

Queen's University 27th Annual Anesthesiology Research Day

Scientific Program Coordinators:

Ian Gilron, MD, MSc, FRCPC

Elizabeth VanDenKerkhof, RN, MSc, DrPH

Scientific Adjudicators:

Eric Dumont, PhD

Ramiro Arellano, MD, MSc, FRCPC

Howard Nathan, MD, FRCPC (Guest)

Queen's Anesthesiology Residency Program Director:

Melanie Jaeger, MD, FRCPC

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John Cain, MD, FRCPC

Queen's Anesthesiology Postgraduate Medical Secretary:

Mrs. Kim Asselstine

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Queen's University 27th Annual Anesthesiology Research Day

SCIENTIFIC PROGRAMME

- 0900 – 0910 **Opening Remarks – Dr. John Cain**
- 0910 – 0920 **Introduction – Dr. Ian Gilron**
- 0920 – 1000 **Dr. Lorna Jean Edmonds, PhD, Director, Office of Research Services, Queen's University**
"Population health research is knocking at your door: Are you going to answer it?"
- 1000 – 1015 **Dr. Kyle Doerksen, PGY-4, Queen's Anesthesiology**
"Post-operative analgesia for radical retropubic prostatectomy" (research update/data presentation)
- 1015 – 1030 **Ms. Annie Hsieh, MA Student, Psychology, Queen's University**
"Experimental pain responses in Caucasian Canadian and Chinese" (research update/data presentation)
- 1030 – 1100 *** * * POSTER PRESENTATIONS** (see list below) and coffee break * * *
- 1100 – 1115 **Mr. James Jeong, MSc Candidate, Pharmacology & Toxicology, Queen's University**
"Delta opioid receptor-mediated analgesia is enhanced following chronic morphine: a role for glial activation?" (research update/data presentation)
- 1115 - 1130 **Dr. Ryan Endersby, PGY-2, Queen's Anesthesiology**
"Identifying the Barriers for Anesthesiology Staff and Residents Using Portable Computers to Record Patient Assessments Using the Theory of Planned Behavior" (research proposal)
- 1130 – 1145 **Dr. Jason Erb, PGY-3, Queen's Anesthesiology**
"The relationship between evoked versus spontaneous pain and peak expiratory flow after laparoscopic cholecystectomy" (research update/data presentation)
- 1145 - 1200 **Ms. Sarah Holdridge, PhD Candidate, Pharmacology & Toxicology, Queen's University**
"Ultrastructural localization of Delta Opioid Receptors in an animal model of neuropathic pain: implications for novel pain treatment?" (research update)
- 1200 – 1300 *** * * LUNCH** (provided) * * *
- 1300 – 1315 **Dr. Esther Ho, PGY-2, Queen's Anesthesiology**
"Barriers to the use of an electronic database to record anesthesia experience." (research proposal)
- 1315 – 1330 **Ms. Samantha Waxman, MA Student, Psychology, Queen's University**
"Psychosocial Factors as Predictors of Relationship Satisfaction in Chronic Low Back Pain" (research update/data presentation)
- 1330 – 1345 **Mr. N'Gai Porte, Medical Student, Queen's University**
"Temporal Artery Scanner Thermography: adequate for the OR?" (research update/data presentation)

- 1345 – 1400 Ms. Glory Prupas, MSc Student, Pharmacology & Toxicology, Queen's University
"Blockade and reversal of morphine tolerance with ultra-low doses of opioid receptor antagonists" (research update/data presentation)
- 1400 – 1430 * * * POSTER PRESENTATIONS (see list below) and coffee break * * *
- 1430 – 1445 Dr. Cara Reimer, PGY-3, Queen's Anesthesiology
"Does gabapentin attenuate morphine analgesic tolerance via actions on the alpha-2-delta-1 subunit of the voltage-dependent calcium channel receptor?" (research update/data presentation)
- 1445 – 1500 Dr. Kara Gibson, PGY-2, Queen's Anesthesiology
"Laser Therapy for Retinopathy of Prematurity: Is a general anesthetic necessary?" (research proposal)
- 1500 – 1515 Mr. Vico Dagnone, Medical Student, Queen's University
"Patients' attitudes and perceptions regarding the use of portable computers at the bedside: A qualitative assessment" (research update/data presentation)
- 1515 – 1530 Mr. Adam van Dijk, MSc Student, Community Health & Epidemiology, Queen's University
"The assessment of pain prevalence in schoolchildren" (data presentation)

EACH 10-MINUTE PRESENTATION WILL BE FOLLOWED BY A 5-MINUTE QUESTION PERIOD

The Judges will be:

Dr. Howard Nathan, Professor, Department of Anesthesiology, University of Ottawa
Dr. Eric Dumont, Assistant Professor, Queen's Depts. of Anesthesiology and Pharmacology & Toxicology
Dr. Ramiro Arellano, Assistant Professor, Queen's Department of Anesthesiology

- 1530 * * * *Guest Speaker:* **Dr. Howard Nathan**, Professor and Vice-Chairman Research, Department of Anesthesiology, University of Ottawa
Speaker of the Royal College of Physicians & Surgeons of Canada, Region 3 Advisory Committee
- "Quality of Life and Cognitive Function 5 Years After Coronary Artery Surgery."
- 1830 Cocktails and Dinner (Donald Gordon Center)
- * * * Presentation of awards following dinner * * *
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Poster Presentations

Stacey Armstrong, Research associate, Pharmacology & Toxicology, Queen's University
Ultra low dose Naltrexone enhances the antihyperalgesic effect of spinal morphine in a model of neuropathic pain

Kim Cottick, 4th year student, Queen's University Life Science Program
"Delta-opioid receptors in the Bed Nucleus of the Stria Terminalis: distribution and function"

Ms. Tara Haley, BSc Student, Psychology, Queen's University **"Individual Differences in Pain Perception in an Acute Pain Induction Task"**

Jibran Khokhar, 4th year student, Queen's University Life Science Program

"Neuronal activity underlying the emotional dimension of pain: a closer look at the Bed Nucleus of the Stria Terminalis"

Natalie Lam, BSc honours candidate, Pharmacology & Toxicology, Queen's University

"The Role of the Alpha-2 Delta (a2d) Calcium Channel Subunit in Opioid Tolerance"

Ms. Chelsea Maddock, BA Student, Psychology, Queen's University

"Factors Effecting Face-to-Face Pain Perception"

Ms. Carrie Ng, BA Student, Psychology, Queen's University

"Effects of Cognitive Intervention to Reduce Catastrophic Thoughts in High Pain Catastrophizing Individuals"

Linda Plong, BSc honours candidate, Pharmacology & Toxicology, Queen's University

"A comparison of inflammation and tactile allodynia in two chronic constriction injury models"

Lihua Xue, Research associate, Pharmacology & Toxicology, Queen's University

"Incomplete Cross-tolerance Between Morphine and Methadone: Role of Delta Opioid Receptors"

Post-operative analgesia for radical retropubic prostatectomy

Kyle Doerksen, MD, Alison Froese MD, FRCPC
Department of Anesthesiology, Queen's University

INTRODUCTION: Multiple analgesic strategies have been employed for Radical Retropubic Prostatectomy (rRPP) following this procedure including spinal or epidural opiates, continuous epidural block, IV ketorolac and intravenous Patient-Controlled Analgesia (PCA-IV). Prior to the year 2000 continuous epidural block was commonly used in our institution. Interestingly, studies on determinants of post-operative stay after rRPP revealed that the use of epidural analgesia may contribute to delay of discharge. This has led to a move away from epidural analgesia towards PCA-IV in this population. Paravertebral Blocks (PVBs) have been employed in our institution as a means to improve on the analgesia provided by PCA-IV alone. The relative effectiveness of these three techniques (continuous epidural, PCA-IV, or PCA-IV with PVB) after rRPP is not known.

METHODS: A descriptive, institution-based, retrospective review was carried out on patients undergoing rRPP from the year 2000 to 2003. A total of 199 patients were returned from the surgical database of which 14 were excluded leaving 185 patients for analysis. Analgesic modality and time to discharge were recorded from all patients. 10 patients from each analgesic modality sub-group were randomly selected for detailed review including maximum VAS scores, narcotic use, time to ambulation, PONV, sedation, pruritis, and length of intestinal ileus.

RESULTS: Analysis of analgesic methods used over the study period revealed that 50% (n=92) received PCA, 30% (n=56) received CEA, 18% (n=34) received PVB + PCA, and 2% (n=3) received spinal opioids. There was an obvious change in analgesic practice over the study period with 54% (15/28) of patients receiving CEA in 1999 compared with 6.0% (6/48) in 2002 and 0.0% (0/15) in 2003. Average length of stay (LOS) for all patients was 105.48 ± 2.77 hrs over the study period, which remained relatively stable across all years. Sub-group analysis showed that there was no difference in LOS based on analgesia modality (PCA 106.68 ± 4.55 hrs, PVB + PCA: 105.07 ± 6.20 hrs, EPIDURAL 102.79 ± 3.40 hrs, SAB 92.63 ± 34.32 hrs). However, in 2001 and 2002 there was a trend towards a decreased LOS with CEA (85.08 ± 5.46 hrs $p < 0.05$). There were no differences in intra- and post-operative blood loss across the groups. VAS scores were not different between PCA and EPIDURAL however there was a trend towards higher VAS scores and morphine consumption > 10 hrs post-op in the PVB + PCA group compared to PCA alone ($p < 0.1$). Side effect analysis showed none of the patients required naloxone. There was a trend towards shorter post-operative ileus in the epidural group as compared with PCA ($p < 0.05$ for time to first PO intake). No differences could be found between groups w.r.t. PONV, pruritus, and sedation.

CONCLUSIONS: Post-operative length of stay appears to depend more on surgical factors than on the type of analgesic modality employed following rRPP. Our data suggest that there is a trend towards shorter post-operative ileus and length of stay when CEA is used. PVB has been used safely in our institution however there is a trend towards a delayed increase in VAS scores and morphine consumption suggesting a rebound hyperalgesic state once the block recedes. This is difficult to explain given the possible spinal-cord wind-up prevention that regional anesthesia may afford. Given that there is little difference in LOS, VAS scores, side-effect profile and surgical outcomes any of the modalities may be safely employed however a prospective study including patient satisfaction would confirm this. Given that epidural analgesia was equivalent to PCA-IV and may slightly decrease LOS and post-op ileus, patients for rRPP should not be denied this method of analgesia if they so wish.

Experimental pain responses in Caucasian Canadian and Chinese

Annie Y. Hsieh B.A, Dean Tripp, PhD. & Samantha E. Waxman B.A.

Department of Psychology, Queen's University

Research shows that there are cross-cultural differences in health care delivery and acute and chronic pain management practices (e.g. Green, 2003). Recent studies using experimental pain paradigm have demonstrated differences among cultural groups in pain experience. However, many of these studies did not explain why such differences exist or how cultural beliefs about pain may affect the experience of pain. Furthermore, most of the cross-cultural research in experimental pain has studied African Americans and Hispanics with little data available for Asian groups. Therefore, this study will investigate differences in pain beliefs and pain responses between Caucasian Canadians and Chinese. We hypothesize that cultural groups will moderate the relation between pain beliefs and pain responses.

56 Caucasian Canadians and 52 Chinese undergraduate students underwent the Cold Pressor (CP) task (2°Celsius water bath into which participants immerse their arm). Pain attitudes questionnaires were administered prior to the CP task. Participants provided pain intensity and unpleasantness (SF-McGill; Melzack, 1987) immediately after the CP task. ANOVA will be conducted to examine pain responses and pain beliefs between the two groups. Multiple regression analysis will be conducted to test the moderating effect of cultural group on pain responses.

References;

Green, C. R., Anderson, K. O., Baker, T. A., Campbell, L. C., Decker, S., Fillingim, R. B. et al., (2003). The unequal burden of pain: Confronting racial and ethnic disparities in pain. *Pain Medicine*, 4, 277-294.

Melzack, R. (1987). The short-form McGill Pain Questionnaire. *Pain*, 30, 191-197.

Delta opioid receptor-mediated analgesia is enhanced following chronic morphine: a role for glial activation?

James Jeong¹, Khem Jhamandas^{1,2}, and Catherine Cahill^{1,2,1} Dept. of Pharmacology and Toxicology,
²Dept. of Anaesthesiology, Queen's University, Kingston, Ontario

Introduction: Mu-opioid receptor agonists such as morphine are commonly used for the treatment of moderate to severe pain, however their clinical usefulness may be limited by the occurrence of analgesic tolerance. The mechanisms underlying tolerance are unclear but recent research suggests a role for the delta opioid receptor (DOR) in this phenomenon. Prolonged exposure to mu agonists such as morphine induces the migration of DORs from intracellular neuronal compartments to the plasma membrane. This exposure produces an increase in sensitivity to the analgesic action of DOR agonists such as deltorphin.

Studies on opioid analgesic tolerance have also implicated the activation of spinal glial cells in the development of this phenomenon. The drug propentofylline, which blocks the opioid-induced glial activation, has been shown to attenuate the development of tolerance to the spinal analgesic action of morphine. However, the relationship between the increased sensitivity to DOR agonists and glial activation seen in opioid analgesic tolerance remains unknown. The goal of this study was to investigate whether spinal glial activation has a role in the increased sensitivity to the DOR agonist, deltorphin, in animals treated with a chronic morphine regimen inducing analgesic tolerance.

Methods: Male Sprague Dawley rats were administered either of saline, morphine (5mg/kg, s.c.), morphine + propentofylline (10µg/30µL, i.t.), or propentofylline alone for 6 days. Thermal nociceptive thresholds were assessed on days 1, 4, and 6 using the 52°C hot water tail flick test to assess the degree of analgesic tolerance. On day 7, animals were injected with the DOR agonist, deltorphin (10µg/30µL, i.t.) via a lumbar puncture and thermal nociceptive thresholds were assessed for 40 minutes following the drug injections. Animals were then perfused with 4% paraformaldehyde and the lumbar region of the spinal cords were removed for immunohistochemical analysis of astrocytic and microglial surface proteins, glial fibrillary acidic protein (GFAP) and CR3/CD11b, respectively.

Results: Animals treated chronically with morphine developed tolerance to its analgesic effect by day 6. On day 7, these animals showed a significant increase in the spinal analgesic action of deltorphin compared with animals chronically treated with saline. The occurrence of analgesic tolerance was accompanied by a significant increase in glial activation as indicated by glial hypertrophy. Co-administration of propentofylline with morphine attenuated the development of tolerance and blocked the increased sensitivity to the spinal analgesic action of deltorphin.

Summary: These results suggest that glial activation occurs in morphine tolerance and this response contributes to the increased sensitivity to a DOR agonist such as deltorphin. Glial activation could contribute to the translocation of delta receptors from intracellular compartments to the plasma membrane in opioid tolerant states.

Identifying the Barriers for Anesthesiology Staff and Residents Using Portable Computers to Record Patient Assessments Using the Theory of Planned Behavior.

Ryan Endersby, MD, Esther Ho, MD, and David Goldstein, MD, FRCPC

Department of Anesthesiology, Queen's University

Annually more than five million Canadians receive an Anesthetic and experience surgical pain. More than 80 Canadian pain experts, (The Canadian Collaborative Acute Pain Initiative) believe sharing acute pain patient outcome information will describe the issues which need to be addressed to reduce pain and suffering. Standardized patient assessment information must be recorded. A portable computer system has been developed with a standardized assessment template. The Theory of Planned Behavior has been developed to elucidate what barriers exist to the adoption of a new behavior. In this theory, adoption of a new behavior is influenced by attitudes, social pressure and perceived control. The aim of this research project is to use the Theory of Planned Behavior to identify the barriers that exist in the adoption of portable computers for patient assessment in acute pain and Anesthesiology.

The population under study is the consultant and resident anesthesiologists at Kingston General Hospital. Following the instructions found in, "Constructing Questionnaires Based on the Theory of Planned Behavior – A manual for Health Service Researchers" by Francis, *J. et. al.*, a general open-ended questionnaire has been created and given to a randomly selected group of Anesthesiology staff and residents. This questionnaire will be modified based on the input from the first group and resubmitted to another randomly selected group of Anesthesiology staff and residents. Subsequently a more detailed specific 41-item questionnaire regarding attitudes, social pressures and perceived control will be created. This questionnaire will then be given to all of the Anesthesia staff and residents. The small number of acute pain staff has warranted the distribution of the questionnaire to all consultant and resident staff. It is believed the barriers identified will apply to all staff, whether in using the portable computer for acute pain or pre-operative Anesthesiology patient assessments. The barriers to using portable computers for patient assessments will be determined from analyzing the data collected from the 41-item questionnaire. After the baseline questionnaires are administered and the barriers reviewed, the Anesthesiology staff and residents will be given an introductory course on the use of a portable computer and the acute pain software. Both staff and residents will be given the opportunity to interview and assess three patients with the acute pain portable computer and software. The 41-item questionnaire will be administered again to look for differences in the responses. The goal of this project is to determine the barriers to adoption and to gain insight into how we may make the use of portable computers for acute pain assessments most convenient.

Reference

1) Francis, Jillian et al.. **Constructing Questionnaires Based on The Theory of Planned Behavior: A Manual For Health Services Researchers.** University of Newcastle, May, 2004.

The relationship between evoked versus spontaneous pain and peak expiratory flow after laparoscopic cholecystectomy

Jason Erb, MD & Ian Gilron, MD, MSc, FRCPC

Department of Anesthesiology, Queen's University

This study is proposing to look at the relationship between evoked versus spontaneous pain and pulmonary function measurements after upper abdominal surgery, in particular laparoscopic cholecystectomy. It is well known that, postoperatively, there are changes in pulmonary function. In particular changes are seen in functional residual capacity, vital capacity and inspiratory capacity. There are several contributors to this phenomenon. Several previous studies have found that pain contributes to inspiratory muscle dysfunction and pulmonary function.

Pain can be described as two components, spontaneous and evoked pain. A patient who has undergone a procedure will have a baseline pain level referred to as spontaneous pain. Activity such as movement or coughing generally results in a pain level that is in excess of the patient's spontaneous pain and can be described as evoked pain. Deep breathing, coughing, incentive spirometry are all means that can trigger this evoked pain. However these maneuvers are necessary for patient rehabilitation and prevention of thromboembolic phenomenon and atelectasis that can lead to pneumonia.

This study proposes to look at measures of pulmonary function FEV1, PEF, and FVC post operatively and the concurrent levels of spontaneous and evoked pain. The study would examine the strength of the correlation between pain scores and pulmonary function changes from baseline. The three hypothesis to be tested for upper abdominal surgery are:

- A. Movement evoked pain is more severe than pain at rest.
- B. Post operative pain is significantly correlated with post operative lung function.
- C. Movement evoked pain is more significantly correlated than rest pain

Study design will consist of ASA 1 or 2 patients undergoing elective laparoscopic cholecystectomy. Expected correlation coefficient value (r) of 0.6 with two tailed $\alpha = 0.05$ and a $\beta = 0.2$ which will give an estimated sample size of 25. Pre operative care will be routine with exception of baseline pulmonary function measurements and teaching in use of spirometer. Anesthetic plan will be flexible except fentanyl will be the only opioid used. Post operative pain will be managed by IV fentanyl.

Data will be collected at 20, 40, 60, 80, 100, and 120 minutes time points. Measurements will include baseline pain at rest, pain on sitting, and cough pain. Visual analog scale will be used to assess pain intensity. Spirometry measurements will include PEF, FEV1, and FVC. Pain scores for performing these maneuvers will be recorded. Patients are to be discharged home from PAR.

Values of pulmonary function will be plotted as a percentage of baseline value against time. Pain scores will be plotted as a function of time. The pain scores will be correlated with the pulmonary function of each patient to estimate the magnitude and statistical significance of correlation coefficients. Correlation analysis will be used to look at the relationship between pain and pulmonary function, both spontaneous and evoked.

Ultrastructural localization of Delta Opioid Receptors in an animal model of neuropathic pain: implications for novel pain treatment?

S.V. Holdridge¹, BScH & C.M. Cahill^{1,2}, PhD

Departments of ¹Pharmacology & Toxicology and ²Anesthesiology, Queen's University

Background: Neuropathic (NP) pain is defined as pain caused by a peripheral and/or central nervous system lesion with sensory symptoms and signs and is estimated to affect more than 1.5 % of Americans. Despite its prevalence and adverse impact on functionality and quality of life, it remains a significant challenge for physicians as it is typically refractory to traditional analgesics. However, research in ours and other laboratories increasingly suggests a therapeutic role of delta-opioid receptor (OR) agonists in treating NP pain. Following induction of NP pain in rats, intrathecal administration of Deltorphin, a selective delta-OR agonist, dose-dependently attenuated mechanical allodynia as assessed using calibrated von Frey filaments. Furthermore, Deltorphin produced enhanced antinociception in NP rats compared to controls in two acute thermal pain paradigms. These data suggest that NP injury induced changes in the delta-OR function. This functional enhancement does not appear to be a result of increased delta-OR biosynthesis, as delta-OR protein did not significantly increase. It is therefore hypothesized that alternative mechanisms, such as increased cell-surface expression, may be responsible.

Methods: In the present study, we examined delta-OR subcellular localization by electron microscopy immunohistochemistry using immunogold labeling in the spinal cords of NP and control rats. The number and proximity to the plasma membrane of silver-enhanced gold particles will be assessed within the dorsal horn with particular attention paid to the distribution of delta-ORs in laminae I & II, and V, as these regions are involved in the processing of pain transmission.

Results: Quantification and analysis are in progress.

Discussion: The recruitment of delta-ORs to neuronal plasma membranes with a corresponding enhancement in antinociceptive effectiveness may represent a compensatory mechanism by which neurons may sustain an inhibitory tone during chronic pain states.

Barriers to the use of an electronic database to record anesthesia experience.

Esther Ho, MD, Ryan Endersby, MD and Ted Ashbury, MD, FRCPC
Department of Anesthesiology, Queen's University

Residents are required to keep a record of their clinical experience throughout residency. Ideally, this record not only provides a means to keep track of the number and variety of cases done but also allows the incorporation of notes which can be written to provide future references and reflection about the cases. The Resident Log Book (RLB) is one of the newest media by which residents can record their daily activities. It is a web based electronic database designed by the Queen's University Anesthesiology Informatics Lab (QUAIL) available to all anesthesiology residents across Canada. The data collected from this program can have great implications for the quality assurance of residency programs across the nation. Residents' experience can be compared between programs. In order for the data to be useful, all residents across the country must enter their data in the RLB.

In order to ensure full resident usage of the RLB, barriers to adoption of the RLB for recording clinical experiences must be determined and incorporated into future upgrades of the RLB. Icek Ajzen, a renowned psychologist has developed a theory describing the motivation of any human actions. In the Theory of Planned Behavior, human actions are guided by: whether the person is in favor of doing it (attitude), how much the person feels the social pressure to do it (subjective norm) and whether the person feels in control of the action in question (perceived behavioral control) (2). Based on the theory, a questionnaire to study these three aspects behind human actions was developed. The questionnaire has been used to study different human behaviors and has repeatedly shown to be a reliable model. Furthermore, it has been adopted in the studying the motivations behind health professionals.

In our proposed study, a questionnaire regarding the attitude, the subjective norm and perceived control over using the RLB will be constructed using the instructions from Constructing Questionnaires Based on The Theory of Planned Behavior – A manual for Health Services Researchers by Francis, J et. al(3). First, a pilot questionnaire will be used to identify accessible attitude, subjective norm and perceived behavioral control. Using the identified beliefs, a second questionnaire consisting of approximately 41 items with rating scale will be created. The results from the second questionnaire will be analyzed using standard algorithms. It is predicted that the Theory of Planned Behavior will allow us to assess the barriers to adopting the RLB and make changes to the program to improve its utilization by residents.

References:

- 1) <http://www.people.umass.edu/aizen>
- 2) www.residentlogbook.com
- 3) Francis, Jillian et. al., *Constructing Questionnaires Based on The Theory of Planned Behavior: A Manual For Health Services Researchers*. University of Newcastle, May, 2004.
- 4) Beatty, PC and SF Beatty, *Anaesthetists' intentions to violate safety guidelines*. *Anaesthesia*, June, 2004; 59(6): 528-40.

PSYCHOSOCIAL FACTORS AS PREDICTORS OF RELATIONSHIP SATISFACTION IN CHRONIC LOW BACK PAIN

Samantha E. Waxman B.A., Dean A. Tripp Ph.D., Annie Y. Hsieh B.A.

Department of Psychology, Queen's University, Kingston, ON Canada

Chronic pain is a leading health issue for Canadians, and chronic low back pain (CLBP) is one of the most commonly experienced forms of chronic pain. CLBP negatively impacts an individual's life, as indicated by decreased quality of life and interpersonal relationships, and increased disability and psychosocial difficulties (Lamé et al., 2005; Moulin et al., 2002). However, little information is available regarding the role of the psychosocial environment in the prediction of relationship satisfaction. The purpose of this study is to examine the contribution of various psychosocial variables in the prediction of relationship satisfaction in patients with CLBP. We hypothesized that relationship satisfaction will be negatively associated with catastrophizing, pain-related fear, and depression, and positively associated with sexual satisfaction. Fifty-four patients with CLBP completed a series of measures assessing physical and psychological functioning. Hierarchical regression will be used to test the unique contribution of psychosocial variables to relationship satisfaction over and above demographic and medical variables. This study will provide a better understanding of the factors that play a crucial role in the decline of relationship quality among CLBP patients. The study is ongoing and final results, as well as clinical implications, will be discussed.

References:

- Lamé, I. E., Peters, M. L., Vlaeyen, J. W. S., Kleef, M., & Patijn, J. (2005). Quality of life in chronic pain is more associated with beliefs about pain, than with pain intensity. *European Journal of Pain*, 9, 15-24.
- Moulin, D. E., Clark, A. J., Speechley, M., & Morley-Forster, P. K. (2002). Chronic pain in Canada: Prevalence, treatment, impact and the role of opioid analgesia. *Pain Research and Management*, 7, 175-184.

Temporal Artery Scanner Thermography: adequate for the OR?

N'Gai Porte, Medical Student, Queen's University; Dr. T. Ashbury, Department of Anesthesiology, Queen's University; Wilma Hopman, Community Health and Epidemiology

Introduction:

Hypothermia is a common complication of general and regional anesthesia. It is associated with increased infection rates, decreased wound healing and increased cardiac morbidity, among others things. Less than one third of American anesthesiologists monitor patient temperatures during regional anesthesia and thus it is likely that significant hypothermia goes unnoticed during these procedures.

Temporal artery thermometry is a relatively new non-invasive method of measuring core temperatures. This study aimed to determine if temporal artery temperature monitoring could be used in the operating room setting when nasal or oral sites are not tolerated.

Methods:

Patients undergoing any surgery involving general anesthesia were recruited for this study. Temperatures were monitored from four different sites (axillary, nasopharyngeal (NP), skin and temporal artery), and were recorded every 15 minutes throughout the case. Temporal artery temperatures were measured with the Exergen Temporal ScannerTM (TS). Axillary and skin temperatures were taken using axillary probes and liquid crystal skin thermometers. NP temperatures were treated as core temperatures and all other sites were compared to NP. Agreement between NP and TS/axillary/skin was calculated using Bland and Altman analysis with 0.5 degrees Celsius chosen as an acceptable variation between temperatures.

Results:

Ninety-five percent of the Temporal Scanner temperatures varied from NP by more than 0.5 degrees Celsius. Axillary and skin temperatures had 45% and 69% variation, respectively. Of the three methods axillary was the best alternative to NP temperatures.

Discussion:

Our results demonstrate that the Temporal Scanner is a poor alternative to NP temperature monitoring in general anesthesia patients. It is not a suitable intraoperative temperature monitoring technique. Axillary temperature agreed most with NP and therefore is the method of choice in cases where NP or oropharyngeal sites are contraindicated.

Limitations of this study are its small sample size and that nasopharyngeal temperatures were used to represent core rather than a more standard location.

References:

1. Frank SM, Nguyen JM, Garcia CM, et al. Temperature monitoring practices during regional anesthesia. *Anesth Analg* 1999;88:373-7.
2. Arkilic CF, Akca A, Taguchi A, et al. Temperature monitoring and management during neuraxial anesthesia: An observational study. *Anesth Analg* 2000;91:662-6.
3. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307-10.

Blockade and reversal of morphine tolerance with ultra-low doses of opioid receptor antagonists.

Glory Prupas¹, Cathy Cahill^{1,2}, and Khem Jhamandas^{1,2}

¹Department of Pharmacology and Toxicology, ²Department of Anesthesiology, Queen's University, Kingston, Ontario

Introduction: The mechanisms underlying the development of opioid analgesic tolerance are largely unclear, but it has been shown that this phenomenon is related to up-regulation of pronociceptive neurotransmitters such as calcitonin gene-related peptide (CGRP) and substance P in the dorsal horn of the spinal cord. We have previously shown that the development of opioid tolerance, as indicated by the loss of morphine potency, can be blocked or reversed by co-treatment of morphine and an ultra-low dose of *non-selective* opioid receptor antagonist, naltrexone. This study examines if: a.) *selective* μ - and d-opioid antagonists, CTAP and naltrindole, share the effect of ultra-low dose naltrexone, and b.) whether ultra-low dose naltrexone acts by preventing or reversing the up-regulation of CGRP at the spinal level.

Methods:

Induction of Tolerance Study: Adult, male Sprague Dawley rats were given a daily intrathecal injection of either 15 mg morphine or in combination with ultra-low dose of an antagonist [naltrexone 0.05 ng, CTAP 0.001 ng, or naltrindole 0.06 ng] from day 1 to day 7. Nociceptive thresholds were assessed using the tailflick and paw-pressure withdrawal tests. On day 8, a cumulative morphine dose-response curve was derived to generate morphine ED50 value, an index of drug potency.

Reversal of Tolerance Study: Morphine analgesic tolerance was induced by daily administration of 15 mcg morphine for 5 days. On day 6 to day 10, animals received either morphine alone or in combination with ultra-low dose of an antagonist [naltrexone 0.05 ng, CTAP 0.001 ng, naltrindole 0.06 ng]. On day 11, a cumulative morphine dose-response curve was derived to generate morphine ED50 value. Rats were perfused with formaldehyde at the end of the behavioral experiments to process their spinal cords for immunohistochemical labeling of CGRP.

Results: Co-treatment with an ultra-low naltrexone prevented the development of morphine analgesic tolerance. In animals rendered opioid tolerant, introduction of an ultra-low dose naltrexone with morphine restored the analgesic potency of morphine. The CGRP-immunoreactivity in the lumbar spinal cord of morphine-tolerant animals was significantly higher than that in non-tolerant animals treated with a combination of morphine and naltrexone, saline, or naltrexone alone. The effect of ultra-low dose of *non-selective* opioid receptor antagonist, naltrexone, in maintaining or restoring morphine potency was shared by ultra-low dose *selective* μ - and d-opioid receptor antagonists, CTAP and naltrindole, respectively.

Conclusion: Co-treatment with ultra-low dose naltrexone prevented and reversed the up-regulation of CGRP that is known to contribute to the development of morphine tolerance. Naltrexone and related opioid receptor antagonists may be useful in maintaining opioid potency during chronic drug administration with opioids. [Supported by Canadian Institute of Health Research].

Does gabapentin attenuate morphine analgesic tolerance via actions on the alpha-2-delta-1 subunit of the voltage-dependent calcium channel receptor?

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Recent evidence suggests that gabapentin (GBP) is an effective agent for the treatment of neuropathic pain.¹ Currently there is a newfound interest in the drug as a perioperative 'coanalgesic'. Over the past 5 years there have been several studies exploring the use of the medication in this context. A single preoperative dose of GBP has been found to significantly decrease pain scores and opioid usage after spinal surgery, mastectomy, hysterectomy and laparoscopic cholecystectomy.² These data, in combination with its relatively benign side-effect profile, has made gabapentin a drug of considerable interest to the anesthesiologist.

The mechanisms of gabapentin action are unknown. A GABA-analogue, gabapentin was originally developed as an anticonvulsant. It binds with high affinity to the alpha-2-delta-1 subunit of the voltage-dependent calcium channels (VDCC) in the CNS.³ This subunit is upregulated in the dorsal root ganglion and dorsal spinal cord in rodent models of neuropathic pain.⁴ Administration of intrathecal antisense oligonucleotides complementary to a region in the alpha-2-delta-1 gene designed to knock down alpha-2-delta-1 subunit expression attenuates tactile allodynia in neuropathic rats, indicating an important role for this subunit in the modulation of neuropathic pain states.⁵

Gabapentin has opioid-sparing effects in humans. In the cold pressor test, it enhances the acute analgesic effect of morphine in healthy volunteers.⁶ Animal studies have shown that GBP administered systemically and intrathecally can block and may reverse morphine tolerance.^{7,8}

Elucidating the mechanism of action of GBP is an important step in exploring the clinical possibilities of this drug. The alpha-2-delta-1 subunit of the VDCC may be a site of action where GBP exerts its effects on morphine tolerance. Indeed, various studies have demonstrated that VDCC antagonists block opioid analgesic tolerance, highlighting the relevance of these channels in the development and maintenance of tolerant states.

The proposed experiment involves intrathecal administration of antisense oligonucleotide designed to block translation of the alpha-2-delta-1 protein. Antinociceptive effects of morphine will then be assessed by determining thermal thresholds of the rat hind paw using a hot-box apparatus. Western blot analysis will then be used to confirm antisense-induced knock down of the alpha-2-delta-1 subunit. We propose that suppressing translation of the alpha-2-delta-1 subunit will attenuate morphine analgesic tolerance. Furthermore, administration of GBP will have no effect on opioid tolerance in antisense treated rats if, indeed, GBP is acting via this protein.

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Laser Therapy for Retinopathy of Prematurity: Is a general anesthetic necessary?

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Background: Retinopathy of prematurity (ROP) affects a very high risk group of infants frequently with chronic lung disease and other serious systemic co-morbidities, making them vulnerable to the complications of the operative treatment and anesthetic. Moreover, laser therapy for ROP often occurs shortly after infants have been weaned from a ventilator. Laser therapy is the newest advance in treatment of ROP. It is potentially less invasive and more portable than cryotherapy for ROP. Anesthetic techniques are adapting to this new surgical technology such that laser therapy is successfully being performed under sedation and analgesia in various centers. However, there is very little in the current literature describing this technique. **Objective:** To retrospectively evaluate and compare the anesthetic technique of sedation and analgesia versus general endotracheal anesthesia (GETA) for laser therapy of ROP. **Methods:** All non-intubated infants less than 42 wks GA who had laser therapy performed for ROP at Kingston General Hospital or Hotel Dieu Hospital under any type of anesthetic were included in the initial retrospective chart review. Cardiorespiratory stability scores (CRSS) were assigned for four days pre- and post-operatively. The CRSS was determined using the parameters of mean daily FiO₂, mode of respiratory support (IPPV, CPAP, NP), apneas, bradycardias, desaturations, and emergency resuscitation. Intra-operative events requiring surgical interruption, anesthetic intervention or conversion to GETA were also noted. Scores reflected (0) improvement from baseline, (1) no change from baseline, (2) mild instability, (3) marked instability, and (4) life-threatening event. Perioperative stability scores of the two groups were trended and compared. This preliminary study will be used to design a randomized prospective study comparing GETA versus sedation and analgesia. **Results:** Preliminary scores suggest that sedation and analgesia can be successfully used to perform laser surgery for ROP. **Conclusions:** Sedation and analgesia offers a comparable technique of anesthesia to GETA for laser therapy of ROP in extubated infants with cardiorespiratory stability.

Patients' attitudes and perceptions regarding the use of portable computers at the bedside: A qualitative assessment

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Objective: To obtain patients' attitudes and perceptions about the impact of documentation on portable computers at the bedside on the clinician-patient interaction

Design: Two consecutive qualitative interview studies (tablet and personal digital assistant)

Participants: Purposive sample of 40 consecutive patients who had undergone a routine assessment which was documented at the bedside using a tablet (n=20) or personal digital assistant (n=20)

Setting: The acute pain management service at Kingston General Hospital in Kingston, Ontario, Canada, July 2004

Results: All patients felt that the use of a tablet or personal digital assistant for documentation at the bedside was unobtrusive and did not adversely impact the clinician-patient relationship. Participants found the technology to be progressive and a valuable tool that could contribute to improving hospital efficiency while ensuring the documentation of a reliable and accurate medical record. Areas of concern were the level of comfort and competency of clinicians using the portable computer and the potential for the technology to "crash".

Conclusion: Patients view the use of portable computers at the bedside as unobtrusive and with no adverse impact on the clinician-patient relationship. Furthermore, many patients view this technology as a valuable tool that can promote an efficient hospital atmosphere, and reliable and accurate medical documentation. This research suggests that the perceived negative effect of portable computers at the bedside may be inaccurate.

PAIN PREVALENCE IN SCHOOLCHILDREN

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Abstract

Despite significant improvement in understanding the epidemiology of chronic pain in adults, relatively little is known about pain in children living in North America. We conducted a population-based study to assess the prevalence of pain in a sample of 9- to 13- year old schoolchildren in Eastern Ontario. Children completed the *Pain Experience Interview – Short Form* which captures information on the lifetime and point prevalence of different types of acute and chronic pain. The questionnaire was completed in class or at home. A majority of the 495 children in the study (96%) had experienced acute pain during the previous month. Headache (78%) was the most frequently reported. The lifetime prevalence for some types of acute pain was significantly different by gender ($p < 0.05$). Fifty-seven percent of the children reported at least one recurrent pain, while 6% were identified as having had or currently having chronic pain. Self-administered school surveys are an efficient means of capturing epidemiological data on pain in children. The prevalence estimates obtained in this Canadian cohort are comparable to international population-based estimates of specific pain sites in children (i.e., headache). Pain related to minor childhood events is common, however a large portion of children also report frequent and disabling pain. The *Pain Experience Interview – Short Form* can be used to assess the level of self-reported pain in 9- to 13- year olds, and may be useful as a screening survey to identify children at risk of developing or maintaining chronic pain conditions.

Critical Appraisal Essay

By: Rejean Gareau, MD, PGY-1

Title of the Publication: *“The Risk of Cesarean Delivery with Neuraxial Analgesia Given Early versus Late in Labor.”*

Authors: *Wong CA, Scavone BM, Peaceman AM, McCarthy RJ, Sullivan JT, Diaz NT, Yaghamour E, Marcus RJ, Sherwani SS, Sproviero MT, Yilmaz M, Patel R, Robles C, Grouper S.*

N Engl J Med. 2005 Feb 17;352(7):655-65.

General:

The contribution of neuraxial analgesia to higher rates of cesarean sections when given early (less than 4 cm dilation of the cervix) rather than late in labour has been questioned. This becomes an important issue not only for the patient and child's safety but also for the practice of obstetrics and anesthesiology. However, the title of this paper from the New England Journal of Medicine is relatively vague as it fails to mention the control used in the experiment. Perhaps a better title would have been, "Neuraxial Analgesia versus systemic opioids: The Risk of Cesarean Delivery with analgesia when given early in labour."

The authors of the paper were both anesthesiologists as well as obstetrician/gynecologists which lends the paper some strength in that both specialties were represented. Of course, more anesthesiologists were represented in the writing committee thus providing a potentially skewed perspective on the matter. In addition, the authors were from the Feinberg School of Medicine at Northwestern University - a reputable institution.

Introduction:

The problem being addressed in this study was whether the initiation of neuraxial analgesia given early in labour, defined as being less than 4 cm dilation of the cervix, increases the risk of cesarean delivery when compared to the alternative administration of systemic opioids. The difficulty with the state of knowledge regarding this issue at present time is that there are discrepancies in thinking between obstetricians and anesthesiologists. Many obstetricians believe that early neuraxial analgesia slows down labour and may contribute to an increased rate of cesarean delivery. Many anesthesiologists, on the other hand, do not believe this to be so. It is thought that an increased rate of cesarean section with prolonged labour is due to other reasons such as dystocia or macrosomia. Thus, the hypothesis tested was that initiating and maintaining neuraxial analgesia early in labour with intrathecal opioids would not increase the risk of cesarean delivery when compared with systemic opioids. The significance of this could potentially change the current standard of practice with respect to pain management in labour and delivery.

Methodology:

This study was prospective, experimental, randomized and not blinded. It was composed of human subjects and is justified. The study performed was ethically sound since a protocol for April 7, 2006

pain management was followed in both the control and experimental groups.

Experimental controls were used and were given intravenous or intramuscular hydromorphone. However, if the subjects asked for pain control more than twice, they were automatically given an epidural anesthetic.

With 750 assigned patients and 22 individuals excluded, a sufficient size (of which 350 were required) was met. However, this study was not powered to detect small differences between the groups.

The similarity between our practice of anesthesiology in Kingston and that expressed in the study is difficult to note in that the obstetrical team at KGH decides when the anesthesiology staff is called to administer an epidural analgesic. Because of this, it is very likely that most if not all of the patients receiving epidurals are further than 4 cm dilated.

Experimental exclusions included non-vertex presentation, scheduled induction, any contraindication to opioid analgesia and cervical dilation of 4 cm or greater when seen. These patients were excluded in order to provide patient safety (both fetus and mother) as well as to test the aforementioned hypothesis.

The experimental protocol was very complex and convoluted. It is sometimes difficult to follow the study design although the introduction of a schematic into the journal article substantially aids in the understanding of the outline. While it was designed to test the hypothesis, limitations and flaws in the study design make some of the results questionable.

Of course, the drugs and equipment are very well laid out in the study design. However, some of the patients were given patient-controlled epidural analgesia which does not allow a completely reproducible study design. In addition, randomization was carried out via a computer generated single block. This randomization was not completely adhered to if the patient asked for subsequent pain management despite having received systemic opioids on two previous occasions.

The primary endpoint of the study was the method of delivery (i.e. vaginal or cesarean). Secondary endpoints included an indication for cesarean section, the method of vaginal delivery (instrumentation vs. none), the quality of analgesia, the use of

oxytocin, the duration of labour, the incidence of non-reassuring fetal states and the neonatal outcome.

This study protocol is not clinically relevant in that it is a very time consuming process requiring the anesthesia house-staff to return on multiple occasions throughout the course of labour. This may not be feasible in a busy setting.

Data was analyzed according to the intention to treat. A $p < 0.05$ was required to reject the null hypothesis. Statistical tests used to analyze the data included the chi-square test, t-test, Mann-Whitney test, Kaplan-Meier test and log rank test. A Cox regression analysis was performed as well. The statistics are appropriate.

Results:

The groups sampled in the study were comparable, although the systemic-analgesia group had a higher percentage of individuals with cervical dilation less than or equal to 1.5 cm when first asking for analgesia. This group also had a higher rate of spontaneous rupture of membranes 12 hours or more before given oxytocin. The intrathecal-analgesia group, on the other hand, had a lower median cervical dilatation at the initiation of analgesia. Twenty-two subjects were eliminated from the study after not meeting the inclusion criteria. Furthermore, neither the rates of cesarean delivery nor those of instrumental vaginal delivery were significantly different between the groups. However, the oxytocin infusion rate was higher in the systemic-analgesia group.

Complete dilatation of the cervix and vaginal delivery were shorter after intrathecal analgesia than after systemic analgesia. Moreover, the pain scores between first and second requests for analgesia were found to be lower in the intrathecal group. However, the time interval between the requests was longer in the systemic analgesia group. Incidence and severity of nausea and vomiting were lower in the intrathecal analgesia group.

While there was an increased incidence of prolonged and late decelerations in fetal heart rates in the intrathecal group, a difference in neonatal outcome was not stated. In fact, Apgar scores below 7 were more frequent in the systemic analgesia group. The tables and graphs provided to describe the study details were adequate and a great help in the organization of the paper.

Discussion:

This study concluded that intrathecal opioid use in labour did not increase the rate of cesarean section as compared to systemic opioid use. This conclusion is supported by the results although there may be flaws in the study design that lead to this assumption.

The authors state that the absence of an association between the epidural and cesarean section suggests that an early request for analgesia or an increased use of analgesia early in labour may be an indication that other risk factors for cesarean section, such as macrosomia or dystocia, may be present. In addition, it is stated that epidural analgesia has a prolonged first stage of labour. This may be due to parasympathetic efferents being blocked by neuraxial local anesthetics but not by neuraxial opioids. For this reason, cervical dilation is faster in combined spinal-epidural analgesia rather than epidural analgesia alone.

Analgesia may have indirect effects on labour and its progress. In previous studies it was stated that intrathecal fentanyl decreased circulating maternal epinephrine concentration while systemic meperidine did not. This decrease in circulating epinephrine may decrease tocolysis which would result in a more rapid labour. Alternatively, it has been shown that opioids decrease uterine activity. Prolonged epidural analgesia may also result in a motor blockade which could potentially increase the rate of instrumental delivery.

The study shows that early use of neuraxial analgesia, statistically, does not lead to a higher rate of cesarean delivery; thus, epidural placement may be initiated early on in labour. This also lends support to a previous study by Chestnut et al which suggests that an association between early epidural analgesia and cesarean delivery did not exist. Further, fetal bradycardia associated with intrathecal opioid analgesia did not differ from that associated with systemic opioid analgesia. This contradicted the findings of a previous meta-analysis. It is important to note, however, that there were prolonged decelerations in the intrathecal analgesia group more frequently than in the systemic analgesia group. For this reason, it may be prudent to say that although neuraxial analgesia may not be an independent precursor to cesarean delivery, it may play a role in this outcome. Finally, those neonates born to mothers in systemic analgesia groups were more likely to have low one minute Apgar scores which differed from a previous study.

Limitations in this study are profuse. The study was not powered to detect small differences between groups in the rate of cesarean section. Only nulliparous women in spontaneous labour or with spontaneous rupture of membranes were studied. Therefore, these results may not apply to other populations.

This study was not blinded and techniques of administration of neuraxial analgesia varied between physicians. This could have led to potential differences amongst the patient population. In addition to this, different obstetrical providers had different management styles which could have lead to different results. It is important to mention that the majority of the study was performed by anesthesiologists which could have influenced the results.

While the experiment hypothesis strives to seek an answer to the dilemma of whether early administration of neuraxial analgesia contributes to cesarean section, if analgesics were asked for greater than two times in the systemic analgesia group, they were given an epidural automatically. Thus, both experimental and control groups received epidural analgesia. Therefore, it is difficult to determine whether cesarean delivery is due to early or late administration of intrathecal analgesia versus some other factor or combination of factors.

Protocol violations occurred during the study. In some cases, patients did not receive their assigned treatments for various reasons. Further, no cervical examination was performed in some instances. It is interesting to note that the only mention of these facts occurred in the comments below the first figure rather than in the text of the article. It is unclear if these subjects were still used in the data but this brings forth the question of whether or not the authors were trying to draw attention away from some of the confounding variables in the experiment.

A faster progress of labour after intrathecal analgesia was suggested to have possibly been due to a greater cervical dilation at the initiation of analgesia. It is important to note that patient controlled epidural analgesia was also utilized in some cases which could have lead to variability within the patient population and may make replication of the study difficult.

In conclusion, some of the results of this study seem promising; however, there are many limitations to the study both in design and practice. While the results of this study would suggest that neuraxial anesthesia may be initiated early in labour with no increase in the rate of cesarean section, this study should be reviewed by obstetricians in order to be clinically appropriate.

Critical Appraisal Essay

By: Ruth-Ann Green, MD PGY-1

Title of Publication: *“Effects of music on target-controlled infusion of propofol requirements during combined spinal-epidural anaesthesia.”*

Authors: Zhang XW, Fan Y, Manyande A, Tian YK, Yin P.

Anaesthesia. 2005 Oct;60(10):990-4.

Music has been long known for its ability to elicit emotion in people. It was in 1914 that this phenomenon was applied in the operating room, when Kane (1) used intraoperative music as a distraction from the “horror of surgery”. Since that point, numerous studies have been conducted which investigate the effects of music on the surgical patient. It has been shown that music during the preoperative period reduces anxiety (2, 3, 5, 7) and can decrease the sedative and analgesic requirements of awake patients intraoperatively (4, 6). Cross-cultural validity was supported when the effect of pre-operative music was found to reduce anxiety in Chinese men (3). Most of the studies conducted to date involve conscious or lightly sedated patients.

This study strove to measure the calming effects of music using bispectral index (BIS) and target-controlled infusion (TCI) propofol during spinal-epidural anesthesia. The authors of this paper are from Tongji Medical College and Guazhong University of Science and Technology, both in China, as well as from the Thames Valley University in London, UK. The authors took a similar stance to previous studies, measuring the sedative effects of music, but varied slightly in that they used a higher degree of sedation and incorporated more objective measures of outcome. Through measuring the amount of propofol required intraoperatively, with and without music, this study adequately addresses the hypothesis that music may have sedative properties.

Methods:

110 ASA grade one or two women who were scheduled for elective total abdominal hysterectomy under combined spinal-epidural anesthesia were enrolled. Their ages ranged from 24 to 59 years and their weight was between 44 and 80 kg. The study design was prospective, randomized and experimental. Informed consent was obtained from all participants and the local ethics committee granted its approval for the study. A computer-generated randomization list was used to assign the women to either the music or the control group. Each group consisted of 55 women. With an accepted statistical significance of $p < 0.05$, a significance level of 5%, power 90%, common standard deviation of 100 and mean values of 178 mg and 250 mg of propofol use, it was determined that the study size was adequate. The estimate of propofol use was gathered from their pilot study.

The authors adequately outlined the type of equipment and the intervals at which they were used. The parameters of the OAA/S (observer's assessment of alertness/sedation) were
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clearly outlined as well as its use perioperatively. A 10 cm VAS (visual analogue scale) was used on post-operative day one to determine, “the patient's level of satisfaction with perioperative care,” however, the time of day, and the manner in which this was approached was excluded. The handling of IL-6 and the assay used for its analysis were clearly delineated. Information which was not included in the paper was the time of day that the surgeries were conducted and specific information regarding the degree of hydration of the patients preoperatively. This information could be useful insofar as reproducibility.

The exclusion criteria for this experiment were ASA class III and IV and weight under 44 kg or over 80kg. The restriction on ASA class permitted the comparison of more similar groups with regard to general health status as well as physiological responses to anesthesia and thus the endpoints of the study. Along a similar thread is the weight restriction. Large variance in weight and height would be a significant confounding variable with the amount of propofol required to achieve the desired endpoint. In addition, obesity coincides with a number of health related comorbidities which would alter the statistical significance of the two samples. Other exclusion criteria were non-elective procedures, and of course men, given that the operative procedure was a hysterectomy. There was no mention of excluding women on the basis of medications that they were taking routinely, however the women were screened for drug abuse. In addition to the above criteria, the women in the study were screened for hearing impairment, known psychiatric or memory disorders, all of which may have altered the study outcomes.

This experiment used a number of endpoints to evaluate the sedative properties of music. These included TCI (Target Controlled Infusion) propofol, BIS, OAA/S score, blood pressure and heart rate, all of which were recorded at 10 minute intervals perioperatively. In addition, the incidences of cardio-respiratory depression were recorded, the induction time of sedation, and the intra-operative amount of propofol. On post operative day one, the patient's level of satisfaction with perioperative care was measured using a 10 cm VAS. Finally, serum interleukin-6 (IL-6), a pro-inflammatory cytokine, was measured before, immediately after and 1 hour following intervention.

Results:

The two groups were comparable with regard to height, weight, average age, and ASA classification. Characteristics regarding

music, such as perception, exposure frequency and level of music education were also similar among the two groups. In addition, cardiovascular variables as well as baseline and target BIS levels were similar. The mean duration of surgery and TCI were alike in the two groups and no one was excluded from the study. A target of OAA/S 3 (responds only after name is called loudly and/or repeatedly) (8) was attained in all patients.

It was found that the patients in the music group required less time for induction: 12 minutes vs. 18 minutes in the control group. Mean intraoperative propofol target concentration differed: 1.6 ug/ml vs. 2.4 ug/ml compared with the control group as well as total propofol requirements of TCI: 171 mg vs. 251 mg, respectively. Only one patient in the control group had temporary respiratory depression with SpO₂ < 90% directly after the loading dose, which resulted in no complications. A high level of satisfaction was reported in all patients with their peri-operative care, with a mean VAS score of 9.7 in the music group and 8.1 in the control group. No memories during the OAA/S 3 period were recalled, and there were no significant differences in the serum values of the IL-6. The results of this study were outlined entirely in table format. The inclusion of some graphs may have made the data less cumbersome to read.

Discussion:

This study's conclusion was: "Music may help patients to achieve appropriate depths of sedation with significantly lower levels of propofol, shorter induction times of sedation and greater satisfaction." (8). This conclusion is in line with the hypothesis stated in the study's introduction. The results outlined support this conclusion, although there were some factors which were not accounted for.

The authors strove to make the two study groups as equal as possible with regard to sex, height, weight, and even level of music education. Not accounted for were the differences in ethnicity as well as their preoperative perception of surgery and relative anxiety with regard to undergoing surgery. Such information is important because it may offer an alternative explanation for the study's results. For example, if the control group had a higher proportion of women who more nervous regarding surgery they may have required higher doses of propofol as well as longer induction periods. This higher level of anxiety with regard to surgical and/or anesthetic procedures may also be reflected in the cultural background of the people involved in the study. Teasing apart this later concept is an idea for future studies, as few studies in this area have been conducted to date. (3)

Along a similar thread are the differences that exist among individual responses to propofol, which again were not accounted for. That is, if one of the groups studied happened to be more sensitive to propofol, this would affect their overall use and their induction time would be quicker if given the same bolus dose to start. With that said, individual variations regarding responses to a drug are a difficult and tedious phenomenon to account for. The authors tried to gain equality in levels of sedation by attaining an OAA/S of 3 in all patients. They also screened participants for a history of drug abuse, which is one factor that may decrease sensitivity to propofol. The screening process, however, was not outlined so the accuracy of the results cannot be determined. Finally, large variances in individual responses to propofol were minimized

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by the random allocation of participants between the two groups. This effect would be further minimized with a larger study.

One feature of the study that was not mentioned was the difficulty and/or ease with which the combined spinal-epidural anesthesia (CSEA) procedure was performed. If attaining the CSEA was a difficult and/or painful process, it may have induced more anxiety in the patient, thus altering the results. Also excluded was any information regarding nausea and post operative pain which may have had an impact on the patients' perception of satisfaction with perioperative care one day after surgery. Including such information is an idea for further research.

Simply by its nature, this study could not be completely blinded. Those in the control group were aware of their group allocation, as no music was played in their headphones. The people who were grading the OAA/S were, however blinded to the two groups. The non-music group was therefore exposed to the regular noises in the operating room, as the headphones were not noise-occlusive. Consequently, one cannot attribute the results exclusively to music itself, as it may simply be the lack of operating room noise or a distraction from it. Conducting a similar study using occlusive headphones, or simply adding a third arm with ear plugs may be another idea for further research, as this has not yet been studied using deep levels of sedation.

The results obtained through this analysis are in line with previous studies that have examined the effects of music on anesthesia. As mentioned previously, statistical analysis was carried out using fixed parameters which supported the validity of the study, provided the study groups contained at least 42 people each.

This study added to the existing literature by using heavier amounts of sedation as well as more objective measures than previous studies. It has left several unanswered questions, some of which have already been mentioned as ideas for further research. Other focal points for future research underpinning this study include the following: Will similar results be found in a male study group? Does music have a more calming effect on individuals who have a greater appreciation of and/or education in music? Would similar results be obtained using local rather than neuraxial anesthesia? How would music affect this patient group under general anesthesia?

Clearly, the use of music in anesthesia has wide reaching possibilities. Numerous investigations have scrutinized the apparent calming effect of music from several different angles, with each study opening the door to more unanswered questions. The applicability of such studies is usually relatively simple and something that perhaps one day I will incorporate in to my practice of anesthesia.

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Critical Appraisal Essay

By: Robin Harwood, MD, PGY-1

Title of Publication: ***“Propofol is superior to thiopental for intubation without muscle relaxants”***

Authors: ***Taha S, Siddik-Sayyid S, Alameddine M, Wakim C, Dahabra C, Moussa A, Khatib M, Baraka A.***

Can J Anaesth. 2005 Mar;52(3):249-53.

Research Hypothesis

A group of researchers from the American University of Beirut Medical Center in Lebanon conducted a randomized double-blind study to determine whether propofol or thiopental (both in combination with lidocaine and remifentanyl) provided the best intubating conditions in the absence of muscle relaxants. The title of the article and the research question are clearly stated. Prior research has suggested that adequate intubating conditions can be achieved without the use of muscle relaxants. The researchers have attempted to compare propofol and thiopental with respect to ease of intubation and cardiovascular changes following induction of anesthesia. The research question posed has clinical significance. In situations where muscle relaxants are either undesirable or contraindicated, it is worthwhile to study the intubating conditions and post-induction consequences produced by propofol and thiopental.

Study Design

The researchers have conducted an ethically sound, randomized double-blind experimental study of 76 ASA I or II adult patients. Researchers received approval from an ethics committee and also obtained written informed consent from all participating patients. An experimental design is appropriate for attempting to address the issue in question. The patients were randomized by computer into two groups. The anesthetists who performed the intubations did not administer the propofol or thiopental and were prevented from seeing the hypnotic agents by drapes and opaque syringes. An argument can be made that the study may not have been truly double-blind. Even though the intubating anesthetist could not see which hypnotic agent was administered, he or she may have been able to deduce the agent based on immediate changes in heart rate and mean arterial pressure. No information is provided regarding the number of participating anesthetists.

The researchers chose to limit the sample population to 76 ASA I and II patients undergoing elective surgery. Patient ages ranged from 16 to 60 yrs old. Patients were excluded from the study for hypertension, asthma, substance abuse, cardiovascular disease, GERD, BMI > 30 and predicted difficult intubations. Given the nature of the study, these exclusion criteria are reasonable. Accepting an unhealthy patient into this study would have been unethical and may have introduced confounding variables that could have distorted the results. The delivery of safe anesthetic care must outweigh any experimental interests. However, the exclusion criteria used significantly limits the clinical applicability of the study results.

A larger sample size may have also strengthened the clinical relevance of the study.

The experimental protocol is adequately detailed and reproducible. The combination of agents given to patients was lidocaine 1.5 mg/kg, remifentanyl 2 µg/kg and either propofol 2 mg/kg or thiopental 5 mg/kg. Cardiovascular changes were measured at defined intervals after hypnotic administration and after intubation. Intubation was attempted 90 seconds after hypnotic administration. Details are provided regarding the use of ephedrine and atropine in situations where mean arterial pressure or heart rate dropped. In case of a failed intubation attempt, the researchers administered rocuronium to facilitate intubation.

The assessment of intubating conditions was based on subjective scores assigned to mask ventilation, jaw relaxation, laryngoscopy, vocal cord position, coughing and limb movement. For example, scoring categories for laryngoscopy are given as easy, fair, difficult and impossible. No definitions are given to distinguish between a fair and difficult laryngoscopy. The skill level of the intubating anesthetist may bias the scoring in either direction.

In addition to evaluating intubating conditions, data was collected regarding heart rate and mean arterial pressure changes. Heart rate and MAP were recorded at baseline, post-induction, post-intubation, at two minutes post-intubation and at 5 minutes post-intubation. Data was not collected beyond five minutes post-intubation. The researchers reported data as mean ± standard deviation and statistics were analyzed with Student's t test, Chi-square and Fisher's exact test. Statistical significance was deemed to be $P < 0.05$.

Results

Characteristics are provided regarding the propofol and thiopental patient groups. The distribution of age, weight and gender is reasonably comparable between the two groups. The initial heart rates and mean arterial pressures were also similar between the two groups. The researchers found that mean arterial pressure values dropped from baseline in both the propofol and thiopental groups, and MAP remained below baseline for the entire five minute interval in both groups. The propofol group had a larger decrease in MAP from baseline and required ephedrine far more often than the thiopental group. Researchers found that heart rates in the propofol group dropped below baseline and remained below baseline for the five minute interval. Heart rates for the thiopental group showed little variance during the five minute interval.

The study results are reported thoroughly via text discussion, tables and line graphs. No subjects or data was eliminated. All 76 patients are included in the statistical analysis.

Discussion

The researchers concluded that propofol (when used in conjunction with lidocaine and remifentanyl) produced superior conditions for intubation than thiopental. They also noted that hypotension and bradycardia are more often induced with propofol versus thiopental. The statistical results of this study support the researchers' conclusions. Excellent intubating conditions (defined as easy mask ventilation, complete jaw relaxation, easy laryngoscopy, open vocal cord position, no coughing and no limb movement) were obtained in 84% of the patients in the propofol group, but only obtained in 50% of the thiopental patients. The data also shows that propofol, while providing superior intubating conditions compared to thiopental, also produces significantly more hypotension and bradycardia. These results directly address the research question posed. The researchers explain these results by citing previous research that suggests propofol decreases muscle tone and suppresses a laryngeal response to intubation to a larger degree than thiopental. The authors also cite a study that showed thiopental induces greater vocal cord adduction than propofol.

The title of this research article ("Propofol is superior to thiopental for intubation without muscle relaxants") is somewhat inaccurate because lidocaine and remifentanyl are also important factors in achieving the intubating conditions produced by this study. The inclusion of lidocaine and remifentanyl raises the issue of drug synergy which is discussed reasonably well in this article. The authors acknowledge that propofol and remifentanyl may affect each other in a synergistic manner. They cite a study that showed the dose of remifentanyl normally required to reduce a response to laryngoscopy or intubation may be decreased by the concurrent administration of propofol. The authors also acknowledge evidence that lidocaine improves intubating conditions by increasing the depth of anesthesia (in addition to providing an antitussive effect). No discussion is given to alternative agents that may have a synergistic effect with thiopental. Before thiopental can be dismissed as an inferior agent for producing intubating conditions in the absence of muscle relaxants, are there any other combinations of drugs which might improve the utility of thiopental? Perhaps this is a question that will be addressed in future research.

The authors disagree with previous research concerning equipotent doses of propofol and thiopental. They note a previous study that suggested 2.5 mg/kg of propofol was

equipotent with 5 mg/kg of thiopental. The researchers of this study have regarded 2 mg/kg of propofol as equipotent with 5 mg/kg of thiopental. They defend this choice by suggesting that a higher dose of propofol in combination with lidocaine and remifentanyl would have only increased the number of easy intubations achieved. But the severity of hypotension and bradycardia would likely also have become more pronounced, possibly to a point that limits the clinical applicability of the technique.

The results of this study are clinically and statistically relevant. The clinical relevance, however, is limited to healthy euvolemic adult patients with predicted easy intubations who can tolerate a transient drop in heart rate and mean arterial pressure. The authors recognize that this technique poses increased risks in elderly and compromised patients. Compared with previous studies, the researchers have achieved an increased percentage of excellent intubating conditions in the absence of muscle relaxants from 50% to 84% of patients. They attribute this increase to the addition of lidocaine 1.5 mg/kg to remifentanyl and propofol. There is no discussion of why this dose of lidocaine was chosen.

In conclusion, this experimental study has answered a clearly stated, clinically relevant research question and is reasonably consistent with other studies of the same question. The study was double-blind and although there may have been a potential for bias, the magnitude and effect of this bias likely did not significantly distort the results of the experiment. The sample size, at 76 patients, is small but enough to demonstrate that propofol produces superior intubating conditions than thiopental (when both are combined with lidocaine and remifentanyl) in the absence of muscle relaxants. The results of this study can be incorporated into clinical practice provided the technique is only used with healthy, low risk patients. The authors provided an adequate description of data collection methods and statistical analysis and accounted for all patients that entered the study. The difference between the propofol and thiopental groups was statistically significant. The authors have presented a plausible explanation of their results and accounted for their improved success rates compared to previous studies.

Critical Appraisal Essay

By: Devin Sydor, MD, PGY-1

Title of Publication: *“Preemptive epidural analgesia and recovery from radical prostatectomy: A randomized controlled trial.”*

Authors: *Gottschalk A, Smith DS, Jobs DR, Kennedy SK, Lally SE, Noble VE, Grugan KF, Seifert HA, Cheung A, Malkowicz SB, Gutsche BB, Wein AJ.*

JAMA 1998 Apr 8; 279(14): 1076-82.

Introduction:

The title of the article clearly states the intentions of the study and defines the surgery and intervention. The authors are based out of the departments of anesthesiology and urology at the Hospital of the University of Pennsylvania in the United States. They have no stated conflicts of interest.

The aforementioned article addresses the ubiquitous problem of postoperative pain, and more specifically, pain after major lower abdominal surgery. As the article points out in the first paragraph postoperative pain of any kind leads to a reduced patient satisfaction, increased patient morbidity, and the potential for development of chronic pain syndromes. This problem places significant burden on patients and an already taxed healthcare system, and thus it is an important issue to address. Radical prostatectomy is a common surgery in men afflicted with prostate cancer, the most common cancer in males, and thus the issue of postoperative pain control and functional recovery after radical prostatectomy is significant.

Postoperative pain is a well studied problem. All surgeries provide some degree of postoperative pain, and major lower abdominal surgery, including radical retropubic prostatectomy, results in a significant amount. Basic science has outlined several mechanisms for the physiologic basis of pain as well as proposed theories of pain perception and modulation. Further research has uncovered that painful stimuli may actually sensitize the central nervous system (CNS) to subsequent stimuli and promote future pain perception. Several studies noted in the article state that appropriately timed analgesia can modulate the CNS response to painful stimuli, but the authors point out that the varied study results make the practice of preemptive analgesia still controversial. This study's hypothesis states, “that preemptive epidural analgesia, initiated prior to a major surgical procedure with adequate doses of local anesthetic or opioid, would favorably impact short-term and long-term postoperative pain and would influence other postoperative outcome variables”. Testing this hypothesis will further define the use of preemptive epidural analgesia in the clinical setting of postoperative pain.

Methodology:

This study can be classified as a prospective double blind randomized controlled experimental trial. Human male patients scheduled to undergo radical retropubic prostatectomy under general anesthesia with a preemptively placed epidural between April 1994 and December 1995 were block randomized (10

groups of 9) to one of three groups: a control group, a fentanyl group, a bupivacaine group. The latter two groups received preemptive analgesia with their respective medications, while all three received aggressive postoperative epidural analgesia. While 417 patients were initially eligible for the study only 100 patients were eventually randomized into the hospital-based portion of the study. Although the study authors stated that the power analysis revealed that only 60 patients were needed for a significant result, this does not detract from the selection bias that was introduced from not including eligible patients because personnel were not available for the study. While the authors admitted the attending anesthesiologist was not blinded to the grouping of the patient in question for safety reasons, they did note that the research assistant/anesthesiologist who collected the data, as well as the patients, were blind to their treatment grouping. This was important to have, as unblinding of the data collector would have introduced serious observational bias to the study.

The population chosen was stated to be “generally healthy” with an average age of 60 and ASA of 2 in all groups. This may be a slight deviation from the typical patient coming for a radical prostatectomy, and this may have introduced a small selection bias to the study. Patients were excluded (n=2) from the study if they had gross neurological impairment, a chronic pain syndrome, or cardiovascular conditions (e.g. severe valvular disease or coronary artery disease). The former two reasons were probably due to altered perception of pain, and the latter reason because of the requirement for fentanyl at induction to blunt the stress response to intubation.

The experimental protocol, including drugs and equipment used, was clearly explained in the article, such that it could be completely reproducible. The protocol was clinically relevant in that the methods used are an important adjunct to anesthesia and pain control in current practice. The methods used were all standardized to the best ability, and the techniques were probably the standard of practice at that time. For information gathering a 10 question health survey detailing physical activity, body pain, and body pain interference with work was performed before surgery, and then at 3.5, 5.5, and 9.5 weeks postoperatively. No mention whether this survey has been validated. A visual analogue scale (VAS) was used for postoperative pain recording during the first 4 postoperative days. Other surrogate markers were also taken including bloodwork, pulse oximetry, and pulmonary function tests. All of these were collected by the aforementioned blinded research assistant.

The primary endpoint for the study was postoperative pain as assessed daily by the VAS during hospitalization and pain scores obtained at the defined times with the health survey. Secondary endpoints included activity levels postoperatively and several blood tests including cortisol levels postoperatively. Statistical analysis included several tests of variance that seemed appropriate.

Results:

The 3 different groups to which randomization was performed were comparable with respect to age, ASA status, and Goldman score (assessment of cardiac risk for non-cardiac surgery). Postoperatively the groups were seen to also be comparable for intraoperative fluid and medication administration (the bupivacaine group did however require a greater amount of ephedrine administration when compared to the control group). Each of the groups also lost similar numbers of participants to elimination for the following reasons: alterations in the surgical schedule after randomization (n=3), epidural catheter not functioning properly (n=3), patient remained intubated post surgery for reasons unrelated to the study (n=2), inadvertent use of NSAIDs after the surgery (n=1), and patient withdrawal (n=1). Finally, all 3 groups lost one third of their participants to follow up. Both losses could potentially have introduced bias into the study results.

The article provided the results in the form of tables and graphs, all of which are complete and easily deciphered. This made the reader share in the interpretation of the data instead of just following along with the text.

Discussion:

The main conclusion of this study is that "Even in the presence of aggressive postoperative pain management, preemptive epidural analgesia significantly decreases postoperative pain during hospitalization and long after discharge, and is associated with increased activity levels after discharge". This statement slightly exaggerates the results, as the significant decreases in pain did occur during hospitalization and at 9.5 weeks follow up, but the decrease in pain was not significant at 3.5 or 6.5 weeks. The authors explain these results as participants resuming normal activity levels after 6 weeks even if there was some degree of discomfort associated with the activity. With regard to improvement in activity levels after discharge, the results were only significant for the first follow up at 3.5 weeks. The authors explained this result as participants engaging in activity only to the point of discomfort, which leads to differences in activity despite uniform pain scores. These results may have changed if all of the participants lost to follow up could have been contacted.

Although the results address and support the initial study hypothesis with statistical significance the paper may not be as clinically significant as emphasized. The reason for this statement is that the health survey components may not be sensitive enough to detect a clinically significant difference in pain or activity levels because of their small number of discrete points (e.g. 6-point scale for pain, 3-point scale for activity). Also it is unknown if the potential bias introduced through the initial enrollment procedure and the loss of patients to follow up may have changed the results.

Several limitations of this study method/analysis have already been discussed in previous paragraphs. The reader also felt that there were two other limitations. First, the study was a uni-center trial. This introduces a potential for selection bias and a loss of representation of the population on the whole. Second, and not really a limitation, is that some of the medications used in the study for anesthesia may not be regularly used in today's practice, and an updated regimen may need to be studied.

The results of this study vary with existing literature. Although consistent with animal studies and phantom limb pain studies regarding the long-term benefit of preemptive analgesia on postoperative pain, the study admits that there are varied results in the literature about the long-term benefits of this practice. This study does offer a positive outlook for preemptive analgesia in lower abdominal surgery, specifically with an epidural technique. Future studies are needed to answer several questions including the following. Does preemptive epidural analgesia still convey similar long-term benefits when post-operative pain control is not so aggressive? Does epidural local anesthetic provide significantly better long-term pain control than epidural opioids? Do other methods of preemptive analgesia compare to the epidural route for long-term pain control?

Applicability:

This paper has stressed the importance of controlling postoperative pain and has shown that an understanding of basic physiology is the backbone to innovative and effective clinical research and practice. As a junior resident my experience is limited with respect to effective postoperative pain control as well as an understanding of the neuroanatomy and neurophysiology of pain. This paper has allowed me to begin to consider these issues and places a focus on prevention of pain instead of just control. Prevention is just as important, if not more crucial, to the practice of modern medicine, and anesthesia is no exception. This study will allow me to consider prevention (of pain, nausea/vomiting, hypotension, etc.) more seriously in my future practice.

**Queen's University Department of Anesthesiology
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