

Queen's University 29th Annual Anesthesiology Research Day

Scientific Program Coordinators:

Ian Gilron, MD, MSc, FRCPC

Elizabeth VanDenKerkhof, RN, MSc, DrPH

Scientific Adjudicators:

Ted Ashbury, MD, FRCPC

Cathy Cahill, PhD

Franco Carli, MD, MPhil (Guest)

Queen's Anesthesiology Residency Program Director:

Melanie Jaeger, MD, FRCPC

Queen's Anesthesiology Department Head:

John Cain, MD, FRCPC

Queen's Anesthesiology Postgraduate Medical Secretary:

Mrs. Kim Asselstine

** The Royal College of Physicians & Surgeons of Canada, Region 3 Advisory Committee, has provided a continuing medical education grant in support of this meeting.**

Held at Donald Gordon Centre, Kingston, Ontario, CANADA, April 11, 2008.

Supported by Educational Grants from:

Fresenius Kabi

Pfizer

Valeant Pharmaceuticals

Abbott Laboratories

Baxter Corporation

Janssen Ortho

GE Healthcare Technologies

Organon/Schering Plough

Bristol Myers Squibb

Arrow Medical Products

Programme booklet cover design by Nicole R. Richardson

© Copyright 2008, Queen's University Department of Anesthesiology

Queen's University 29th Annual Anesthesiology Research Day

SCIENTIFIC PROGRAMME

- 0830 – 0840 Opening Remarks – Dr. John Cain**
- 0840 – 0850 Research Day Introduction – Dr. Ian Gilron**
- 0850 – 1000 Dr. Khem Jhamandas, PhD, Professor Emeritus, Department of Pharmacology & Toxicology and Professor, Department of Anesthesiology, Queen's University**
"Reflections on 40 Years in Experimental Opioidology: Pain transmitters, opioid analgesia and tolerance"
- 1000 – 1030 Oral presentations** (see list below)
- 1030 – 1100 Poster presentations** (see list below) **and nutrition break**
- 1100 – 1200 Oral presentations** (see list below)
- 1200 – 1300 * LUNCH** (provided) *
- 1300 – 1415 Oral presentations** (see list below)
- 1415 – 1445 Poster presentations** (see list below) **and nutrition break**
- 1445 – 1515 Oral presentations** (see list below)

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

The Judges will be:

Dr. Franco Carli, Professor, Department of Anesthesia, McGill University

Dr. Edwin L. Ashbury, Associate Professor, Queen's Depts. of Anesthesiology and Pediatrics

Dr. Catherine Cahill, Assistant Professor, Queen's Depts. of Pharmacology & Toxicology and Anesthesiology

-
- 1515 Dr. Franco Carli**, Professor, Department of Anesthesia, McGill University, Speaker of the Royal College of Physicians & Surgeons of Canada, Region 3 Advisory Committee
"The postoperative recovery process and meaningful outcomes. Any role for anesthesia research?"
- 1830 Cocktails & Dinner** (Donald Gordon Center), *** Awards Presentation following dinner ***
-

Poster Presentations

Edmund Ong, Cathy Cahill. **Opioid Receptor Heterooligomer Translocation in Neuropathic Pain**

K.A. Sutherland, C.M. Cahill. **In vivo heterodimerization of the delta and mu opioid receptors.**

T.A. Mattioli, B. Milne, C.M. Cahill. **Attenuation of morphine-induced glial activation and tolerance development by ultra-low dose opioid antagonist.**

Julian Mackenzie-Feder, Nicole J. Bailey, Eric C. Dumont. **Dopamine produces bidirectional modulation of synaptic transmission in the bed nucleus of the stria terminalis.**

Meredith J. Kuipers, Dasha V. Ianovskaia, Adam Schizkoske, Eric C. Dumont. **Dopamine in the bed nucleus of the stria terminalis is critical in the reinforcement produced by natural or pharmacological rewards.**

Scott Hayton, Mary Cella Olmstead, Eric C. Dumont. **Acquisition of response inhibition produces shift in synaptic strength. An engram for executive control?**

Tania J. Morano, Nicole J. Bailey, Catherine M. Cahill, Eric C. Dumont. **Nuclei- and condition-specific responses to pain in the bed nucleus of the stria terminalis.**

Order of Oral Presentations

Dr. Kyle McKechnie, PGY-4, Queen's Anesthesiology

"Flo-Trac pulse contour analysis versus pulmonary artery catheter thermodilution for the determination of cardiac output during aortic valve replacement surgery for aortic stenosis" (research update)

Dr. Chantelle Peter, PGY-2, Queen's Anesthesiology

"Retrospective Chart Review: Post-operative Respiratory Events in Patients with Obstructive Sleep Apnea Monitored by Overnight Remote Oximetry" (research proposal)

Dr. Kara Gibson, PGY-4, Queen's Anesthesiology

"Can laser therapy of retinopathy of prematurity (ROP) be safely and successfully achieved with local anesthetic, sedation and analgesia?" (research update/data presentation)

Dr. Rejean Gareau, PGY-3, Queen's Anesthesiology

"Quality of a Bier Block with or without the use of an Esmarch bandage" (research update/data presentation)

Dr. Stacy Ridi, PGY-2, Queen's Anesthesiology

"The CaRMs Game: What factors influence Anesthesia applicant's rank list?" (research proposal)

Dr. Andrew Lee, PGY-2, Queen's Anesthesiology

"The effects of intraperitoneal ketorolac on postoperative pain following laparoscopic cholecystectomy" (research update/data presentation)

Ms. Niousha F. Ghazni, MSc Candidate, Queen's Pharmacology & Toxicology

"Functional magnetic resonance imaging of light touch and brush sensations in the human spinal cord and brainstem." (data presentation)

Dr. Samia Ali, PGY-3, Queen's Anesthesiology

"The impact of anesthetic induction drugs on the intraoperative electroencephalogram" (research proposal)

Dr. Ruth-Ann Green, PGY-3, Queen's Anesthesiology

"Pharmacokinetics of Ametop application to oral mucosa" (research update)

Dr. Angela Hogan, PGY-3, Queen's Anesthesiology

"Postoperative Analgesia After Total Knee Replacement: Comparing the analgesic efficacy of the lumbar paravertebral block and the femoral "3-in-1" nerve block" (research proposal)

Dr. Tammy Henderson, PGY-3, Queen's Anesthesiology

"An In Vitro Study Of MRI-Related Heating At 3.0 Tesla Of An Epidural Catheter" (research update/data presentation)

Dr. Patrick Wong, PGY-2, Queen's Anesthesiology

"Gender differences in chronic neuropathic pain: Analysis of clinical features and treatment patterns" (research proposal)

Dr. Robin Harwood, PGY-3, Queen's Anesthesiology

"Do the laryngoscopy techniques of experienced anesthesiologists match classically taught methods?" (research update/data presentation)

Flo-Trac pulse contour analysis versus pulmonary artery catheter thermodilution for the determination of cardiac output during aortic valve replacement surgery for aortic stenosis

Resident presenter: Kyle McKechnie

Supervisor: Tarit Saha

Background: Cardiac output (CO) is often measured by anesthesiologists during aortic valve replacement surgery. Knowledge of CO facilitates the direction of therapies to improve the performance of the heart and optimize oxygen delivery to the body's tissues. The gold standard method of measuring CO in anesthetized patients is thermodilution using a pulmonary artery catheter (PAC), although pulsed Doppler transesophageal echocardiography (TEE) has also been shown to be effective. Unfortunately, PACs have been associated with rare but serious complications and TEE requires both special equipment and an experienced operator. The newly-developed Flo Trac™ system (Edwards Lifesciences LLC) represents an alternative method of estimating CO using the waveform from a patient's arterial line. It offers the potential ability to measure CO intraoperatively without exposing patients to the risks associated with PAC. Minimal operator training is required. At this point the performance of the Flo Trac system has only been sparsely validated in comparison with PAC thermodilution.

Study Questions: 1) What is the measurement error of the Flo Trac™ system in comparison with thermodilution via PAC? 2) Is this error small enough to justify use of the Flo Trac to guide anesthetic management during aortic valve replacement surgery?

Methods: Prospective trial involving 30 elective aortic valve replacement surgery patients. Exclusion criteria will include refusal of consent, presence of either tricuspid regurgitation or aortic regurgitation and symptomatic peripheral vascular disease. CO values will be obtained simultaneously via both Flo Trac™ and PAC thermodilution at the following time points: post induction of anesthesia, 15 minutes post sternotomy, 1 hour after arrival in postoperative recovery and 6 hours after arrival at the postoperative recovery. Bland-Altman plots will be used for data analysis.

Retrospective Chart Review: Post-operative Respiratory Events in Patients with Obstructive Sleep Apnea Monitored by Overnight Remote Oximetry

Resident presenter: *Chantelle Peter*

Supervisors: Kim Turner and Alison Froese

The purpose of this research is to explore the relationship between post-operative oxygen desaturations captured by remote oximetry in patients with Obstructive Sleep Apnea Syndrome (OSAS) and the possible association of these events with: perioperative CPAP use/treatment, surgical procedure, type of anesthetic and post-operative analgesia, and extraneous oxygen use.

During the last 10 years OSAS has become widely recognized not only by the medical but also lay community, as an important disease with significant implications on the cardiovascular and cerebrovascular systems, not to mention, the daily functional impairment associated with sleep-fragmentation. It is believed that patients with OSAS are at particular risk for worsening of their disease during the perioperative period because of the effect of surgery on sleep architecture and the use of sedatives, hypnotics, and narcotics used during the anesthetic and for post-operative analgesia. Concern for the care of these patients prompted the American Society of Anesthesiologists (ASA) to appoint a task force to review published evidence and poll expert opinion to build consensus for practice guidelines for the perioperative management of patients with OSAS. Many Canadian hospitals, including Kingston General Hospital (KGH), have adopted a version of these 2006 guidelines.

To date there are no published studies evaluating the use of these guidelines and any change in patient morbidity and mortality since their institution. Currently at KGH all patients undergoing post-operative remote oximetry have a comprehensive printed report detailing the frequency and magnitude of oxygen desaturations experienced during their first night after surgery. Although such data is available, no formal evaluation has been made to correlate respiratory events in these patients with the clinical aspects of their surgical and post-surgical care. The current proposed study is intended as a pilot project to analyze previously collected but not evaluated data from overnight remote oximetry and find relationships between respiratory events and peri-surgical care. Our hope is to then design a prospective trial to see if perioperative interventions as directed by the ASA guidelines are in fact impacting morbidity and mortality in patients with OSAS.

The proposed study is a retrospective chart review in conjunction with analysis of already existing remote oximetry data. The sample size for this pilot study will be a minimum of 50 patients who underwent surgery between January 1, 2007 and the present. Individual patient charts will be examined for key information in the anesthetic record, post-anesthetic care unit record, sleep lab reports, respiratory consult letters, and nursing progress notes.

This pilot project relies heavily on the availability of adequate patient records with a readable documentation of events, which may not be obtainable. The presented study offers no control for comparison. As well, this small study may be inefficient for evaluation of rare events like respiratory depression and death. Because this project is purely observational as opposed to interventional, all associations demonstrated cannot be ascertained to be causal. Pending approval by the Queen's University Research Ethics Board, it is anticipated that the project will be initiated in April of 2008. Preliminary results of this pilot study will be available in summer of 2008, with plans of a larger, prospective trial projected for fall of this year.

Is sedation and analgesia with midazolam and fentanyl an acceptable alternative to general anesthesia for laser therapy of retinopathy of prematurity?

Resident presenter: Kara Gibson

Authors: Kara Gibson, Sylvia Rodriguez, David Gale and Ted Ashbury

Supervisors: Ted Ashbury and David Gale

Background: The use of laser therapy rather than cryotherapy for treatment of retinopathy of prematurity (ROP) has meant that many of these procedures are occurring under sedation outside the operating room. The use of laser therapy is less painful, and the equipment is more portable than its predecessor, cryotherapy, and lends itself well to more innovative anesthetic approaches for this high-risk neonatal population. It has been debated for years if a general anesthetic is necessary or possibly harmful for these premature infants. Although the recent Ophthalmology literature frequently mentions that these treatments are being performed under sedation and analgesia, to our knowledge there is only one report in the literature describing the experience with a similar anesthetic technique for ROP laser therapy.

Purpose: To determine if sedation and analgesia with midazolam and fentanyl is an acceptable alternative to general endotracheal anesthesia for laser therapy of retinopathy of prematurity.

Methods: A retrospective chart review was conducted on 19 neonates undergoing laser therapy for threshold retinopathy of prematurity from January 2001 to January 2006. All neonates included received either general anesthesia with elective endotracheal intubation or sedation with fentanyl and/or midazolam without intubation for their procedure. Cardiorespiratory parameters were used to score neonatal stability for a period of four days pre- and post-procedure.

Results: The cardiorespiratory stability scores were similar between groups pre- and post-procedure, but the average stability score of the general anesthesia group showed more instability in the 24 hours following the procedure than the sedation group. All neonates in both groups had successful completion of laser therapy. Both techniques provided the surgeon with satisfactory operating techniques. No neonate in either group required emergency intubation at any time following the procedure. There was one conversion to general anesthesia in the SED group due to minor desaturation and bradycardia. All other intraprocedural events, 2 in SED group and 1 in GETA group, were minor and easily treated without impacting the success of the laser therapy or surgeon satisfaction.

Conclusions: This study shows that sedation and analgesia with midazolam and fentanyl for non-intubated premature infants is an acceptable alternative to general anesthesia for laser therapy of retinopathy of prematurity and suggests this sedation technique provides improved cardiorespiratory stability over general anesthesia in the first 24 hours following the procedure.

Quality of a Bier Block with or without the use of an Esmarch bandage

Resident presenter: Rejean Gareau

Supervisors: Scott Duggan and Conrad Watters

Background: Intravenous regional anesthesia, also known as the Bier block, has been used in anesthetic practice for over 90 years and is currently used for anesthesia in upper extremity surgeries including carpal tunnel release, Dupuytren's contracture repairs and reduction of fractures. The procedure is employed with the use of an esmarch bandage to exsanguinate the extremity prior to the infiltration of local anesthetic. This benefit of a bloodless field and an adequate block with the use of the Esmarch has often been assumed in the past; however, currently the literature supplies little information to provide proof for or against this assumption. Because the use of the Esmarch bandage may be potentially painful and its benefit has not been proven, this study will attempt to prove equivalence of anesthetic block both with and without the Esmarch bandage.

Objectives: To assess the need to use the Esmarch bandage for the Bier block.

Methods: An equivalence study has been employed in order to determine if the time to tourniquet pain with and without the use of an esmarch bandage is 45 +/- 15 minutes. Similarly, the duration of block is deemed to be equivalent between the two groups if the block length is 60 +/- 15 minutes. A sample size of 56 patients receiving upper extremity surgery will consist of 28 patients receiving a Bier block with the use of an Esmarch bandage and a control 28 patients without the Esmarch. The patients are randomized to either the control or the experimental group using a set of envelopes chosen by the anaesthesiologist for the case. The surgeon is blinded as to the technique used. Lidocaine is injected intravenously in order to induce analgesia following the inflation of a double cuffed tourniquet. Quality of block is assessed post-operatively with the use of a questionnaire using a number scale to determine patient satisfaction. Further, surgical satisfaction using a similar number scale is applied to the surgeon performing the surgery in order to assess adequate surgical visualization. Intra-operative assessment of analgesia and anesthesia are assessed verbally with primary endpoints including injection of additional local anesthetic by the surgeon and secondary endpoints including the conversion of anesthetic technique to a general anesthetic.

Results: Fifteen patients (9 male and 6 female) have undergone their upper extremity procedures without the esmarch bandage to this point while 11 patients (7 male and 4 female) in the study have had the use of the esmarch. Of the "without" group, none of the patients required conversion to GA while one required supplementation of the field. Surgical satisfaction measured 3.57 +/- 0.42 while patient satisfaction measured 4.57 +/- 0.45. Of the "with" group, no patients required neither conversion to GA nor supplementation. Surgical satisfaction measured 3.09 +/- 0.30 while patient satisfaction measured 4.73 +/- 0.74. Tourniquet times varied between groups with the Esmarch group having a tourniquet time of 41.82 +/- 9.0 min and the without Esmarch group having a tourniquet time of 50.28 +/- 21.64 min.

Conclusions: The quality of block during upper extremity surgery with the use of a Bier block appears to be equivalent with and without the use of an esmarch bandage. There is a trend towards a wetter surgical field in the group in whom an Esmarch bandage is not utilized.

The CaRMs Game: What factors influence Anesthesia applicant's rank list?

Resident presenter: Stacy Ridi

Supervisors: Melanie Jaeger and Lindsey Patterson

Knowledge Gap: There is currently little to no research on how graduating Canadian medical students rank the various residency programs in their chosen specialty. Although residency programs spend significant resources, both human and monetary, on the CaRMs interview process, there is no data available to measure how effective these efforts actually are in attracting top candidates. In fact, it is unknown if the measures these programs take to attract candidates have any bearing on the factors that influence a candidate's rank list.

Aim: To define and explore the major factors influencing a CaRMs applicant's decision to choose one Anesthesia residency program over another. To provide a strategy to implement changes to the Queen's Anesthesia CaRMs process to better meet these influencing factors. A secondary aim is to determine whether or not applicants prefer to have CaRMs Anesthesia residency program interviews in one centralized location vs multiple locations.

Reason for study: There currently is insufficient data on what factors influence CaRMs applicants when ranking anesthesia residency programs in Canada. Queen's University Anesthesia Residency Program spends significant resources on the CaRMs process. Resources are spent on selecting applicants for interviews, as well as the interview process, which is rather involved. Specific dollar figures are currently unavailable but would cover: fourteen staff days, fourteen resident days, provision of food and drinks on interview days, post-interview socials, file review, and the administrative work surrounding the entire process. In addition to the resources spent by residency programs, significant resources are spent by the applicants in turn. CaRMs Anesthesia applicants apply to individual programs. If an invitation to interview is received, they then travel to each individual university for the interview. This is a time-consuming and expensive process for the applicant and there is no data available to know if this expenditure provides any information that ultimately influences their program rank list. In addition to the expense, applicants may be concerned about their safety as the interview process takes place in February in Canada and there is often inclement weather. It is unknown whether financial constraints, travel time and safety influence applicants' decision on where to apply interview. There is currently no system in place that allows feedback on the Queen's Anesthesia Residency Program interview process. As such, it remains unknown whether or not the resources spent are actually effective in influencing candidates' rank list order. Previous Research: A literature search revealed a dearth of information on factors influencing Canadian medical students' residency program selection. There is minimal data on factors influencing medical students in other countries (including the US) on their residency program selection and on the factors influencing medical students' selection of a surgical vs. a non-surgical specialty (The Influence of Quality-of-Life, Academic, and Workplace Factors on Residency Program Selection, Nuthalapaty F.S., Academic Medicine, Vol. 79, No. 5/May 2004). None of the studies are specific to Anesthesia residency programs and all except one,

are from the 1980's and 1990's, and are, therefore, less applicable to today's medical school graduates. CaRMs conducts an optional post-match survey of all CaRMs applicants. These results are not easily accessible by residency programs. Moreover, this survey is not specific to either Anesthesia applicants or to the individual residency programs. There is some research on how residency programs in Canada can effectively choose appropriate candidates. However, none of these studies are looking at the factors influencing the applicants' program selection.

Study Design: The required information will be obtained from a survey. The population of the study will be all 2007-08 CaRMs applicants interviewing for Queen's University Anesthesia Residency program. The survey will be conducted via two modalities. The first modality will be a paper survey provided to the interviewee following their Queen's University Anesthesia interview. Surveys can be returned via a self-addressed stamped envelope (also included) or be deposited in a locked box present on the premise immediately after the interview. This box will not be opened until after Match Day and a sign will be placed on the box to remind interviewees of this, with the implication that their responses will not affect their interview in any way. The second modality will be the option of an online survey should the interviewees prefer it. For this, the interviewees will provide an active email address as a contact after first giving consent for obtaining such information. They will then be emailed a link to an online anonymous survey resource, such as Survey Monkey. CaRMs has provided information obtained in the 2006-07 post-match survey. This information has been used to design the following sample survey, which will be similar to the one given to interviewees.

Follow-up: A follow-up survey in the resident's PGY5 year will be done at 'Making the Mark' conference. This will provide comparison data on if the initial influencing factors are still deemed significant factors. Ethics Interviewees will be asked for consent for their email address. The study will be administered by an individual who has no influence on the ranking of applicants. Similarly, the applicant's decision to participate in the survey will not influence the rank list order. Candidates will be provided with numerous anonymous options for survey completion, including a locked box on the interview day, a stamped envelope to mail the survey at a later date, and an online resource. Timeline: A sample survey is provided in this proposal for approval from the Resident Research Advisor/Board. After implementing suggestions provided by the Resident Research Board, an application will be made to the Ethics Committee, with a request for immediate attention at the next Ethics Committee meeting. After Ethics approval is obtained, the survey will be administered to 2007-08 CaRMs applicants who are interviewing at Queen's University Anesthesia Residency program. The surveys will be collected in the two months following interviews and the results will then be collated and analyzed.

The effects of intraperitoneal ketorolac on postoperative pain following laparoscopic cholecystectomy

Resident presenter: Andrew Lee

Supervisor: John Murdoch

The aim of this study is to determine the analgesic effectiveness of intraperitoneal ketorolac for postoperative analgesia following laparoscopic cholecystectomy. This route of administration is to be compared to intravenous administration. Secondary analysis will include incidence of nausea and vomiting and time to recovery post-anesthesia.

The study population includes patients undergoing outpatient laparoscopic cholecystectomy. There is a goal of 40 patients (120 total) in each group (intraperitoneal ketorolac, IV ketorolac, placebo/control).

Follow-up will be made at 24 hours post surgery with a telephone questionnaire (VAS pain scores, side-effects profile). Descriptive statistics will include frequencies and percents on nonparametric data and measures of central tendency (mean, median, standard deviation) on normally distributed data.

UPDATE: All 120 patients have been recruited and data obtained and unblinded for analysis.

**Altered spinal cord and brainstem activation in response to peripheral sensitization:
a spinal fMRI study**

Student presenter: Niousha Ghazni

Authors: Niousha Ghazni, Catherine Cahill, Caroline Pukall, Pat Stroman

Supervisor: Catherine Cahill

Functional magnetic resonance imaging (fMRI) studies have identified multiple brain structures involved in the pain experience. However, most of the imaging studies performed to date have focused on brain structures rostral to the thalamus, although the first level of sensory information and pain transmission occurs at the spinal cord.

Objectives: The primary goal of the present study is to map activity using fMRI, from the entire cervical spinal cord and brainstem following innocuous and noxious stimuli before and after peripheral sensitization in normal human volunteers.

Materials and Methods: Functional MRI studies of the spinal cord were carried out in 26 healthy individuals in a 3T Siemens Magnetom Trio. We examined the activity of brush and innocuous and noxious touch (von Frey filaments) before and after peripheral sensitization. Stimuli were randomly applied in a block paradigm consisting of three stimulation periods interleaved with baseline periods. After each block, volunteers were asked to rate the pain and unpleasantness on a numerical 11 point scale from 0 to 10. Peripheral sensitization was induced by topical application of capsaicin for 30 minutes. Functional image data were acquired with a half-fourier single-shot fast spin-echo (HASTE) sequence, TE=38 msec and TR=1 sec per slice. Signal intensity changes observed in the image data upon a change in neuronal activity were the result of signal enhancement by extravascular water protons (SEEP), as well as a contribution from BOLD. Sagittal image slices were selected to span from the C7/T1 disc to the superior edge of the thalamus. Areas of activity were superimposed onto anatomical transverse drawings and identified visually with comparison to a stereotaxic atlas

Results: The brush stimulus, before sensitization activated typical areas expected of non-painful sensory transmission. These include the ipsilateral dorsal horn, gracile and cuneate nuclei in the medulla and areas surrounding the dorsal column medial lemniscal pathway. Peripheral sensitization produced activation patterns typical of a pain response, such as the contralateral ventral horn. The touch stimulus produced activity in typical sensory centres in the dorsal horn and brainstem before sensitization, but after sensitization, we observed a pain response as evidenced by the activity in the spinal cord and higher brainstem structures. Interestingly, the noxious stimuli showed similar activation patterns even though the force of the von Frey filaments used to evoke these responses were different.

Conclusions: The results from this study strongly indicate that a non-noxious stimulus translates into a pain response after peripheral sensitization. In all experiments there was indication of descending modulation as activity was observed in and around areas of the periaqueductal gray, midbrain red nuclei and pontine reticular formation. This study is unique in that it shows how peripheral sensitization induces changes in non-noxious stimuli-induced activation patterns that correlate with pain sensory transmission.

Intravenous Anesthetic Agent with Best Potential for Preservation of the Electroencephalogram in Patients Undergoing Carotidarterectomy: Comparison of the Impact of Single Induction doses of Propofol, Thiopental and Etomidate

Resident presenter: *Samia Ali*

Authors: Samia Ali, Joel Parlow and Donald Brunet

Supervisor: Joel Parlow

BACKGROUND: While an ideal monitor of cerebral perfusion during carotid endarterectomy under general anesthesia has yet to be discovered, the use of electroencephalography (EEG) as an indicator of the adequacy of cerebral perfusion is a well established modality that has been validated since the 70's. There are, however several limitations to the use of EEG in this context, one of which is the impact of anesthetic agents. Extensive studies have been done on EEG in relation to anesthetics in the context of carotid surgery. However, most of the literature relates to the purposeful use of repeated bolus doses or continuous infusions of induction agents to induce a burst suppression pattern as a cerebroprotective mechanism. It has been well documented in the literature that propofol, etomidate and thiopental all cause a burst suppression pattern. However, comparison of the onset and duration of EEG changes following a single induction dose of each of these drugs in carotid endarterectomy patients has not been studied

OBJECTIVE: To compare the impact of a standard induction dose of propofol, etomidate and thiopental on the EEG during carotid endarterectomy from the time of induction to carotid cross clamping.

METHODS: After obtaining approval from the ethics committee, 30 patients will be enrolled in this prospective clinical trial. The patients will be randomly assigned to one of 3 groups, each containing 10 patients. Group P patients will be induced with propofol, group T patients with thiopental and group E patients with etomidate. The doses of each of the induction agents shall be titrated to loss of consciousness. Defined doses will not be set as patients undergoing CEA are generally older, with decreased anesthetic requirements. Following induction, desflurane will be used as a maintenance agent in all patients. In order to minimize confounding factors, defined amounts of narcotics shall be used, and benzodiazepines shall not be part of the anesthetic. The 12 channel intraoperative EEG tracing will be stored on computer disk, and then analyzed at the following intervals: prior to induction, then at 2, 5, and 10 minutes post induction, then prior to and 1 and 5 minutes post cross clamping. The neurologist analyzing the EEG shall be blinded to the induction agent used. 30 second epochs of EEG will be analyzed by Fast Fourier Transformation yielding EEG power for each channel. Statistical comparisons of power pre and post clamping will be made between the groups using a polynomial model. This will result in a statistic describing the difference between the groups.

IMPLICATIONS: We anticipate that this study will enable us to determine which, if any of the induction agents may have residual impact on the EEG at the time of cross clamping.

Pharmacokinetics of Ametop application to oral mucosa

Resident presenter: Ruth-Ann Green

Supervisor: Ramiro Arellano

Background:

Tetracaine, the active ingredient in Ametop®, is an ester local anesthetic that is often used for topicalization of the skin in preparation for percutaneous anesthesia. In our institution, Ametop® is frequently used for anesthetizing the mucous membranes in preparation for bronchoscopy or awake intubation. The manufacturers of Ametop®, however, state that application to mucous membranes is a contraindication to its use. Despite this contraindication, Ametop® is routinely and safely used on oral mucosa for cancer patients in order to help with the pain of mucositis. In our institution it is used as an effective means of topicalizing the airway prior to awake intubation or bronchoscopy without adverse reactions. The literature is sparse with regard to studying the effects of tetracaine absorption after application to mucous membranes with the exception of two papers published in JAMA in the 1950's:

1. Adriana, J., Campbell, D. Fatalities following Topical Application of Local anesthetics to Mucous Membranes. JAMA 162: 1527-1530. (Dec. 1956).
2. Weisel, W., Tella, A.,. Reaction to Tetracaine Used as Topical Anesthetic in Bronchoscopy. JAMA 147: 218 – 222. (Sept. 1951).

These papers outline the adverse reactions of patients receiving tetracaine via mucous membranes, but were severely limited by confounding variables. It is my intention to revisit this topic with my resident research project, which will entail a small study including 10 healthy volunteers who can be categorized as either ASA 1 or 2. Women will be asked to take a pregnancy test to ensure they are not pregnant and be required to be using a reliable form of contraception. Participants will undergo a short history and physical as well as blood work to be sure they don't meet the exclusion criteria.

Volunteers will be asked to have nothing to eat or drink for 6 hours prior to commencement of the study. 1 gram of Ametop® (40 mg of tetracaine) will be applied to the mucous membranes (500 mg to each side) over an area of 18cm² and secured under an occlusive dressing. The application time will be 10 minutes, after which the occlusive dressing will be removed. Blood samples will be taken at 0, 2, 4, 6, 8, and 10 minutes after the initial application for a total of 60 mL of blood per individual. Blood will be analyzed for concentration of tetracaine.

This experiment will ultimately lead to a better understanding of the pharmacokinetics of application of Ametop® to oral mucous membranes and add to the paucity of literature on this topic.

Postoperative Analgesia After Total Knee Replacement: Comparing the analgesic efficacy of the lumbar paravertebral block and the femoral “3-in-1” nerve block

Resident presenter: Angela Hogan

Supervisors: Tarit Saha and Richard Henry

Abstract: Pain control after total knee arthroplasty (TKA) can be challenge. Regional anesthesia has been shown to produce better pain control than IV PCA morphine alone in the early postoperative period, however the most optimal technique is still up for debate. Femoral nerve blocks (FNB) do provide good pain control after TKA, as well as facilitate early ambulation and reduce the length of acute hospitalization as compared to IV PCA Morphine alone. The obturator nerve is not consistently blocked with this technique, and the addition of a sciatic nerve block to the femoral nerve block has not been shown to provide significant improvement in pain control. Lumbar paravertebral nerve blocks (LPNB) have been shown to provide adequate pain control after TKA and significantly reduce early morphine consumption, however no study has yet compared the LPNB with the femoral nerve block (FNB) for analgesic efficacy after TKA. The study we are proposing is a prospective double blind, randomized quality control trial that compares post-operative pain control with the LPNB at the L3-4 level with the femoral “3 in 1” block, both using 20mL 0.5% Ropivacaine. Study subjects undergoing single TKA will receive a standardized spinal anesthetic for surgery, after which they will be randomized to either the LPNB group or the FNB group, which will be performed in the recovery room after the operation. All patients will receive IV PCA morphine 1.5 mg q 6 minutes for pain control post-operatively, as well as regular Tylenol and Ketoprofen. Our primary outcome will be total narcotic usage (morphine equivalence consumption) recorded at 12, 24, 48, and 72 hours post-operatively. Secondary outcomes include degree of pain as assessed by the Visual analog scale (VAS) scores at rest and with activity at 4, 8, 12, 24, 48, and 72 hours, as well as by the Brief Pain Inventory (BPI) short form which will be administered by telephone 30 days following surgery.

An In Vitro Study of MRI-Related Heating at 3.0 Tesla of an Epidural Catheter

Resident presenter: Tammy Henderson

Supervisors: Lindsey Patterson and Pat Stroman

Background

Epidural hematoma is a rare but dreaded complication of epidural anesthesia. When this diagnosis is suspected prior to epidural catheter removal, catheters are left in situ for fear of worsening a bleed. The imaging modality of choice to diagnose such a complication is MRI. Many epidural catheters, including Flex-tip Plus Epidural Catheter, contain a ferromagnetic stainless steel coil. Metal containing epidural catheters, however, are deemed MRI-unsafe and CT scans must be carried out instead.

There is research available suggesting the linear movement and torque caused by placing Arrow's Flex-tip Plus Epidural Catheter in the magnet are within safe limits. No studies have looked at this device or any other coil-containing catheter with respect to heating.

Objectives

We propose to demonstrate the safety of Flex-tip Plus Epidural Catheters in a 3.0 Tesla MRI based on a lack of heating in excess of greater than 1 degree.

Methods

A pilot study was conducted in July 2007 by Dr Henderson and Dr Patrick Stroman at Queen's MRI (Department of Diagnostic Radiology). We successfully demonstrated negligible artifact due to the presence of Flex-tip Plus Epidural Catheter in zucchinis. In the absence of artifact, we are hopeful that Arrow epidural catheters will not cause clinically significant heating either.

We propose to place epidural catheters into gel phantoms designed to approximate human tissue. The catheters will be placed in various configurations, either straight or looped, to approximate possible in vivo configurations. These configurations will be imaged and temperature changes monitored using a fiber optic thermometer. Temperature change of greater than 1 degree will be sought and documented (FDA states that heating of a medical implant of less than 1 degree is clinically safe.)

We are currently awaiting funding to purchase the fibre optic thermistors to allow us to complete our investigations.

Future Directions

Our hope is that our investigation will demonstrate the safety of Arrow Flex-tip Plus Epidural Catheters and allow their use in the MRI in cases of suspected epidural hematoma. This will allow for more accurate and expedient detection of pathology thereby improving patient outcomes.

Gender differences in chronic neuropathic pain: Analysis of clinical features and treatment patterns

Resident presenter: *Patrick Wong*

Authors: Patrick Wong, Joan Bailey, Ian Gilron

Supervisor: Ian Gilron

Introduction

It is generally accepted that patient's gender can affect the clinical features of chronic pain. Women have been reported to be prone to recurrent pain, lower pain threshold, experience more disabling pain, and have pain in multiple body regions.¹ However this generalization has been criticized as over-simplified. Gender difference might be even less pronounced in the setting of chronic pain.

Only a handful of human studies have investigated gender differences in neuropathic pain. A series of 829 patients diagnosed with RSD in the Netherlands suggested that women are three times more likely than men to develop RSD.² On the other hand, some have found no differences between gender for neuropathic pain.³

Little is known regarding gender differences in treatment patterns for pain. Simoni-Wastila analyzed the 1987 National Medical Expenditures Survey from US and found that the female gender is an independent predictor for narcotic and anxiolytic use.⁴ On the other hand, Raftery et al reported that perception of pain, rather than gender, is a predictor for number of pills and the strength of medication given in ER.⁵ There are currently no published articles describing gender differences in treatment regimen.

The goal of this study is to identify any differences in clinical features and treatment patterns between males and females suffering from neuropathic pain.

Methods

Gender based secondary analyses were conducted using data from a previous survey of neuropathic pain patients.⁶ Following REB approval, questionnaires were completed by patients pursuing clinical trial enrollment (80 women, 71 men). Information gathered included demographics, pain intensity, duration of pain, current treatments, and previously tried treatments. Proportions data were analyzed with Chi-square tests and parametric data were analyzed with t-tests.

Preliminary Results

Females have significantly higher average pain intensity on a 10-point pain scale (F=5.6 vs M=4.8, $p<0.05$). Higher proportion of females were using weak opioids (F=30.9% vs M=13.2%, $p<0.05$). A significantly larger portion of males were not taking any pain medications for their neuropathic pain (M=35.3% vs F=17.3%, $p<0.05$).

Discussion

Our results suggest that females suffering from neuropathic pain report higher pain intensity and are more likely to receive analgesic drugs than males. Additional research is needed to replicate these findings and to further examine the cause of such differences. Further understanding of gender difference in neuropathic pain may ultimately help to better understand and treat this devastating disorder.

References

1. Unruh, A. M. (1996). Gender variations in clinical pain experience. *Pain*, 65(2-3), 123-167.
2. Veldman, P. H. (1993). Signs and symptoms of reflex sympathetic dystrophy: Prospective study of 829 patients. *Lancet*, the, 342(8878), 1012.
3. Berkley, K. J. (1997). Sex differences in pain. *Behavioral and Brain Sciences*, 20(3), 371-380.
4. Simoni-Wastila, L. (2000). The use of abusable prescription drugs: The role of gender. *Journal of Women's Health & Gender-Based Medicine*, 9(3), 289-297.
5. Raftery, K. A., Smith-Coggins, R., & Chen, A. H. (1995). Gender-associated differences in emergency department pain management. *Annals of Emergency Medicine*, 26(4), 414-421.
6. Gilron, I., & Bailey, J. M. (2003). Trends in opioid use for chronic neuropathic pain: A survey of patients pursuing enrollment in clinical trials. *Canadian Journal of Anaesthesia = Journal Canadien d'Anesthesie*, 50(1), 42-47.

Do the laryngoscopy techniques of experienced anesthesiologists match classically taught methods?

Resident presenter: Robin Harwood

Supervisor: Rick Zamora

Research Question

Do the laryngoscopy techniques of experienced anesthetists match the classically taught method of laryngoscopy with respect to laryngoscope grip and angle of use?

Related Area of Clinical Need

Laryngoscopy is an essential skill for several health care disciplines. A study of in-vivo laryngoscopy may reveal significant differences from classically taught laryngoscopy technique. An opportunity may exist to increase the intubating success rate of student laryngoscopists.

Current Knowledge Gaps in this Area

No standardized investigations have been performed regarding laryngoscope grip and angle of use during in vivo intubations.

Hypothesis to be Tested

This project seeks to test the hypothesis that experienced anesthetists employ a laryngoscope grip and angle of use (ie the angle of the laryngoscope handle relative to horizontal) which significantly differs from the technique taught to beginning laryngoscopists (ie locked wrist and a laryngoscope handle at 45 degrees above horizontal).

Proposed Study Design

We propose to evaluate the laryngoscopy technique of twenty experienced anesthetists in a prospective, controlled observational study. Photographs of laryngoscope grip and angle of use will be digitally analyzed to arrive at a standardized assessment of laryngoscopy technique. Each anesthetist will be photographed performing five intubations on patients with known or anticipated easy airways.

Possible Pitfalls, Feasibility and Expected Project Timeline

This project will require two years to complete. One possible pitfall involves obtaining laryngoscopy photographs from a consistent perspective. Operating room layout and congestion caused by necessary surgical and anesthetic equipment may present challenges to the photographer.

Critical Appraisal Essay

By: **Jason-Denis Cyr, MD, PGY-1, Queen's Anesthesiology**

Title of the Publication: "A Randomized Trial of Tranexamic Acid to Reduce Blood Transfusion for Scoliosis Surgery"

Authors: *Neilipovitz DT, Murto K, Hall L, Barrowman NJ, Splinter WM.*

Anesth Analg. 2001 Jul;93(1):82-7.

Scoliosis surgery is a major orthopedic surgery in which the pediatric population is at increased risk of blood product transfusion and its associated risks. For this reason, Dr Neilipovitz, Murto, Hall, Barrowman and Splinter have published "A Randomized Trial of Tranexamic Acid to Reduce Blood Transfusion for Scoliosis Surgery". These authors are based out of Children's Hospital of Eastern Ontario (CHEO) in Ottawa.

The etiology of blood loss in patients undergoing surgery to correct scoliosis is multifactorial, potential contributors are coagulation factor deficiencies and increased fibrinolysis. As prophylactic tranexamic acid (TXA) is known to reduce blood loss and transfusion requirements in cardiac surgery, the authors have hypothesized that TXA administration would decrease transfusion requirements for pediatric patients undergoing posterior spinal fusion.

Methodology

The design of this experimental study was such that the patient, surgeon, anesthesiologist, as well as the investigator collecting the data were all blinded. The authors' experimental protocol, as described in the article, offers enough detail to be reproducible and is designed to adequately test the hypothesis.

The authors received IRB approval for this study. Consent was obtained from parents of children undergoing posterior spinal fusion for both primary and secondary scoliosis. Exclusion criteria were limited to a history of a bleeding disorder, thrombocytopenia (<150), abnormal INR or PTT, BMI greater than 30, previous thromboembolic event, or a family history of thromboembolism.

This study recruited forty patients, age nine to eighteen, divided into two groups. This allowed for detection of 25% absolute change in the amount of blood transfused with a significance level of 0.05, an 80% power and 5% dropout rate.

The anaesthetic technique in the study design included standard monitoring, sufentanil and thiopental induction, maintenance being accomplished with sufentanil infusion, nitrous oxide and isoflurane. Deliberate

hypotension to a mean arterial pressure of 55 mm Hg +/- 5 was generated with isoflurane until spinal straightening at which time the mean arterial pressure returned to 20% of baseline. Cell saver was used for all patients.

The primary outcome was the total amount of blood transfused in the perioperative period. A uniform transfusion policy was established, excluding cell-saved blood. The transfusion threshold was set at 7.0 g/L or less during the intraoperative period and the first 24 hours after surgery. Use of plasma, platelets and other products was left to the discretion of the attending physicians. All fluids were administered via volumetric infusion pumps.

Results

The authors present their results adequately in a concise and clear manner aided by the use of tables. Demographic values for their study groups are comparable. No subjects were eliminated from this study. Perioperative blood loss was not compared between groups, as operative drains were not placed in all patients. Six patients in each group received at least 1U of blood at values above threshold.

The most significant results to report are statistically significant reduction in total blood transfused (1784 mL vs 1253 mL) and a strong trend towards reduction in transfused packed cells (1254 mL vs 874 mL). Intraoperative blood loss was not significantly different (2453 mL vs 2703 mL).

Discussion

The main conclusion of this study is that TXA has the potential to reduce the perioperative transfusion requirements in pediatric patients undergoing posterior spinal fusion for scoliosis. The results presented with this trial are in support of this conclusion, although the sample size and power are somewhat limited. They also state that although the safety of TXA in this patient population has not been established, no thrombotic complications or other adverse effects were detected in this clinical trial.

A similar previous study by Dell et al. was unable to demonstrate benefit of TXA in scoliosis surgery. The current authors state that Dell et al. had less power and

smaller sample size. Furthermore, Dell et al. only involved primary scoliosis patients, who tend to bleed less.

The authors of this study discuss in good detail the limitations and interpretations they make of their results. The first major point of interest is the fact that estimating blood loss by conventional methods has been demonstrated to be highly imprecise. For this reason, they have judiciously opted to use the surrogate end point of blood transfusions. This is also the most clinically relevant of outcomes.

Upon further review, the basic demographics of the two groups might skew the results in favor of the control group. The TXA group had a larger proportion of patients with secondary scoliosis, which has been proven to increase blood loss. Also, the authors identify one patient in the TXA group who had complicated surgery requiring higher volumes to be transfused. Despite this difference, the TXA group still required fewer transfusions than the control group indicating that there might be more advantage to TXA than that demonstrated.

Potential limitations of this study according to the authors are the use of cell-saved blood as well as transfusions at a hemoglobin value above threshold. Allowance of this practice was justified, if nothing else, on the basis of safety.

Interestingly, although prevention of allogeneic blood products was not an outcome of this study, a post hoc analysis was performed to determine the potential benefit conferred by TXA. Although the number of patients who averted allogeneic blood was not significant, this study demonstrates a decrease in exposure by approximately one unit. Cost alone would justify this benefit, not to mention reduced alloimmunization potential and blood-borne pathogens.

This study raises important issues for the care of our paediatric population undergoing posterior spinal fusion

surgery. It is known that TXA reduces blood loss, and therefore transfusion requirements, in other surgeries. It is only logical to think that this would also apply to scoliosis surgery.

The authors have designed a sound study to attempt to prove this. The primary end point, although arguably surrogate, was the most adequate estimation of reduction in blood loss, as it is known that estimation of intraoperatively losses is highly imprecise.

Their methods were appropriate and this study could be easily reproducible. Anaesthetic technique was comparable to that used commonly. Interestingly, the patient population included patients suffering from both primary and secondary scoliosis allowing for a broader range of applicability and more accurate picture of the population this study can potentially be applied to.

Although sample size limits the power of this study to demonstrate clear benefit, it has proven statistically that patients who receive TXA have a reduction in total blood transfusion. Furthermore, it seems to set a trend towards reduction in packed cell transfusion and blood loss perioperatively. It is also important to note that TXA doesn't appear to be associated with thromboembolic events, as suggested by Benoni et al. This study has not had any adverse effects with the use of TXA, but it did exclude patients at increased risk of thromboembolic events from the protocol.

Blood product transfusions come at a price, both financial and immunologic. Reduction in transfusion requirements as demonstrated by this study, although potentially minimal, may have significant clinical outcome.

In light of the information brought forth by this study, it would be in the paediatric patients best interest to receive TXA for posterior spinal fusion, with further benefit seemingly conferred to patients suffering from secondary scoliosis.

Critical Appraisal Essay

By: **Mathew Kuruvilla, MD, PGY-1, Queen's Anesthesiology**

Title of the Publication: "Randomized Comparison of General Regional Anesthesia for Cesarean Delivery in Pregnancies Complicated by Severe Preeclampsia"

Authors: *Leveno KJ, Cunningham FG, Giesecke AH, Shearer VE, Sidawi JE.*

Obstet Gynecol. 1995 Aug;86(2):193-9.

INTRODUCTION

Many advantages and disadvantages of different anesthetic techniques in the caesarean delivery of women with severe preeclampsia have been postulated. In preeclampsia women, spinal and epidural anesthesia were thought to potentially cause pulmonary edema, in response to the use of pressors and large IV fluids to correct iatrogenically induced hypotension. This drop in hypotension was also believed to lower uteroplacental perfusion. Furthermore, women with preeclampsia were thought to be very sensitive to vasopressors. On the other hand, general anesthesia also had the potential to cause pulmonary edema, cerebral edema, or intracranial hemorrhage in response to the hypertension secondary to increased stimulation by tracheal intubation.

Given that there was no universal agreement on which method was better, this study hopes to compare the maternal and fetal effects of the three anesthetic methods. The hypothesis being tested was that none of the three anesthetic methods had a significant advantage or disadvantage over the other. By testing this hypothesis, it was hoped to eliminate the bias towards using only one anaesthetic method exclusively in women with severe pre-eclampsia.

METHODOLOGY

The study was a prospective study that was randomized and not blinded. The patient base that was looked at is not entirely reflective of the population here in Kingston as the study used women, half of who were nulliparous, 35% Hispanic, 35% African-American, and 30% white. The study is ethically sound as all the potential problems with each anesthetic method were anticipated and appropriate standard of care was provided.

There were two requirements for the women to be included in the study: 1) systolic BP 160 mmHg or greater and diastolic BP 110 mmHg or more or 2) proteinuria of 100 mg/dl (2+) or more. The women excluded were - women with thrombocytopenia, defined by platelet count less than 100,000/mm³; and those with

eclampsia or medical complications (including heart disease, diabetes mellitus, or chronic renal disease). This study was also limited to pregnancies requiring caesarean delivery for indications other than non reassuring fetal heart rate patterns.

Once the women had given consent to be a part of the study, they were assigned according to a random-number table and numbered sealed envelopes to receive one of the three anesthetic methods. The method, drugs and equipment used with each method were explained in detail.

Demographic data, duration of labor, oxytocin use, and indications for caesarean were all recorded, although specific details of these were not included in the article. The highest and lowest systolic and diastolic maternal BP's in the labor room and at various points in the operating room were recorded, along with IV fluid volumes and urine output. Infant outcomes such as gestational age, birth weight, apgar scores, umbilical artery blood gas, admission to special care nursery, incidence of small for gestational age infants, those with respiratory distress requiring mechanical ventilation, and those with intracranial haemorrhage were also recorded.

Statistical analysis used the Fisher exact test and analysis of variance. Repeated measures analysis of variance was used for maternal weight, urine output, and mean arterial pressures across key time posts. Bonferroni multiple comparison procedures were used to refine the results of the analysis of variance. $P < 0.5$ (two-tailed was considered significant).

RESULTS

There were 80 women randomly assigned to general (26 women), epidural (27), or combined spinal-epidural (27) anesthesia. While the demographics within each group wasn't specified, the group as a whole had half that were nulliparous, 35% were Hispanic, 35% were African American, and 30% were white. Furthermore, 6 of the women were excluded as they changed their mind when asked to provide written consent. While another subject

assigned to epidural anesthesia, which failed, was then administered general anesthesia. Most common reason for cesarean was dystocia and abnormal fetal presentation.

Adequate details of results were provided. It was seen that general anesthesia had significantly shorter anesthesia induction to skin incision times (3min of GA vs. 25-35 min for RA) and a shorter skin incision to delivery interval (3 mins shorter with GA).

Among the three anesthesia groups, the mean highest and lowest BPs were approximately 170/110 mmHg. Hypotension with RA had been treated with fluid boluses and ephedrine and they had details how of how much fluids were used along with no. of times ephedrine was used. None of the women required transfusions as their pre-operative and postoperative hematocrits were not significantly different between the 3 groups. Blood pressures at different time points during the surgery were also recorded with the only real difference being a higher blood pressure for GA compared to the other 2 RA. It was also noted that women with RA received significantly more fluids compared to GA. Urine flow was increased in all 3 groups and no oliguria developed in any of the women. There was no significant maternal weight loss among the three anesthesia groups as well.

There were no neonatal deaths and the infants were about 34-36 weeks gestation at delivery, but with a wide range (26-41 weeks). It was found that the spinal epidural group often delivered larger and more mature infants. Infant apgar scores, and cord ph were not affected by the type of anesthetic used.

DISCUSSION

Given the exclusion criteria, none of the three anesthetic methods stood as being more beneficial or harmful than the other. Unlike previous studies, the results of this study showed that general anesthesia was not contraindicated nor was regional anesthesia indicated exclusively in women with severe preeclampsia. Platelet count of less than 100,000/mm³ was chosen to avoid the risk of epidural hematoma; women with cesarean for non reassuring FHR patterns were also excluded to avoid confounding variables that could obscure interpretation of the BP effects of regional anesthesia. The study also admits that none of the women were predicted as being difficult to intubate which is usually not the case in clinical practice. Given the rarity of several maternal or fetal outcome measures, their study was not able to achieve a larger sample size due to time constraints. The results in the study supports the conclusions of the study, and addresses the hypothesis of the study.

APPLICABILITY OF THE PAPER

The study does seem to show that all three anesthetic methods were equally acceptable options for women with severe pre-eclampsia as long as all the precautionary steps for each method were taken. It seems that given the situation, I could be more flexible in choosing the method that I'm most comfortable with. If I felt a patient was difficult to intubate, I would be comfortable using the regional approaches. And, if I felt that the anesthetic induction to skin incision time was of utmost importance, then I'd probably be more inclined to choose general anesthesia. However, I realize the limitations of the study, and I'd have to make sure that my patients fit the criteria for the study participants.

Critical Appraisal Essay

By: **Drew McLaren, MD, PGY-1, Queen's Anesthesiology**

Title of the Publication: ***“A randomized crossover comparison of the effects of propofol and sevoflurane on cerebral hemodynamics during carotid endarterectomy.”***

Authors: ***McCulloch TJ, Thompson CL, Turner MJ.***

Anesthesiology. 2007 Jan;106(1):56-64.

Carotid endarterectomy is a commonly performed procedure in which anesthesia needs to be supplied to an often unhealthy population with numerous comorbidities. General anesthesia continues to be a common technique employed during these procedures. One of the complications of utmost concern during carotid endarterectomy is cerebrovascular events. With the concern of cerebral perfusion in mind, and knowing the differing effects that anesthetic agents have on perfusion, an anesthesiologist must carefully decide on the agents that they choose to employ. Consequently, any clinical research that aims to enlighten the topic of cerebral perfusion during carotid endarterectomy would be of considerable value to practicing anesthesiologists. The purpose of this critical appraisal is to review one such article: A Randomized Crossover Comparison of the Effects of Propofol and Sevoflurane on Cerebral Hemodynamics during Carotid Endarterectomy. In the course of this critical appraisal, the aforementioned article will be briefly summarized and subsequently critiqued.

Summary

Introduction

In this article, the authors McCulloch, Thompson and Turner report on their study in which the effects of propofol and sevoflurane on cerebral hemodynamics are evaluated during carotid artery clamping. A number of different hemodynamic measurement techniques and values need to be defined to have a complete understanding of the article. Internal carotid artery pressure (ICAP) during clamping is also known as “stump pressure” since it is measured distal to the carotid artery clamp.¹ In a previous article by Bakay,² it was demonstrated that ICAP is equal to the pressure at the origin of the middle cerebral artery (MCA), and thus ICAP can be used to measure changes in perfusion pressure for the ipsilateral side of the brain.¹

During the article in review, the concept of critical closing pressure (CCP) is also addressed and the authors theorize that the perfusion pressure driving cerebral

circulation could in fact be the difference between arterial pressure and CCP rather than intracranial pressure (ICP).¹ An additional hemodynamic value, apparent zero flow pressure (aZFP) had been previously hypothesized as an estimate of CCP,³ and so in this article the authors also set out to determine aZFP during carotid clamping.¹

Material and Methods

The experimental protocol utilized a randomized crossover design to compare sevoflurane to propofol. The propofol-sevoflurane group (PS) was induced and maintained by propofol until after the arteriotomy was performed, at which time the patients were crossed over to sevoflurane. The opposite occurred in the sevoflurane-propofol (SP) group.

For analysis, the MAP, ICAP and mean MCABV were determined at two times during clamping: (1) immediately before starting cross-over and (2) before removal of the internal carotid artery catheter. The aZFP was calculated based on ICAP and MCABV.

Results

In the SP group, the authors found the ICAP increased during cross-over causing the MAP-ICAP gradient to decrease by a mean of 10 mmHg (95% CI 6-14 mmHg, $P < 0.0001$).¹ In the PS group, there was a smaller change in opposite direction with ICAP pressure decreasing and a mean increase of MAP-ICAP of 5 mmHg (95% CI 2-7 mmHg, $P = 0.002$).¹

The authors reported the transcranial doppler data as incomplete but did find that in the SP group, crossover was associated with a significant decrease in ipsilateral MCABV. Data was complete in only five of the PS group and 4 had increases in ipsilateral MCABV during cross-over but there was no significant change in the mean. In the fifth patient the MCABV decreased during the cross-over period which the authors felt was due to a steal phenomenon. The aZFP was compared between the groups prior to cross-over and significant differences were found; in the SP group the mean aZFP was 22 ± 10

mmHg compared to 30 ± 13 mmHg in the PS group (95% CI 3-14 mmHg, $P < 0.01$). There was also a difference in the slope of the pressure-velocity curve; SP slope = 1.8 ± 0.9 cm/s, compared to PS 1.4 ± 0.9 cm/s ($P = 0.01$).

Discussion

The authors concluded from their results that the vasodilating effect of sevoflurane was confirmed during clamping by a lower aZFP, a higher MCABV and a higher slope of the velocity-pressure relation when compared to propofol. They found that when crossing over from sevoflurane to propofol there was an increase in ICAP, and hence a decrease in the gradient between MAP and ICAP, and they interpreted this to suggest that cerebral perfusion pressure was better maintained with propofol. The authors acknowledge that CBF, not arterial pressure is of utmost importance during carotid clamping. Thus, sevoflurane may be the preferred agent since it is associated with an increase in MCABV. However, they feel that based on the one episode of intracerebral steal they witnessed, sevoflurane carries the risk of diverting flow away from marginally perfused regions. They contrast this to propofol which although it had a decreased CBF, they believe it maintained a higher perfusion pressure which would preserve flow to regions that were already maximally vasodilated. The authors thus concluded that while there is no outcome-based evidence favouring either anesthetic agent, the results from their study may indicate a hemodynamic advantage of propofol over sevoflurane during carotid clamping.

Critical Appraisal

The authors of the paper are Timothy McCulloch, Christopher Thompson and Martin Turner. They are associated with the University of Sydney in Sydney and Royal Prince Alfred Hospital in Camperdown, both in New South Wales, Australia.

Introduction

The purpose of this study was to investigate and compare the effects of sevoflurane and propofol on cerebral hemodynamics during the carotid clamping phase of carotid endarterectomy surgery. This is to address one of the most concerning risks of endarterectomy surgery: cerebral ischemia. To minimize the risk of ischemia it is critical to maintain optimal cerebral perfusion during carotid artery clamping. However there is no clear consensus on the ideal general anesthetic agent to use and it is well known that different agents have different effects on cerebral hemodynamics. The authors have thus chosen a worthwhile topic of investigation, since practicing anesthesiologists are likely to value new information that can guide them in their choice of anesthetic agents. By comparing propofol and

sevoflurane, two commonly used general anesthetic agents, the authors may be able to provide information to guide practice. They hypothesized that during carotid clamping, sevoflurane would be associated with cerebral vasodilation, resulting in a lower ICAP, and possibly an increase in MCABV, a decrease in aZFP and/or an increase in the slope of the velocity-pressure relation. By testing their hypothesis, they could learn which of these two agents better maintains cerebral perfusion and thus could be superior for use during carotid endarterectomy to minimize risk of cerebral vascular related co-morbidities.

Materials and Methods

This study was completed as a randomized cross-over design. The physicians carrying out the anesthetics were clearly not blinded to the agent in use and there is no specific mention in the article as to whether the investigators conducting statistical analysis were blinded. Randomization took place by use of a handheld computer immediately prior to induction. There was no control group who did not undergo any cross-over and the authors acknowledge in their discussion that this is a weakness. Without a control group they are unable to exclude the possibility that changes may have occurred during the course of clamping regardless of whether a cross-over of agents took place.

The study was ethically justified as both sevoflurane and propofol are used for these procedures and neither agent has been proven to be superior. Furthermore, the investigators did not prolong the length of surgery to achieve the cross-over. Depth of anesthesia during cross-over was ensured by use of a BIS monitor. MCABV was measured by a transcranial doppler ultrasound; a non-invasive technique. ICAP was initially measured by a needle distal to the clamp. This was never stated to be routine practice for the procedure, but given that the surgeons used ICAP to guide their decision on the needs for a bypass shunt, it seems likely that this is a routine maneuver. After arteriotomy, ICAP was monitored by a balloon catheter in the internal carotid artery; a relatively non-invasive technique.

The authors make no mention of power analysis in this study and this should have been completed. There is also no mention of why or how 37 patients were recruited. They make no mention of specific inclusion criteria or if all patients in a consecutive time period were enrolled.

The patients included in this study and the general methodology are similar to that conducted at our own institution. In regards to patients, the average age seems similar to that which would be expected in Kingston. In regards to the anesthetic approach, the vast majority of carotid endarterectomies completed here are carried out under general anesthesia. Both sevoflurane and propofol are used for induction of anesthesia here, but for maintenance of anesthesia during carotid endarterectomy

surgery, volatile anesthetics are used almost exclusively. In the study the researchers used a target-controlled infusion pump for maintenance propofol dosing, a method which we currently do not employ in Kingston. Surgical technique differed from our hospital in that the vascular surgeons in this study utilized the ICAP shortly after carotid clamping to help in their decision as to whether an arterial bypass shunt was required. The surgeons at our institution do conduct bypass shunts as needed but use only EEG monitoring to guide their decision. BIS monitoring, remifentanyl and phenylephrine infusions were all used in the study and are common practice at our institution.

For the most part, the authors provide excellent details regarding technique, drug use and equipment use to allow the study to be reproducible. They however did not give any clear guidelines on when patients required an arterial shunt. Reference was only made to a low stump pressure, electroencephalographic changes or concerns with both.¹

The authors stated their primary outcome as the change in the MAP-ICAP pressure gradient.¹ Secondary outcomes included the MCABV and the aZFP. The cross-over technique was a good design to evaluate these changes since it allowed comparison of how these hemodynamic variables changed while changing anesthetic agents. By using a cross-over design, the intrinsic variability of each patient's ICAP and cerebral flow was controlled for. The disadvantage of the cross-over was that the agents were incompletely eliminated at the time of the second hemodynamic recordings. The authors state that based on the infusion pump algorithm, propofol effect site concentration had only decreased by 62% in the PS group at the end of clamping.¹ End-tidal sevoflurane concentration had decreased by 91% in the SP group.¹ Since variable amounts of the first agent were lingering at the end of clamping, the second set of measurements were not solely due to the steady-state effects of only one drug. The study was also well designed because the investigators directly measured their primary outcomes: MAP was measured via a radial artery catheter and ICAP was measured via a needle and balloon catheter placed into the distal stump of the internal carotid artery.

Data collection was completed in an organized and appropriate manner with an analog-to-digital recording system logging systemic arterial pressure, ICAP and the waveform of MCABV. Measurements of the MCABV were limited because the investigators had difficulty achieving adequate doppler ultrasound signals.¹ From the continuous recordings the authors analyzed their two target time points: (1) immediately prior to cross-over and (2) prior to removal of the balloon catheter. These are the two optimal points to analyze since they most closely represent a steady state for each of the anesthetic

agents. However, as discussed above, the second time point is affected by the incomplete elimination of the first agent. While ICAP and MCABV were directly measured variables, the aZFP and slope of the pressure-velocity relationship were calculated. The authors of this study followed suggestions from a previous study by Aaslid et al.,⁸ to analyze their pressure measurements and subsequently calculate the aZFP.¹

In regards to statistical analysis, the authors appropriately selected a two-tailed paired t test to compare the mean values of the MCAP-ICAP gradient, MCABV and aZFP. They calculated the pressure-velocity relationships for the two groups, PS and SP, separately due to the incomplete clearance of the first anesthetic agent prior to recording of the second time point measurements.¹

Results

The authors state that the two groups were similar except that the mean age of the SP group was older: 73 ± 7 yr vs. 66 ± 11 yr ($P=0.04$). No other patient demographic data is presented except for sex, and thus we are unable to evaluate for ourselves that the groups are in fact similar. One piece of information that may have been useful to analyze and report would have been severity of disease in the carotid arteries prior to surgery. This may have impacted on which patients required an arterial bypass shunt and were thus excluded from the study. Patients with less severe disease may have had less collateral circulation and hence upon carotid artery clamping may have shown more signs of inadequate cerebral perfusion. An unequal number of patients required bypass shunts between the two groups, (4 of 21 from the SP group and 1 of 16 from the PS group)¹ and it would be best to explore all possible reasons for this before suggesting it may be due to the vasodilatory effect of the volatile anesthetic.

All of the 32 patients that remained in the trial were included in the analysis. However, because of difficulty the investigators had with measuring MCABV, not all patients contributed to this measurement or subsequently the aZFP. In fact, in the PS group, only 5 of the 15 patients had ipsilateral MCABV measurements. Aside from the previously mentioned lack of demographic data reporting the authors do an adequate job of reporting their results.

Discussion

The authors main conclusion from this study is that: "the gradient between MAP and ICAP during carotid clamping was lower with propofol than with sevoflurane anesthesia, suggesting that cerebral perfusion pressure was better maintained with propofol".¹ Their hemodynamic results are in agreement with their conclusion regarding the pressure gradient. However,

whether a smaller pressure gradient can be taken as evidence of superior cerebral perfusion is less clear, and the authors do acknowledge this in the discussion. They make note that the aZFP was higher with propofol and this would suggest a higher CCP, and hence a decreased perfusion pressure according to the CCP model.¹ Thus, the authors have two different possible conclusions regarding propofol compared to sevoflurane: (1) a smaller MAP-ICAP gradient could suggest a better perfusion pressure (2) a higher aZFP could suggest a higher CCP and thus worse perfusion pressure. The authors settle this dispute by pointing to their one patient that demonstrated a steal phenomenon while switching from propofol to sevoflurane. With this in mind, they conclude that while sevoflurane may produce increased cerebral blood flow, it is not well targeted and puts patients at risk for steal phenomenon.¹ The authors compare this effect of sevoflurane to that of hypercapnia which has been demonstrated to cause vasodilation and cerebral steal.^{1,9}

The authors' interpretations of cerebral perfusion by the two anesthetic agents are mostly well supported by their data. One particular concern however is the inadequate MCABV data collection. Measurements of ipsilateral MCABV were collected on 76% of the SP patients but only 33% of the PS patients. Furthermore, bilateral MCABV were obtained in only 34% of the total patients. The MCABV was measured using the transcranial doppler ultrasound, a technique with which the authors state they had "difficulty obtaining and maintaining a reliable signal throughout the period of carotid clamping".¹ Yet, as noted above, the authors cite the steal phenomenon as a key point in concluding that there may be improved cerebral perfusion with propofol. By emphasizing the steal phenomenon they place considerable faith in a technique that they clearly had difficulty reproducing. So while the interhemispheric cerebral steal phenomenon may certainly have been accurate, caution does need to be taken in placing too much weight, or conclusion on a single event. However with that statement in mind, the authors also make astute comparisons, as stated above, between the cerebral vasodilatory effects of sevoflurane and carbon dioxide. Considering these similarities, the authors could still make the same conclusions regarding perfusion with sevoflurane to at risk regions, even if the steal phenomenon had not been witnessed.

The clinical relevance of this study is debatable, and the authors state as much. The study was successful in demonstrating that the MAP-ICAP gradient was smaller during propofol anesthesia compared to sevoflurane. The authors have concluded that by witnessing a steal phenomenon and comparing the vasodilatory effects of sevoflurane to carbon dioxide, propofol may have a hemodynamic advantage during carotid clamping. However, the results may be insufficient to convince

anesthesiologists to change their clinical practice. Some aspects of their data collection were incomplete and only one case of a cerebral steal was demonstrated using a technically difficult method. But the authors do present important parallels between sevoflurane and carbon dioxide that should draw the attention of vascular anesthesiologists. In a debate where there is no clear benefit between inhalational anesthetics and propofol, this article presents some convincing clinical data and interpretation that suggests a perfusion benefit of propofol during carotid artery clamping.

References

1. McCulloch TJ, Thompson CL, Turner MJ: A randomized crossover comparison of the effects of propofol and sevoflurane on cerebral hemodynamics during carotid endarterectomy. *Anesthesiology* 2007; 106:56-64
2. Bakay L, Sweet WH: Cervical and intracranial intra-arterial pressures with and without vascular occlusion. *Surg Gynecol Obstet* 1952; 95:67-75
3. Aaslid R: Cerebral hemodynamics, Transcranial Doppler, 1st edition. Edited by Newell DW, Aaslid R. New York, Raven Press, 1992, pp 49-55
4. Matta BF, Mayberg TS, Lam AM: Direct cerebrovasodilatory effects of halothane, isoflurane, and desflurane during propofol-induced isoelectric electroencephalogram in humans. *Anesthesiology* 1995; 83:980-5
5. Matta BF, Heath KJ, Tipping K, Summors AC: Direct cerebral vasodilatory effects of sevoflurane and isoflurane. *Anesthesiology* 1999; 91:677-80
6. Artru AA, Shapria Y, Bowdle TA: Electroencephalogram, cerebral metabolic, and vascular response to propofol anesthesia in dogs. *J Neurosurg Anesthesiol* 1992; 4:99-109
7. Ludbrook GL, Visco E, Lam AM: Propofol: Relation between brain concentrations, electroencephalogram, middle cerebral artery blood flow velocity, and cerebral oxygen extraction during induction of anesthesia. *Anesthesiology* 2002; 97:1363-70
8. Aaslid R, Lash SR, Bardy GH, Gild WH, Newell DW: Dynamic pressure-flow velocity relationships in the human cerebral circulation. *Stroke* 2003; 34:1645-9

Queen's University Department of Anesthesiology Publication List – 2006-2007

(in alphabetical order of 1st author, Department members/cross-appointees highlighted in bold)

Abdul-Husn N.S., Sutak M., **Milne B., Jhamandas K.** Augmentation of spinal morphine analgesia and inhibition of tolerance by low doses of mu and delta receptor antagonists. *British Journal of Pharmacology* 151:877-887, 2007.

Alain T., Wong J.F., **Endersby R.**, Urbanski S.J., Lee P.W., Muruve D.A., Johnston R.N., Forsyth P.A., Beck P.L. Reovirus decreases azoxymethane-induced aberrant crypt foci and colon cancer in a rodent model. *Cancer Gene Therapy* 2007 Oct;14(10): 867-72.

Bardell T, **Brown PM.** Smoking inside Canadian acute care hospitals. *Can Respir J.* 2006 Jul-Aug;13(5):266-8.

Beique, F., **Ali M.**, Hynes M., et al. Canadian guidelines for training in adult perioperative echocardiography. *Canadian Journal of Anesthesia* 2006; 53: 1044-60.

A.M. Bourgault, C.A. Brown, S.M.J. Hains, J.L. **Parlow.** Effects of Endotracheal Tube Suctioning on Arterial Oxygen Tension and Heart Rate Variability. *Biological Research for Nursing* 2006; 7:268-78.

Boscariol R, Gilron I, Orr E. Chronobiological characteristics of postoperative pain: diurnal variation of both static and dynamic pain and effects of analgesic therapy. *Can J Anaesth* 2007;54:696-704.

Cahill CM, Holdridge SV, Morinville A. Trafficking of delta-opioid receptors and other G-protein-coupled receptors: implications for pain and analgesia. *Trends Pharmacol Sci.* 2007 Jan;28(1):23-31. Epub 2006 Dec 5.

Cload B, Howes DW, Sivilotti ML, Ross JJ, **Murdoch JA.** Where is the ET tube? *CJEM.* 2006 Nov;8(6):436, 446-7.

Dagnone D.V., Wilson R., Goldstein D.H., Murdoch J., Rimmer MJ, VanDenKerkhof E.G., Patients' attitudes and perceptions regarding the use of portable computers at the bedside: A qualitative assessment. *Journal of Healthcare Quality* 2006; 28(4): 37-44

Deshpande MA, Holden RR, Gilron I. The impact of therapy on quality of life and mood in neuropathic pain: what is the effect of pain reduction? *Anesth Analg.* 2006 May;102:1473-9.

Dumont E.C., Rycroft B.K., Maiz J., Williams J.T. Chronic morphine produces excitatory neuroplasticity in a circuit-specific way in the bed nucleus of the stria terminalis. In Press, *Neuroscience*, 2007.

Erb J, Orr E, Mercer CD, Gilron I. Interactions between pulmonary performance and movement-evoked pain in the immediate postsurgical period: Implications for perioperative research and treatment. *Regional Anesthesia and Pain Medicine* 2008 (In Press).

Ewaschuk J., **Endersby R.**, Thiel D., Diaz H., Backer J., Ma M., Churchill T., Madsen K. Probiotic bacteria prevent hepatic damage and maintain colonic barrier function in a mouse model of sepsis. *Hepatology* 2007 Sep; 46(3):841-50.

Froese A. Anesthesia and the role of short-term service delivery in developing countries. *Can J Anaesth.* 2007 Nov;54(11):940-6.

Froese AB. Gravity, the belly, and the diaphragm: you can't ignore physics. *Anesthesiology.* 2006 Jan;104(1):193-6.

Gendron L., Esdaile M.J., Mennicken F., Pan H., O'Donnell D., Vincent J.P., Devi L.A., **Cahill C.M., Stroh T., Beaudet A.** Morphine increases the anti-hyperalgesic potency of deltorphin but induces tolerance to its antinociceptive properties in animals with chronic inflammatory pain. *Pain* (in press).

Gilron I, Coderre TJ. Emerging drugs in neuropathic pain. *Expert Opinion in Emerging Drugs* 2007;12(1):113-26.

Gilron I, Flatters SJ. Gabapentin and pregabalin for the treatment of neuropathic pain: A review of laboratory and clinical evidence. *Pain Res Manag.* 2006;11 Suppl A:16A-29A.

Gilron I. Analgesia controlled with patience: towards a better understanding of analgesic self-administration behaviour. *Can J Anaesth.* 2008 Feb;55(2):75-81.

Gilron I. Combination drug therapy for neuropathic pain. *Eur J Pain* 2007; 11(1) Suppl 1: 2.

Gilron I. Gabapentin and pregabalin for chronic neuropathic and early postsurgical pain: Current evidence and future directions. *Current Opinion in Anesthesiology* 2007;20:456-472.

Gilron I. Review article: the role of anticonvulsant drugs in postoperative pain management: a bench-to-bedside perspective. *Can J Anaesth.* 2006;53:562-71.

Gilron, I., Watson, P., Cahill, C., Moulin, D. Neuropathic pain: a practical guide for the clinician.

Canadian Medical Association Journal 175 (3): 265-75, August 1, 2006.

Gratadour P, Cividjian A, Sagnard P, **Parlow J**, Viale JP, Quintin L. Unusual sinus arrhythmia. *Int J Cardiol*. 2007 Aug 17; [Epub ahead of print].

Greenspan JD, Coghill RC, **Gilron I**, Sarlani E, Veldhuijzen DS, Lenz FA. Quantitative somatic sensory testing and functional imaging of the response to painful stimuli before and after cingulotomy for obsessive-compulsive disorder (OCD). *Eur J Pain*. 2008 Mar 5; [Epub ahead of print].

Henry R, Morales A, Wyllie MG. TEMPE: Topical Eutectic-Like Mixture for Premature Ejaculation. *Expert Opin Drug Deliv*. 2008 Feb;5(2):251-61.

Holdridge SV, Armstrong SA, Taylor AM, **Cahill CM**. Behavioural and morphological evidence for the involvement of glial cell activation in delta opioid receptor function: implications for the development of opioid tolerance. *Mol Pain*. 2007 Mar 12;3:7.

Holdridge SV, **Cahill CM**. Spinal administration of a delta opioid receptor agonist attenuates hyperalgesia and allodynia in a rat model of neuropathic pain. *Eur J Pain*. 2007 Aug;11(6):685-93. Epub 2006 Dec 18.

Hopman W.M., Berger C., Joseph L., Towheed T., **VanDenKerkhof E.G.**, et al. CaMos Research Group. The Natural Progression of Health-Related Quality of Life: Results of a Five-year Prospective Study of SF-36 Scores in a Normative Population. *Quality of Life Research* 2006; 15(3): 527-36.

Izard JP, Sowery RD, **Jaeger MT**, Siemens DR. Parameters affecting urologic complications after major joint replacement surgery. *Can J Urol*. 2006 Jun;13(3):3158-63.

Jhamandas K, **Milne B**, Sutak M., Gouarderes C., Zajac J.M., Yang H.Y.T. Facilitation of spinal morphine analgesia in normal and morphine tolerant animals by neuropeptide SF and related peptides. *Peptides* 27: 953-963 2006.

Kabli N, **Cahill CM**. Anti-allodynic effects of peripheral delta opioid receptors in neuropathic pain. *Pain*. 2007 Jan;127(1-2):84-93. Epub 2006 Sep 8.

Landau AM, Yashpal K, **Cahill CM**, St Louis M, Ribeiro-da-Silva A, Henry JL. Sensory neuron and substance P involvement in symptoms of a zymosan-induced rat model of acute bowel inflammation. *Neuroscience*. 2007 Mar 16;145(2):699-707.

McMullen MC, Girling LG, Graham MR, Mutch WA. Biologically variable ventilation improves oxygenation and respiratory mechanics during one-lung ventilation. *Anesthesiology*. 2006 Jul;105(1):91-7.

McNaull B, Trang T, Sutak M, **Jhamandas K**. Inhibition of tolerance to spinal morphine antinociception by low doses of opioid receptor antagonists. *Eur J Pharmacol*. 2007 Apr 10;560(2-3):132-41. Epub 2007 Jan 17.

Morano T.J., Bailey N.J., **Cahill C.M.**, **Dumont E.C.** Nuclei- and condition-specific responses to pain in the bed nucleus of the stria terminalis. In press, *Progress in Neuropsychopharmacology and Biological Psychiatry*, 2007.

Moulin D.E., Clark A.J., **Gilron I**, et al. Pharmacologic Management of Chronic Neuropathic Pain-Concensus Statement and Guidelines from the Canadian Pain Society. *Pain Research and Management* 2007; 12(1): 13-21.

Mukhida K., Mendez I., McLeod M., Kobayashi N., Haughn C., **Milne B.**, Baghbaderani B., Sen A., Behie L.A., Hong M. Spinal GABAergic transplants attenuate mechanical allodynia in a rat model of neuropathic pain. *Stem Cells*. First published online August 16, 2007.

Nickel JC, Mullins C, **Tripp DA**. Development of an evidence-based cognitive behavioral treatment program for men with chronic prostatitis/chronic pelvic pain syndrome. *World J Urol*. 2008 Feb 22; [Epub ahead of print]

Nickel JC, **Tripp DA**, Chuai S, Litwin MS, McNaughton-Collins M, Landis JR, Alexander RB, Schaeffer AJ, O'Leary MP, Pontari MA, White P, Mullins C, Nyberg L, Kusek J; NIH-CPCRN Study Group. Psychosocial variables affect the quality of life of men diagnosed with chronic prostatitis/chronic pelvic pain syndrome. *BJU Int*. 2008 Jan;101(1):59-64. Epub 2007 Oct 8.

Nickel JC, Baranowski AP, Pontari M, Berger RE, **Tripp DA**. Management of men diagnosed with chronic prostatitis/chronic pelvic pain syndrome who have failed traditional management. *Rev Urol*. 2007 Spring;9(2):63-72.

Odreich M., **Bailey J.M.**, **Cahill C.M.**, **Gilron I**. Chronobiological characteristics of painful diabetic neuropathy and postherpetic neuralgia: Diurnal pain variation and effects of analgesic therapy. *Pain* 2006; 120:207-12.

Parlow J.L., **Ahn R.**, **Milne B**. Obesity is a risk factor for failure of "fast track" extubation following coronary artery bypass surgery. *Can J Anesthesia* 2006; 53:288-94.

Parlow J.L., van Vlymen, J. Rationale, design, and organization of the PeriOperative Ischemic Evaluation (POISE) Trial: A randomized controlled trial of metoprolol versus placebo in patients undergoing noncardiac surgery. *American Heart Journal*, 223-30, August 2006.

Parlow J.L., vanVlymen J.M. The methylene blues: anticipating adverse reactions to non-anesthetic drugs/Le blues du méthylène : prévenir les réactions indésirables aux médicaments non anesthésiques *Can J Anesthesia: In Press*.

Roth ML, **Tripp DA**, Harrison MH, Sullivan M, Carson P. Demographic and psychosocial predictors of acute perioperative pain for total knee arthroplasty. *Pain Res Manag.* 2007 Autumn;12(3):185-94.

Smith KB, **Tripp D**, Pukall C, Nickel JC. Predictors of sexual and relationship functioning in couples with Chronic Prostatitis/Chronic Pelvic Pain Syndrome. *J Sex Med.* 2007 May;4(3):734-44. Epub 2007 Apr 19.

Smith KB, Pukall CF, **Tripp DA**, Nickel JC. Sexual and relationship functioning in men with chronic prostatitis/chronic pelvic pain syndrome and their partners. *Arch Sex Behav.* 2007 Apr;36(2):301-11. Epub 2006 Dec 21.

Silcox L., Ashbury T., VanDenKerkhof E.G., Milne B. Residents' and Program Directors' attitudes to research during anesthesiology training: A Canadian perspective. *Anesthesia & Analgesia* 102 (3): 859-64, 2006 Mar.

Strum DP, Pinsky MR. Modeling ischemia-induced dyssynchronous myocardial contraction. *Anesth Analg.* 2006 Oct;103(4):846-53.

Sullivan MJ, Adams H, **Tripp D**, Stanish WD. Stage of chronicity and treatment response in patients with musculoskeletal injuries and concurrent symptoms of depression. *Pain.* 2008 Mar;135(1-2):151-9. Epub 2007 Jul 23.

Sullivan MJ, Martel MO, **Tripp DA**, Savard A, Crombez G. Catastrophic thinking and heightened perception of pain in others. *Pain.* 2006 Jul;123(1-2):37-44. Epub 2006 Mar 24.

Sullivan MJ, Martel MO, **Tripp D**, Savard A, Crombez G. The relation between catastrophizing and the communication of pain experience. *Pain.* 2006 Jun;122(3):282-8. Epub 2006 Mar 20.

Trang T, Sutak M, **Jhamandas K.** Involvement of cannabinoid (CB1)-receptors in the development and

maintenance of opioid tolerance. *Neuroscience.* 2007 May 25;146(3):1275-88. Epub 2007 Mar 28.

Trang T, Ma W, Chabot JG, Quirion R, **Jhamandas K.** Spinal modulation of calcitonin gene-related peptide by endocannabinoids in the development of opioid physical dependence. *Pain.* 2006 Dec 15;126(1-3):256-71. Epub 2006 Aug 28.

Tripp DA, VanDenKerkhof E.G., McAlister M. The prevalence of chronic pain and pain-related interference in a predominantly rural region of Southeastern Ontario. *Pain Research and Management (in press)*.

Tripp DA, Nickel JC, Wang Y, Litwin MS, McNaughton-Collins M, Landis JR, Alexander RB, Schaeffer AJ, O'Leary MP, Pontari MA, Fowler JE Jr, Nyberg LM, Kusek JW; National Institutes of Health-Chronic Prostatitis Collaborative Research Network (NIH-CPCR) Study Group. Catastrophizing and pain-contingent rest predict patient adjustment in men with chronic prostatitis/chronic pelvic pain syndrome. *J Pain.* 2006 Oct;7(10):697-708.

Tuan T., Ma W., Chabot J.G., Quirion R. **Jhamandas K.** Spinal modulation of calcitonin gene-related peptide by endocannabinoids in the development of opioid physical dependence. *Pain, In Press* 2006.

Turner K., VanDenKerkhof E.G., Lam M., Mackillop W. Perioperative care of patients with obstructive sleep apnea – a survey of Canadian anesthesiologists. *Can J Anesth* 2006 53: 299-304.

VanDenKerkhof E.G., Hopman W.M., Towheed T., Wilson R., Murdoch J., Rimmer M., Schmidt Stutzman, S., Tod, D., Dagnone V., Goldstein D.H. Pain, health-related quality of life, and health-care utilization after inpatient surgery: A pilot study. *Pain Research and Management*, 2006;11(1): 41-47.

VanDijk A., McGrath P.A., Pickett W., **VanDenKerkhof E.G.,** Pain prevalence in schoolchildren. *Pain Research and Management (In Press)*.

Waxman SE, **Tripp DA**, Flamenbaum R. The Mediating Role of Depression and Negative Partner Responses in Chronic Low Back Pain and Relationship Satisfaction. *J Pain.* 2008 Feb 28; [Epub ahead of print]

Yang H., Raymer K., Butler R., **Parlow J.L., Roberts R.** The effects of perioperative β -blockade: results of the Metoprolol after Vascular Surgery (MaVS) Study. *American Heart Journal* 2006; 152:983-90.

Zamora, J.E., Murdoch, J., Simchison, B., Day, A. Contamination: a comparison of 2 personal protective systems. *CMAJ* 175 (3): 249-54, August 1, 2006.