AND SOS2 EXPRESSION IN THE RAT STRIATUM IN VIVO

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INTRODUCTION: Guanine nucleotide exchange factors (GEFs) function to activate a large family of small GTPases in mammalian cells by converting inactive GDP-bound GTPases to an active GTP-bound form. Prominent among the GEF family is mammalian Son-of-sevenless (Sos) that specifically activates a subclass of GTPases (i.e., Ras) to link receptor signals to Ras-triggered mitogen-activated protein kinases (Ras-MAPKs). Stimulation of dopamine receptors by psychostimulant cocaine is known to activate the Ras-MAPK pathway in striatal neurons¹, although the direct effect of cocaine on the Ras-MAPK activator Sos is unknown. In this study, we hypothesized that cocaine exposure alters Sos expression in brain neurons and this hypothesis was tested in the rat striatum in vivo.

METHODS: Wistar male adult rats were randomly divided into four groups (n =4 per group) and were treated with a single intraperitoneal injection of saline or cocaine at different doses (5, 10, or 20 mg/kg). The rats were anesthetized and sacrificed 1 h after injection. Brains were quickly removed and the forebrain structures, including the ventral striatum/nucleus accumbens, dorsal striatum/caudate putamen, hippocampus, and amygdala, were dissected for protein extraction, followed by Western blot analysis. The densities of immunoblots were measured and the data were analyzed using ANOVA.

RESULTS: Cocaine at all doses reduced Sos1 in the nucleus accumbens and caudate putamen. Cocaine at the two higher doses (10 and 20 mg/kg) also reduced Sos2 protein levels in the two structures. In contrast, cocaine at all doses did not alter protein levels of actin in the same samples. No significant change in Sos1 or Sos2 levels in the hippocampus and amygdala was detected following cocaine injection.

DISCUSSION: As a rate-limiting step, Sos-mediated activation of Ras is critical for linking extracellular signals to the Ras-MAPK cascade. While this cascade was rapidly activated 5-10 min after cocaine

injection², the Ras-MAPK activator Sos (both Sos1 and Sos2 isoforms) was reduced in abundance 1 h after drug injection, which possibly serves as a negative feedback mechanism to prevent Ras overactivation. The Ras-MAPK system is a key modulator of a wide array of inducible cellular and synaptic activities, including synaptic plasticity related to addictive properties of cocaine. The dynamic change in Sos expression is therefore an important step in integrated these responses to cocaine and critical for the production of cocaine action.

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S-188.

TITLE: EFFECTS OF PHOSPHODIESTERASE (PDE) INHIBITORS ON RAT BRONCHIAL SMOOTH MUSCLE CONTRACTION

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INTRODUCTION: The Cyclic nucleotide phosphodiesterase (PDE) hydrolyzes adenosine 3,5-cyclic monophosphate (cAMP). The inhibition of PDE may cause the relaxation of airway smooth muscle (ASM) by increasing intracellular cAMP concentrations, suggesting PDE inhibitors may act as bronchodilator. Since both PDE3 and 4 are high-affinity cAMP-selective isozymes and exist in ASM, PDE3 and 4 inhibitors may be considered as useful for therapy and anesthetic managements of asthmatic patients. In this study, we examined the effects of both PDE3 (olprinone, milrinone) and 4 (rolipram, ICI63197) inhibitors on rat ASM contracted by acetylcholine (ACh).

METHODS: Ring strips (width 200 µm, diameter 500 µm) from intrapulmonary bronchus of male Wistar rat were placed in 400 µL organ baths containing Krebs-Henseleit solution (95%O₂-5%CO₂, 37°C, resting tension 50mg). After obtaining stable contraction with 30 µM ACh (confirmed as EC₅₀ preliminarily), isometric forces were measured with the following protocols.

#1: rolipram or ICI63197 (0.01-100 µM) was cumulatively applied.
#2: milrinone or olprinone (0.1 µM-1mM) was cumulatively applied.
#3: Effects of pretreatment with milrinone on the force by ACh were investigated. ACh (0.1 µM-1mM) was cumulatively applied for 2 strips. For one strip, milrinone (0.1 µM or 10 µM) was added, prior to the application of ACh and through the experiment.

RESULTS: #1: Rolipram and ICI63197 produced concentration-dependent relaxation of rat ASM. However, both agents even at highest concentrations (100 µM) failed to achieve the complete relaxation.

#2: Milrinone and olprinone, even at highest concentrations (1mM), had no significant effect on the force by ACh.

#3: Pretreatment with milrinone had no significant effect on concentration-response curves for ACh.

DISCUSSION: Although PDE4 inhibitors showed the concentration-dependent relaxation, relaxation by these agents was slight even with high concentrations. Some investigators demonstrated that rolipram significantly relaxed ASM contracted by muscarinic agonists. However, like the result of this study, Moriuchi et al. showed that rolipram, even at high concentrations, showed only slight relaxation on the methacholine-contracted contraction in bovine ASM, while rolipram completely relaxed the same preparations contracted by histamine. The reason for this differential sensitivity to agonists is unknown, however, there is a possibility that this difference exists also in our preparation.

PDE3 inhibitors did not relax rat ASM, and pretreatment with milrinone failed to show the inhibition of the force by ACh, suggesting, at least in our experimental environment, PDE3 inhibitors are not supposed as bronchodilator.

Further investigation will be needed to elucidate entirely the effects of PDE inhibitors on ASM.

CONCLUSION: PDE4 inhibitors rolipram and ICI63197 slightly relax rat ASM contracted by ACh.

PDE3 inhibitors olprinone and milrinone had no effects on rat ASM contraction.

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- 3) Anesth Analg. 2001; 93:230-3

S-189.

TITLE: DIFFERENTIAL EFFECTS OF OPIATES IN THE FELINE PULMONARY VASCULAR BED

AUTHORS: A. D. Kaye¹, A. Fields², A. Bajwa¹, J. Hoover³;

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The aim of this study was to ascertain relative potencies of different clinically relevant opioids compared with traditional vasodepressor agents in the feline pulmonary vascular bed. A second aim was to study the effects of morphine and other opiate agents, and to identify the receptors involved in the mediation or modulation of these effects. This was a prospective vehicle controlled study involving an intact chest preparation of adult mongrel cats. The effects of various opioids, morphine, fentanyl, remifentanyl, sufentanyl, and meperidine, were compared with other vasodepressor agents. Additionally, the effects of L-N⁵-(1-Iminoethyl) ornithine hydrochloride (L-NIO) (nitric oxide synthase inhibitor), nimesulide (selective cyclooxygenase (COX)-2 inhibitor), glibenclamide (ATP-sensitive K⁺ channel blocker), naloxone (non-selective opiate receptor antagonist), and diphenhydramine (histamine H₁-receptor antagonist), were investigated on pulmonary arterial responses to morphine and other selected agonists in the feline pulmonary vascular bed. The systemic pressure and lobar arterial perfusion pressure were continuously monitored, electronically averaged, and recorded. In the cat pulmonary vascular bed of the isolated left lower lobe, morphine, remifentanyl, fentanyl, sufentanyl, and meperidine induced a dose-dependent moderate vasodepressor response and it appeared that sufentanyl was the most potent on a nanomolar basis. The effects of all opiates studied were not significantly altered after administration of L-NIO, nimesulide, and glibenclamide. However, the vascular responses to all opiates were significantly attenuated following administration of naloxone and diphenhydramine. The results of the present study suggest that sufentanyl appears to have slightly more potency and morphine the least of the five opioid agonists studied on a nanomolar basis. Additionally, all opiates studied had moderate vasodilatory action in the feline

pulmonary vascular bed and this response appeared to be mediated or modulated by both opiate receptor and histamine receptor sensitive pathways.

S-190.

TITLE: NEUROMUSCULAR BLOCK (NMB)-VERSUS-DOSE RELATIONSHIP: A POSSIBLE INTERPRETATION OF THE EXPONENT IN THE HILL EQUATION

AUTHORS: V. Nigrovic, S. B. Bhatt, A. Amann;

AFFILIATION: College of Medicine, University of Toledo, Toledo, OH.

INTRODUCTION: Kopman and coworkers (1) compared the exponent γ in the Hill equation obtained in 62 experimental NMB-versus-dose studies with 11 muscle relaxants (MRs). The range, 4.0 to 5.8, is remarkably narrow. The goal of the current study was to explore in simulations the factors that might influence the value of γ and to define the possible reasons for the narrow range.

METHODS: Twitch was simulated in a model of neuromuscular transmission (2) and calculated from the peak concentration of the activated receptors, [ARA], and two parameters: γ_A and [ARA50] (2): $T_w = [ARA]^{\gamma_A} / ([ARA]^{\gamma_A} + [ARA50]^{\gamma_A})$. NMB was calculated from the difference in twitch strength in the absence and the presence of a MR. The parameters [ARA50], and in turn γ_A , are a function of the occupancy of the postsynaptic receptors when NMB=0.5 (Occ_{NMB50}). To estimate γ_A and [ARA50], we assigned 31 values to Occ_{NMB50} (0.6 to 0.9). The pharmacokinetics (PK) of the hypothetical MRs were defined by a 3-compartment model. The rate constant for the transport between plasma and the effect compartment was identical for all MRs ($k_{e1}=0.2 \text{ min}^{-1}$). Three MRs shared identical PK properties, but differed 100-fold in the affinities for the postsynaptic receptors ($K_{D1}=(0.316, 3.16, \text{ and } 31.6) \cdot 10^{-7} \text{ M}$). Three other MRs shared identical affinities ($K_{D1}=10^{-7} \text{ M}$), but were assigned systemic clearance of 1, 5, and 25 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. NMB-versus-dose relationship was examined for each of six MRs injected in 15 doses and the peak concentrations in the effect compartment as well as the associated peak [ARA] calculated. NMB was calculated using peak [ARA], and one of seven pairs of γ_A and [ARA50] ($Occ_{NMB50}=0.60, 0.65, 0.70, 0.75, 0.80, 0.85, \text{ or } 0.90$). The Hill equation was fitted to the 42 simulated NMB-versus-dose curves (6 MRs: 7 pairs of γ_A and [ARA50]) and the parameter γ estimated.

RESULTS: Increasing values of Occ_{NMB50} decrease γ_A and [ARA50].

The seven pairs of γ_A and [ARA50], one for each of the seven Occ_{NMB50} were used to calculate NMB for each MR. The estimated values of γ in the fitted Hill equation decreased with increasing Occ_{NMB50} (from 5.2 to 3.9) independent of the MRs.

DISCUSSION: Assuming that MRs act by occupying the postsynaptic receptors, then the slopes of the NMB-versus-dose curves are a function of Occ_{NMB50} and, in turn, of γ_A and [ARA50]. The value of Occ_{NMB50} in humans is not known. Exponent γ in the Hill equation is a function of the muscle and not of the MRs.

REFERENCES: (1) Anesth Analg 2000;90:1191. (2) J Pharmacokinetic Pharmacodyn 2003;30:23.

S-191.

TITLE: INHALED ANESTHETICS ACTIVATE TRPA1 HETEROLOGOUSLY EXPRESSED IN HEK CELLS.

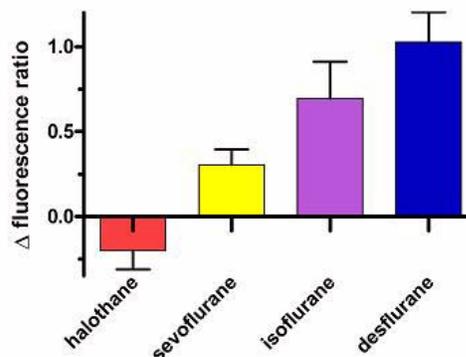
AUTHORS: C. Chu, M. A. Schumacher, N. W. Bunnett, H. Eilers;
AFFILIATION: University of California, San Francisco, San Francisco, CA.

INTRODUCTION: Despite significant efforts, no present theory explains the molecular mechanisms of inhaled anesthetic actions. Evidence from animal experiments shows that inhaled anesthetics can excite nociceptors (1), which may explain the hyperalgesia observed at low subanesthetic concentrations (2). Moreover, irritating anesthetics can elicit strong airway responses, including cough and laryngospasm, which can compromise recovery. The presented study investigates the transient receptor potential cation channel A1 (TRPA1) as possible target of inhaled anesthetics. TRPA1 is expressed in C-fiber nociceptors and is activated by a large number of irritant chemicals including plant derivatives such as allyl isothiocyanate (mustard oil) and environmental irritants like acrolein (3).

METHODS: The effect of anesthetics on TRPA1 was assessed by measurement of intracellular calcium in a heterologous expression system. TRPA1 expression inducible by tetracycline was achieved in the HEK Flp-In T-Rex 293 cell line (Invitrogen, Carlsbad, CA). Cells were loaded with Fura-2 AM and assayed by ratiometric fluorescence measurement (340 and 380 nm) in a cuvette based fluorescence spectrophotometer system (F-2500, Hitachi, San Jose, CA). Application of anesthetics from saturated solutions in Hanks buffer as well as TRPA1 specific agonists was achieved by injection into the cuvette. Measurements were done in Hanks buffer with 20 mM HEPES at room temperature. Results are displayed as mean \pm SD.

RESULTS: HEK cells expressing rat TRPA1 were exposed to equianesthetic doses (equivalent to \sim 1MAC) of halothane, sevoflurane, isoflurane, and desflurane. Sevoflurane, isoflurane, and desflurane produce an increase in intracellular calcium indicated by an increase in fluorescence ratio (340/380 nm). This response is absent in control cells not expressing TRPA1. The magnitude of the response correlates with the irritant potential of the anesthetics. The decrease in fluorescence

ratio observed after halothane exposure would indicate a decrease in intracellular calcium. Earlier experiments with halothane performed at 37°C had revealed a small increase in intracellular calcium (not shown). TRPA1 expressing samples showed the expected response when challenged with allyl isothiocyanate (mustard oil, not shown).



DISCUSSION: The presented data support the hypothesis that inhaled anesthetics activate TRPA1 with a potency that correlates with their irritant potential. Considering the TRPA1 expression profile this activation may play a role in anesthetic induced airway irritation and hyperalgesia.

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S-192.

TITLE: METHYLNALTREXONE (MNTX) ATTENUATED PROTEASE INHIBITOR INDUCED NAUSEA/VOMITING IN A RAT PICA MODEL

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INTRODUCTION: Protease inhibitors, especially ritonavir, cause significant nausea/vomiting (1). Previous reports showed that symptomatic treatment using combined anti-emetics can partially reduce this gastrointestinal discomfort (2). In this study, we evaluated the effects of opioid receptor antagonists, especially a peripherally acting opioid antagonist, MNTX (3), on ritonavir-induced nausea/vomiting using a rat pica model.

METHODS: The experimental protocol was approved by the IACUC. Rats react to nauseous and emetic stimuli with pica, manifested by increased intake of a non-nutritive substance, kaolin (4). Rats received 20 mg/kg ritonavir orally for two consecutive days. Naloxone or MNTX pretreatment were administered intraperitoneally 30 min prior to each ritonavir dose. Kaolin and food pellets were weighed daily. Blood samples were collected and plasma naltrexone levels were measured by HPLC. Data were analyzed using a two-way analysis of variance (ANOVA).

RESULTS: Naloxone alone did not affect kaolin intake or pica. Ritonavir-induced pica was attenuated by 10-30 μ g/kg pretreatment with naloxone ($P < 0.01$). The pica was also attenuated with MNTX in a dose-dependent manner ($P < 0.01$; Fig. 1). Food intake was not significantly affected. No detectable naltrexone after 3.0 mg/kg MNTX suggested that MNTX was not demethylated in our experimental paradigm

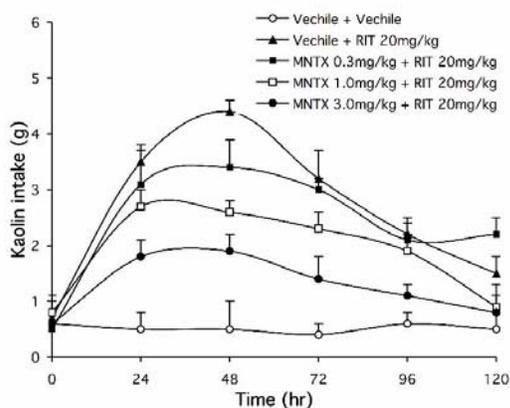


Fig. 1. Effects of pretreatment with MNTX on kaolin intake induced by ritonavir in rats. Ritonavir-induced increase in kaolin intake was attenuated with MNTX in a dose-related manner ($P < 0.01$). $n = 6-7$ per group. MNTX, methylnaloxone; RIT, ritonavir.

DISCUSSION: MNTX is a quaternary derivative of naltrexone (3). Non-selective opioid antagonist such as naloxone or naltrexone can compromise opioid analgesia. MNTX may have a clinical utility in reducing nausea/vomiting in AIDS patients receiving ritonavir to increase their medication compliance and improve their quality of life.

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S-193.

TITLE: CREATININE CLEARANCE CALCULATION IN PERIOPERATIVE PATIENTS WITH VARYING BODY MASS
INDEX: A COMPARISON OF TWO FORMULAS: COCKROFT-GAULT VERSUS MODIFICATION OF DIET IN RENAL DISEASE

AUTHORS: G. D'souza¹, E. R. Viscusi²;

AFFILIATION: ¹A I Dupont Hospital for Children, Wilmington, DE, ²Thomas Jefferson University, Philadelphia, PA.

INTRODUCTION: There is currently an epidemic of obesity. Increasing weight has serious implications in perioperative care. Several methods of estimating renal function are available: BUN/Creatinine values, or by calculating creatinine clearance using either the Cockcroft-Gault formula (C & G) or the Modification of Diet in Renal Disease (MDRD) formula. The MDRD calculation is not affected by patient weight.

METHODS: After IRB approval, a retrospective analysis of admission laboratory values on 10 patients each in BMI <25, BMI 25-30, BMI 30-35, BMI > 35 was performed. Patients were randomly selected from a database of all Total Joint Replacement (TJR) patients from January to June 2005. Data collected was age, sex, race, weight (BMI), & plasma creatinine. Creatinine clearance was calculated using the C & G formula and MDRD formula. Statistical analysis was performed.

Cockcroft-Gault formula: $((140 - \text{age(ys)}) \times (\text{weight (kg)})) / (72 \times \text{serum creatinine(mg/dl)})$

Multiply by a factor of 0.85 if female

Intended for ages 18-110, weight 35-120 kg, serum creatinine 0.6-7 mg/dl

MDRD formula:

$\text{GFR (mL/min/1.73 m}^2) = 175 \times (\text{serum creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$ (conventional units)

RESULTS:

	C & G	MDRD
BMI < 25 (SD)	32.43	34.59
(Mean)	72.51	78.6
BMI 25 -30 (SD)	23.44	21.83
(Mean)	99.4	82.9
BMI 30-35 (SD)	29.97	16.28
(Mean)	108.6	75.4
BMI > 35 (SD)	60.8	27.27
	138.5	84.9

For BMI < 25, C & G underestimates clearance by 7.74% compared to MDRD

For BMI >25 & < 30, C & G overestimates clearance by 19.90%

For BMI >30 & < 35, C & G overestimates clearance by 44.03%

For BMI > 35, C & G overestimates clearance by 63.10%

CONCLUSIONS: The results demonstrate that as the weight increases, C & G progressively overestimates creatinine clearance compared to MDRD calculation. This may have serious implications for drug dosing such as low molecular weight heparin which should be based on renal function. For obese patients, the MDRD method of calculating renal function may be more reliable

S-194.

TITLE: EVIDENCE OF PALONOSETRON'S MOLECULAR DIFFERENTIATION DISTINGUISH IT AS A UNIQUE ANTINAUSEA AND ANTIEMETIC AGENT.

AUTHORS: C. Rojas¹, J. Zhang¹, E. B. Rubenstein², S. Cantoreggi³, B. S. Slusher¹;

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INTRODUCTION: Despite multimodal approaches, an unmet need remains for therapies that can protect patients from PONV out to 3 days. Palonosetron (PALO) can be distinguished from older 5-HT₃ receptor antagonists (RAs) by its unique chemical structure, greater binding affinity, and substantially longer half-life. Clinical trials have shown a single IV dose of PALO superior to older 5-HT₃ RAs in preventing chemotherapy (CT)-induced nausea and vomiting through 5-days post-CT. The purpose of this research was to elucidate differences in the molecular interactions of PALO and older 5-HT₃ RAs with the receptor. These findings could help explain the established differentiated clinical profile.

METHODS: Receptor site saturation binding experiments were carried out with each [³H]-antagonist to obtain the corresponding Scatchard analyses and Hill coefficients. Diagnostic equilibrium binding experiments and kinetic dissociation experiments were conducted in order to examine competitive vs. potential allosteric interactions between ondansetron (OND), granisetron (GRAN) and PALO and the 5-HT₃ receptor. Finally, long term effect of the three antagonists on receptor function as measured by Ca²⁺ influx in HEK 293 cells expressing the 5-HT₃-receptor was compared.

RESULTS: Scatchard plots derived from saturation binding isotherm experiments revealed linear relationships for OND and GRAN consistent with simple bimolecular binding. In contrast, the Scatchard plot for PALO was curvilinear downward, suggestive of positive cooperativity. Hill coefficients for OND and GRAN approximated unity, indicative of no receptor cooperativity. The Hill coefficient derived for PALO was 1.5, indicative of positive cooperativity. Diagnostic tests showed that OND and GRAN competing with each

other or with themselves exhibited linear correlations. In contrast, when PALO was in competition with OND or GRAN functions were indicative of allosteric binding. PALO accelerated the rate of dissociation from the 5-HT₃ receptor of both [³H] OND and [³H] GRAN also indicative of an allosteric modifier. Neither OND nor GRAN had an effect on the rate of dissociation of the other [³H] antagonists. Prolonged inhibition of serotonin-induced Ca²⁺ influx (60% reduction vs. control cells, p < 0.001) was observed in cells that had been incubated with PALO even after the antagonist was allowed to dissociate from the cells. In contrast, cells incubated with OND or GRAN showed little or no inhibition of Ca²⁺ influx after antagonists were allowed to dissociate.

DISCUSSION: The results provide strong evidence that PALO exhibits allosteric binding and positive cooperativity when binding to the 5-HT₃ receptor. The prolonged inhibition of serotonin-induced Ca²⁺ influx also indicates that PALO triggers functional effects that persist beyond its immediate binding to 5-HT₃ receptors. To our knowledge, this is the first report showing PALO's unique interaction with the 5-HT₃ receptor at the molecular level, clearly differentiating it from the older 5-HT₃ RAs.

Data also will be submitted as a manuscript to A&A fall 2007

S-195.

TITLE: EFFECTS OF VOLATILE ANESTHETICS ON CAROTID BODY RESPONSE TO HYPOXIA AND HYPERCAPNIA IN ANIMAL STUDIES

AUTHORS: J. J. Pandit, K. O'Gallagher;

AFFILIATION: John Radcliffe Hospital, Oxford, United Kingdom.

INTRODUCTION: A previous non-systematic review concluded that in animals, 'hypoxic chemosensitivity of the carotid body is minimally affected by inhaled anesthetics'¹. This conclusion is at variance with humans where doses of just ~0.1 MAC halve the ventilatory response to hypoxia (2). We wished to re-examine the issue by systematic review (meta-analysis).

METHODS: We searched Medline, PubMed and Ovid from 1966 using appropriate keywords and also manually searched reference lists of retrieved papers (excluding abstracts, letters and human studies). For inclusion, the effect of anesthetic had to be localisable to the carotid body. Thus, just two types of experimental approaches were included: (a) protocols that measured activity directly in the carotid sinus nerve (the response in this case being afferent firing frequency); (b) protocols that exposed anesthetic (and/or hypoxia) to an isolated (or separately perfused) carotid body. The response in this case was carotid sinus nerve activity, or phrenic nerve activity or minute ventilation. Data were expressed as a 'standardised hypoxic response' (SHR) - ie, the relevant response to hypoxia with anesthetic, divided by the response without anesthetic. Statistical significance was assessed using ANOVA with factors being 'anesthetic', 'dose', 'species' and 'neuromuscular blockade'.

RESULTS: Only 7 papers met the inclusion criteria for hypoxia, and 6 papers for hypercapnia. Halothane, enflurane and isoflurane were studied in rabbits and cats. Anesthetic (mean dose \pm SD 0.75 ± 0.40 MAC) modestly but significantly reduced carotid body response to hypoxia (mean reduction 24% ($p < 0.05$)) but anesthetic (mean dose 0.81 ± 0.42 MAC) did not affect hypercapnic response. None of dose, species or neuromuscular blockade influenced the results.

S-196.

TITLE: ACROLEIN IMPAIRS THE MOVEMENT OF ISOFLURANE FROM LIPID TO SOLUBLE PROTEIN

AUTHORS: J. E. Johnson¹, E. E. Fibuch¹, N. W. Seidler²;

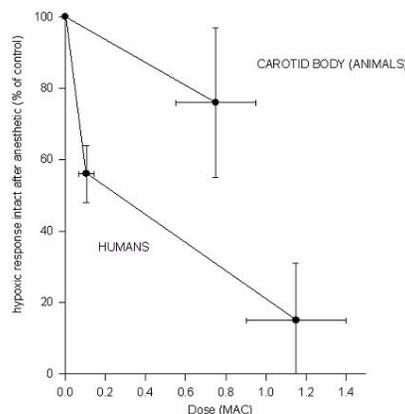
AFFILIATION: ¹University of Missouri - Kansas City School of Medicine, Kansas City, MO, ²Kansas City University of Medicine and Biosciences, Kansas City, MO.

INTRODUCTION: Postoperative cognitive dysfunction (POCD) occurs following surgery with inhaled anesthetics (IAs) particularly in the elderly [1,2]. While the molecular mechanisms are unknown, certain properties of IAs suggest that they may be affected by the chemical environment. Sevoflurane, for example, is not miscible with water [3] and partitions into lipid. IAs also bind to soluble proteins [4-6]. Acrolein, a lipid peroxidative product that is implicated in aging [7], may affect partitioning dynamics of IAs. This study examined the role of acrolein/isoflurane interactions with lipid and bovine serum albumin (BSA).

METHODS: A three-phase in vitro system was used consisting of a lower phase of isoflurane, a middle phase of water/acrolein and an upper phase of lipid (glyceryl trimyristate (GTM); glyceryl trioleate, (GTO)). Following incubation with GTM, the middle phase was removed, incubated with BSA, and tested for conformational changes using intrinsic fluorescence. Following incubation with GTO, the upper lipid phase was removed, layered over BSA, incubated and the BSA was tested for changes in structure using chromatography.

RESULTS: Middle phase aliquots, which were incubated with GTM in the presence and absence of acrolein and isoflurane, decreased intrinsic fluorescence of BSA in the acrolein and isoflurane groups, but not when acrolein and isoflurane were combined (Figure below). The transferred GTO layer, which was incubated over an aqueous layer with and without acrolein and isoflurane, affected the protein structure of acrolein and the isoflurane groups, but not when acrolein and isoflurane were combined.

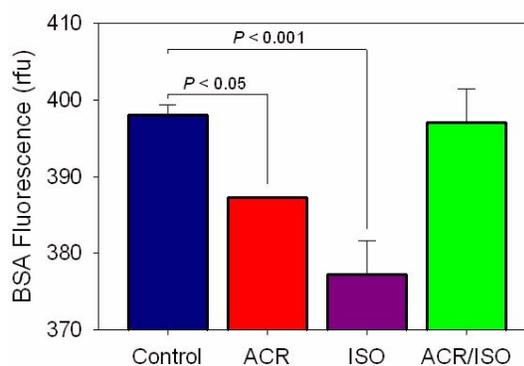
Fig. 1. Depression of hypoxic response in animal carotid bodies (this study) compared with depression of human hypoxic ventilatory response (from refs (2,3)) vs MAC. Error bars are SEM.



CONCLUSIONS: Volatile anesthetics depress the carotid body response to hypoxia. The animal carotid body appears more resistant than the intact human (2) (Fig. 1). This may be due species difference in the carotid body (animal vs human). However, lack of anesthetic effect in hypercapnic response parallels what is observed in humans (3), and suggests that in these effects on chemoreflexes, anesthetics act directly on the carotid body.

REFERENCES:

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- (2) Anaesthesia 2002; 57: 632-43
- (3) Anaesthesia 2005; 60: 139-45.



DISCUSSION: Isoflurane and acrolein individually affected the structure and the function of BSA. When acrolein and isoflurane were both present, no effect was detected, suggesting that both isoflurane and acrolein are retained in the lipid layer preventing their interaction with soluble protein. These observations suggest that acrolein promotes the retention of isoflurane in the lipid domain, which may contribute to the mechanism associated with POCD. Increase in the focal concentration of these co-lipid solutes, isoflurane and acrolein, may have a sustained and deleterious affect on lipid function. In conclusion, co-administration of acrolein-scavengers may play a role in moderating these effects.

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S-197.

TITLE: OPTIMIZATION OF ADLEA EXPOSURE TIME IN RAT PAW INCISION MODEL

AUTHORS: D. Liang, W. Williamson, D. Phan, P. Chiechi, S. Kramer, L. Sangameswaran;

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INTRODUCTION: Adlea™ (formerly 4975) is a novel formulation of capsaicin that is currently in clinical development as a long-acting non-opioid analgesic for moderate-to-severe pain associated with orthopedic surgery or osteoarthritis. Clinical trials have demonstrated that a single administration of Adlea via local instillation into open surgical wounds provides long-acting analgesia for postoperative pain, with no apparent adverse effects on other sensory or motor functions. The objective of the current study was to provide nonclinical evidence of the efficacy of Adlea dosed by local instillation in a surgical pain model. A secondary objective was to determine the optimal exposure time for Adlea within the surgical wound to elicit the efficacy as evaluated by behavioral endpoints.

METHODS: The study protocol was approved by the Anesiva IACUC. The paw incision in male Sprague-Dawley rats, weighing 200-250 g, was as described by Brennan et al., (1996) under isoflurane anesthesia. 100 µl of 2% lidocaine was injected in the paw 15 min prior to the incision. Adlea doses (5, 15, 75 µg) were formulated in either 25 or 50% PEG 300. 20 µl of either Adlea or vehicle was instilled into the incision for a prespecified period of time, the liquid aspirated at the end of the incubation and wound closed with 4 nylon sutures. Thermal and mechanical hyperalgesia were behaviorally assessed by von Frey filament test and Hargreave's method respectively on post-surgery days 1, 2, 3 and 6. The positive reference compound was buprenorphine, dosed subcutaneously each day 30 min prior to testing for behavioral outcomes.

RESULTS: A 5 µg (0.25 mg/mL) dose of Adlea was instilled for 2, 5 or 10 min to determine the optimal exposure time. Both 5 and 10 min exposure times were significantly better in increasing the paw withdrawal latency (PWL) than 2 min, vehicle or sham group in the Hargreave's test.

A single dose administered by local instillation in the incised paw elicited a reversal in thermal hyperalgesia in a dose-dependent manner with statistical significance on days 1, 2 and 3 post-surgery. Adlea, at the highest tested dose, caused a statistically significant reversal of mechanical hyperalgesia on day 1 after the incisional surgery.

DISCUSSION: Several publications discuss the pharmacological action of capsaicin dosed by intraplantar injection. This is the first report of delivering a single low dose of capsaicin by local instillation to provide direct preclinical evidence of efficacy that is dose-dependent and exposure time-dependent. The results showed that a single 5 or 10-minute instillation of Adlea into the incised paw produced significant reductions in postoperative thermal hyperalgesia that lasted up to 3 days. The highest tested dose of Adlea resulted in a reversal of mechanical hyperalgesia lasting up to 24 hours.

REFERENCE:
Pain, 64, 493-501, 1996

S-198.

TITLE: "CAINE" CATCHER

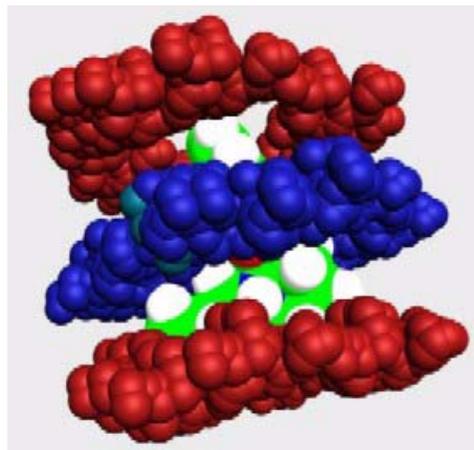
AUTHORS: R. Glassenberg¹, R. Eckenhoff²;

AFFILIATION: ¹Northwestern University, Chicago, IL, ²University of Pennsylvania, Philadelphia, PA.

INTRODUCTION: Beta cyclodextrins are hemolytic by leaching cholesterol from red cell membranes. This toxicity was tempered to create anionic cyclodextrins that have a natural affinity for monoamine, steroidal muscle relaxants. Is it possible to synthesize a macrocycle local anesthetic scavenger to prevent cardiac arrest following inadvertent intravascular injection or when given intrathecally have the ability to reverse a total spinal?

METHODS: We ran a series of isothermal calorimetric titrations to measure the binding of bupivacaine to a series of sulfated or carboxylated beta and gamma cyclodextrins, cucurbiturils, and calixarenes.

RESULTS: Cucurbit[7]uril binds dibucaine (K_d=0.1) and rocuronium (K_d=0.02), but not bupivacaine. Fig(1)



DISCUSSION: Cucurbiturils chelate cationic diamines. Lidocaine diamines have been synthesized in the form of dimers(1). The beast in bupivacaine could be tamed by creating a bup-lido chimera more suitable for binding than the monomer. Alternatively, a cyclopentapeptide trap modeled after sodium channels could be effective. Unfortunately, the only guanidinium steroidal local anesthetic which could be bound by a cyclodextrin, batrachiotoxin, from South American tree frogs is not readily available for clinical use. However, cucurbit[6]uril is small enough to bind sodium ions with a K_a=1000 and may potentiate local anesthetics. It would not have the mitochondrial toxicity of bupivacaine which acts as a powerful protonophore(2)

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S-199.

TITLE: NEUROPROTECTIVE EFFECTS OF A NOVEL PACAP DERIVATIVE DEPENDING ON PRESENCE OF RAT GLIA CELLS

AUTHORS: M. Miyamoto;

AFFILIATION: Tokyo Medical University, Tokyo, Japan.

Astrocytes represent at least 50% of the volume of the human brain. Besides their roles in various supportive functions, astrocytes are involved in the regulation of stem cell proliferation, synaptic plasticity and neuroprotection. Astrocytes also influence neuronal physiology by responding to neurotransmitters and neuropeptides and by releasing regulatory factors termed gliotransmitters. Pituitary adenylate cyclase activating polypeptide (PACAP) is a neuropeptide first isolated from ovine hypothalamic tissue. This peptide stimulates adenylate cyclase activation. However, few details were known of the function of this peptide on stimulus-secretion coupling in neuronal cells. Despite the neuroprotective properties of PACAP, its use as a drug is limited by its susceptibility to endopeptidases. In this experiment, we examined the neuroprotective effects of a novel PACAP derivative, ac-PACAP30, on brain neuronal death induced by exposure to 1 mM glutamate (Glu). Primary cultured rat cerebellar granule cells were prepared to the neuron rich cell group (neuron:glia=9:1) and the neuron/glia cocultured cell group (neuron:glia=6:4). The concentrations from 1 to 1000 fM of ac-PACAP30 were incubated with Glu contained Krebs-HEPES buffer for 20 hr at 37°C. Cell injury was assayed with calcein-AM. Extracellular levels of IL-6 and GM-CSF were measured using rat ELISA kits, respectively. Significant inhibitions of ac-PACAP30 on the cell death induced by Glu were observed at concentrations more than 10 fM in the cocultured cells, but not the neuron rich cells. In addition, ac-PACAP30 given 30min after Glu treatment was significantly neuroprotective. In the cocultured cells, but not the neuron-rich cell cultures, ac-PACAP30 significantly increased IL-6 and GM-CSF levels for 30min in stimulated condition, dose-dependently. These results indicate that ac-PACAP30 showed a strong neuroprotective property at its low concentration due to the increasing IL-6 and GM-CSF from astrocyte.

S-200.

TITLE: A PIGLET MODEL OF CYANIDE TOXICITY

AUTHORS: H. Singh, D. Beebe, T. E. Reihsen, H. Pham, S. E. Patterson, K. G. Belani;

AFFILIATION: University of Minnesota, Minneapolis, MN.

INTRODUCTION: Cyanide toxicity can occur during vasodilator therapy with sodium nitroprusside (NTP). It can also occur from smoke inhalation and possibly bio-terrorism. Being an extremely toxic compound, cyanide is difficult to work with experimentally. Evaluation of antidotes requires a reproducible animal model. In this study, we describe a piglet model where cyanide toxicity was induced using NTP.

METHODS: Ten piglets (20-35 kg) were anesthetized with Telazol and isoflurane, and mechanically ventilated. Two piglets received a low-dose intravenous infusion of NTP (35 mg/hr) for 4 hours, and 3 piglets received a high-dose infusion of NTP (100 mg/hr). The systolic blood pressure was supported at values within 20% of control with an infusion of phenylephrine. Two piglets received an infusion of phenylephrine alone, and 3 piglets did not receive an infusion of either NTP or phenylephrine. Mixed venous oxygen tensions (VpO₂) and serum lactate levels were determined hourly. Cyanide levels were determined at the beginning and end of the experiment. Data were reported as mean ± SD. Significance (p<0.05) was determined by ANOVA, and paired and unpaired t tests

RESULTS: The cyanide levels increased from 0.067±0.001 and 0.112±0 mg/L to 4.52±0.74 mg/L and 18.72±4.6 mg/L in the piglets that received low-dose and high-dose NTP, respectively. The cyanide levels did not increase in piglets that did not receive NTP. The lactate levels increased significantly in all pigs that received NTP from 1.98±0.75 to 10.56±5.6 mg/dL, but did not change in the control animals. The lactate levels increased more in those receiving high-dose NTP (14.4±0.5 mg/dL) than low-dose (4.7±3.9 mg/dL). The VpO₂ increased in all the animals receiving NTP from 46.6±6.3 to 67.8±18.1 mmHg (p<0.05) 2 hours after beginning the infusion, and remained elevated throughout the experiment. However the VpO₂ fell in the hour prior to death in 2 animals receiving high-dose NTP from 87 to 67 mmHg and 83 to 73 mmHg respectively, but increased in one animal

from 76 to 85 mmHg. The VpO₂ did not change in the control animals throughout the experiment. All of the animals receiving high-dose NTP died during the planned 4-hour infusion. All other animals survived following the experiment, and were sacrificed two weeks after the study.

DISCUSSION: Piglets tolerate low doses of NTP to produce lactic acidosis. With the higher doses the lactic acidosis is severe and fatal. This study demonstrates that cyanide toxicity can be induced with a NTP infusion in a piglet model.

(supported by : Grant 1U01NS058087-01, National Institutes of Health, USPHS)

REFERENCE:

1. Occupational Medicine, volume 48, 427-31, 1998.

S-201.

TITLE: METHYLNALTREXONE-INDUCED RECEPTOR TYROSINE PHOSPHATASE MU (RPTPM) ACTIVATION REGULATES ENDOTHELIAL CELL PERMEABILITY

AUTHORS: P. A. Singleton, J. G. Garcia, J. Moss;
AFFILIATION: University of Chicago, Chicago, IL.

Endothelial cell (EC) barrier dysfunction, i.e., increased vascular permeability, is observed in inflammatory states, tumor angiogenesis, atherosclerosis and in both sepsis and acute lung injury. Therefore, agents that preserve vascular integrity have important therapeutic implications. We examined the effects of methylnaltrexone (MNTX), a peripherally active mu opioid receptor antagonist (PAMORA) in late-stage development for opioid-induced constipation in advanced illness, on human pulmonary EC barrier disruption produced by edemagenic agents including morphine, the peptide mu opioid receptor (MOR) agonist DAMGO, thrombin and lipopolysaccharide (LPS). We utilized a preparation of human pulmonary EC as previously described and assessed barrier integrity by transelectrical resistance (Am J Respir Cell Mol Biol 37:222-231, 2007). Pretreatment of EC with MNTX (100 nM, 1 hour) or the uncharged MOR antagonist naloxone (100 nM, 1 hour) attenuated morphine and DAMGO-induced barrier disruption in a concentration dependent manner. However, MNTX (but not naloxone) pretreatment of EC inhibited thrombin- and lipopolysaccharide (LPS)-induced barrier disruption, indicating a potential MOR-independent effect of MNTX. Silencing the MOR attenuated the morphine- and DAMGO-induced EC barrier disruption, but not the permeability response to either thrombin or LPS. Further, treatment of human EC with MNTX (100 nM), but not naloxone (100 nM), increased Receptor Protein Tyrosine Phosphatase mu (RPTPμ) activity suggesting a mechanism independent of MOR expression. Silencing RPTPμ expression (siRNA) in human EC inhibited MNTX protection from EC barrier disruption with edemagenic agents. Mechanistically, silencing RPTPμ increased Src and RhoA activation as well as tyrosine phosphorylation (inactivation) of the negative regulator of RhoA, rhoGAP. These results indicate that MNTX provides barrier protection against edemagenic agonists via RPTPμ activation and suggests that the compound may have activity in syndromes of increased vascular permeability.

S-202.

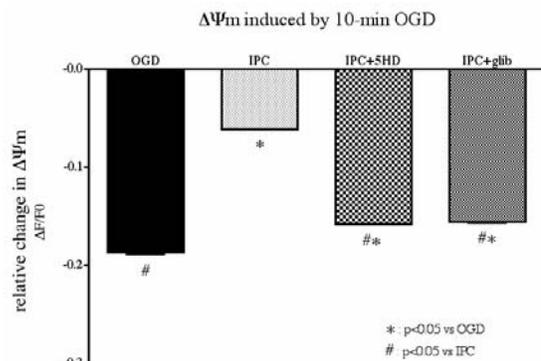
TITLE: RAPID ISCHEMIC PRECONDITIONING ATTENUATES MITOCHONDRIAL MEMBRANE DEPOLARIZATION EVOKED BY OXYGEN GLUCOSE DEPRIVATION IN RAT NEURONAL CELLS

AUTHORS: M. Shizukuishi¹, S. Yamada¹, N. Matsuoka¹, H. Ishida², Y. Kobayashi¹, T. Kazama¹;
AFFILIATION: ¹National Defence Medical College, Saitama, Japan, ²Tokai University School of Medicine, Kanagawa, Japan.

INTRODUCTION: Multiple intracellular signaling mechanisms are involved in ischemic tolerance in many organs. As in the heart, rapid ischemic tolerance was recently reported in the brain. The mitochondrial K_{ATP} channel plays one of the central role in rapid ischemic tolerance of the brain, similar to the heart(1). When the brain ischemia is induced, mitochondrial depolarization occurs in the neuron(2). We hypothesize that rapid ischemic preconditioning attenuates ischemia-induced mitochondrial depolarization.

METHODS: Acute hippocampal slices were preloaded with a fluorescent indicator, Rhodamine 123 (R-123) for mitochondrial membrane potential ($\Delta\Psi_m$). Ischemia was simulated by subjecting the slices to a 10-minute oxygen glucose deprivation (OGD) and then the slices were recovered for 5 minutes. As an ischemic preconditioning (IPC), a 1-minute OGD was performed 15 minutes before the 10-minute OGD. Relative changes of fluorescent intensities in pyramidal neurons of the hippocampal CA1 field were monitored during 10-minute OGD and 5-minute recovery phases.

RESULTS: The fluorescence of R-123 started to decrease at 2-3 minutes after the beginning of the OGD, reached its plateau at 7-10 minutes and then further decreased during the recovery phase. The IPC dramatically reduced these changes in fluorescent intensity caused by the OGD: depolarization of the mitochondrial membrane potential (Figure 1). This protective effect of the IPC was abolished by 5-hydroxydecanoic acid (5HD) and glibenclamide (glib).



DISCUSSION: In this study, IPC attenuated the mitochondrial membrane depolarization. K_{ATP} channel blockers inhibited the protective effects of the IPC. These results suggested that the tolerant cells maintained $\Delta\Psi_m$ below the critical level and prevented initiation of the process to neuronal death. The attenuation of $\Delta\Psi_m$ depolarization induced by activation of K_{ATP} channels may be one of the key mechanisms of rapid tolerance in rat hippocampal slices. The limitation of our study is that we did not evaluate the survival rate in every slice, because rat acute hippocampal slices were used in our experiment.

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- 2) J Neurophysiol, 84(1): 311-24, 2000.

S-203.

TITLE: DEXMEDETOMIDINE EXTENSION OF LOCAL ANESTHETIC EFFECT OF BUPIVACAINE IN A PERIPHERAL NERVE BLOCK IN RATS

AUTHORS: J. C. Petruska¹, R. Trainer¹, P. A. Seidman¹, P. S. Glass¹, R. G. Soto²;

AFFILIATION: ¹Stony Brook University, Stony Brook, NY, ²Beaumont Hospital, Royal Oak, MI.

BACKGROUND: Dexmedetomidine (DEX) is an alpha-2 agonist with an alpha-2 specificity seven times greater than clonidine. Clonidine has been used successfully as an adjunct to local anesthetics for neuraxial and regional anesthesia, but no data exists describing the safety or efficacy of DEX for similar uses. We therefore designed an in vivo rat study to quantify the effects of DEX alone and in conjunction with bupivacaine.

METHODS: Two models were used. 1) The cutaneous trunci muscle reflex (CTMR): a nociceptive specific reflex in which the dorsal trunk skin visibly flicks or puckers and is driven by noxious stimuli applied to the skin or high-threshold electrical stimuli applied to the dorsal cutaneous nerves. In CTMR behavioral assays, equal volumes of bupivacaine + (Lactated Ringer's or DEX) were injected subcutaneously targeting the L3 and L4 dorsal cutaneous nerves bilaterally, a manner that modeled a clinical peripheral nerve block. The CTMR was then tested by applying noxious pinch to the L3/4 dermatomes bilaterally (and elsewhere to test for systemic effects) every 10 minutes until the reflex returned. In CTMR electrophysiological assays, the dorsal cutaneous nerves were exposed for electrical stimulation and the CTM instrumented for EMG recordings. After baseline responses were recorded, equal volumes of bupivacaine + (Lactated Ringer's or DEX) were injected along the course of a single nerve inside the intact superficial fascia bilaterally. The CTMR was then tested every 10 minutes by delivering electrical stimulation to the treated nerves with the return of the CTMR defined by the EMG recording. 2) Nerve conduction assays: the responses to electrical stimulation of the common peroneal nerve were recorded from both dorsal and ventral spinal roots. DEX was applied directly to the sciatic nerve via a pool

created at the hip.

RESULTS: The CTMR model (using both the behavioral and EMG readouts) indicated that the addition of DEX significantly extended the local anesthetic actions of bupivacaine, by 25-30%. This was not due to volume effects or nerve compression. Application of DEX temporarily suppressed the CTMR globally, though the CTMR always returned in non-treated regions well before those served by the bupivacaine-treated nerves. Nerve conduction assays indicated that DEX has little to no effect on conduction of A-fibers, even at 2x indicated dosage.

CONCLUSIONS: Although DEX alone lacks significant local anesthetic properties, it prolongs local anesthetic action of bupivacaine. This effect was reversible with administration of an intravenous alpha-2 antagonist suggesting a mechanism of action independent of conduction block, but synergistic with the blocking effects of bupivacaine.

S-204.

TITLE: A COMPUTATIONAL STUDY OF NETWORK MECHANISMS MEDIATING ANESTHESIA-INDUCED PARADOXICAL EXCITATION

AUTHORS: M. M. McCarthy¹, N. Kopell¹, E. Brown²;

AFFILIATION: ¹Boston University, Brockton, MA, ²Boston University, Boston, MA.

INTRODUCTION: The anesthetic propofol paradoxically produces both behavioral and electroencephalographic (EEG) manifestations of excitation at low doses. Specifically, we see a rise in the EEG beta frequency band (12-20 Hz). To understand the source of this system-wide excitation, we look at the emergent properties of the underlying cortical networks in the presence of increasing doses of propofol.

METHODS: We construct biophysical models of cortical cells and track the evolving behavior of the population as we potentiate the GABA_A receptor consistent with propofol. Hodgkin-Huxley-type formulations describe the intrinsic and synaptic conductance changes of our model neurons. Intrinsic currents are minimized to the spiking currents and the M-current. Increasing both the time-constant and conductance of the GABA_A conductance mimics the addition of propofol to the system. We consider neural networks ranging in size from 2 to 220 neurons. Our output measure is either the population spiking activity or the simulated EEG, which we approximate as the sum of the population AMPA activity in our model pyramidal cells.

RESULTS: The spiking frequency of our two-cell model unexpectedly increases from the alpha to beta frequency with the potentiation of the GABA_A receptor. The presence of the M-current in the pyramidal cell is critical to this phenomenon. We find GABA_A-induced suppression of the M-current during the interspike interval responsible for the increased spiking frequency. Larger magnitude GABA_A potentiation results in dominance of the GABA_A-current over the M-current, leading to the expected spike frequency slowing. Our three-cell model produces an even larger increase in spiking frequency from theta to mid-beta (around 20 Hz) frequency following GABA_A potentiation. In this network, the interneurons spontaneously form an anti-synchronous rhythm following GABA_A potentiation. The formation of this rhythm

results from a loss of phase dependence of post-inhibitory rebound spiking due to GABA_A-induced M-current suppression. Larger networks manifest increased beta power in the simulated EEG, as well as decreases in delta, theta and alpha power. The rise in beta power correlates with a switch in the activity of the interneurons from a sparsely spiking and largely synchronous pattern to a continuous, rhythm of anti-synchronous interneuron clusters spiking in the mid-beta frequency range. Pyramidal cells pattern their behavior after the interneuron rhythm. Interneuronal M-current is necessary for the emergence of paradoxical excitation in the larger network models.

DISCUSSION: Our studies suggest that GABA_A potentiation can suppress the membrane M-current leading to increased neuronal excitability and the establishment of interneuron anti-synchrony. These represent possible mechanisms behind the CNS excitation observed with low doses of propofol anesthesia. Excitation in this context, similar to that seen clinically, is a dose-related phenomenon manifest only at low levels of GABA_A potentiation. These results may help inform experiments to further elucidate cortical network mechanism generating anesthesia-induced excitation.

S-205.**TITLE: EFFECTS OF ROPIVACAINE AND BUPIVACAINE ON GLUTAMATE CURRENTS IN CULTURED RAT HIPPOCAMPAL NEURONS**

AUTHORS: L. Xu, Y. Jiang, H. Zhang;

AFFILIATION: PLA General Hospital, Beijing, China.

INTRODUCTION: The aim of the study was to observe and compare the effects of ropivacaine and bupivacaine on glutamate-evoked currents in cultured rat hippocampus neurons.

METHODS: Rat hippocampal neurons were dissociated and cultured. Glutamate-evoked currents were recorded by whole cell patch clamp recording. Effects of ropivacaine and bupivacaine on glutamate-evoked currents were observed. Drugs were given by pressure ejection or applied in the bath.

RESULTS: Glutamate (100mmolL^{-1}) can activate inward currents in cultured rat hippocampus neurons and these currents could be blocked by non-NMDA antagonists DNQX. At the concentration of 10, 50, 100 mmol L^{-1} , bupivacaine and ropivacaine all could obviously decrease glutamate-evoked currents in cultured rat hippocampus neurons. At higher concentration of 50 and 100mmolL^{-1} , the reduced amplitude of glutamate currents by ropivacaine was larger than that of bupivacaine ($P < 0.01$).

DISCUSSION: Ropivacaine and bupivacaine have obvious inhibition effect on glutamate-evoked currents in cultured rat hippocampus neurons. The inhibition effect of ropivacaine on glutamate-evoked currents was stronger than that of bupivacaine.

Pharmacology-Clinical

S-206.

TITLE: CEREBROSPINAL FLUID BIOAVAILABILITY OF ORAL PREGABALIN

AUTHORS: A. Buvanendran¹, J. S. Kroin¹, S. S. Reuben², M. Kari¹, K. J. Tuman¹;

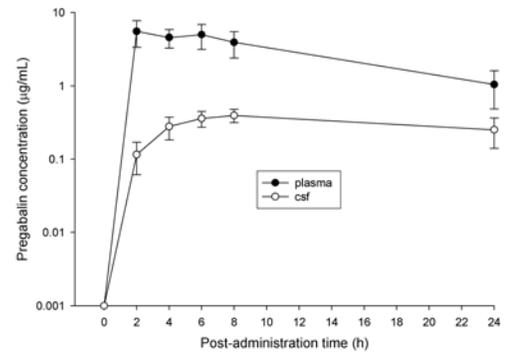
AFFILIATION: ¹Rush Medical College, Chicago, IL, ²Baystate Medical Center, Springfield, MA.

INTRODUCTION: Pregabalin is an anticonvulsant that is effective for treatment of neuropathic pain. When administered in the perioperative period, pregabalin reduces postoperative pain (Anesth Analg 2007;104:1545). Oral pregabalin reaches peak concentration in plasma 1 h after administration in humans (Epilepsia 2005;46:1407). In rat brain tissue, peak pregabalin concentration is not attained until 100 min after oral administration, but peak plasma concentration is reached by 20 min, indicating that there is a delay entering brain (Eur J Drug Metab Pharm 2001;26:123). However, in humans it is not known when the peak pregabalin concentration is reached in brain or spinal cord, and how the brain or spinal cord concentration relates to the plasma level.

METHODS: Following IRB approval, subjects (n=9) undergoing total knee arthroplasty were consented for the study (as part of a larger study to evaluate the effect of perioperative pregabalin on postoperative pain). Patients received a 300 mg oral dose of pregabalin prior to surgery. Before incision, patients were prepared for continuous spinal anesthesia, with placement of an intrathecal catheter. Cerebrospinal fluid (CSF) was withdrawn (0.5 mL) at 2 h after oral pregabalin, and simultaneously, a 2 ml sample of venous blood obtained. Paired samples were also obtained at 4, 6, 8, and 24 h after oral pregabalin. Samples were analyzed for pregabalin concentration using a validated HPLC assay (Epilepsia 2005;46:1407).

RESULTS: Mean age of subjects was 66.6 yr (range, 61-72), and mean weight was 90.1 kg (range, 73-127); with 7 female and 2 male subjects. The figure shows plasma and CSF concentrations (mean ± SD) of pregabalin measured over 24 h after a single 300-mg oral dose in 9 subjects. Median time to peak concentration was at first sampling time for plasma (2 h) and 8 h for CSF. AUC(0-24h) values for plasma and CSF were 73.9 ± 19.3 and 7.07 ± 1.46 µg·h/mL respectively. AUC(0-

24h) CSF/plasma ratio was 0.098 ± 0.015 and mean CSF/plasma ratio increased with time postdose.



DISCUSSION: This is the first human study to investigate the pharmacokinetics of pregabalin in CSF. The important finding of this study is that plasma pregabalin enters the CSF with an AUC(0-24h) (CSF/plasma) drug concentration ratio of approximately 10%, and this spinal pregabalin may account for much of the efficacy of pregabalin in pain states.

S-207.

TITLE: DELAYED INHIBITION OF AGONIST-INDUCED GRANULOCYTE-PLATELET AGGREGATION AFTER LOW-DOSE SEVOFLURANE INHALATION IN HUMANS

AUTHORS: E. Lucchinetti, J. Wacker, M. Jamnicki, L. Härter, M. Keel, M. Zaugg;

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INTRODUCTION: An increasing body of evidence supports the potent anti-ischemic, preconditioning-mimicking effects of halogenated ethers. Our group previously demonstrated that low-dose sevoflurane inhalation protects the endothelium against ischemia-reperfusion injury in a human forearm model [1]. We further showed in healthy volunteers that sevoflurane inhalation at subanesthetic concentrations modifies human blood transcriptome and decreases the expression of the proinflammatory L-selectin (CD62L) on granulocytes for up to 48 hours, consistent with the occurrence of a “second window of protection” [2]. Ischemic preconditioning was previously shown to selectively downregulate pro-coagulant granulocyte-platelet aggregation [3]. Analogous to ischemic preconditioning, we hypothesized that low-dose sevoflurane inhalation would reduce expression of platelet markers and render them refractory to agonist-induced aggregation. Therefore, we tested whether low-dose sevoflurane inhalation provides inhibition of granulocyte-platelet aggregation in humans.

METHODS: Ten healthy male volunteers were enrolled in this crossover study. Each subject inhaled for one hour sevoflurane at 0.5-1 vol.-% end-tidal concentration in oxygen (50 vol.-%). Inhalation of oxygen (50 vol.-%) alone served as control. Venous blood samples were collected at baseline before inhalation, immediately after inhalation, and 24 hours thereafter, and were used for flow cytometry to determine platelet surface marker (CD41, CD42b, CD62P (P-selectin), and PAC-1) on platelets and granulocytes and for kaolin-induced clot formation, as assessed by thrombelastography. In flow cytometry measurements, platelets were stimulated with arachidonic acid (AA, 30 µM), adenosine diphosphate (ADP, 1 µM), and thrombin receptor agonist peptide-6 (TRAP-6, 6 µM). Thrombelastographic measurements

were also determined at baseline, one hour after sevoflurane inhalation, and 24 hours later in control and sevoflurane-treated blood samples.

RESULTS: AA, ADP, and TRAP-6 markedly increased the expression of CD62 on platelets, while CD42b (shedding) and PAC-1 (formation of microparticles) expression decreased. The amount of granulocyte-platelet aggregates increased upon agonist stimulation. Low-dose sevoflurane inhalation reduced CD62P expression on platelets 24 hrs after inhalation, and inhibited the formation of granulocyte-platelet aggregates under stimulation with AA and ADP after one and 24 hours, and with TRAP-6 after 24 hours compared to control. Inhibition of granulocyte-platelet aggregates was accompanied by reduced clot firmness, as measured by thrombelastography 24 hours after sevoflurane inhalation compared to control.

DISCUSSION: We demonstrate for the first time that low-dose sevoflurane inhalation (<1 vol.-%) inhibits agonist-induced granulocyte-platelet interactions 24 hours after application and promotes late anti-coagulant effects.

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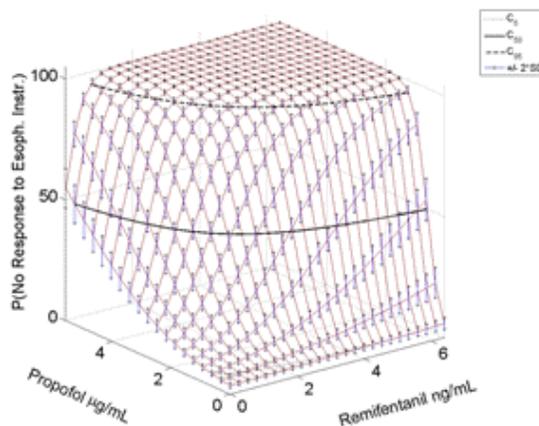
TITLE: ESTIMATING INTER-SUBJECT VARIABILITY FOR A REMIFENTANIL PROPOFOL RESPONSE SURFACE OF ESOPHAGEAL INSTRUMENTATION

AUTHORS: C. D. LaPierre, K. B. Johnson, N. Syroid, T. D. Egan;
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INTRODUCTION: 3D response surfaces are commonly used to visualize predicted population responses where two drugs are concurrently administered. Response surfaces model the central tendency of a population, but an individual's response is likely to vary from the surface. We explored inter-subject variability of a remifentanyl (R) propofol (P) response surface describing the loss of response to esophageal instrumentation (EI).

METHODS: Following IRB approval, 24 volunteers received 15 escalating target controlled infusions of P and R. Effect site concentrations were estimated using Marsh kinetics^{1,2} ($ke_0 = 0.51$)³ for P and Minto kinetics⁴ for R. At each target concentration pair, responses to EI were recorded and used to build a response surface model using a Logit construct. To estimate inter-subject variability, predicted responses for 24 surfaces were calculated using data from N-1 subjects, removing each subject once. The resulting response standard deviations (SD) were used to create error bars in the probability of no response (PrNR) to EI for R-P concentration pairs throughout the response surface.

RESULTS: The response surface for loss of response to EI and the associated SDs are presented in Figure 1. The dashed, solid, and dotted lines represent the 5, 50, and 95% isobols for PrNR to EI. At the 50% isobol, for R=1.3, P=2.2, the SD is 1.9%. Below the 5% isobol, for R=0.5, P=0.3, the SD is 0.5% and above the 95% isobol for R=2.4, P=2.8 the SD is 0.7%. Along the 50% isobol, R=0 & P=5.3 and R=6.1 & P=0.6 the SDs were 3.9% and 4% respectively.



DISCUSSION: Inter-subject variability in response to EI is largest at the transition from responsive to unresponsive. SD increases from 5 to 50% and decreases from 50 to 95%. Variability along the 50% isobol tends to decrease with combinations of R and P compared to when one drug is predominantly used. The analysis did not account for the Pk variability of either drug. Better interpretation of response surface predictions of combined drug effects warrants the exploration of improved methods to describe response surface variability.

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S-209.

TITLE: RECOVERY OF TRAIN-OF-FOUR RATIO IS DELAYED IN DIABETIC PATIENTS RECEIVING VECURONIUM

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AFFILIATION: Fukuoka University School of Medicine, Fukuoka, Japan.

INTRODUCTION: Diabetes mellitus causes motor nerve degeneration, loss of axon terminals and neuromuscular junctions. Delayed recovery of train-of-four (TOF) count in diabetic patients has been reported.¹ In present study, we evaluated the spontaneous recovery profile of neuromuscular block induced by vecuronium in patients with diabetes mellitus and in control patients with first dorsal interosseous electromyogram (EMG) until TOF ratio ≥ 0.9 was recorded. We measured first dorsal interosseous EMG, as there is a good correlation between adductor pollicis mechanomyogram (MMG) and first dorsal interosseous EMG at a TOF ratio ≥ 0.75 .

METHODS: Fourteen adult patients with Type 2 diabetes mellitus (DM group) and 14 otherwise healthy patients of ASA physical status I or II (control group), who were scheduled to undergo elective surgery entered this study. Diabetic patients with renal dysfunction were excluded. Neuromuscular monitoring was recorded from the first dorsal interosseous muscle using EMG with stimulation of the ulnar nerve. After induction of general anesthesia with propofol 1.5-2.5mg/kg, fentanyl 50-100mcg, a 50Hz tetanic stimulation of 2 seconds duration was applied at 40mA. After the calibration, TOF stimuli were delivered every 20 seconds at the ulnar nerve. Following 5 minutes stabilization period, vecuronium 0.1mg/kg was given to facilitate tracheal intubation. General anesthesia was maintained with propofol and fentanyl. The neuromuscular block was assessed until a TOF ratio $\geq 90\%$ was achieved spontaneously.

RESULTS: There were no significant differences between DM and control groups with regard to age, height, or weight. Onset times of 0.1mg/kg vecuronium were similar between the groups. Recovery times of TOF ratio in DM and control group after 0.1mg/kg of vecuronium

are shown in Table 1. Times from vecuronium administration to the TOF ratio 0.9 in DM group were significantly longer than those in control group. Times from TOF ratio 0.25 to 0.9 were also significantly longer in DM group than those in control group. In DM patients, times from TOF ratio 0.25 to 0.9 took more than an hour in 5 of 14 patients.

Table 1. Recovery of train-of-four (TOF) ratio after 0.1 mg/kg vecuronium

	DM group	Control group
Time to 0.7 TOF ratio (min)	90 ± 29.1	72 ± 17.4
Time to 0.9 TOF ratio (min)	130 ± 60.9*	90 ± 27.3
TOF ratio 0.25 to 0.7 (min)	27 ± 17.7	18 ± 7.6
TOF ratio 0.25 to 0.9 (min)	67 ± 49.8*	36 ± 18.7

Mean ± SD, *P<0.05 versus control group.

DISCUSSIONS: Since the recovery of vecuronium neuromuscular block was delayed in DM patients, routine quantitative monitoring is recommended until the return of TOF ratio is confirmed.

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S-210.

TITLE: THE IMPACT OF COMBINED PROPOFOL-REMIFENTANIL ANESTHESIA ON SEIZURE DURATION AND RECOVERY TIME DURING ELECTROCONVULSIVE THERAPY

AUTHORS: K. Suga, M. Komai, R. Takao, H. Yamazaki, A. Yoshida, Y. Kobayashi;

AFFILIATION: National Hospital Organization Tokyo Medical Center, Tokyo, Japan.

INTRODUCTION: Electroconvulsive therapy (ECT) under general anesthesia with muscle paralysis is commonly used for treatment of depression. Recently, propofol was reported to produce a dose-dependent decrease in the duration of seizure activity during ECT 1). However, a decrease in propofol dose could neither provide adequate hypnosis nor minimize acute hemodynamic changes. We hypothesized that remifentanil in combination with a small dose of propofol would attenuate hyperdynamic responses to ECT without a decrease in the seizure activity and also provide a rapid and reliable recovery.

METHODS: After obtaining approval from the human ethics committee of our hospital and written patient consent, we enrolled a total of five ASA I-II patients (range 46-75yr) in a randomized study, and a total of 38 ECT sessions were evaluated. Anesthesia was induced in one of two protocols in random order: (1) thiamylal IV - Group T; (2) propofol + remifentanil - Group R. Propofol was administered with a target-controlled infusions system (TCI) until loss of verbal contact. Then, an air tourniquet was inflated on the left leg and succinylcholine IV was administered for muscle relaxation. Noninvasive systolic blood pressure (SBP) and heart rate (HR) were recorded before the electrical stimulus and after the end of seizure, respectively, in order to calculate the percent changes. Patients were discharged when they met the following criteria: stable hemodynamic and respiratory status and response to verbal command similar to pre-ECT status. Duration of seizure on electroencephalography (Seizure Duration), Recovery Time (time from the end of seizure to discharge), adverse events and therapy were also recorded. Statistical analysis between the two groups was based on unpaired t tests. P-values <0.05 were considered significant.

RESULTS: The percent changes of HR was lower in Group R than in Group T (23.7% vs. 51.6%, P=0.003). The percent changes of SBP, Seizure Duration and Recovery Time did not differ significantly between groups. The 95% confidence intervals for the difference between the means in the percent changes of SBP, Seizure Duration and Recovery Time were -8.1 to 25.7%, -16.7 to 7.0 sec and -2.1 to 2.6 min, respectively.

DISCUSSION: In this study, a TCI system could minimize blood concentration of propofol and also be effective in avoiding relatively shorter seizures compared to barbiturate anesthesia. In view of recovery profile, we could not demonstrate any superiority of combined propofol-remifentanil anesthesia during ECT in comparison to conventional anesthetics. However, the hemodynamic changes were similar in both groups. In conclusion, propofol-remifentanil combination attenuated acute hemodynamic responses after ECT stimulus without adversely affecting the seizure activity.

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S-211.

TITLE: INVESTIGATION FOR A PREFERRED REMIFENTANIL PROPOFOL COMBINATION AND DOSING SCHEDULE FOR ESOPHAGEAL INSTRUMENTATION

AUTHORS: C. D. LaPierre, K. B. Johnson, T. D. Egan;

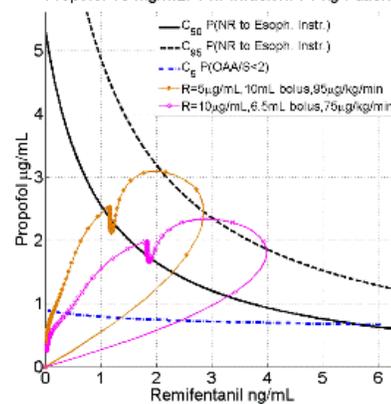
AFFILIATION: University of Utah, SLC, UT.

INTRODUCTION: Propofol (P) and remifentanil (R) are often combined to achieve desired anesthesia and analgesia for esophageal instrumentation (EI). These drugs interact synergistically, and have rapid kinetics. These properties lead to a therapeutic dosing window that changes with drug combination. We hypothesized that a preferred drug combination and dosing scheme exists at which a majority of people would tolerate EI while minimizing time at effect site concentrations where adverse events occur.

METHODS: Following IRB approval, EI was attempted on 24 volunteers at 15 random, predefined P and R target controlled effect site concentrations (Marsh kinetics^{1,2} ($ke_0 = 0.51$)³ for P and Minto kinetics⁴ for R). A measure of sedation (OAA/S) and response to EI were recorded at each pair and response surface models were constructed using a Logit construct. Drug combinations, bolus doses and infusion rates for a one hour induction were simulated in Stanpump⁵ and plotted on the response surfaces. Preferred was defined as rapid time to C₉₅ for EI, sitting at C₅₀ until the infusion was stopped, then returning rapidly to C₅ for sedation.

RESULTS: Simulation determined that C₉₅ for EI could be reached in under two minutes while recovery depended on the dosing. Two dosing schemes (shown in Figure 1; markers appear at whole minutes) were developed: P=10mg/mL, R=5µg/mL, 10mL bolus, P infusion rate (PIR)=95µg/kg/min and P=10mg/mL, R=10µg/mL, 6.5mL bolus, PIR=75µg/kg/min. With a two minute pause after the bolus in the first combination, EI C₉₅ was reached in 100 seconds (total time above C₉₅=90 seconds) and time to sedation C₅ was 20 minutes. With the second combination, EI C₉₅ was reached in 110 seconds (total time above C₉₅=110 seconds) and time to sedation C₅ was 12.2 minutes.

Proposed Dosing for Esophageal Instrumentation. Propofol Rate, Remifentanil and Bolus As Indicated. Propofol 10 mg/mL. 1 hr Infusion. 71 kg Patient.



DISCUSSION: The preliminary bolus aided rapid time to EI C₉₅, yet allowed a rapid drop to EI C₅₀. Recovery times decrease when higher R, lower P combinations are used, but an increase in airway complications was noted in the study. It was also noted that pharmacokinetic modeling of propofol after initial bolus doses does not reflect observations³. Continued exploration by simulation and experimentation are needed to further define a preferred dose.

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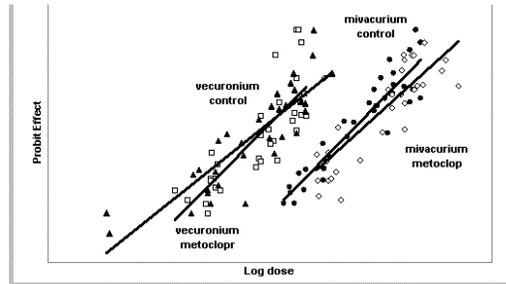
TITLE: VECURONIUM POTENCY AFTER METOCLOPRAMIDE: A COMPARISON TO MIVACURIUM

AUTHORS: D. Steinberg¹, G. H. Steinberg²;
AFFILIATION: ¹Hospital Clinicas Caracas & Policlinica Mendez Gimon, Caracas, Venezuela, ²School of Medicine, Central University Venezuela, Caracas, Venezuela.

INTRODUCTION: During the intense efforts for an antiemetic efficacious therapy, metoclopramide (MET) and vecuronium (VEC) have been widely and coincidentally used together. Although MTC is a very active metabolic agent, no interaction is described for this combination. Instead, both prolongation and reduction on infusion rate to maintain muscular relaxation were reported when mivacurium (MIV) was used after MTC⁽¹⁻²⁾. The aim of present trial is to compare VEC and MIV potencies after a previous MTC administration.

MATERIAL & METHODS: Following consenting, 2 groups (n= 11 e/a) of elective patients received either VEC or MIV fractional doses (control) during induction with intravenous agents and nitrous oxide. Two additional similar groups were treated with the same drugs after MTC (study) was included as part of pre-anesthetic medications. Using EMG, maximal block was assessed following a stable previous effect and used to develop a cumulative dose-response curve after log dose-probit response transformation. T test and p<0.05 level for significance were used for statistical comparison of control and study groups

RESULTS: Final doses and effect were: 87±11 µg.Kg⁻¹ and 87±9%, 93±5 and 93±7 for MIV control and MTC groups respectively, 37±6 µg.Kg⁻¹, 76±20% and 37±1, 77±17 for VEC. Neither 0 nor 100% block were noticed (Fig 1).



	VEC ^{cntl}	VEC ^{mtcpl}	p	MIV ^{cntl}	MIV ^{mtcpl}	p
ED ₅₀	29±10	30±10	0.704	57±9	61±12	0.121
ED ₉₀	59±20	60±21	0.780	92±16	95±20	0.553
ED ₉₅	75±26	76±26	0.804	109±19	110±23	0.791

DISCUSSION: Potent non-competitive and dose dependent inhibitions of both plasma cholinesterase and erythrocyte acetyl cholinesterase have been reported for MTC⁽³⁾. Such an effect can be linked to the prolongation of succinylcholine action⁽⁴⁾ and probably to MIV-induced blockade. These effects may also explain the above mentioned findings related to lower MIV infusion rates⁽¹⁻²⁾. Experimentally, MTC produced calcium antagonistic action and inhibited twitch contraction at the rat diaphragm⁽⁵⁾, but present results doesn't support any potentiating clinical action on VEC or MIV neuromuscular blockade.

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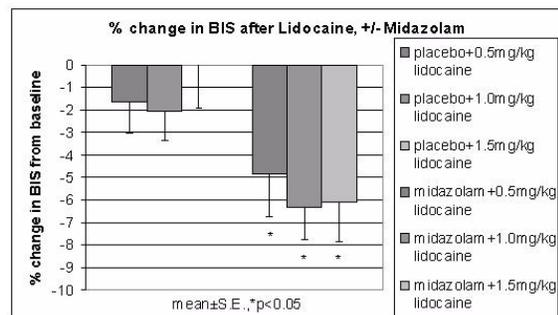
TITLE: LIDOCAINE POTENTIATES THE EFFECT OF GABAERGIC SIGNALING ON BISPECTRAL INDEX

AUTHORS: A. McKay, Z. M. Malik, M. Forbes, M. E. Durieux, D. S. Groves, J. Huffmyer;
AFFILIATION: UVA Health System, Charlottesville, VA.

INTRODUCTION: Intraoperative systemic lidocaine shortens postoperative ileus duration and hospital stay (1). However, it affects bispectral index (BIS): IV lidocaine during propofol or sevoflurane anesthesia reduces anesthetic doses required to achieve target BIS values (1, 2), and an inadvertently high dose of lidocaine decreased BIS to 0 during sevoflurane anesthesia (3). We therefore studied the interaction between lidocaine and BIS. First, we hypothesized that lidocaine may not affect BIS directly. We therefore examined the effect of IV lidocaine on BIS in the absence of anesthetic. Second, lidocaine's effects on BIS changes induced by propofol and sevoflurane suggests that it may potentiate effects of GABAergic compounds (1,2). Therefore, we hypothesized that lidocaine would affect BIS in the presence of midazolam.

METHODS: The study was randomized, double-blinded and placebo-controlled. After obtaining IRB approval and written informed consent, 96 patients to undergo general anesthesia were assigned randomly to one of six treatment groups. They received either midazolam (0.03 mg/kg) or placebo, followed approximately 5 min later by one of three pre-induction doses of lidocaine: 0.5, 1 or 1.5 mg/kg. Baseline BIS values were recorded before administration of lidocaine, and at 30 second intervals afterwards for three minutes. Propofol was then administered for anesthetic induction. Primary endpoint was the average BIS level recorded. Statistical analysis was performed using repeated-measures t-test, p<0.05.

RESULTS: Baseline BIS values were lower in the midazolam group (94±4 vs. 90±7, p<0.001). There was no significant decrease in BIS values in the placebo group for any of the three lidocaine doses. There was a significant decrease in BIS in the midazolam groups (85±9, 84 ± 7, and 86±8, respectively; see Figure).



DISCUSSION: IV lidocaine decreases BIS values in the presence of midazolam, but not in its absence. This suggests that the effect of IV lidocaine on BIS is not direct, but instead results from modulation of midazolam-facilitated GABAergic signaling. This may explain why significant effects of lidocaine on BIS were observed in the presence of other GABAergic drugs (propofol, sevoflurane).

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S-214.

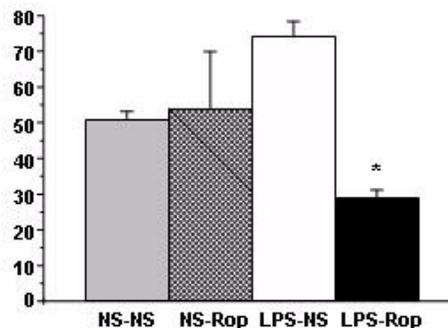
TITLE: ROPIVACAINE EXERTS ITS PROTECTIVE EFFECT IN ENDOTOXIN-MEDIATED LUNG INJURY VIA MECHANISMS OTHER THAN ICAM-1 INHIBITION

AUTHORS: R. Koshy, E. Votta-Velis, M. Castellon, R. Minshall;
AFFILIATION: University of Illinois, Chicago, IL.

INTRODUCTION: A recent study revealed that ropivacaine provided a beneficial effect in reducing markers of acute lung injury caused by lipopolysaccharide (LPS), an endotoxin. That study also revealed that, in-vitro, there was an attenuation of LPS-induced stimulation of intracellular cell adhesion molecule 1 (ICAM-1) mRNA in wild-type mouse lung cells given ropivacaine. This study serves to find out whether lung PMN transmigration following LPS exposure plus high tidal volume ventilation in ICAM-1 knockout mice would be reduced by ropivacaine.

METHODS: ICAM-1 knockout mice were placed in a nebulizer for 1 hour and were exposed to either nebulized LPS or nebulized normal saline (NS). The mice were then given either IV NS or IV ropivacaine (one micromolar) two hours after initiation of the study. The mice were placed on a volume-control ventilator and were given high tidal volumes (28 cc/kg) for a total of two hours in order to further induce acute lung injury. At the end of the four hour protocol, the mice received a bronchoalveolar lavage (BAL) three times, gently instilling and removing one milliliter PBS each time. This fluid was then Cytospun to collect the BAL cells on the slides, which were subsequently stained and visualized under fluorescence microscopy. Using 20X magnification, four representative fields were visualized per slide and the average neutrophil count high-powered field was analyzed and the means compared by ANOVA.

RESULTS: Figure 1: Determination of BAL neutrophils per high-powered field in ICAM-1-knockout mice given either nebulized NS followed by IV NS (NS-NS), nebulized NS followed by IV ropivacaine (NS-Rop), nebulized LPS followed by IV NS (LPS-NS) or nebulized LPS followed by IV ropivacaine (LPS-Rop). * p<0.05 vs LPS-NS.



DISCUSSION: In this study, endotoxin plus high tidal volume ventilation-mediated PMN transmigration into the lung was attenuated in ICAM-1-knockout mice by IV ropivacaine. No such attenuation is seen in mice receiving purely ventilator-induced lung injury, so the anti-inflammatory effect of ropivacaine appears to be specific to endotoxin-induced injury. Plus, since ropivacaine attenuated the LPS response in the knockout model, ICAM-1 may not be the sole mechanism by which local anesthetic attenuates such injury. Other proteins involved in transcellular signaling may also be the target and are currently under investigation.

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Ropivacaine Decreases Inflammation in Experimental Endotoxin-induced Lung Injury: Anesthesiology 104:961-969, 2006.

S-215.

TITLE: SAFETY AND EFFICACY OF DEXMEDETOMIDINE USED FOR SEDATION DURING ELECTIVE AWAKE FIBEROPTIC INTUBATION: THE MULTICENTER TRIAL

AUTHORS: S. Bergese¹, K. Candiotti², A. Zura³, P. Bokesch⁴, A. Bekker⁵;

AFFILIATION: ¹The Ohio State University, Columbus, OH, ²University of Miami, Miami, FL, ³Cleveland Clinic Foundation, Cleveland, OH, ⁴Hospira Worldwide, Inc., Lake Forest, IL, ⁵New York University, New York, NY.

INTRODUCTION: An awake fiberoptic intubation (AFOI) is indicated for patients with an anticipated difficult airway secondary to anatomy, airway trauma, morbid obesity or unstable cervical spine injuries.¹ Although patients may be sedated for an AFOI, they need to be responsive and capable of maintaining their own airway without assistance. In this multicenter study we evaluated the safety and efficacy of dexmedetomidine (DEX) versus placebo (PBO) used for sedation during elective AFOI.

METHODS: This Phase III, randomized, double-blinded placebo-controlled study was conducted at 17 US sites with institutional approval and informed written patient consent. One hundred-twenty four subjects (DEX=63; PBO=61) entered the study. All subjects' vital signs were continuously monitored. A baseline Ramsay Sedation Scale (RSS) score was documented. They received glycopyrrolate premedication. DEX subjects received 1mcg/kg DEX loading dose over 10 min followed by 0.7 mcg/kg/hr DEX maintenance infusion. PBO subjects an equal loading and maintenance dose of NaCl. Following the beginning of maintenance infusion any subject with an RSS score equal 1 received rescue 0.5 mg midazolam (MDZ) until RSS score was >2. After topical anesthesia (lidocaine) and RSS score >2 achieved, nasal or oral intubation using a flexible fiberoptic bronchoscope was performed. MDZ was given as needed to maintain RSS score >2. Following successful intubation drug infusion was discontinued, general anesthesia induced and scheduled procedure proceeded. The anesthesiologists were queried about the AFOI. At 24-hour followup, the subjects were assessed for AFOI satisfaction. Blood analysis was

performed to assess safety.

RESULTS: Fewer DEX subjects than PBO subjects required rescue MDZ to achieve and/or maintain targeted sedation for AFOI (47.3% v 86.0%, p<0.001). The total dose of rescue MDZ was lower in DEX subjects than PBO subjects (1.07mg v 2.85mg, p<0.001). One DEX patient required additional medication other than MDZ to achieve targeted RSS; four PBO patients required supplemental fentanyl or propofol to maintain RSS>2. The anesthesiologists rated both groups similar in ease of intubation, hemodynamic stability and subject cooperation. The majority of the subjects in both groups did not recall feeling anxiety or pain during the AFOI and were highly satisfied with the procedure. Among subjects with the most difficult airways (Mallampati Class IV), fewer DEX subjects than PBO subjects required rescue MDZ for successful AFOI (66.7% v 91.7%). There were no statistically significant differences in the number of adverse events experienced by the two groups.

DISCUSSION: DEX was efficacious for sedation in subjects undergoing awake fiberoptic intubation. DEX was superior to PBO when rescue MDZ was required. DEX was safe and well tolerated. The incidence of treatment-emergent adverse events was similar among DEX-treated and PBO-treated subjects.

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S-216.

TITLE: EFFECT OF DEXMEDETOMIDINE USE ON POSTOPERATIVE NAUSEA AND VOMITING IN BARIATRIC SURGERY: A RETROSPECTIVE ANALYSIS

AUTHORS: J. J. Wright, R. E. Carter, A. R. Budak, T. K. Byrne, K. A. Morgan, M. D. McEvoy;

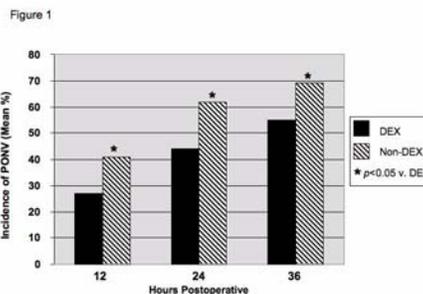
AFFILIATION: Medical University of South Carolina, Charleston, SC.

INTRODUCTION: Laparoscopic gastric bypass (LGB) is a commonly performed operation for morbid obesity, with a significant number of patients experiencing postoperative nausea and vomiting (PONV). The purpose of this study was to determine the effect, if any, of intra-operative dexmedetomidine (DEX) use on PONV.

METHODS: With IRB approval, patients who underwent LGB for morbid obesity from February 2005 until July 2007 at our institution were included in this retrospective analysis. The unadjusted comparison of the incidence of PONV between groups (DEX, n=120 and non-DEX, n=120) was computed using the product limit estimator and log rank statistic. A sensitivity analysis was conducted using a Cox proportional hazards model that utilized propensity scoring to adjust for gender, age, body mass index, weight, history of asthma, COPD, smoking, sleep apnea, PONV, hypertension, chronic pain, diabetes, as well as anesthesia and procedure time, opioid use and use of ketoralac.

RESULTS: The DEX group had a significant reduction in the rate of developing PONV in both unadjusted and adjusted comparisons. In particular, the use of DEX was associated with a 34% risk reduction in the rate of developing PONV over the entire 36-hour period of study (Hazard Ratio=0.659, p=0.019; Log Rank Statistic, p=0.0107). The largest relative difference was observed during the first 12 hours postoperatively; however, as illustrated in Figure 1, the magnitude of the difference in the cumulative incidences of PONV, as quantified by the relative risk, were clinically relevant at all three time points. The relative risk for the DEX v. non-DEX group of developing PONV at 12, 24, and 36 hours postoperatively was 0.667 (95% CI: 0.462, 0.962), 0.708 (95% CI: 0.551, 0.910) and 0.790 (95% CI: 0.644, 0.969), respectively. Of note, the total opioid usage between the two groups was

not different at any intra-operative or postoperative time-point.



DISCUSSION: PONV is a common complication following LGB. Our analysis indicates that intra-operative DEX use was associated with a significant reduction in PONV at 12, 24 and 36 hours postoperatively. Furthermore, after adjusting for PONV risk factors, patients receiving DEX infusions had a decreased incidence of PONV and experienced PONV at a slower overall rate. Further randomized studies will be needed to better quantify this effect.

S-217.

WITHDRAWN

S-218.

TITLE: SUGAMMADEX REVERSES NEUROMUSCULAR BLOCKADE AFTER CONTINUOUS INFUSION OF ROCURONIUM IN PATIENTS UNDER SEVOFLURANE OR PROPOFOL MAINTENANCE ANESTHESIA

AUTHORS: S. Wagner¹, F. K. Pühringer², C. Spies³, J. Scholz⁴, M. Heeringa⁵, H. Wulf¹;

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BACKGROUND: Sugammadex provides rapid and safe reversal of neuromuscular blockade (NMB) induced by single and repeat bolus doses of rocuronium. In this study, we assessed equivalence in recovery from NMB with sugammadex after continuous infusion of rocuronium in patients randomized to maintenance anesthesia with either sevoflurane or propofol.

METHODS: Patients were enrolled if they were aged 20-65 years, ASA class 1-3 and scheduled to undergo surgery of 2-5 hours with general anesthesia requiring the use of rocuronium. Anesthesia was induced with intravenous (IV) propofol and an opioid and maintained with an opioid and either sevoflurane or propofol according to randomization. All patients received a single IV dose of rocuronium 0.6 mg/kg followed by continuous infusion of rocuronium. The rocuronium infusion was adjusted to maintain NMB at zero response to train-of-four (TOF) stimulation and a post-tetanic count of ≤ 10 responses over ≥ 90 min. A single IV bolus dose of sugammadex 4.0 mg/kg was administered at the end of the rocuronium infusion at a T1 of 3-10%. NMB was monitored by acceleromyography (TOF-Watch® SX) at the adductor pollicis muscle. The primary efficacy variable was time from start of administration of sugammadex to recovery of the TOF ratio to 0.9. Equivalence between groups was shown if the 95% confidence

interval (CI) for the between-group difference was within ± 60 sec. Pharmacokinetics (rocuronium) and safety were also assessed.

RESULTS: A total of 52 patients were randomized, 51 of whom received sugammadex (sevoflurane group, n=26; propofol group, n=25). Median recovery time from start of sugammadex administration to a TOF ratio of 0.9 was 1.3 min in the sevoflurane group and 1.2 min in the propofol group. The estimated difference in recovery time between groups was 9 sec (95% CI -6, +20 sec). Since this CI is entirely within the pre-defined interval, equivalence was shown. Rocuronium infusion rate was slightly lower and the duration of infusion was shorter under sevoflurane compared with propofol maintenance anesthesia (median 0.43 versus 0.46 mg/kg/h and 2.1 versus 2.6 hours, respectively). Plasma concentrations of rocuronium before administration of sugammadex were 33% lower in the sevoflurane group than in the propofol group, with similar variability in both groups. Sugammadex was well-tolerated and no serious adverse events were reported. There were no reports of reoccurrence of NMB based on neuromuscular monitoring and no patients had clinical evidence of reoccurrence of NMB or residual NMB.

CONCLUSION: Sugammadex 4.0 mg/kg is equally effective and well tolerated for reversal of NMB after continuous infusion of rocuronium in patients in whom anesthesia is maintained with either sevoflurane or propofol.

S-219.

TITLE: RESPIRATORY COMPROMISE PRECEDES ADEQUATE ANESTHESIA FOR ESOPHAGEAL INSTRUMENTATION WHEN USING REMIFENTANIL AND PROPOFOL COMBINATIONS

AUTHORS: B. R. Randall, K. B. Johnson, C. D. LaPierre, D. R. Westenskow, T. D. Egan;

AFFILIATION: University of Utah, Salt Lake City, UT.

INTRODUCTION: Respiratory depressant effects of propofol (P) and remifentanil (R) are worrisome when used in a monitored anesthesia care setting with spontaneously breathing patients. Recent work has led to the development of modeling tools that characterize drug effects (analgesia, sedation, etc) for selected drug combinations. We explored how well various R-P concentration pairs would allow esophageal instrumentation (EI) yet avoid respiratory compromise (RC). Our hypothesis was that there exist R-P concentration pairs that allow EI yet avoid RC.

METHODS: Twenty four volunteers received 15 different combinations of R & P. Responsiveness to EI with a 42 Fr bougie, sedation level (using the observer assessment of alertness/sedation (OAA/S) scale), and presence of RC were measured at each concentration pair. An inductive plethysmograph was used to measure chest wall movement. A tight fitting face mask attached to a flow meter was used to measure airway flow. Respiratory depression was defined as fewer than 2 respiratory efforts in 30 seconds and airway obstruction was defined as absence of airway flow in the presence of a respiratory effort. RC was defined as the presence of respiratory depression or airway obstruction. Models were built to predict the probability of an OAA/S < 2, no response to EI, and presence of RC across a range of clinically relevant R-P concentration pairs. Model predictions of 50% probability of each response were superimposed to identify concentration pairs that provide no response to EI but avoid RC.

RESULTS: Figure 1 presents model predictions for OAA/S < 2, no response to EI, and RC. When concentration pairs were high enough to permit EI, volunteers had to be prompted to breathe or the airway had to be opened. Low P and high R concentrations required volunteers to be

prompted to breathe despite EI. High P low R concentrations led to airway obstruction requiring head tilt/chin lift. EI often relieved airway obstruction. We identified no region of R-P concentration pairs that had a high probability of no response to EI yet a low probability of RC.

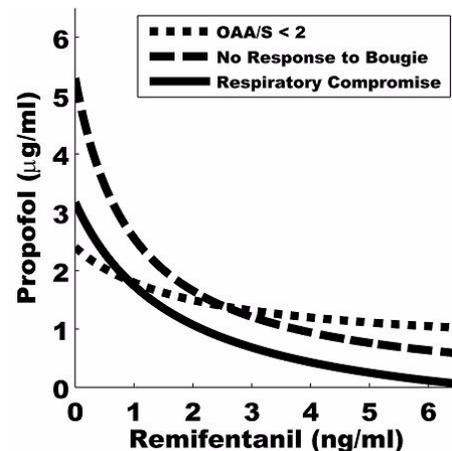


Figure 1

DISCUSSION: Our results did not confirm our study hypothesis. Our analysis revealed that RC preceded adequate anesthesia for EI. These results suggest that maintaining R-P concentration pairs at levels that blunt response to EI would lead to unacceptable RC.

S-220.

TITLE: ECONOMICS OF RETURN OF PATIENTS WITH POSTOPERATIVE NAUSEA AND VOMITING: SHOULD WE TREAT ALL SURGICAL PATIENTS PROPHYLACTICALLY?

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INTRODUCTION: Patients rank postoperative nausea and vomiting (PONV) in the top five most undesirable outcomes of surgery and are willing to pay \$100 out of pocket to prevent it.(1) Thirty percent of all surgical patients experience PONV.(2-4) This hospital profit/loss study was conducted to determine whether it is financially feasible to prophylactically treat all surgical patients for PONV regardless of predetermined PONV risk.

METHODS: This retrospective study was done with institutional approval and with waiver of patient consent. We anonymously reviewed all surgical cases from June 2005 to June 2007 with the PONV billing code (787.01). The PONV risk factors for these patients were assessed as well as the cost associated with readmission with PONV as the chief complaint. Risk factors assessed were 1) history of PONV or motion sickness, 2) history of nonsmoking 3) postoperative opioid use and 4) female gender (5).

RESULTS: Of the total number of surgeries performed during the specified two-year time period (56,532 surgeries), 1,783 (3.15%) billed for PONV. Twenty-eight of these PONV patients (1.57%) returned to the hospital with PONV. Four (0.22%) were admitted to the hospital. The remainder were treated in the emergency department and released. Of the returning PONV patients, two had one risk factor, five had two risk factors, 20 had three risk factors and two had all four risk factors. The total billable charges for PONV for these returning patients were \$83,674; the total reimbursements were \$25,816. The reimbursement rate was 31%. The total expenses for these patients were \$24,123 yielding a net profit of \$1,693 for the hospital to treat these returning patients. The average charge/dose of antiemetic drug is \$3.66. If we had treated every surgical patient in this period with three doses of an antiemetic drug on average, regardless of PONV risk factors, then the

total reimbursement (assuming the 31% rate) would have been \$192,424. The drug cost would have been \$51,557 (average cost/dose = \$0.304). The net profit to the hospital would have been \$140,866.

DISCUSSION: Our economic model shows that it would have been feasible to treat our entire surgical population prophylactically for PONV. We should do a better job recognizing and treating patients who are at high risk for PONV. Since most patients with post discharge PONV do not return for treatment, further studies are needed to determine if it is medically warranted to treat all patients prophylactically for PONV to improve comfort and satisfaction.

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S-221.

TITLE: OFFSET / ONSET RATIO FOR MUSCLE RELAXANTS: CLINICAL ASSESSMENT FOR COMPARISON

AUTHORS: D. Steinberg¹, G. H. Steinberg²;

AFFILIATION: ¹Hospital Clinicas Caracas & Policlínica Mendez Gimón, Caracas, Venezuela, ²School of Medicine, Central University of Venezuela, Caracas, Venezuela.

INTRODUCTION: Offset/Onset ratio for rocuronium has been shown to be greater than for other muscle relaxants when a special blood flow free model is used⁽¹⁻²⁾. The aim of present trial is to further investigate if this findings are supported by regular clinical monitoring and could be extensive to other drugs similar and dissimilar to rocuronium.

MATERIAL & METHODS: Four groups of elective and consenting patients received equieffective doses of either rocuronium (n=25, maximal effect 92±3%), vecuronium (n=30, 94±3%), mivacurium (n=20, 93±4%) or rapacurium^(*) (n=25, 93±6) during induction with intravenous agents and nitrous oxide. Using electromyography, initial onset time (up to 80% block), maximal blockade, onset time, recovery time between 10 and 25% block and clinical duration (from administration to 25% spontaneous recovery), were assessed. For onset, speed of action (SEC%) were calculated as the ratio between fractional time and block: **initial** until 80% (ONS^{INI}), **final**: from 80% to maximal block (ONS^{FIN}) and from drug administration to maximal block (SA). For offset, speed of recovery (SEC%) was calculated as the ratio between fractional time of recovery and block: between maximal block and first 10% spontaneous recovery (^{1st}REC), from 10 to 25% recovery (^{2nd}REC) and for the time of clinical duration (SR). Offset/onset ratio was used for comparisons and Wilcoxon signed rank test for statistical analysis.

RESULTS: Poor correlation was found between parameters (R² range: 0,000033 and 0,3229874). Consistently offset/onset ratio was statistically significant greater for rocuronium than other muscle relaxants (Table 1).

Table 1	ROC	VEC	MIV	RAP
^{1st} REC/ONS ^{INI}	757±481	304±243 ^{ff}	274±194*	228±112 ^{ff}
^{1st} REC/ONS ^{FIN}	133±71	104±106 ^{ff}	135±136*	56±47 ^{ff}
^{1st} REC/ONS ^{SR}	22±9	9±2 ^{ff}	6±2**	5±2*
^{2nd} REC/ONS ^{FIN}	4±1	2±1 ^{ff}	3±2**	1±0.9*
^{1st} REC/SA	418±204	222±190 ^{ff}	222±162*	143±71 ^{ff}
^{2nd} REC/SA	12±4	6±2 ^{ff}	5±1*	4±1**
SR/SA	31±8	16±7 ^{ff}	17±8*	13±5 ^{ff}

^{ff}): p= 0.0001. (*): p= 0.020. (**): p= 0.022 vs= ROC

DISCUSSION: Present results support previous findings regarding comparisons of rocuronium to slow onset and short, intermediate or long lasting relaxants⁽¹⁻²⁾ and is now extensive to the fast and short acting rapacurium. In addition shows that usual clinical monitoring methods can be used for such an assessment. Suggestions are driven that comparisons can also be made with rapid or slow onset or offset drugs but still, this findings do not clarify their mechanism of action.

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(*) rapacurium's data comes from a previous presentation: Anesthesiology 2003; 99: A1128

S-222.

TITLE: A PROPOFOL/REMIFENTANIL PHARMACODYNAMIC MODEL PREDICTS PATIENT RESPONSE TO ENDOSCOPY

AUTHORS: D. J. Wiest¹, C. LaPierre², K. Johnson², N. Syroid², P. L. Gambus³, E. W. Jensen⁴,

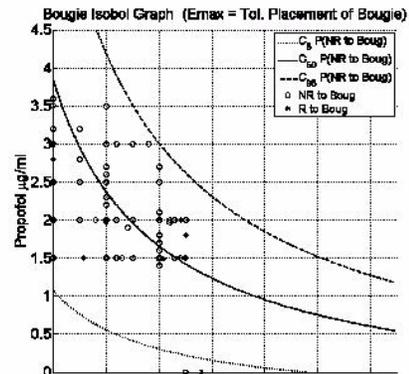
AFFILIATION: ¹Oregon Health & Science University School of Medicine, Portland, OR, ²Department of Anesthesiology, University of Utah, Salt Lake City, UT, ³Anesthesia Department, Hospital Clinic de Barcelona, Barcelona, Spain, ⁴Centre de Recerca en Enginyeria Biomedica (CREB), Universitat Politècnica de Catalunya, Terrassa, Spain.

INTRODUCTION: Pharmacokinetic and pharmacodynamic drug interaction models describe the synergistic relationship between remifentanyl and propofol for loss of consciousness, return of responsiveness, and response to noxious stimuli (1-2). Should the models predict patient responses with sufficient accuracy, their use in real time may bring more sophisticated clinical pharmacology information to the point of care. We measured how accurately propofol and remifentanyl models predicted patient responses during endoscopic procedures.

METHODS: We delivered increasing amounts of propofol and remifentanyl to volunteers, recorded their responses to insertion of a bougie, and constructed a response surface model using a Logit model construct (3-4). Controlled amounts of propofol and remifentanyl were given to 110 patients undergoing endoscopic procedures using Schnider and Minto (5-8) pharmacokinetic models (9). These two separate studies both used effect site target controlled infusion pumps. Levels of sedation and responses to insertion and extraction of an endoscope and bougie were measured.

RESULTS: The effect site concentrations at the time the endoscope was inserted are shown in figure 1. The curves show the drug concentrations where 5%, 50%, and 95% of volunteers did not respond to the insertion of a bougie. There were 88 patients that did not respond (open circles) and 15 that responded with a gag reflex (stars). At the time of endoscope insertion patients had a 45 +/- 23% probability of responding to bougie insertion. Those patients who had a gag response during the insertion of the

endoscope had a 31 +/- 22% probability of responding to bougie insertion. Those that did not respond had a 48 +/- 22% probability of responding.



DISCUSSION: The results show that a propofol and remifentanyl pharmacodynamic model developed using data collected in volunteers accurately predicted patients response to the insertion of an endoscope. If used in real time, the model may improve drug management by predicting patient responses before they actually occur.

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S-223.

TITLE: A RANDOMIZED, DOUBLE-BLINDED ASSESSMENT OF THE USE OF DEXMEDETOMIDINE FOR AWAKE FIBEROPTIC INTUBATIONS

AUTHORS: M. Dorsey, C. Aveyard, A. Ovassapian, D. B. Glick;

AFFILIATION: University of Chicago, Chicago, IL.

INTRODUCTION: To achieve proper sedation during awake fiberoptic intubation (AFI), clinicians commonly administer a regimen of fentanyl and midazolam. These drugs are anxiolytic, sedative and amnestic to ensure the patient's comfort, but fentanyl decreases ventilatory drive, which may lead to hypoxemia or apnea, especially when combined with midazolam.¹ The alpha-2 agonist dexmedetomidine (DEX) has been identified as a potentially useful adjunct during AFI, because it does not decrease ventilatory drive, and patients can be easily roused during sedation if stimulated. A number of case reports have documented the efficacy of DEX during AFI.^{2,3} This study is the first to examine the potential benefits of DEX as an adjunct to AFI in a double-blinded randomized clinical trial.

METHODS: IRB approved written consent was obtained from patients who required AFI. All patients were premedicated with 1 - 2 mg of midazolam and 0.2 mg of glycopyrrolate. Infusion of either saline or DEX (at a rate of 0.7 mcg/kg/hr) began in the pre-op holding area. The airway was anesthetized using 5% lidocaine ointment to the base of the tongue, 4% lidocaine spray to the oropharynx, and a transtracheal injection of 4% lidocaine to anesthetize the chords before intubation was performed. Hemodynamic parameters were recorded at one-minute intervals. Fentanyl was titrated in doses of 25-50 mcg to achieve the desired level of sedation. The time required to intubate was recorded as well as patient satisfaction post-operatively. T-tests were performed on continuous normalized data.

RESULTS: We enrolled 28 patients, randomized to either the DEX or placebo group. We found that DEX significantly attenuated the rise in heart rate during AFI. On average, patients receiving DEX were intubated faster and were given less fentanyl. Assignment to either the DEX or placebo groups did not significantly affect satisfaction. There were 2 cases of hypoxemia (defined as spO₂s of <90%) in the placebo

group, lasting 13 and 4 minutes, and one case in the DEX group, lasting 1 minute.

	DEX (n = 14)	Placebo (n = 14)	p
Percent increase in Heart Rate	13±16%	28±20%	0.04
Time to Intubate (sec)	129±77	197±164	0.17
Fentanyl (mcg/kg)	1.2±0.9	1.6±0.7	0.20

DISCUSSION: DEX is a safe, useful adjunct for AFI. Compared to placebo, DEX attenuates the rise in heart rate and may decrease the time to intubate as well as the fentanyl required for sedation during AFI.

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S-224.

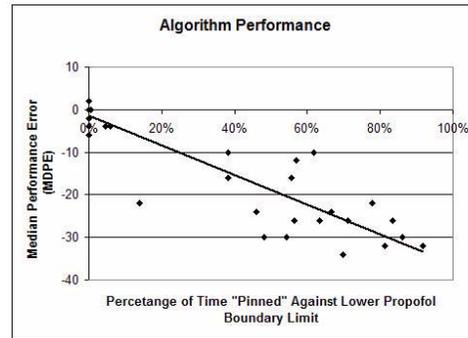
TITLE: EVALUATION OF A TARGET-CONTROLLED PROPOFOL DELIVERY ALGORITHM BASED ON STATE ENTROPY

AUTHORS: D. M. Mathews, P. Cirullo, D. Kopman, A. Divan;
AFFILIATION: St Vincent Catholic Medical Center, New York, NY.

INTRODUCTION: This study was done to assess the performance of a target-controlled, proportional-integral-derivative (PID) algorithm for propofol delivery utilizing state entropy (SE, GE Healthcare, Helsinki, Finland). The algorithm was designed to work in conjunction with a closed-loop remifentanyl delivery system previously described.¹

METHODS: Forty patients undergoing lower extremity surgery were studied as part of an IRB approved protocol. Target-controlled infusions of propofol and remifentanyl were delivered via RUGLOOP (M Struys and T DeSmet, Ghent, Belgium). Initial effect-site concentrations (Ce) were 4.0 ng ml⁻¹ for remifentanyl and 5.0 mcg ml⁻¹ for propofol. Following induction, closed-loop administration of remifentanyl was initiated. The state entropy value was entered manually every five seconds into an Excel spreadsheet that contained the PID algorithm and displayed the suggested propofol Ce; propofol target Ce was adjusted manually. Lower and upper boundaries for propofol were 1.5 and 9.0 mcg ml⁻¹ and for remifentanyl were 2.5 and 10.0 ng ml⁻¹, respectively. The PID algorithm was written to maintain the SE at 50. The median performance error (MDPE) and the percentage of time that the propofol Ce was "pinned" against the lower propofol boundary limit (SE<50, propofol Ce =1.5 mcg ml⁻¹) during surgery were determined.

RESULTS: In 20 patients the percentage of time pinned (PTP) was 10% or less; in these patients the MDPE (median, range) was 0, -6 to 2. In 20 patients the PTP was >10%; in these patients the MDPE was -26, -10 to -34. The figure demonstrates the significant relationship between PTP and MDPE (r²=0.82, p<.001). The average (SD) remifentanyl concentration (ng ml⁻¹) was significantly greater in the elevated PTP group, 6.9 ± 1.7, compared to the low PTP group, 4.4 ± 1.3 (t-test, p<0.001).



DISCUSSION: The algorithm performance was excellent in the 20 patients whose propofol Ce was maintained above 1.5 mcg ml⁻¹. Performance deteriorated with increasing PTP. Typically, in these patients, the remifentanyl closed-loop infusion led to comparatively higher levels, resulting in combinations of high remifentanyl/low propofol Ce. These data suggest that as a closed-loop controller for propofol administration, the SE-based PID algorithm will demonstrate better performance measures in patients who are not maintained in a high remifentanyl/low propofol state.

REFERENCE: ¹Anesthesiology 2007; 107, A-735.

S-225.

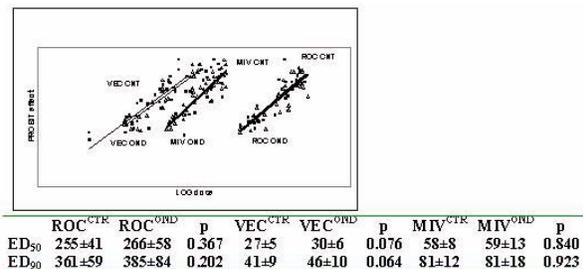
TITLE: THE EFFECT OF ONDANSETRON ON ROCURONIUM, VECURONIUM AND MIVACURIUM POTENCY

AUTHORS: D. Steinberg¹, G. H. Steinberg²;
AFFILIATION: ¹Hospital Clinicas Caracas & Policlínica Mendez Gimón, Caracas, Venezuela, ²School of Medicine, Central University of Venezuela, Caracas, Venezuela.

INTRODUCTION: Ondansetron (OND), a 5-HT₃ antagonist is prophylactically used to reduce postoperative nausea and vomiting⁽¹⁾ and sometimes for prevention of pain from injection of both propofol and rocuronium⁽²⁾. After OND any significantly change on atracurium dose-response curves was reported⁽³⁾. The aim of present trial is to investigate potency changes induced by OND on rocuronium (ROC), vecuronium (VEC), and mivacurium (MIV).

MATERIAL & METHODS: Three similar groups (n= 66) of adult elective and consenting patients received fractional successive doses of ROC, VEC or MIV, during induction with intravenous agents and nitrous oxide; either alone (control) or preceded by OND (study) as part of pre-anesthetic medications. Using electromyography, maximal effect was assessed. After log-dose/probit-effect transformation a regression line was developed and slope of the cumulative curve obtained. ED₅₀, ED₉₀ and ED₉₅ were calculated for each patient. T test and 0.05 level of significance were used for intra-group (control vs study) comparisons.

RESULTS: Patients in the study groups received 11±2 µg·Kg⁻¹ OND (mean ± SD). ED₅₀, ED₉₀ and ED₉₅ are shown in Table 1 and Fig 1.



DISCUSSION: The possibility exists for the presence both centrally and peripheral of 5-HT₃ receptors and that OND may affect neuromuscular transmission (NMT)⁽³⁾. In fact, NMT in human non-voluntary isolated detrusor muscle is facilitated by 5-HT₄ subtype receptor⁽⁴⁾ and experimentally a biphasic response to OND is elicited at the guinea-pig ileum⁽⁵⁾. But so far present results shows that in humans no interaction between OND and the muscle relaxant's potency should be expected.

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S-226.

TITLE: THE CORRELATION BETWEEN KETAMINE AND PTSD IN BURNED SERVICE MEMBERS

AUTHORS: L. L. McGhee¹, C. V. Maani¹, T. H. Garza¹, K. M. Gaylord¹, I. H. Black²;

AFFILIATION: ¹US Army Institute of Surgical Research, Ft Sam Houston, TX, ²Brooke Army Medical Center, Ft Sam Houston, TX.

BACKGROUND: Up to 17% of returning OIF/OEF uninjured veterans reported symptoms consistent with PTSD. Predisposing factors for PTSD include: experiencing a traumatic event, threat of injury, and untreated pain. Ketamine is used at low doses as part of a multi-modal analgesia. However, since ketamine is associated with psychosomatic effects, there is a concern that ketamine may increase the risk of developing PTSD. This study investigated the prevalence of PTSD in OIF/OEF service members who were treated for burns in a military treatment center and compared the prevalence of PTSD in patients receiving ketamine during their operation(s) compared to patients not receiving ketamine

METHODS: After IRB approval, the charts of all OIF/OEF soldiers with burns who completed the PCL-M screening tool (2002-2007) were reviewed. Morphine equivalent units were calculated using standard conversion factors.

RESULTS: The United States Army Institute of Surgical Research (USAISR) received 603 burned casualties from OIF/OEF, of which 241 completed the PCL-M. Of those, 147 soldiers underwent at least one operation at the USAISR. During surgery, 119 received ketamine and 28 did not receive ketamine. Of those receiving ketamine, the prevalence of PTSD was 26.9% (32/119) versus 46.42% in those not receiving ketamine (13/28)*** p=0.044 by Mann Whitney test.

Ketamine correlates with PTSD

Ketamine	r=-0.166 * (p=0.044)
TBSA	r=-0.085 (p=0.308)
ISS	r=-0.092 (p=0.266)
ICU days	r=0.087 (p=0.295)
Morphine equivalents/ operation	r=-0.049 (p=0.555)
Total morphine equivalents in OR	r=0.046 (p=0.584)
Number of operations	r=-0.045 (p=0.588)

S-227.

TITLE: A COMPARITIVE STUDY USING PRIMARILY DEXMEDETOMIDINE OR MIDAZOLAM FOR SEDATION DURING ELECTIVE AWAKE FIBEROPTIC INTUBATION

AUTHORS: S. D. Bergese, S. Bender, T. McSweeney, S. Fernandez, K. Sage;

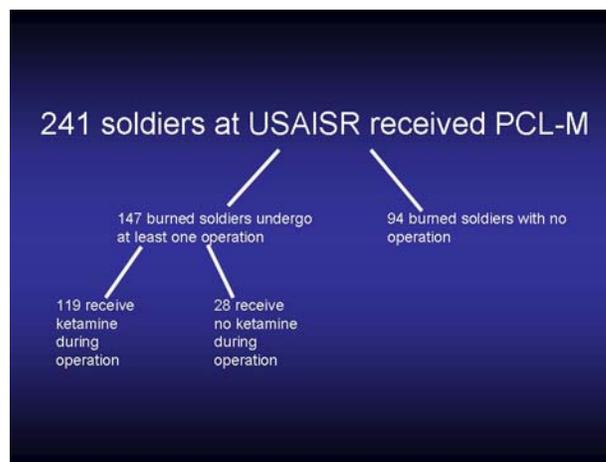
AFFILIATION: The Ohio State University, Columbus, OH.

INTRODUCTION: An awake fiberoptic intubation (AFOI) is indicated for patients with an anticipated difficult airway secondary to the anatomy, airway trauma, morbid obesity or unstable cervical spine injuries.¹ Although patients may be sedated for an AFOI, they need to be responsive and capable of maintaining their own airway without assistance. The objective of this study was to evaluate the efficacy of dexmedetomidine (DEX) versus midazolam (MDZ) for sedation during elective AFOI.

METHODS: This double-blinded comparison study was conducted with institutional approval and informed written patient consent. Fifty-five subjects (DEX=31; MDZ=24) entered the study. All subjects' vital signs were monitored at one-minute intervals during the AFOI. All subjects received 0.2 mg glycopyrrolate IV premedication. MDZ subjects received 0.05 mg/kg IV MDZ with additional doses given until the subject was adequately sedated. DEX subjects received 0.02 mg/kg MDZ followed by 1 µg/kg DEX. DEX subjects then received an infusion of 0.1 µg/kg/hr DEX and titrated to 0.7 µg/kg/hr until the subject was adequately sedated. AFOI was then performed in both groups. The anesthesiologist rated the AFOI ease of placement. An observer rated the subjects' reaction to placement. Within 24 hours post surgery, the subject was asked whether they recalled the AFOI and to rate their satisfaction of the intubation.

RESULTS: There were no demographic differences between the two subject groups. The DEX subjects were observed to be significantly calmer than the MDZ subjects during AFOI and had less adverse reaction to the AFOI. The DEX subjects were more satisfied with the AFOI than the MDZ subjects. There were no significant hemodynamic differences between the two subject groups.

DISCUSSION: DEX was more effective than MDZ for sedation in



DISCUSSION: A score of 44 or higher on the PCL-M is considered a positive screen for PTSD. The prevalence of PTSD in burned soldiers (241 soldiers) at USAISR (27.7%) using the PCL-M is similar to averages of 8-45% found in civilian burn populations. There are multiple mechanisms that might explain this including: better pain control, NMDA antagonism, and memory encoding and consolidation decrements.

CONCLUSIONS: Patients receiving ketamine had a lower prevalence of PTSD than soldiers receiving no ketamine during their surgeries despite having larger burns, higher injury severity scores, undergoing more operations, and spending more time in the ICU.

non-intubated patients with high-risk airways undergoing AFOI. DEX was well tolerated in comparison to MDZ sedation.

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S-228.

TITLE: THE INFLUENCE OF GENDER ON MIVACURIUM PHARMACODYNAMICS: A COMPREHENSIVE STUDY

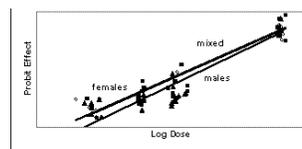
AUTHORS: D. Steinberg¹, G. H. Steinberg²;

AFFILIATION: ¹Hospital Clinicas Caracas & Policlinica Mendez Gimón, Caracas, Venezuela, ²School of Medicine, Central University Venezuela, Caracas, Venezuela.

INTRODUCTION: Gender studies have been extended to anesthesiology⁽¹⁾. Controversy about the effect of gender on vecuronium neuromuscular block has recently been clarified⁽²⁾. But no apparently studies with mivacurium (MIV) have been reported. This is the aim of present trial.

MATERIAL & METHODS: Three groups (n= 15 e/a) of elective, mixed gender (MIX) and consenting patients received single doses of MIV (20, 40 and 100 µg.Kg⁻¹). Using electromyography, maximal effect was assessed and after log-probit transformation ED₅₀, ED₉₀ and ED₉₅ obtained for each patient from the regression line. Two additional groups (males (MAL) n=26, females (FEM) n=27) received single dose of MIV and ED₅₀, ED₉₀ and ED₉₅ were obtained by the same method. Three additional groups (MAL, n=26, FEM, n=26 and MIX, n=20) received 100 µg.Kg⁻¹ and early onset time (EOT), up to 80% of block, onset time (OT), maximal block (MAX), recovery between 10-25% (Rec10-25), clinical duration (DUR) assessed by same method. Speed of action as the ratio between fractional block and time were calculated during initial phase, up to 80% blockade (INI), final between 80% and MAX (FIN) and global as OT/MAX ratio (GLO) and speed of recovery as the ratio between fractional recovery and time (SR) were calculated. Analysis of variance, Student, Newman, Keuls and T test used for statistical comparisons.

RESULTS: Slope for the curves did not differ statistically (p=0.866). Not statistical significant differences were noticed between potencies for MIX, MAL and FEM groups. Any statistical differences were noticed among pharmacodynamic parameters when 100 µg.Kg⁻¹ were given to MIX, MAL or FEM (Fig & Table 1)



	1)FEMALE	2)MALE	3)MIXED	SIG
ED ₅₀	46±10	51±11	47±12	p=0.310
ED ₉₀	79±17	83±18	80±20	p=0.777
ED ₉₅	95±21	98±21	97±24	p=0.895
E.O.T.	205±51	221±74	206±59	p=0.618
MAX	90±9	88±12	93±4	p=0.233
O.T.	312±62	317±55	283±43	p=0.09
DUR	11±5	14±8	15±7	p=0.177
Initial	2.5±0.6	2.7±0.9	2.5±0.7	p=0.619
Final	9.5±5.5	10±13	5.9±2.7	p=0.230
Global	3.5±0.9	3.7±1.2	3.04±0.5	p=0.060
Recv. Speed	46±25	56±31	53±29	p=0.484

DISCUSSION: Although an increased sensitivity to vecuronium has been described for females⁽³⁻⁴⁾, this has not been reproduced by a recent comprehensive study⁽²⁾. Gender has no significant effect on the relation between post-tetanic-count and T1 for rocuronium⁽⁵⁾. Time course for atracurium is not significantly different between female and male patients⁽⁶⁾. In conclusion: present results did not show any pharmacodynamic changes for MIV between male, female and mixed group of patients.

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Regional

S-229.

TITLE: REAL-TIME 3-DIMENSIONAL ULTRASOUND FOR CONTINUOUS INFRACLAVICULAR BRACHIAL PLEXUS BLOCKADE

AUTHORS: S. R. Clendenen, J. E. Freidenstein, N. J. Clendenen;
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BACKGROUND: There are a variety of techniques for targeting placement of an infraclavicular blockade, paresthesias, nerve stimulation and 2-dimensional ultrasound(2-D US) guidance all varying success and potential complications. 2-D US allows direct visualization of the advancing needle and neurovascular structures but only in a 2 dimensional plane.

METHODS: We describe a 3-dimensional ultrasound (3-D US) technique in which a Philips X 7-2 ultrasound probe (3-D IU-22, Andover, MA) is used for placement of an infraclavicular nerve block with improved spacial relationship of the advancing needle and nerve bundle with real-time manipulation of the US images. The 3-D US probe was positioned 2 cm medially and 2 cm caudal of the coracoid process. A 17- gauge insulated 50- mm Arrow® needle connected to a nerve stimulator (pulse duration 0.3 ms, current 1.5 mA, frequency 2 Hz) was advanced laterally toward the nerves under 3-D US visualization. (Fig. 1) After correct positioning was confirmed by appropriate distal motor nerve response, a19-ga stimulating catheter (Stimcath® Arrow International, Reading,PA) was advanced 5 cm under continuous stimulation and ultrasound guidance. The flow of local anesthetic from the catheter and its advancement and tracking around the nerve could be seen by real-time 3-D manipulation of the ultrasound images. After injection of 30 cc of local anesthesia the catheter was visualized lying across the nerve bundle. (Fig. 2)

The patient had a complete nerve block as confirmed by motor and sensory testing prior to undergoing successful total elbow arthroplasty.

DISCUSSION: The Philips matrix X 7-2 US probe provides a higher 3- D US frequency allowing for imaging of nerve bundles which can be manipulated in real-time to provide further evidence of a correctly positioned needle placement and spread of local anesthesia. This approach is especially useful in nerve blocks involving the brachial

plexus and any area of anatomy that has a dense population of neurovascular structures and individual anatomic variations. The 3-D US imaging can provide information of the entire anatomic region including nerve thickness and 360 -degree spatial relations.



Figure 1

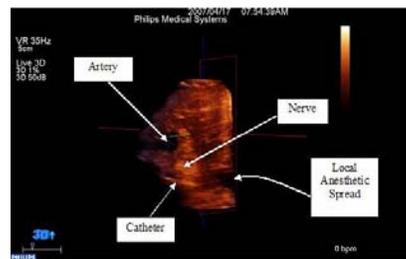


Figure 2

CONCLUSIONS: Advantages of 3-D US may include the ability to monitor correct needle placement and spread of local anesthetic along the nerve while manipulating the images real-time to provide additional information that cannot be identified with 2-D ultrasound alone.

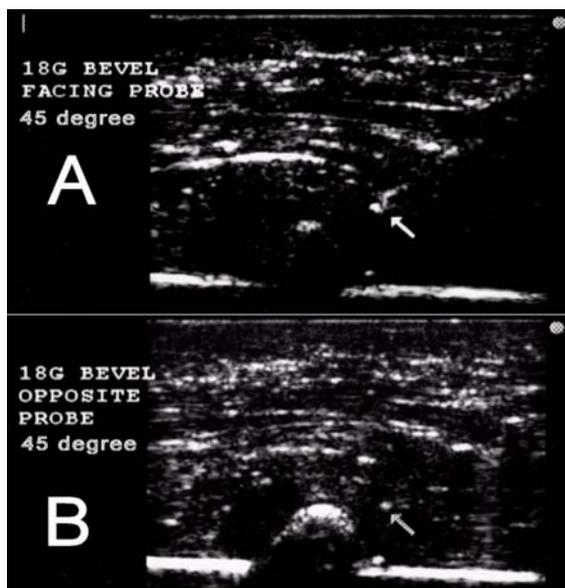
S-230.

TITLE: EFFECT OF VARIOUS NEEDLE TIPS AND THEIR BEVEL ORIENTATION ON THE QUALITY OF ULTRASOUND IMAGES WITH LINEAR AND CURVILINEAR TRANSDUCERS.

AUTHORS: N. S. Sandhu¹, N. H. Karuvannur²;
AFFILIATION: ¹University of California San Diego, San Diego, CA,
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INTRODUCTION: This study aimed to determine which needle tip and bevel orientation obtain the best ultrasound (US) image. The images of two types of needle tips in a chicken breast at 45 and 90 degree to US beam were studied. Their bevels were rotated to three different positions; bevel facing the transducer, opposite to transducer or bevel facing sideways. These were studied using both linear and curvi-linear probes. **METHODS:** Eighteen gauge needles with Touhy-Schiff tip(B.Braun) and 14 degree bevel tip (Arrow, Reading PA) were imaged in chicken breast muscles using a 7 MHz curvilinear probe (C 11, Sonosite, Bothell, WA) and a 13 MHz linear probe (Sonosite). The needle tip was imaged with bevel pointing towards or away from the transducer and rotated sideways with needle at 45 and 90 degrees to US beam. The needle tip images were observed and printed. **RESULTS:** All needles at 90 degrees to US beam provided the best needle tip image irrespective of tip or bevel orientation to transducer with both linear and curvilinear probes. With a curvilinear transducer the Touhy- Schiff needle at 45 degrees angle to US beam with the bevel facing towards the transducer provided the best quality image (Fig A). The needle bevel facing away from transducer procured the poorest image quality (FigB). The image quality with needle bevel facing sideways is intermediate. Using a linear probe and 14 degree needle at 45 degrees to US beam the needle shaft is not clearly seen but Touhy tip with its bevel facing the transducer is seen as a distinct dot. The image of tip was poor with tip bevel sideways or facing opposite to transducer. The 14 degree bevel needle provided less distinct image with bevel facing the transducer, sideways and opposite to probe had increasingly diminished quality respectively.

DISCUSSION: The Touhy tips were best seen with bevel facing the transducer when needle was aligned at 45 degrees due to its curved tip which reflects the ultrasound beams better than other needle orientations. 14 degree bevels had poor quality image especially with linear transducers. The needle tip image was not affected by bevel orientation or tip type when needles were at 90 degree to US beam with both linear and curvilinear transducers.



DISCUSSION: The Touhy tips were best seen with bevel facing the transducer when needle was aligned at 45 degrees due to its curved tip which reflects the ultrasound beams better than other needle orientations. 14 degree bevels had poor quality image especially with linear transducers. The needle tip image was not affected by bevel orientation or tip type when needles were at 90 degree to US beam with both linear and curvilinear transducers.

S-231.

TITLE: THE IMPACT OF ADDING MIDAZOLAM IN THREE DIFFERENT DOSES TO SPINAL BUPIVACAINE

AUTHORS: K. Radwan, H. Khafagy, M. El-Barr, M. A. Abosedira;
AFFILIATION: Theodor Bilharz Research Institute, Cairo, Egypt.

INTRODUCTION: Several investigators have demonstrated prolongation of bupivacaine -induced spinal anaesthesia adding midazolam (1-3). The optimum dose of midazolam has not identified. This prospective, randomised, double blind study was designed to evaluate the impact of adding midazolam to in three different doses to the quality & characteristics of spinal bupivacaine.

METHODS: Forty ASA I or II patients undergoing inguinal herniorrhaphy under were included & divided into 4 groups. Group B: received bupivacaine 10mg + 0.3 ml saline, group BM1 received bupivacaine 10 mg + midazolam 0.5mg in 0.1ml + 0.2 ml saline, group BM2 received bupivacaine 10 mg + midazolam 1mg in 0.2ml + 0.1 ml saline, group BM3 received bupivacaine 10 mg + midazolam 1.5 mg in 0.3ml. Spinal anaesthesia was performed at L2-3 level using 25G needle after administering a preload one litre of Hartmann's solution IV.

RESULTS: Patients were matching regarding demographic data, ASA status and operative time. The vital signs & the sedation score showed no significant differences between the four groups throughout the study period.

None of the patients in both groups exhibited post-operative complications, delay in recovery or home discharge.

Table 1. the characteristics of spinal anaesthesia & post-operative analgesia of the four groups.
*: p < 0.05

	B	BM1	BM2	BM3
No of Sensory blocked segments	16 ± 1.2	15.6 ± 0.8	16.5 ± 1	17 ± 0.7
Onset of sensory block (min)	10.2 ± 2	7.4 ± 1.7*	6 ± 1.3*	4.6 ± 0.5 *
duration (min)	275 ± 54	288 ± 50.2	295 ± 52*	377 ± 42.3 *
Rate of 2 segments regression (min)	21 ± 6.5	21.8 ± 7.5	19.8 ± 7.3	20 ± 7.1
No of Motor blocked segments	11 ± 0.6	12 ± 0.4	13 ± 0.7	12 ± 0.4
Onset of Motor block (min)	9 ± 1.4	7.3 ± 2.1*	6.1 ± 2*	6 ± 1.6*
Time to first Analgesia Request (hours)	4.2 ± 0.8	4.8 ± 0.8	5.7 ± 0.6 *	6 ± 0.4 *
24 Hr diclofenac Requirement (mg)	135 ± 62.5	90 ± 33.5*	75 ± 43.2 *	75 ± 25 *

S-232.

TITLE: COMPARISON OF STIMULATING VERSUS NON-STIMULATING CATHETER TECHNIQUE FOR CONTINUOUS INTERSCALENE BRACHIAL PLEXUS BLOCK BY POSTERIOR APPROACH FOR SHOULDER SURGERY

AUTHORS: G. Gopalakrishnan, R. Edward, S. Ram, P. Venkat;
AFFILIATION: Hull Royal Infirmary, Hull, United Kingdom.

BACKGROUND: There is continuing debate whether the use of stimulating catheters for continuous nerve blocks leads to improved clinical outcome such as reduction in pain scores and opioid consumption. We compared stimulating with non stimulating catheter for ISB by posterior approach for shoulder surgeries for its analgesic efficacy and patient satisfaction.

METHODOLOGY: 40 patients undergoing shoulder surgery were randomised to receive ISB using the posterior approach with a stimulating catheter (Group A) or non stimulating catheter (Group B). The block technique was standardised in both groups. Catheter placement time, onset, distribution of sensory and motor block were assessed by a blinded observer after injection of 2% lignocaine with 1:200,000 adrenaline 30-35mls.

Post-op care was standardized with 0.2% Ropivacaine(L.A) infusion 5mls/hr, bolus PCA 3 mls every 20 mins. Post-op pain score; opioid, L.A consumption and patient satisfaction were observed.

RESULTS: Post op pain score at 24 hrs, 36hrs and rescue opioids required were significantly high in Nonstimulating group. (Tables).

	Stimucath(A)	NonStimucath(B)	P value
Catheter Placement Time(min)	5.8 (2.2)	5.7 (2.2)	NS
Sensory Block onset (min)	11 (6.3)	9.4 (4.6)	NS
Motor Block Onset (min)	8.3 (4.4)	10.8 (5.9)	NS

Mean (Standard Deviation) NS- statistically not significant

DISCUSSION: The results of this study reveal that the addition of midazolam to spinal bupivacaine speeds the onset of sensory & motor blockade, prolongs the time to first analgesic requirement & reduces the post-operative analgesic requirement in a dose dependent manner & without increasing morbidity or delaying the rate of recovery from spinal anaesthesia.

These results confirm the results of other investigators who reported the prolongation of spinal anaesthesia by spinal midazolam (1-3). The improvement of adding the lower dose of midazolam seems clinically modest compared to the higher two doses. Of the three doses used, the higher dose (1.5mg) seems to the optimum.

The finding that adding midazolam to low dose spinal anaesthesia improves the quality of anaesthesia without delaying recovery from spinal anaesthesia or increasing the complications rate, favours its use in ambulatory surgery.

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3. Eur J Anaesthesiol. 2003; 20(11):904-10

Pain score	Stimucath	Non-Stimucath	P value
VRS r 24hrs	0[0,0]	1[0,1]	0.001
VRSm 24hrs	1[0,1]	1[1,1]	0.074
VRS r 36hrs	0[0,0]	1[0,1]	NS
VRSm 36hrs	1[0,1]	1[0,2]	NS
No. of patients required Opioids	5	13	0.009
Patient satisfaction	9[8,10]	8[5,10]	NS
L.A (first 24 hrs) Consumption(mgs)	211(108)	215(151)	NS

Median [Lower, upper quartile],
VRS-verbal rating score r-rest, m-movement

CONCLUSION: Compared to non-stimulating catheter group, pain score and opioid consumption were significantly less in the stimulating catheter group.

REFERENCE:

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S-233.

TITLE: THE ADDITION OF MIDAZOLAM TO ROPIVACAINE FOR CAUDAL ANALGESIA FOR HAEMORRHOIDECTOMY : DOES IT MAKE A DIFFERENCE?

AUTHORS: M. A. Abosedira, M. A. Abosedira, H. Khafagy, K. Radwan, M. El-Barr;

AFFILIATION: Theodor Bilharz Research Institute, Cairo, Egypt.

INTRODUCTION: Several investigators have demonstrated prolongation of bupivacaine-induced caudal analgesia in children by adding midazolam (1-3). There are no reports on the use of ropivacaine-midazolam admixture in adults.

This prospective, randomised, double blind and controlled study was designed to evaluate the impact of adding midazolam to ropivacaine caudally.

METHODS: Forty ASA I or II patients undergoing haemorrhoidectomy under GA were included. After induction of standardized general anesthetic technique, all patients received 0.5 ml.kg⁻¹ of either ropivacaine 0.2% (R group) or ropivacaine 0.2% plus midazolam 50 µg.kg⁻¹ (MR group). Intra and postoperative vital signs, post-operative visual analogue pain score (VAS), Bromage score, sedation score, the time to first analgesia request, analgesic consumption and adverse effects were assessed.

RESULTS: Patients were matching regarding age, weight, gender distribution, ASA status and operative time.

The vital signs showed no significant differences between the two groups throughout the study period.

The duration of analgesia was significantly longer (26.8%) in the MR group (5.2 hours) compared to the R group (4.1 hours). All patients in both groups exhibited a pain score of zero during the first two post-operative hours. After that, 14.3% of patients in the MR group exhibited mild pain (VAS <3) compared to 80% in the R group. During the fourth hour, 57.2% of patients in the MR group exhibited mild pain compared to 100% in the R group. By the fifth hour, 42.9% of patients in the MR group exhibited moderate pain (VAS score ≥ 3) requiring rescue analgesia compared to 100% in the R group. The 24 hours meperidine requirement was reduced by 41.7% in the MR group.

The sedation score were higher in the MR group (85.7%, 28.6% respectively) compared to the R group (60% and 20%, respectively) only upon admission to the recovery room and at 15 minutes later.

There was no evidence of motor blockade throughout the study period except at recovery room admission when significantly more patients with evidence of Bromage 1 or 2 were reported in the MR group (85%) compared to the R group (60%). None of the patients in both groups exhibited post-operative complications or delayed recovery or home discharge.

DISCUSSION: These results reveal that the addition of midazolam to caudal ropivacaine significantly prolongs its post-operative analgesia without significant side effects. These findings are consistent with the findings of previous studies performed on children (1-3).

The higher sedation score suggests systemic absorption of caudally administered midazolam. A pharmacokinetic study of this admixture is warranted. The use of this admixture seems suitable for ambulatory surgery in adults and optimum midazolam dosage needs to be investigated.

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S-234.

TITLE: VASOPRESSIN IS ASSOCIATED WITH ADVERSE OUTCOMES IN RESUSCITATION OF RATS FROM BUPIVACAINE-INDUCED ASYSTOLE

AUTHORS: G. Di Gregorio¹, R. Ripper², K. Kelly², G. Weinberg³;

AFFILIATION: ¹University of Illinois at Chicago and Universita' Degli Studi di Padova, Chicago, IL, ²University of Illinois at Chicago, Chicago, IL, ³University of Illinois at Chicago and Jessie Brown VA Medical Center, Chicago, IL.

INTRODUCTION: The combination of vasopressin (V) and epinephrine (EPI) has been proposed for treatment of bupivacaine-induced cardiac arrest¹. It has also been previously demonstrated in an in vivo rat model that intravenous lipid emulsion (L) improves survival in resuscitation from bupivacaine-induced cardiac toxicity². We compared the efficacy and metabolic effects of V plus EPI, with V alone and L alone in a rat model of resuscitation from bupivacaine-induced asystole.

METHODS: Cardiac arrest was induced with an intravenous bolus of bupivacaine, 20mg/kg. The end of bupivacaine infusion was taken as zero-time. All rats developed asystole and CPR was initiated immediately and comprised mechanical ventilation with 100% oxygen plus chest compressions (240 bpm) that were continued to return of spontaneous circulation (ROSC taken as native rate-pressure product, RPP= HR x [LVSP-LVDP], greater than 20% of baseline). Rats were randomly assigned to one of three treatment groups (n=5 for each): V-alone (0.4U/kg X 3); EPI+V(30µg/kg + 0.4U/kg, respectively, X 3); or L (30% soy oil emulsion, 5mL/kg bolus followed by a continuous infusion at 1mL/kg/min until ROSC. ECG and arterial blood pressure were continuously monitored and arterial and central venous blood samples were drawn at baseline and after 10 min. of resuscitation for the determination of pH, lactate levels, and O₂ saturation.

RESULTS: All rats in group L successfully recovered RPP greater than 20% of the baseline value by 10 min. Only 3 of 5 rats in the EPI+V group and none in the V-alone group survived. All animals in the V-alone and EPI+V groups developed severe, hemorrhagic pulmonary

edema as well as pH, lactate and SvO₂ levels that differed significantly from those of the L group.

10min values	Lipid	V	EPI + V
RPP (mmHg min ⁻¹)	27195 ± 9153	3311 ± 1845	12532 ± 3743
pH	7.22 ± 0.07	7.18 ± 0.07	7.13 ± 0.13
LACT (mmol L ⁻¹)	2.40 ± 0.84	7.70 ± 0.99	7.33 ± 2.5
SvO ₂ (%)	77.6 ± 18.5	41.9 ± 22.9	38 ± 21.9

DISCUSSION: Vasopressin, in this model, alone and in combination with epinephrine, causes severe pulmonary edema and is associated with reduced survival and metabolic evidence of poor tissue oxygenation. These findings suggest that vasopressin might be detrimental during resuscitation from bupivacaine-induced cardiac arrest. Lipid emulsion infusion, by contrast, resulted in better survival rate, hemodynamics and tissue perfusion.

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2. Anesthesiology 88:1071-1075,1998

S-235.

TITLE: EFFECT OF GENDER DIFFERENCES ON PHARMACOKINETICS AND TOLERANCE STUDY OF HIGH DOSE ROPIVACAINE FOR SINGLE SCIATIC NERVE BLOCK IN DOGS

AUTHORS: X. Dong, Y. Huang;

AFFILIATION: Department of Anesthesiology, Peking Union Medical College Hospital, Peking Union Medical College, Beijing, China.

INTRODUCTION: It is taught that sex differences have important effect on absorption, distribution, metabolism and elimination of drug, so the application of individualized medication in clinical treatment should be considered. The pharmacodynamics and pharmacokinetics of ropivacaine used for epidural, brachial plexus and caudal block had been studied, but was not found in gender differences. This study was to investigate the effect of gender differences on pharmacokinetics and tolerance of high dose ropivacaine for single sciatic nerve block in dogs.

METHODS: Twelve healthy adult mongrel dogs (6 male, 6 female) weighing 13-16kg were divided into 2 gender groups (n=6 each): male group and female group. The animals were anesthetized with intramuscular 3% pentobarbital 30 mg/kg. A polyethylene catheter was surgically inserted into the sheath of sciatic nerve for nerve block with ropivacaine. Femoral artery was cannulated for BP monitoring and blood sampling. ECG and BP were continuously monitored before and after ropivacaine injection. 0.5% ropivacaine 10 mg/kg was injected into the sheath of sciatic nerve through the catheter at 48 hours after cannulation. Arterial blood samples were taken for determination of plasma ropivacaine concentration (using HPLC) before and at 10, 20, 30, 60, 90, 120, 150, 180, 240, 360 and 720 min after ropivacaine injection. The pharmacokinetic parameters were determined from concentration-time data using DAS 1.0 software package.

RESULTS: The concentration-time curve in two groups were adequately matched to two-compartment open model. No signs of cardiovascular or CNS toxicity were observed after sciatic nerve block with ropivacaine in the two groups. The main pharmacokinetic parameters in male and female mongrel dogs after 10mg/kg ropivacaine

for sciatic nerve block were Cmax (4.57±1.24) µg/ml, (4.76±1.47) µg/ml, Tmax (0.40±0.09) h, (0.38±0.11) h, T_{1/2α} (0.31±0.12) h, (0.35±0.17) h, T_{1/2β} (4.67±1.48) h, (4.96±1.69) h, AUC_{0-12h} (19.19±2.57) mg.h.l⁻¹, (19.00±2.36) mg.h.l⁻¹, respectively. No statistically significant differences were found regarding the pharmacokinetic parameters between the study groups (p > 0.05).

DISCUSSION: 10mg/kg ropivacaine can be used safely in dog single sciatic nerve block and no systemic toxic reactions were found in this dog study setting. The gender has no significant effect on pharmacokinetics of ropivacaine for sciatic nerve block in dogs.

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S-236.

TITLE: NEEDLE VISIBILITY WITH ULTRASOUND

AUTHORS: N. S. Sandhu¹, N. H. Karuvannur²;

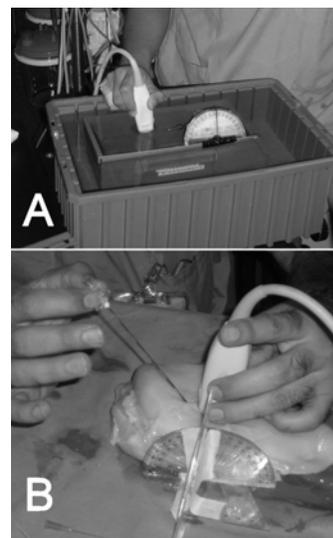
AFFILIATION: ¹University of California San Diego, San Diego, CA, ²Canyon Crest Academy, San Diego, CA.

INTRODUCTION: Ultrasound (US) is used to guide needles for nerve blocks, vascular access and tissue biopsy. Schaffhalter-Zoppoth et al(1) have studied various needles using a linear probe using a gel bath which has uniform echogenicity unlike any human or animal tissue. This study was conducted in a water bath (uniform echogenicity) and chicken breast which is similar to human muscle. Both *linear* and *curvilinear* probes were used.

METHODS: Various size (18, 22, 25 gauge) needles were imaged in a water bath and in chicken breasts using linear and curvilinear probes. The needle was rotated from 0-90 degrees in a water bath (Fig 1A) and chicken breast model (Fig 1B) and images were recorded in a videoclip. Images were recorded at 10 degree increments.

Imaging in water bath: *Linear probe:* needle is clearly seen as a continuous line at 90-70 degrees to US. At 70-60 degrees needle appears as dotted line at 60 to 30 degree there is only indirect evidence of acoustic shadow. Between 30 to 0 degree needle is not seen. *Curvilinear probe:* the needle is clearly seen as a continuous line between 90-60 degrees, a dotted line of decreasing intensity from 60 to 10 and indistinct dotted line at between 10-0 degree.

Imaging in Muscle tissue: *Linear probes:* needles are clearly imaged between 90 -70 degree. Between 70-50 degrees it becomes a dotted line. Beyond that the needle is not seen though there may be indirect evidence of tissue movement and post-acoustic shadowing. *Curvilinear probe:* needle image is best with needle between 90-60 degree to incident beam. Needle is seen as a dotted line between 50-0 degrees.



DISCUSSION: The thickness of needle improves needle visibility. Curvilinear probe provides needle visibility in a wider range than linear probe. Curvilinear probes therefore are better suited where needles have small angle to incident US beam such as infraclavicular block, supraclavicular block, sciatic in gluteal area or femoral nerve block in obese patients. Linear probes are ideal where needle can be introduced at 90 degree to US beam such as axillary, interscalene and popliteal fossa blocks.

REFERENCE:

- Schaffhalter-Zoppoth I, McCulloch, C, Gray A: Ultrasound visibility of needles used for regional nerve block: An in vitro study. RAPM 2004; 29: 480-88.

S-237.

TITLE: REGIONAL ANESTHESIA AND RESIDENT EDUCATION: IMPLEMENTATION OF A DEDICATED REGIONAL ANESTHESIA RESIDENT AND ITS IMPACT ON OPERATING ROOM EFFICIENCY AND RESIDENT TRAINING.

AUTHORS: J. Nagafuji, P. Hess, P. Panzica;

AFFILIATION: Beth Israel Deaconess Medical Center, Boston, MA.

INTRODUCTION: Efforts to improve resident education in regional anesthetic techniques must be balanced with the economic pressures of maintaining operating room efficiency. In this observational study, we studied how the creation of a dedicated regional resident impacted operating room efficiency and resident training. Previously, the primary anesthesia team (attending and resident) was responsible for administering regional anesthesia in cases assigned to their operating room. We redesigned this process to identify a regional anesthesia team composed a resident who has the sole responsibility of providing peripheral nerve blocks throughout the operating room suites. This resident is supervised by an attending, who may have additional assignments.

METHODS: In this observational study, we collected data from the four month periods immediately prior to and following the implementation of our dedicated regional anesthesia team. We reviewed all of the cases of seven orthopedic sports medicine surgeons whose cases are often amenable to regional anesthesia. Cases were excluded when: the surgical case was the first case of the day, the surgeon had two rooms with over lapping start times, or the case involved neuraxial techniques. We compared operating room turnover times, number and types of regional anesthetics performed, as well as the types of adjunct anesthesia used intraoperatively. Chi-squared was used for incidence, and Mann-Whitney test used for continuous variables. $P < 0.05$ used for significance.

RESULTS: 1,337 cases were identified, and 478 were excluded for reasons listed above, leaving 859 cases. Compared to the period prior to the regional team, we found a significant improvement in turnover time when cases involved regional anesthesia (35.2min vs. 40.5min;

$P=0.004$). There was no difference in cases that did not receive regional anesthesia. An improvement in resident training was reflected in 42% increase in the number of regional anesthetics placed (69 vs. 98 blocks; $P=0.065$). Additionally we performed a greater variety of regional techniques.

DISCUSSION: There are numerous studies that demonstrate the benefits of regional anesthesia (patient satisfaction, reduction in PACU time, reductions in anesthesia controlled time).^(1,2,3) Other studies have identified the need for improvement in resident training in regional techniques.^(4,5) Our observational study shows that process redesign can improve resident education in regional anesthesia by increasing the number of peripheral nerve blocks performed without detrimental impact on room turnover times.

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S-238.

TITLE: TITLE: PREDICTORS OF PULMONARY EMBOLISM FOLLOWING PRIMARY HIP AND KNEE ARTHROPLASTY

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INTRODUCTION: The prevention of thromboembolic complications in patients undergoing hip and knee arthroplasty has typically relied on protocol thromboprophylaxis. However, given that not all patients are at equal risk for pulmonary embolism (PE), routine prophylaxis is not always successful. This study is designed to determine the predisposing factors for PE despite thromboprophylaxis following primary hip and knee arthroplasty at a tertiary care hospital.

METHODS: We performed a cohort study using prospectively collected data from our institutional arthroplasty complication database. We include 9,247 patients whom underwent primary hip or knee arthroplasty from January 2001 to December 2006. Patients gender, age, ethnicity, ASA score, operative time, pre and postoperative labs (hemoglobin, INR, creatinine, WBC, glucose) and patient comorbidities were included for analysis.

RESULTS: Among the numerous variables tested we found that older age, female gender, higher BMI, knee surgery, bilateral surgery, lower postoperative hemoglobin value, higher preoperative and postoperative glucose value, congestive heart failure and hypercholesterolemia were significant predisposing factors for PE.

DISCUSSION: Patients undergoing hip or knee arthroplasty are at risk of developing PE. Identification of factors predisposing patients to PE may be helpful in categorizing patients into different risk groups. The latter could in turn help determine the type and the duration of thromboprophylaxis.

S-239.

TITLE: INTRAOPERATIVE LEVEL OF SEDATION AND POSTOPERATIVE DELIRIUM

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INTRODUCTION: The role of sedative and analgesic medications as iatrogenic risk factors for delirium has recently been described in both surgical and ICU patients^{1,2}. However, the role of intraoperative sedation as an iatrogenic risk factor for delirium is controversial. We hypothesize that limiting level of sedation during spinal anesthesia for hip fracture repair will reduce the incidence of postoperative delirium. This hypothesis was tested in a randomized, controlled, clinical trial.

METHODS: After obtaining IRB approval and informed consent 67 patients undergoing spinal anesthesia with propofol sedation for repair of hip fracture were randomized to one of two levels of sedation during surgery: light sedation or heavy sedation. Level of sedation was determined using both the observer assessment of alertness/sedation scale score (OAA/S) and bispectral index (Bis). Light sedation was defined by an OAA/S of 4-5 and Bis > 80 and heavy sedation was defined by an OAA/S score of 0 and Bis < 50. Patients in both groups were assessed for postoperative delirium as defined by DSM-IV criteria, during their post-operative in-hospital stay using the Confusion Assessment Method (CAM). Rates of postoperative delirium were compared between the experimental (heavy sedation) and control (light sedation) groups with Chi-square.

RESULTS: The two groups were similar in age and prevalence of dementia. Bispectral index and OAA/S were clearly different between the two experimental groups, at levels targeted by treatment assignment. The incidence of postoperative delirium in the light sedation and heavy sedation groups was notably different (see Table; chi square = 0.033)

	Heavy Sedation	Light Sedation	Total
No Post-op Delirium	21	27	48
Post-op Delirium	14 (40%)	5 (16%)	19
Total	35	32	67

DISCUSSION: This randomized experiment suggests that the incidence of postoperative delirium after spinal anesthesia might be reduced by as much as 50% if minimal sedation is applied. This novel approach might also lead to better cognitive outcomes in high risk elderly patients. If this finding can be replicated in a larger randomized controlled trial, it would lead to a major change in geriatric anesthesia practice and intraoperative management, especially in patients with dementia.

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S-240.

TITLE: EPIDURAL VERSUS PERIPHERAL NERVE CATHETERS FOR ANALGESIA POST TOTAL KNEE ARTHROPLASTY

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INTRODUCTION: The aim of analgesia post total knee arthroplasty (TKA) is to provide excellent analgesia, limit side-effects and allowing maximal movement. While epidural catheters provide analgesia, there is potential for side effects. The use of femoral nerve and sciatic nerve catheters may provide optimal analgesia with minimal side-effects.

METHODS: The aim of this retrospective study of 172 patients undergoing primary TKA was to observe which technique achieved optimal analgesia, i.e. 0 on the visual analog scale (VAS). The epidural (E) group received epidural anesthesia and analgesia while the catheter (C) group received spinal anesthesia and continuous infusion of local anesthetic via a femoral nerve catheter and intermittent bolus of local anesthetic via a sciatic nerve catheter. Demographic, visual analog score of zero, length of stay and side-effects were measured. The two groups were compared using Chi square analysis, p< 0.05.

RESULTS: There was no difference in demographics or length of stay (3.6 days) Table 1 shows the incidence of VAS 0 and Table 2 depicts the side effects.

Table 1: VAS “0” Epidural group versus Catheter group

	Epidural group N=50	Catheter group N=122	P
Day1 Rest	6 (11%)	30 (25%)	NS
Day 1 Active	6 (11%)	26 (21%)	NS
Day 2 Rest	11 (20%)	36 (30%)	NS
Day 2 Active	5 (9%)	23 (19%)	NS
Day 3 Rest	18 (33%)	44 (36%)	NS
Day 3 Active	13 (25%)	29 (24%)	NS

Table 2: Side Effects

	Epidural group N=50	Catheter group N=122	P
Pruritis	3 (6%)	1 (0.1%)	S
Urinary catheter	38 (70.04%)	2 (1.6%)	S

DISCUSSION: Both the E and C groups achieved optimal analgesia however the E group had a greater number of side-effects. Urinary catheters has the risk for infection and the potential for infected joint replacement.

CONCLUSION: Although different regional techniques may provide equal optimal analgesia, side effect profile need to be examined for each technique.

S-241.

TITLE: QUANTITATIVE EVALUATION OF THE ECHOGENICITY OF PERIPHERAL NERVE IN YOUNG AND ELDERLY

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INTRODUCTION: The echo intensity (EI) of muscles is significantly increased in the elderly.¹ There are no data comparing the EI of peripheral nerves in the young and the elderly which this study was designed to evaluate.

METHODS: 13 healthy young volunteers (<30 years old, Group Y) and 11 elderly (>60 years old, ASAII-III, Group E) patients were recruited for this study. The ultrasound examination was performed using a high frequency linear array transducer (13 MHz) and a MicroMaxx (Sonosite Inc) system. The settings of the ultrasound system were standardized for all subjects. A transverse scan of the median nerve (MN) and the flexor digitorum superficialis (FDS) muscle in the forearm was obtained. Three video loops (AVI format, 6 sec) were recorded and stored for each subject. Still images (TIFF format) were captured from the video loops and they were normalized. Computer assisted gray scale analysis² (Adobe® Photoshop CS2) was performed on these images to measure the EI of the MN and FDS. T-test (for independent samples) and ANOVA (Univariate analysis) were used to analyze the data.

RESULTS: The mean (SD; CI) EI of the MN in Group E, 171.32 (15.75; 159.87-178.98), was significant higher than the mean EI in Group Y, 137.41 (14.41; 130.28-147.76), $p < 0.0001$. The mean EI of the FDS muscle in Group E, 109.85 (20.48; 101.58-120.61), was also significantly higher than in Group Y, 72.13 (6.25; 62.37-79.78), $p < 0.0001$. ANOVA showed that age affected the EI of the MN and the FDS, $p < 0.05$, but gender did not.

DISCUSSION: The increased echogenicity of muscles and nerves in the elderly may explain why musculoskeletal structures appear whiter and are more difficult to delineate in elderly patients during ultrasound

guided regional anaesthesia.

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S-242.

TITLE: EARLY MORTALITY FOLLOWING TOTAL JOINT ARTHROPLASTY

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INTRODUCTION: With the demographic tendency towards an elderly society the number of joint replacements is expected to increase. Although total joint arthroplasty (TJA) is considered safe, cardiovascular and thromboembolic complications with the potential for fatal outcome may occur following TJA. This study was designed to elucidate the incidence of in hospital mortality, and determine risk factors for this condition following TJA.

METHODS: The study consists of 13,949 patients undergoing TJA at a single institution. Multivariate analysis was performed to evaluate the role of various factors.

RESULTS: A total of 22 patients (0.15%) died in the hospital setting, 10 deaths (0.07%) following primary joint arthroplasty (5 hips, and 5 knees) and 12 (0.55%) after revision surgery (9 Hips, 3 Knees). Patients died 12.4 days (mean, range 0 to 76 days) following index surgery. Autopsy was performed in only 4 cases. The principal cause of death included anoxic brain injury after aspiration or respiratory failure (5), pulmonary embolism (3), acute myocardial infarction (3), Arrhythmias (3), unspecified cardiopulmonary arrest (3), sepsis (3), hypovolemic shock (2) secondary to iliac vessels injury and following massive retroperitoneal bleeding in post ischemic colitis. Older age, longer operative time, revision surgery and higher ASA scores were significant predictors for early mortality following joint arthroplasty.

DISCUSSION: This study suggests that catastrophic complications leading to early mortality following elective joint arthroplasty do occur. Older age, longer operative time, revision surgery and higher ASA score are associated with a higher likelihood of a fatal outcome during hospitalization.

S-243.

WITHDRAWN

S-244.

TITLE: THE PORCINE EPIDURAL SPACE CONTAINS IMMUNOACTIVE CELLS

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INTRODUCTION: Spinal-epidural abscesses are seen very infrequently, perhaps due to a protective mechanism present in the epidural space. This study aims to determine whether there are resident immunologically active cells in the epidural space that could protect against infection after epidural anesthesia.

METHODS: After approval from the Institutional Animal Care and Use Committee, saline washings of the epidural space of six 40-kg pigs were obtained. Three of the pigs were intubated and being ventilated when the washings were taken, and three of the pigs had been euthanized less than an hour prior to the study. A Tuohy needle, with the bevel pointed caudad, was introduced into the epidural space with a loss of resistance technique in the lower thoracic region, and another epidural needle, with the bevel cephalad, was advanced to the epidural space 1-2 vertebral levels below the first. Approximately 50 ml of saline needed to be injected into one needle for a small amount to exit the second needle. If gross blood was visualized exiting the needle or in the epidural washing fluid, the sample was eliminated. The samples were spun onto slides ("cytospins" at 1800 RPM x 5 min.) and stained with Wright-Giemsa stain. The slides were analyzed under a microscope to identify cells associated with peripheral blood, such as erythrocytes or monocytes, and those associated with the local tissue site, such as macrophages.

RESULTS: One of the samples from a live animal was eliminated due to the presence of visible blood, leaving 2 epidural space washings that were analyzed from pigs that were alive and 3 from pigs that were not. Three of the specimens- 2 from live animals and 1 from a recently euthanized pig- were characterized as hemorrhagic. But each of these samples also contained macrophages, which would be expected to originate from the local tissue (i.e. the epidural space) and not the peripheral blood. The remaining 2 epidural space washings contained

amorphous material but no identifiable cells.

CONCLUSION: The macrophages that we identified in the epidural space of 3 of 5 of the pigs would not be expected to come from the peripheral blood that was seen in the samples. If these cells are present in the epidural space of humans, they may help to explain why the incidence of epidural abscess is so low after epidural anesthesia.

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