Welcome to another monthly issue of Anesthesia Abstracts. Providing the discerning anesthetist with up-to-date information for evidence based anesthesia practice.

This month we welcome the contributions of Dr. Nina E. McLain. Dr. McLain is a nurse anesthesia educator and clinician. She has experience in many areas of clinical anesthesia and special expertise in outpatient anesthesia and regulatory issues. Prior to accepting her current faculty position she created and organized anesthesia services at a freestanding outpatient surgery center in Mississippi.

As you read this issue I am working on obtaining Continuing Education approval. You can use the "contact us" link or send email to anesthesiaabstracts@mac.com to let me know how many CE credits you would like to see offered through Anesthesia Abstracts.

And, as always, your suggestions and constructive criticism are welcome at any time. Our desire is that Anesthesia Abstracts makes it fast and economical to keep abreast of the volumes of anesthesia information available every month.

Best Regards,

Michael A. Fiedler, PhD, CRNA

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THE EFFECTS OF FENTANYL ON THE CONTRACTILE RESPONSE OF OVALBUMIN-SENSITIZED RAT TRACHEA

Anesth Analg 2007;104:1103-1108

Nishioka K, Shibata O, Yamaguchi M, Makita T, Sumikawa K

Abstract

Purpose The purpose of this study was to measure the effect of intravenous (IV) fentanyl on antigen-induced tracheal constriction in vitro and in vivo.

Background Exposure to an antigen induces an IgE mediated release of bronchoconstrictive substances including acetylcholine (ACh) and serotonin (5-HT). Fentanyl has been reported to increase airway resistance in some studies and to decrease it in others. The mechanism of any fentanyl airway effect is not well understood. Opioids, however, have been reported to inhibit cholinergic neurotransmission in humans and animals.

Methodology In this prospective, laboratory study, the effects of fentanyl, sevoflurane, and atropine were measured on rat trachea stimulated by an antigen. Ovalbumin (OA) was first used to make the airways of some rats sensitive to bronchoconstriction while others served as non-sensitized controls. OA was then used as an antigen to stimulate bronchoconstriction.

Four different concentrations of fentanyl, differing by a factor of 10, were administered in vitro to observe any effect on the tracheal contraction caused when airways were stimulated by a dose of OA. In some cases, tracheal tissue was pretreated with two different concentrations of naloxone to assess whether the effect of fentanyl on bronchoconstriction was mediated by opioid receptors.

In vivo, respiratory system resistance was measured in rats paralyzed with vecuronium. Resistance was measured in sensitized rats experiencing OA induced bronchoconstriction after IV saline administration, fentanyl 3 µg/kg and 10 µg/kg, atropine 0.01 mg/kg, or sevoflurane 1.5 MAC.

Result Once sensitized, administering OA resulted in contraction of tracheal rings both in vitro and in vivo. No tracheal contraction occurred in non-sensitized rats when OA was administered. Fentanyl did not increase airway resistance in sensitized or non-sensitized rats. In vitro, fentanyl resulted in a dose dependent reduction in the tracheal contraction seen following OA administration. Prior administration of naloxone only partially antagonized this effect of fentanyl. In vivo, when bronchoconstriction was not induced with OA, fentanyl had no effect on respiratory system resistance. But fentanyl did reduce the increase in respiratory system resistance when OA was administered to sensitized rats. Fentanyl 3 µg/kg reduced the increase in respiratory system resistance by 7.5% (P not significant) and fentanyl 10 µg/kg reduced the increase in respiratory system resistance by 37% (P<0.001). Atropine 0.01 mg/kg (55%)(P<0.001) and sevoflurane (59%)(P<0.001) reduced the increase in respiratory system resistance to a significantly greater extent than fentanyl.

Conclusion Fentanyl up to 10 µg/kg does not increase airway resistance. Fentanyl reduces the increase in airway resistance that occurs following antigen administration. Both relatively high dose IV atropine and 1.5 MAC sevoflurane reduce the increase in airway resistance to a greater extent than fentanyl.

Comment

Because fentanyl class opioids decrease heart rate, one might tend to think of them as “vagotonic.” But with respect to the airways, this appears not to be the case. Constriction of the trachea and large conducting airways (bronchoconstriction) is mediated by parasympathetic (cholinergic) stimulation. This study shows that fentanyl dose dependently reduces the bronchoconstriction seen following antigen administration. Fentanyl appears to reduce the release of ACh in the trachea. Since we frequently use fentanyl during general anesthesia and are quite familiar with it, using fentanyl to attenuate bronchoconstriction due to antigen exposure should be fairly straightforward. Also, a close look at the study data suggests that even larger doses of fentanyl are likely to further attenuate tracheal constriction, though where this effect will be maximized is unknown. (Of course, many anesthetists would consider 10 µg/kg a fairly large dose for most cases so this information may not be all that helpful.) Unfortunately, it appears that commonly used doses of fentanyl (3 µg/kg) had little effect on the trachea.
While this is a good study, there are several important things it does not tell us. We don’t know how long fentanyl will partially protect against bronchoconstriction. We don’t know whether the effect is additive with the bronchodilation seen with potent inhalation agents like sevoflurane. And we don’t know whether fentanyl inhibits bronchoconstriction from other causes (chemical irritants like desflurane, for example) or only from antigen exposure.

While not the primary purpose of the study, it is notable that both IV atropine and 1.5 MAC sevoflurane both attenuated bronchoconstriction to a greater degree than 10 µg/kg of fentanyl alone. Only one dose of atropine was studied so we don’t know if the effect of atropine was dose dependent. I would be hesitant to use 0.01 mg/kg atropine IV (0.85 mg in an 85 kg patient) because of the expected increase in heart rate. Smaller doses administered down the endotracheal tube work wonders on bronchoconstriction. Over the years I’ve seen several cases of bronchoconstriction immediately following ETT insertion that was severe enough to prevent adequate ventilation. In each case 0.4 mg atropine down the ETT resulted in immediate bronchodilation and the ability to ventilate.

Michael Fiedler, PhD, CRNA
The purpose of this study was to assess the effect of cricoid pressure on the proper placement of, and ventilation with, the ProSeal laryngeal mask airway (LMA) in anesthetized, paralyzed adults.

Failed rapid sequence intubation prolongs a patients risk of aspirating gastric contents. When endotracheal intubation fails during a rapid sequence induction, the LMA is often used for ventilation, especially if ventilation with a facemask is difficult. The difficult airway algorithm recommends that an LMA be inserted in the “can’t intubate, can’t ventilate” situation. Cricoid pressure, a standard component of rapid sequence induction and intubation, is normally maintained until the airway is secure. Cricoid pressure has been shown to impede placement of, and ventilation with, the classic LMA. The ProSeal LMA is modified to improve the glottic seal. Without cricoid pressure “excellent” ventilation has been reported following 81% to 100% of ProSeal LMA placements.

This prospective, cross-over study included 50 ASA I patients who required general anesthesia. Patients with a body mass index > 30 and pregnant women were excluded. The ProSeal LMA size for each patient was selected according to manufacturer’s instructions. General anesthesia was induced with fentanyl 2 µg/kg, propofol 2 mg/kg, and vecuronium 0.1 mg/kg. The patient’s head was placed in the sniffing position and the ProSeal LMA was inserted according to manufacturer’s instructions using the introducer tool. Cricoid pressure was applied (30 N of force) during LMA insertion and maintained during assessment of ventilation.

After placing the LMA, the cuff was inflated to 60 cm H₂O pressure. The patient was ventilated manually. Ventilation quality was rated as 1 = excellent, 2 = adequate but with a leak, or 3 = impossible to ventilate adequately. The pop-off valve was then partially closed and pressure allowed to build up in the circuit. The pressure at which a leak occurred was used to assess the seal produced by the LMA cuff. Peak inspiratory pressure was assessed during standardized ventilation of 10 mL/kg x 12. After ventilation, the position of the LMA cuff in the airway was assessed with a fiberoptic bronchoscope. LMA position was assessed as 1 = only vocal cords visible, 2 = vocal cords and posterior epiglottis visible, 3 = vocal cords and anterior epiglottis visible, or 4 = vocal cords not visible.

Cricoid pressure was used in all patients during the initial observations. For the second set of observations, cricoid pressure was released and the LMA repositioned. All observations were then repeated without cricoid pressure. Each patient had observations made with and without cricoid pressure.

Participants ranged in age between 18 years old and 51 years old and included 22 men and 28 women.

The volume of air needed to inflate the LMA cuff to 60 cm H₂O pressure was smaller when cricoid pressure was used: 20±5 mL with cricoid pressure vs. 25±5 mL without cricoid pressure (P<0.05). The seal provided by the LMA was better without cricoid pressure. When the LMA was inserted with cricoid pressure it leaked at 21±7 cm H₂O pressure, while the LMA inserted without cricoid pressure didn’t leak until 27±7 cm H₂O pressure. Ventilation through the LMA was much improved when it was positioned without cricoid pressure. When cricoid pressure was used during LMA placement ventilation was “excellent” or “adequate” in 28% of patients compared to 100% of patients without cricoid pressure during LMA placement (P<0.05). Inadequate ventilation was due to airway obstruction or large leaks during ventilation. Higher peak airway pressure was produced when cricoid pressure was maintained during ventilation through the LMA; 28±5 cm H₂O with cricoid pressure versus 14±2 cm H₂O without cricoid pressure (P<0.05).

Fiberoptic examination showed that often LMAs placed during cricoid pressure were not inserted far enough into the airway. This resulted in a suboptimal seal more often when LMAs were placed during cricoid pressure than when they were placed without cricoid pressure. Fiberoptic examination of the LMA cuff position in the airway showed optimal or near optimal positioning (anatomic position grades 1 or 2) in only 34% of LMAs inserted during cricoid pressure but in 76% of LMAs inserted without cricoid pressure (P<0.05).

Cricoid pressure applied during the insertion of a ProSeal LMA impedes its proper positioning, resulting in a higher likelihood of difficulty with ventilation. Releasing cricoid pressure during insertion results in a greater likelihood of optimal LMA placement.
Comment

Cricoid pressure is an important contribution to the safety of our patients but it is not without its disadvantages. Like everything else, the more we know about it, the more we are able to use it intelligently, and sometimes intelligently choose not to use it. When we are unable to intubate a patient during a rapid sequence induction we are taught to continue holding cricoid pressure during mask ventilation while plan “B” for securing the airway is put into effect. But a number of years ago it was shown that holding cricoid pressure during ventilation with a face mask increased peak inspiratory pressure (PIP) and reduced the tidal volume, resulting in complete airway obstruction and the inability to ventilate in 11% of patients. (1) Similar observations have been made during ventilation via a conventional LMA. (2) So, while cricoid pressure is important, Airway and Breathing are more important and there are times when we may choose to let up on the cricoid pressure.

This study is an important addition to our understanding of airway management because it shows how cricoid pressure adversely affects the proper placement of a ProSeal LMA. LMAs have become an important part of emergency airway management, recommended as a first step in the “can’t intubate, can’t ventilate” scenario. When intubation and ventilation fail during a rapid sequence induction, it is important to know that releasing cricoid pressure during LMA placement will make it more likely that the LMA will be optimally positioned. And better positioning means better ventilation at a time when everyone is probably getting pretty anxious to ventilate the patient.

This study shows us that holding cricoid pressure during ProSeal LMA insertion (and, presumably, other LMA types as well) often prevents the LMA from being inserted far enough to make a good seal around the glottis. Releasing cricoid pressure during insertion avoided airway obstruction, lead to a better seal, the ability to ventilate with more pressure before a leak occurred, and thus to ventilate with larger tidal volumes.

Michael Fiedler, PhD, CRNA


TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING AFTER ELECTIVE LAPAROSCOPIC CHOLECYSTECTOMY

Abstract

Purpose The purpose of this study was to examine the effectiveness of Transcutaneous Electrical Nerve Stimulation (TENS) for the prevention of Postoperative Nausea and Vomiting (PONV) in laparoscopic cholecystectomy patients.

Background PONV may be related to a large number of patient, anesthetic, and surgical factors. Despite treatment, the incidence of PONV is 20% to 40%. The incidence of PONV is higher in patients with movement disorders. PONV may result from labyrinthine stimulation. Neural pathways involved in the control of PONV are not well understood. The neural connection between the labyrinth and the medullary vomiting center, if any, is also not well understood. Little is known about the effects of TENS on the vestibular system. TENS has been reported to reduce nausea and vomiting in cancer chemotherapy patients and in surgical patients when combined with ondansetron administration.

Methodology This placebo controlled, double-blind study included 40 ASA class I and II patients undergoing laparoscopic cholecystectomy. Patients with a history of dizziness, PONV, or antiemetic, anticholinergic, or antihistaminic medication within 24 hours before the study period were excluded. All patients received 2.5 mg midazolam. Induction consisted of 5 mg/kg sodium pentothal and 0.1 mg/kg vecuronium. Anesthesia was maintained with sevoflurane 1% (inspired), nitrous oxide 65% and oxygen 35%. A nasogastric tube was placed after induction and suctioned and removed before emergence. Before extubation, all patients received 0.02 mg/kg atropine and 0.04 mg/kg neostigmine (2.8 mg in a 70 kg patient).

Patients were divided into two groups. Both groups had TENS electrodes applied to the neck (anode) and the mastoid area (two cathodes). The TENS group electrodes were stimulated at 5 Hz, 50 millisecond duration, at 0.5 to 4 mA current for the first six hours postoperatively. The non-TENS group electrodes were not stimulated.

A verbal descriptive scale was used to assess PONV as follows: 0 = no complaint, 1 = mild nausea, 2 = moderate nausea, 3 = frequent vomiting, 4 = severe vomiting. Patients with two or more points were given metoclopramide IV.

Result The duration of anesthesia and surgery was similar between the two groups. During the first 24 hours postoperatively, nausea and vomiting both occurred three times more commonly in the non-TENS group than in the TENS group (P<0.05). The incidence of nausea was 75% in the non-TENS group and 25% in the TENS group. Dizziness was three times as common in the non-TENS than the TENS group. The amount of analgesic medication consumed over the first 24 hours after surgery was also greater in the non-TENS than the TENS group (P=0.005).

Conclusion TENS of the vestibular system is an effective treatment for PONV in laparoscopic cholecystectomy patients.

Comment

PONV studies I’ve read that involved other electrical devices, such as electrical stimulation at the wrist, have not been all that impressive. This is the first TENS study I’ve read and I’m impressed. Most importantly, the difference in PONV between the TENS group and the non-TENS group is unequivocal. But there are a couple of other interesting points. Despite the fact that the TENS unit was only used for the first six hours postoperatively, the PONV incidence was lower for 24 hours. The data was broken down into postoperative hours 0-6 and hours 6-24. In hours 6-24, after the TENS was no longer being used, all TENS patients reported a “0” for PONV (“no complaint”) while non-TENS patients reported a median of “1” (“mild nausea”) with some reporting “moderate nausea” (P=0.001). Since most PONV occurs after our patients leave the PACU, this finding is especially important.

It is also interesting that the TENS patients used less analgesic medication. The analgesic being used was metamizol, an NSAID not available in the US since 1977. Since the analgesic was not an opioid, the reduction in PONV in the TENS group was unlikely to be the result of less opioid use in the TENS group. One must wonder, then, if a reduction in PONV resulted in less pain.

With currently available drugs, we are able to get PONV rates in laparoscopic cholecystectomy patients down below the 25% seen in the TENS group in this study. I’m anxious to learn if the antiemetic effect of TENS will further reduce PONV in combination with our current drug therapy.

Michael Fiedler, PhD, CRNA
ANALYSIS OF THE CLINICAL VARIABLES ASSOCIATED WITH RECRUDESCENCE AFTER MALIGNANT HYPERThERMIa REACTIONS

Anesthesiology 2007;106:901-906
Burkman JM, Posner, KL, Domino, KB

Abstract

Purpose  When a malignant hyperthermia episode is promptly and accurately diagnosed and treated, it has been identified that some patients develop a reoccurrence of signs and symptoms following the initial and successful treatment time frame. Many questions remain as to what a re-emergence of signs and symptoms can be attributed to after successful treatment. Questions such as what patient and clinical variables exist, if any, that are predictive of a re-occurrence of a malignant hyperthermia episode? The purpose of this research was to identify commonplace clinical and/or patient variables that would pre-dispose one to a resurgence of a malignant hyperthermia event. This would perhaps warn the caregiver to monitor at a greater intensity and/or prepare for further treatment without any delays. While recrudescence has been reported in documented case studies, research on identification of who may be most vulnerable is lacking. There are several limitations to a study of this type, mostly due to the fact that all data is retrospectively obtained from the Adverse Metabolic Reaction to Anesthesia (AMRA) reports from the North American Malignant Hyperthermia Registry (NAMHR). Within these reports, one of the biggest limitations is that there exists a moderate amount of non-substantiated data reported by the providers.

Background  Malignant hyperthermia is not a common clinical syndrome; it is rarely seen but when it does manifest itself it mandates prompt diagnosis and treatment or death will ensue. Certain anesthetic agents trigger the intracellular release of calcium from the sarcoplasmic reticulum leading to abnormal and often fatal metabolic physiologic processes within the body. Recrudescence is defined as the development of additional signs of malignant hyperthermia after adequate treatment of the initial event in the opinion of the anesthesiologist on the AMRA report. Treatment of an episode is with Dantrolene Sodium. The clinical signs of recrudescence include an increasing heart rate, increasing minute ventilation to maintain end-tidal carbon dioxide, and increasing temperature. There is a two hour time period after the initial event used to define recrudescence.

Methodology  This study was conducted as a retrospective chart review. Information was obtained from the Adverse Metabolic Reaction to Anesthesia reports for 528 patients that exist in the North American Malignant Hyperthermia Registry database since January 1, 2005. When an anesthesia provider calls the Malignant Hyperthermia (MH) Hotline to request guidance with the management of a patient with suspected MH, the consultant requests that the AMRA report be sent to the provider if it is felt the episode is a true MH episode. The provider then completes the AMRA instrument, which includes clinical indicative variables, and returns it to the NAMHR. A record does not exist of the exact date of the episode or the date of the receipt of the AMRA from the provider. Unfortunately, there is no attempt to obtain the original documents to support any reliability or validity of the ARMA data due to protecting the patient’s health information. The MH experts, however, use a clinical grading score based on patient presentation of signs and symptoms (on the AMRA data) which represents a clinical diagnosis; the confirmed clinical diagnosis can only be done via contracture test or genetic testing. Patients are eligible for inclusion in this specific analysis, if they received a general anesthetic in which a suspected MH event occurred and they had a clinical grading score of 20 or higher, indicating a strong likelihood of a MH reaction. Exclusion criteria included a score of less than 20. In addition, this analysis included the year of the event, age, gender, weight, body habitus, family medical history, surgical procedures, anesthetic duration and agents used, MH signs and symptoms, timing of the MH event, and dantrolene dose comparing patients in the recrudescence and non-recrudescence groups. The statistical analysis was robust to detect what variables seemed to place patients at risk for recrudescence.

Result  Recrudescence of MH signs and symptoms occurred in 20% of the 308 records that were reviewed. Evidence of signs occurred between 2.5 and 72 hours after the initial MH reaction. Approximately 50% of patients demonstrated clinical signs within 9 hours of the initial event and the majority showed signs of recrudescence within 16 hours.

The statistical analysis did not identify any differences between those with signs of recrudescence compared to those without signs in relation to the year of the event or the type of surgery. Age, gender and body weight were similar between the groups also. A difference did not exist in family history of MH between the two groups or previous anesthetic exposure. About half the patients did have previous general anesthesia. It was noted, however, that the patients with recrudescence were more likely to have a muscular body habitus compared with patients without recrudescence (P<0.01). Other specific characteristics of the MH episode did differ between groups. Those in the recrudescence group had a clinical grading scale (of symptoms) greater than 35 (P<0.01) and were more likely to exhibit a temperature increase during the original MH episode (P<0.01). The time frame from induction to adverse event was longer in the recrudescence group (P<0.05). Thirty five percent of the patients who did exhibit signs of recrudescence did not exhibit their initial signs of MH until 151 minutes after the induction of anesthesia. This was statistically significant. The total dantrolene dose given for the initial treatment was greater in the recrudescence group (P<0.05). Summarizing, recrudescence was associated with muscular body habitus, longer time between induction and initial MH reaction, and a temperature increase.

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**Conclusion**
While the study was not without key limitations, including a lack of totally “clean” data due to a variety of causes and a small sample size, it did demonstrate that those with recrudescence were most likely to have a muscular body habitus. The re-occurrence of signs and symptoms could be related to the proportionately larger amount of hypermetabolic tissue. The fact that those who recrudesced did not show their initial MH signs and symptoms until 2.5 hours after induction may be a result of a longer exposure to inhalation triggering agents. Of equal interest is that recrudescence was related to temperature increases, but not muscle rigidity, muscle breakdown, or respiratory acidosis. This finding is not consistent with what others have suggested in case reports. It may be that an elevated core temperature facilitates the development of an MH episode. It would be in error to omit the fact that dantrolene in therapeutic concentrations does bind to the RyR1 receptor to block calcium release, but in low concentrations it has been postulated that it may activate the same receptor actually producing calcium release and possibly the re-occurrence of MH. There was not enough data regarding the dosing of dantrolene in the reports that would warrant appropriate conclusions.

**Comment**
Because the incidence of malignant hyperthermia is rare, as anesthesia experts we can never become too comfortable believing that we may never experience its occurrence. We simply do not have the luxury of believing the saying “that which we do often we do well” relative to an event of malignant hyperthermia. We may only experience having to treat one, if any, incidences of MH in our careers. This unique situation truly mandates a vigilant and constant review for adequate preparedness and knowledge of the algorhythm on how to treat. While the hotline is an overwhelmingly valuable resource when MH signs are suggestive of an event and guidance is needed, prompt recognition and treatment is key together with consultation with the experts who are the MH hotline respondents. The event of an MH episode can be considered one of the most perplexing for us as anesthesia experts because of the variability in presentation. The concept of recrudescence of an MH episode is in a league of its own; we have to be of the mindset that this will happen. This research provides useful scientific information; more than we previously had, albeit not perfect nor definitive, to guide us in preparedness of individuals who may be “more” predisposed for a re-occurrence of signs and symptoms. It is this type of work, while preliminary, that increases our knowledge base while focusing on improved patient outcomes. It is also this type of work that no doubt will be expanded upon in future studies.

Mary A. Golinski, PhD, CRNA
Abstract

Purpose To compare anesthesia complication rates between hospitals where obstetrical anesthesia care was provided exclusively by either nurse anesthetists or physician anesthesiologists.

Background Some hospitals have decided to subsidize physician practices in order to obtain obstetrical anesthesia services while rural hospitals are often challenged to find physician anesthesia coverage for both obstetrical and surgical services. One potential long-term solution might be to increase the use of Certified Registered Nurse Anesthetists (CRNA) practicing without supervision from physician anesthesiologists; however, there have been assertions that care provided by CRNAs is of lesser quality.

Methodology Administrative records of 134,806 patients requiring Cesarean delivery in hospitals where, between 1993 and 2004, obstetrical anesthesia care was provided exclusively by either anesthesiologists or CRNAs without anesthesiologist supervision were extracted from the Washington state Comprehensive Hospital Abstract and Reporting System database. Anesthesia complications were identified using ICD-9-CM codes 668.0 through 668.9 and Patient Safety Indicator data were collected using 15 specific ICD-9-CM codes. Regression analysis was used to examine differences in outcomes.

Result Obstetrical anesthesia care was provided by CRNAs to 33,236 patients in 27 of Washington’s 68 hospitals offering obstetrical services, including 79% of the state’s rural hospitals. Anesthesiologists provided direct care for 101,570 patients in 28 hospitals. Nurse anesthetists provided care more commonly in hospitals with less than 100 or more than 200 beds while anesthesiologist-only services were available most commonly in hospitals with between 100 and 200 beds. CRNA-only hospitals were more likely rural (30% vs. 2%) or teaching facilities (9% vs. 4%), admitted more patients of less than 17 years of age (2% vs. 1%), had a higher percentage of Medicaid patients (43% vs. 30%), admitted a greater proportion of patients requiring urgent care (61% vs. 27%), and received from other hospitals a higher percentage of transfer patients (1.44% vs. 0.82%). Hospitals with anesthesia care provided exclusively by anesthesiologists had higher percentages of emergency admissions (6% vs. 2%) and patients older than 35 years-of-age (20% vs. 15%). Patient comorbidities differed between hospital types. The incidences of generalized infection during labor, insufficient prenatal care, postpartum hemorrhage, pulmonary complications, uterine rupture, and “other complications of labor and delivery” (including maternal hypotension, distress, shock, and cardiac arrest) were higher in hospitals where anesthesia care was provided by CRNAs. The rates of fetal cardiac anomalies and problems affecting the mother’s health; maternal diabetes, hypertension, and maternal obesity; multiparity; obstructed labor; and umbilical cord complications were higher in hospitals with anesthesiologist-only anesthesia care. No differences were detected in the frequencies of maternal embolism, eclampsia, placental abruption or previa, or prolonged labor.

Anesthesia complications were documented in 965 patients (2.90%). The unadjusted complication rate for hospitals where obstetrical anesthesia care was provided by CRNAs was 0.58% compared to 0.76% in hospitals with anesthesiologist-only anesthesia services (p < .0006). After controlling for patient and hospital attributes, patient acuity, and anesthesia staffing characteristics; there was no statistically significant difference in the risk of anesthesia complications based on provider type. There were 17 deaths reported, although only one of these patients was among the group having an anesthesia complication. Predictors of anesthesia complications (independent of provider type) were postpartum hemorrhage (odds ratio OR = 1.80); “other complications of labor and delivery” (OR = 1.74); and emergency admission (OR = 1.59).

Conclusion Analysis of data compiled over a 12-year period did not detect any differences in overall anesthesia complication rates between patients receiving anesthesia care for Cesarean delivery in CRNA-only or anesthesiologist-only hospitals. Additionally, there was no evidence that one type of hospital provided care for higher acuity patients. These data provide evidence of the safety and quality of care administered by exclusively by nurse anesthetists; consequently, anesthesia staffing decisions can be based on factors such as provider availability, hospital financial resources, or percentage of Medicaid patients.

Comment

The law of parsimony (Occam’s razor) asserts that the explanation making the fewest assumptions is often the best. When examining anesthesia outcomes, the research methodology making the fewest assumptions is the one adopted by Simonson, Ahern, and Hendryx. They investigated the quality of nurse-administered anesthesia by analyzing the incidences of reported anesthesia complications, rather than attempting to infer quality from less tangible indicators such as failure to rescue or years of life saved. Unfortunately, as noted by Simonson, Ahern, and Hendryx; the ICD-9-CM codes used for reporting anesthesia complications in this study are not available for non-obstetrical procedures.
But quality of care is only one of three elements commonly used to evaluate health care delivery systems. The second element of the triad is access to care. The American Association of Nurse Anesthetists (AANA) claims that CRNAs provide the majority of anesthesia care in rural communities. The current study provides evidence to support the AANA’s assertion: CRNAs provided anesthesia care in 92% of Washington’s rural hospitals, and were the sole providers of obstetrical anesthesia services in 79% of rural hospitals. The important contribution of CRNAs as “front-line” providers is amplified when one considers that 63% of the Cesarean delivery patients cared for by CRNAs in this study were admitted either emergently or urgently (compared to 33% for anesthesiologists). Moreover, the incidence of both postpartum hemorrhage and uterine rupture were higher in hospitals where care was administered solely by CRNAs. These findings would suggest that there are many patients and surgeons who are grateful for the immediate access to anesthesia care provided by CRNAs in rural communities.

The final element of the evaluation triad is cost of care. Abouleish, Prough, and Vadhera reported that labor analgesia costs for patients enrolled in the Texas Medicaid program were higher when the anesthesia services were provided by CRNAs without anesthesiologist direction. The conclusions drawn by this Texas Medicaid study are hindered by some nuanced methodology; but more importantly, there is a broader perspective on cost that must be considered, particularly in rural communities. Anesthesia services are essential for the survivability of rural hospitals where the availability of surgical and obstetrical services may make the difference between a hospital’s continued operations and closure. The economic impact of lost hospital services may be much more significant than the extra $36-$45 cost per patient claimed by Abouleish, Prough, and Vadhera for CRNA-only labor analgesia care.

The philosophical issue of whether CRNAs should be allowed to practice without medical direction will never be answered through any one particular study, but Simonson, Ahern, and Hendryx, have provided a strong piece of evidence that the practice of CRNAs working alone is both safe and necessary.

Alfred E. Lupien, Ph.D., CRNA


2. Abouleish AE, Prough DS, Vadhera, RB. Influence of the type of provider on costs of labor analgesia to the Texas Medicaid program. Anesthesiology 2004; 101:991-8


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EFFECT OF AGE ON PULMONARY GAS EXCHANGE DURING LAPAROSCOPY IN THE TRENDELLENBURG LITHOTOMY POSITION

Acta Anaesthesiol Scand 2007;51:687-692


Abstract

Purpose The purpose of this study was to assess the gradient between arterial and end tidal CO\textsubscript{2} over time in Young, Middle-aged, and Elderly participants undergoing general anesthesia and laparoscopy in lithotomy / Trendellenburg position.

Background End Tidal CO\textsubscript{2} (P\textsubscript{ET}CO\textsubscript{2}) is commonly monitored during general anesthesia to assess the adequacy of ventilation. The normal arterial to end tidal CO\textsubscript{2} gradient with modern monitoring equipment has been determined to be between 2.3 torr and 4.6 torr. A number of factors increase the gradient between arterial and P\textsubscript{ET}CO\textsubscript{2}, including: advanced age and increased dead space ventilation. During general anesthesia, factors that shift the diaphragm cephalad, including Trendellenburg’s position, increase dead space ventilation. Pathophysiologic pulmonary changes associated with aging may also increase the arterial to P\textsubscript{ET}CO\textsubscript{2} gradient.

Methodology This prospective, observational study included 51 patients scheduled for gynecologic surgery in lithotomy and Trendellenburg’s position during general anesthesia. Patients with a Body Mass Index (BMI) grater than 27 were excluded. All patients had an epidural catheter placed in the lower thoracic or upper lumbar region for intraoperative and postoperative use. The epidural catheter was dosed with 3 mL to 5 mL of 1% to 1.5% lidocaine intraoperatively. General anesthesia was induced with 1-2 mg/kg propofol and 0.1 mg/kg vecuronium. A 7.0 mm ETT was placed after induction. Anesthesia was maintained with sevoflurane, nitrous oxide, and 33% and 50% oxygen. Patients were mechanically ventilated using a pressure-controlled mode with a rate of 10-12 breaths a minute, a tidal volume of 3.9 to 13.9 mL/kg (median tidal volume was 8.9 to 10.3 mL/kg in various groups), and an I:E ratio of 1:2. Peak Inspiratory Pressure (PIP) was limited to 35 cm H\textsubscript{2}O. Ventilation was varied to maintain P\textsubscript{ET}CO\textsubscript{2} values between 30 and 35 torr. When PIP reached 35 cm H\textsubscript{2}O, respiratory rate was varied rather than tidal volume. An Ohmeda RGM gas analyzer (Ohmeda USA) was used to monitor P\textsubscript{ET}CO\textsubscript{2} after calibration according to manufacturers instructions.

Arterial blood gasses (ABG) were measured and compared with P\textsubscript{ET}CO\textsubscript{2} values. The baseline ABG was measured after induction of general anesthesia while the patient was in the supine lithotomy position and before abdominal insufflation with CO\textsubscript{2}. After the baseline ABG, patients were positioned in lithotomy and 22° to 25° Trendellenburg’s position and the abdomen insufflated with CO\textsubscript{2} for laparoscopy. Additional ABGs were sampled at 0, 15, and 30 minutes after positioning and abdominal insufflation.

Participants were divided into three groups for comparison: Young (less than 45 years old), Middle-aged (45 years to 64 years old), and Elderly (65 years old or older).

Result P\textsubscript{O}\textsubscript{2} was significantly higher in the Young group than in the Middle-aged or Elderly group at baseline and all time points after positioning and abdominal insufflation (P<0.05). While clinically different, the lowest median P\textsubscript{O}\textsubscript{2} in any group at any time point was 140 torr. The absolute lowest P\textsubscript{O}\textsubscript{2} in any single participant, however, was 73.5 torr. The Middle-aged group had at least one individual with a P\textsubscript{O}\textsubscript{2} below 100 torr at all four time points. The Elderly group had at least one individual with a P\textsubscript{O}\textsubscript{2} below 100 torr at two of the four time points.

Median P\textsubscript{CO}\textsubscript{2} went up over time in all three groups despite the P\textsubscript{ET}CO\textsubscript{2} being maintained between 30 and 35 torr. In the Elderly group, the median P\textsubscript{CO}\textsubscript{2} after 30 minutes of abdominal insufflation with CO\textsubscript{2} was approximately 41 torr with some participants achieving P\textsubscript{CO}\textsubscript{2} above 50 torr.

The arterial to end tidal CO\textsubscript{2} gradient (a-ET CO\textsubscript{2}) was higher in the Elderly than in the Young group at pre-insufflation baseline and at each of the post-insufflation measurements. The a-ET CO\textsubscript{2} tended to rise over time in each group but the increase was only significant in the Elderly group. After 30 minutes of lithotomy / Trendellenburg and CO\textsubscript{2} insufflation, the a-ET CO\textsubscript{2} gradient was as high as approximately 8 torr in the Middle-aged and Elderly groups.

Conclusion During abdominal CO\textsubscript{2} insufflation and lithotomy / Trendellenburg position, the a-ET CO\textsubscript{2} gradient is higher in elderly patients than reported norms and the gradient increases over time.
Comment

Over the last year or so I’ve been regularly providing anesthesia for laparoscopic prostatectomies performed with a DaVinci Robot (Intuitive Surgical, Inc., Sunnyvale, CA). These cases are done laparoscopically, in the maximum Trendellenburg the OR table will supply, and typically last about three hours. This study caught my eye because it relates to these robot prostatectomy cases. It raises some important issues to take into consideration when providing general anesthesia for elderly patients either in steep Trendellenburg’s position or with abdominal CO\textsubscript{2} insufflation or both. The study itself has some important limitations and, candidly, is a little confusing in places, but does, nevertheless, provide some useful information. With modern capnography monitors we are used to very small gradients between arterial and end tidal CO\textsubscript{2} values. This study shows that, in older patients, laparoscopy and even moderate Trendellenburg’s position for only 30 minutes may increase the gradient to twice what I expect it to be. And, it shows that the gradient increases over time. As I do anesthetics for older patients with a lot of pressure on the diaphragm (e.g. laparoscopy, Trendellenburg, Trendellenburg and obesity) I’ll be thinking that the gradient between arterial and end tidal CO\textsubscript{2} may be greater than I’m used to. As a result, I’ll be more likely to ventilate these patients to a lower ET\textsubscript{CO} \textsubscript{2} than I would have in the past.

The choice to limit PIP to 35 cm H\textsubscript{2}O in this study was interesting, especially when it resulted in some participants receiving a tidal volume as low as 3.9 mL/kg (273 mL in a 70 kg patient). As the tidal volume gets smaller, whatever dead space is present becomes a larger \textit{percentage} of the tidal volume. The wide range in tidal volumes (3.9 mL/kg to 13.9 mL/kg) were not correlated to the a-ET CO\textsubscript{2} gradient. I wonder if the small tidal volumes may have had an effect on the a-ET CO\textsubscript{2} gradient. Depending upon what patients got the small tidal volumes and what patients had the greatest a-ET CO\textsubscript{2} gradient, in a worst case the small tidal volumes may have accounted for some of the results of this study.

Michael Fiedler, PhD, CRNA

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ELECTROLYTE CHANGES DURING CRANIOTOMY CAUSED BY ADMINISTRATION OF HYPERTONIC MANNITOL


Hassan ZU, Kruer JJ, Fuhrman TM

Abstract

Purpose: This case report describes hyperkalemia and hyponatremia following mannitol administration during a craniotomy.

Background: The osmotic diuretic, mannitol, is commonly administered during craniotomies to move water extracellularly and, thus, reduce brain size, improving surgical visualization. Mannitol administration is known to cause changes in electrolyte concentrations but this complication occurs almost exclusively with prolonged infusion and/or large doses. An associated risk factor is renal insufficiency. While hyperkalemia is often suggested by ECG changes, hyponatremia is difficult to detect in an unconscious patient. Both may result in serious harm.

Methodology: A 31 year old, 86 kg woman underwent a frontal craniotomy for debulking of an astrocytoma. She had received mannitol during one of two previous craniotomies without incident. Her preoperative labs included a sodium of 136 mmol/L, potassium of 3.7 mmol/L, BUN 8 mg/dL, and creatinine 0.8 mg/dL. Preoperative medications included phenytoin and dexamethasone. Her 12-lead ECG was normal. Vital signs in the holding area were: BP 109/65, HR 52, Respirations 16, room air oxygen saturation 98%. In the OR her ECG appeared normal. She was induced with propofol 200 mg, lidocaine 120 mg, fentanyl 250 µg, and rocuronium 50 mg. Before incision dexamethasone 10 mg and clindamycin 900 mg were administered. Anesthesia was maintained with isoflurane 0.5% and sufentanil 0.3 µg/kg/hour. The patient was ventilated to keep the PaCO2 approximately 30 torr.

The surgeon requested mannitol administration twice and a total of 80 gm of mannitol was administered by slow IV infusion over 45 minutes.

Result: Fifteen minutes after the mannitol infusion, peaked T waves were visible on the ECG monitor and electrolytes were drawn. Serum sodium was 119 mmol/L and potassium was 6.1 mmol/L. The patient was then given CaCl 1 gm, regular insulin 6U, and glucose 25 gm. Hyperventilation and diuresis, often effective at quickly lowering serum potassium, were already underway for surgical reasons. In the PACU, after completion of the procedure, serum sodium was 134 mmol/L and potassium was 4.5 mmol/L. The patient appeared not to have suffered any adverse effects.

Conclusion: Though uncommon, mannitol administration of less than 1 gm/kg in patients with normal renal function may result in hyperkalemia and/or hyponatremia. Prior to craniotomy and mannitol administration the authors recommended: 1) a baseline 12-lead ECG, 2) baseline electrolytes, 3) a rhythm strip be run in the OR for later comparison, and 4) repeat electrolytes after mannitol administration.

Comment: While experience is an insufficient teacher, it is an important teacher. This case report teaches us from the experience of others. While the incidence of this complication appears to be quite low in otherwise healthy individuals, the authors advice still has merit. I’ve given a lot of mannitol during craniotomies and I’ve yet to see this complication. But you can bet I’ll be thinking about this case report the next time I give mannitol.

Michael Fiedler, PhD, CRNA
THE EFFECT OF INITIATING A PREVENTATIVE MULTIMODAL ANALGESIC REGIMEN ON LONG-TERM PATIENT OUTCOMES FOR OUTPATIENT ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION SURGERY


Reuben SS, Ekman EF

Abstract

Purpose The purpose of this study was to assess the effect of celecoxib as a component of preemptive multimodal analgesia on six month rehabilitation outcomes in patients who underwent outpatient arthroscopic anterior cruciate ligament (ACL) repair.

Background Patients who have undergone outpatient ACL repair often experience significant pain. Pain, in turn, may hinder the patient’s participation in rehabilitation, thus delaying recovery and/or resulting in complications. Beginning analgesic treatment preoperatively (preemptive analgesia) may control pain more effectively than responding to reports of pain postoperatively. Preemptive analgesia may also prevent chronic postoperative pain and the development of disabling complications. Multimodal analgesia described for ACL reconstruction includes nonsteroidal anti-inflammatory drugs (NSAIDs), intraarticular local anesthetics, ketamine, opioids, regional anesthesia, and local application of cooling.

Following a surgical procedure, prostaglandin E2 has been shown to increase in the central nervous system (CNS) despite subarachnoid block (“spinal”) anesthesia. This is possible because peripheral inflammation results in central pain sensitization by two mechanisms. One is via neural impulses originating from the inflamed area. This stimulus is blocked by peripherally acting NSAIDs and by regional anesthesia. The second is via a humoral mechanism that can circulate to the CNS and activate cyclooxygenase-2 (COX-2). COX-2 inhibitors that cross the blood brain barrier (such as celecoxib) can prevent central pain sensitization via the humoral mechanism.

Preoperative administration of nonspecific NSAIDs contributes to postoperative analgesia but their use is controversial due to the possibility of platelet mediated increases in bleeding. The investigators observed increased bleeding associated with ketorolac and ibuprofen in ACL reconstruction patients. The COX-2 specific NSAID celecoxib has no effect on platelet aggregation or bleeding time.

While NSAIDs have been linked to cardiovascular morbidity under some circumstances (high doses, long periods of administration, cardiac surgery patients) these complications have not been observed in orthopedic patients taking therapeutic doses for two weeks or less.

Methodology This prospective, randomized, double-blind, placebo-controlled study included 200 patients scheduled for outpatient ACL repair. Patients were divided into two groups. The celecoxib group received celecoxib 400 mg 1-2 hours preoperatively while the control group received a placebo identical in appearance.

All patients received acetaminophen 1000 mg 1-2 hours preoperatively. General anesthesia was induced with propofol 2 mg/kg, fentanyl 2 µg/kg, and ketamine 30 mg. Anesthesia was maintained with nitrous oxide in oxygen and 1% to 2% sevoflurane. All patients received ondansetron 4 mg for PONV prophylaxis. Before incision, 20 mL of 0.25% bupivacaine with 50 µg clonidine was injected into the knee of all patients. Likewise, they received 20 mL of intraarticular 0.25% bupivacaine with 50 µg clonidine, and 5 mg morphine before emergence from anesthesia. A cooling pad was applied to their knee before being moved to the PACU.

After discharge, all patients took acetaminophen 1000 mg every six hours for 14 days. Along with the acetaminophen, patients took either celecoxib 200 mg or placebo. Oxycodone was used as a rescue analgesic.

All patients participated in an accelerated rehabilitation program that emphasized full weight bearing and knee extension on the first postoperative day and a return to normal activities within six months. Patients were assessed for anterior knee pain, flexion contracture, quadriceps weakness and complex regional pain syndrome at six months postoperatively. Activity level was assessed preoperatively and again at six months postoperatively.

Result Of the 200 patients enrolled, 191 completed the six month study. Celecoxib patients reported less pain during strength testing at one month (pain scores 3.1±0.6 vs control 4.8±1.3) and at six months (pain scores 1.0±0.4 vs control 3.2±0.9).
Overall, fewer patients in the celecoxib group developed patellofemoral complications than those in the control group (P=0.001). At the six month follow up, anterior knee pain was reported by 4% of celecoxib patients and 15% of control patients. Flexion contracture was present in 2% of celecoxib patients and 9% of control patients. Flexion strength was no different between groups but extension strength was greater in celecoxib patients than in control patients at both the one month and six month assessment (P<0.05). Complex regional pain syndrome was diagnosed in 1% of celecoxib patients and 7% of control patients. Additionally, scar tissue developed which required a second arthroscopy in only 2% of celecoxib patients compared to 8% of control patients.

More patients in the celecoxib group returned to a more demanding type of activity (85% vs. 65%) (P=0.01), a more competitive level of activity (P<0.02), and more celecoxib patients returned to their full preinjury level of sports participation (P<0.05).

**Conclusion**  
Added to a multimodal postoperative analgesic strategy, celecoxib reduced patient’s perception of pain, reduced the incidence of patellofemoral complications, and reduced the need for a second arthroscopy following ACL surgery. Celecoxib patients were also more likely to return to their preinjury level of physical activity than were control patients.

**Comment**

This is the strongest evidence I have read to date showing just how important adequate pain relief is to the quality of recovery of function after orthopedic surgery. It is quite impressive to see surgical complications being reduced by 75% or more with the addition of celecoxib. It is important to remember, though, that this benefit was not due exclusively to celecoxib. It was due to the multimodal approach to pain management that included celecoxib.

Indirectly, his study also shows how important it is for anesthesia and surgery to work together in order to achieve these improved patient outcomes. The wide variety of interventions used to prevent pain, from ketamine to cold packs and NSAIDs to clonidine, fall into different areas commonly managed exclusively by one service or the other. For the patient to benefit, both anesthesia and surgery will need to be involved, each sharing their knowledge and experience.

I do have one bone to pick with this study (pun intended). I did not report the statistical significance of the differences in pain scores at one and six months because of an all too common mistake in the method of analysis. (While recorded as numbers, the pain scores were interval data and cannot be credibly compared with a student’s T test. Neither can a mean be calculated.) While the differences in pain scores at one month are smaller and more suspect, the difference at six months is quite noticeable and probably would be statistically significant if properly analyzed. We must also remember that the celecoxib group was more active when these scores were reported and, thus, could have been expected to have had more pain to begin with. I do not mean to suggest that there was no difference in the pain between the celecoxib group and the control group. The celecoxib group probably did report less pain, at least at the six month assessment. I am simply saying that we can’t use the statistical test reported here to make a convincing case that they reported less pain. Skepticism is warranted.

Michael Fiedler, PhD, CRNA

The companion article to this one was summarized and reviewed last month in Anesthesia Abstracts 2007, Volume 1 Number 3 (June issue).

Epidural Clonidine for Postoperative Pain After Total Knee Arthroplasty: A Dose-Response Study

Anesth Analg 2007;104:1230-1235

Huang YS, Lin LC, Huh BK, Sheen MJ, Yeh CC, Wong CS, Wu CT

Abstract

Purpose The purpose of this study was to identify the optimal concentration of clonidine added to 0.2% ropivacaine and 0.1 mg/mL morphine for epidural analgesia following total knee replacement. A secondary goal was to quantify any hemodynamic, anesthetic, or central nervous system side effects attributable to clonidine at any of the concentrations studied.

Background Total knee replacement generates significant postoperative pain that can be challenging to relieve. Pain, in turn, can impede physiotherapy, the most important factor in knee replacement outcomes.

Effective pain control from epidural analgesia is associated with improved outcomes following several types of surgical procedures and reduces the incidence of thromboembolism. Multimodal analgesia with other agents may improve analgesia. Adding the alpha2 agonist clonidine to solutions used for postoperative epidural analgesia has been shown to increase the intensity of analgesia produced. The antinociceptive effect of clonidine is mediated by alpha2 receptors in the dorsal horn of the spinal cord which are believed to act like descending inhibitory neural pathways. Like vasoconstrictors, clonidine may also prolong both sensory and motor block when added to local anesthetics. Both the facilitation of regional block and the improvement in analgesia produced by clonidine appears to be dose dependent. Though an alpha agonist, clonidine can cause hypotension by reducing central nervous system sympathetic outflow.

Methodology This double-blind, randomized study included 80 ASA physical status I-III patients scheduled for primary total knee replacement. Patients who had used opioids, NSAIDs, corticosteroids, or drugs for chronic pain within one week preoperatively or who had a diastolic blood pressure greater than 100 torr were excluded.

Study patients were divided into four groups of 20 patients each. All groups received 0.2% ropivacaine and 0.1 mg/mL morphine via lumbar epidural patient controlled analgesia (PCEA) beginning postoperatively. Group C0 received PCEA with only ropivacaine and morphine. Groups C1 through C4 had 1, 2, 3, and 4 µg/mL clonidine respectively added to their PCEA ropivacaine and morphine solution. The PCEA included no basal infusion rate. Pressing the dosing button infused 4 mL of the PCEA solution with a 15 minute lock out and no total dose limitation.

Anesthesia for the total knee replacement was provided with an epidural bolus and infusion of 2% lidocaine with 5 µg/mL epinephrine. All procedures were performed by the same surgeon.

Observations were made at 1, 2, 4, and 12 hours postoperatively and on the morning of postoperative days 1, 2, and 3. Pain was assessed with a 10 cm Visual Analogue Scale during rest and during knee movement. Hypotension was defined as a systolic blood pressure less than 80 torr. Sedation was scored as 1) awake and alert, 2) awake but drowsy, 3) drowsy but resposes to physical stimuli, or 4) unarousable. Sensory block was assessed with pinprick and alcohol. Motor block was classified with the Bromage scale. Physiotherapy was begun on the first postoperative day. Both passive and active range of knee motion was assessed.

Result All 80 patients enrolled completed the study. Their ages ranged from 40 to 80 years. Patients in the clonidine groups (C1 through C4) reported statistically significantly less pain during knee flexion at all time points during the first three days postoperatively (P=0.002). During the first three days, group C0 used an average of 71.8±19.5 mL of PCEA solution (about 18 doses). Groups C1 through C4 used an average of between 49.6±12.3 and 39.4±9.0 mL (10 to 12 doses).

There was no significant difference in blood pressure or heart rate between the groups that included clonidine and the group that did not. No patient met the criteria for hypotension at any of the data collection points. One patient in the C4 group experienced sedation to the point that physical stimuli were necessary to arouse him (sedation score 3). Nausea, vomiting, and itching were more common in group C0 (no clonidine) than in groups C1 through C4 (P<0.05). There were no significant differences in the degree of active or passive knee flexion between groups.

Conclusion In the authors judgment, the optimal concentration of clonidine in a ropivacaine / morphine PCEA for post-total knee replacement was 1 µg/mL.
Multimodal postoperative analgesia is clearly essential for the control of pain following many types of surgical procedures. A growing body of evidence shows clonidine to provide multiple advantages when added to local anesthetics for both anesthetic blocks and for postoperative analgesia. With that information in mind, adding clonidine to a local anesthetic for postoperative analgesia following total knee replacement seems like a no brainer. And this study does show statistically significantly lower pain scores in patients who had clonidine added to their PCEA compared to those who did not. This is, however, one of those cases where statistical significance does not indicate clinical significance. This is true for two reasons.

A close look at the graph of the pain scores shows the values for the group without clonidine and the groups with clonidine clustered closely around a VAS pain score of 4 at 1 hour, 2 hours, 4 hours, 12 hours, and one day postoperatively. The second and third day pain scores are similarly clustered around a VAS of 3. The difference between the group without clonidine and the groups with clonidine appear to be far less than half a VAS unit (less than half a cm). Clinically, when a patient tells me their pain is 4 or 4.5 I don’t see that as being much different. When a patient feels better I’m used to them telling me their pain has gone from an 8 to a 4. Furthermore, this clinically insignificant difference in pain scores was not analyzed with the most appropriate statistically test and may not have been real. The test used (ANOVA) is quite robust and is often used with VAS scores without ill effect when the difference in the scores is larger. I suspect that if the raw data (not included in the study) were analyzed with a more appropriate nonparametric test the difference in pain scores would not even be statistically significant. If my scrutiny of the pain scores is correct, this study shows similar pain relief whether or not clonidine was added to the PCEA solution of ropivacaine and morphine.

Other studies that have examined different analgesia strategies have shown better rehabilitation outcomes in patients who had better pain relief. In this study there was no difference in the degree of active or passive knee flexion between groups at any time point. This may be further evidence that there was no clinically significant difference in pain relief.

So, did this study have anything worthwhile to teach us? Yes it did. Despite the lack of improvement in analgesia, the addition of clonidine clearly reduced the volume of the ropivacaine / morphine PCEA solution needed to keep patients comfortable. The C0 group, without clonidine, used over 70 mL of PCEA solution over three days. The C1 group, with the lowest concentration of clonidine added (1 µg/mL), used just under 50 mL, 31% less. Using less ropivacaine and morphine reduces the likelihood of side effects from those drugs. And since the patients were self administering the PCEA solution on demand with no total dose limit, it also suggests they were comfortable for longer periods between doses. (While the investigators didn’t discuss this observation, I wonder if being comfortable for longer isn’t just as important as being more comfortable.) Using less of the PCEA solution probably accounts for the fact that the clonidine groups (C1 through C4) experienced less nausea, vomiting, and itching than the group without clonidine (C0). This is especially important information given how difficult spinal and epidural morphine induced side effects are to treat. The last bit of good news I see is that there is a concentration of clonidine added to epidural analgesia that doesn’t result in problematic hypotension or bradycardia. Early studies with clonidine in regional anesthesia used larger doses and had sometimes severe problems with hypotension. While these investigators used a fairly liberal definition for hypotension (systolic below 80 torr) a look at the blood pressure graphs shows that average systolic blood pressure dipped only to about 110 torr. This low point occurred four hours postoperatively when patients are generally still being watched quite closely. Later blood pressures were higher despite the continuing use of PCEA with clonidine.

Michael Fiedler, PhD, CRNA
Abstract

Purpose To investigate the incidence of acute renal dysfunction (ARD) and injury, as well as associated risk factors, in open abdominal aortic surgery.

Background The relationship between elective infrarenal abdominal aortic surgery and acute renal dysfunction has been well studied, although wide variations exist in the reported incidence of ARD. Research guided by specific, standardized criteria can offer invaluable information about ARD, its associated risk factors, and yield consistent reports of its incidence. This information can be used to potentially decrease the mortality rate associated with this severe, and sometimes fatal, complication. Opinions differ regarding pre-hydration for renal patients scheduled for surgeries, even those with the potential for significant blood loss. Further investigation addressing this issue in the attempt to standardize care for the ARD patient, may serve to provide evidence-based care and to improve quality.

Methodology In a prospective, randomized control trial, 69 subjects underwent elective aortic repair using an infrarenal approach. Subject ages ranged from 58 to 77 years. Standardized target ranges for hemodynamic values were set. These included a mean arterial pressure (MAP) of 70-90 mmHg, pulmonary artery occlusion pressure (PaOP) of 12-14 mmHg, and cardiac index ≥ 2.41 l/min/m². Kidney injury was measured using urinary albumin-creatinine and N-acetyl-B-D-glucosaminidase-creatinine ratios. For clarification, ARD was defined using the RIFLE renal failure classification system.

Result 22% of the subjects developed ARD, while 4% developed acute renal failure. Overall, the patients that developed ARD were older (68-77 yrs) and had higher preoperative levels of plasma creatinine and estimated glomerular filtration rate (GFR). Intraoperative hypotension (MAP <60 mmHg for >15 min) and low cardiac index (<2.4 l/min/m²) were found to be significant indicators of ARD development (P=0.006 and P=0.017, respectively).

ARD was associated with intraoperative hypotension. Intraoperative hypotension and postoperative low cardiac output were independent risk factors for ARD in multivariate analysis.

Conclusion Most patients incur some kidney injury during infrarenal aortic surgery with 22% developing ARD despite similar hemodynamic management target levels. ARD is associated with intra-operative hypotension as well as low cardiac output. Awareness and adept perioperative management of these two factors may reduce the incidence of ARD during elective infrarenal aortic surgery.

Comment Findings in this study indicated a high incidence of acute kidney injury (22%) in elective infrarenal abdominal aortic surgical repair subjects. This is important to consider in light of the growing population of renal failure patients and the potential anesthetic complications that can occur as a result of cross-clamping. The fact that the reported incidence of kidney injury occurring from the infra-renal approach is considerable offers robust support to investigate this problem.
The authors investigated renal damage resulting from aortic cross-clamp times ranging from 46-95 minutes using multiple protocols for colloid, vasopressor, and inotrope administration. The study evaluated the renal protective attributes of N-acetylcysteine (NAC) using a double-blinded approach with two randomized groups. The groups received either NAC or a placebo.

In the past, there have been conflicting reports of N-acetylcysteine’s (NAC) renal protective ability. However, there seems to be more support for NACs use in recent literature. Apparently, free radicals can impact renal blood flow and cause tissue damage. NAC as a precursor to glutathione seems to promote scavenging of these toxins.

Historically, anesthesia providers have attempted to reduce the incidence of renal damage using methods such as low dose dopamine infusions, mannitol, diuretics, inotropes, and crystalloids. Maintaining MAP (50-55mm/Hg) using these methods during aneurysm repair is the widely accepted practice for organ perfusion and prevention of renal damage. This study reports that even when MAP is maintained between 70-90 mm/Hg with inotropes and vasopressors, ARD occurred in 20% of the subjects. This leads me to question the widely accepted practice of maintaining MAP between 55-60 mm/Hg. However, as with any new practice question, further investigations would be required.

In this study no significant differences were found with NAC administration when compared with crystalloids, colloids, vasopressors, and inotropes; all anesthesia mainstays aimed at maintaining or improving renal function during cross-clamping. Although the findings were insignificant, anesthesia providers may benefit from familiarizing themselves with NAC (Parvolex) as more studies become available that evaluate its efficacy.

Of additional interest to me was the Risk, Injury, Failure, Loss, End Stage Renal Disease (RIFLE) criteria, which were developed as an international renal failure classification system. The RIFLE system can serve to clarify the stages of renal disease, something many CRNAs are not likely familiar with. Classification is determined by specific lab values. The classifications range from risk, injury, failure, loss, and end stage kidney disease. More complete information about the RIFLE classification system is available in the following reference.

Nina E. McLain, PhD, CRNA

An informative article about the RIFLE classification system is Bellomo, R., Kellum, J., & Ronco, C. *Intensive Care Medicine* 2007;33:409-413.
DESFLURANE HEPATITIS ASSOCIATED WITH HAPTON AND AUTOANTIGEN-SPECIFIC IGG4 ANTIBODIES

Anesth Analg 2007;104:1452-1453

Anderson JS, Rose NR, Martin JL, Eger EI, Njoku DB

Abstract

Purpose This case report describes desflurane induced hepatitis in a previously healthy individual.

Background Drug-induced liver injury (DILI) is the third most common cause of acute liver failure in the USA. Potent inhalation agents are a rare cause of DILI. When inhalation anesthetics are the cause, hepatitis develops between 1 and 3 weeks after an inhalation anesthetic. Most reported cases have involved halothane or isoflurane but there are 3 previous reports of hepatitis following desflurane anesthesia. Risk factors include: previous exposure to a potent inhalation agent, female gender, and autoimmune disease.

Methodology A healthy 22 year old, 123 lb women underwent an exploratory laparotomy and left oophorectomy under general anesthesia. She received 175 mg propofol, 150 µg fentanyl, 35 mg rocuronium, and 6% to 8% desflurane in oxygen and air. The case lasted 85 minutes and the patient was discharged the following day.

The woman had no history of blood transfusion. Her HIV test was negative. She had received the hepatitis A vaccine. She had a general anesthetic six years earlier.

Result Sixteen days later the patient developed fever and nausea. Over the next five days she developed dark urine, itching, vomiting, she became dehydrated, and was readmitted to the hospital.

A work up for cholecystitis was negative and her lipase was normal. Liver enzymes were significantly elevated. Screens for infectious or autoimmune hepatitis were negative. Enzymes consistent with DILI were significantly elevated.

Conclusion These findings support an allergic / autoimmune induced hepatitis triggered by desflurane.

Comment

With the era of halothane anesthetics in adult patients behind us in the developed world, it is easy to forget “halothane hepatitis.” But hepatitis following exposure to a potent inhalation agent can still occur, though it is rare. One theory suggests that inhalation agent metabolites play a role in the development of hepatitis following an inhalation anesthetic. But desflurane, which is only about 0.02% metabolized, can still promote hepatitis, however rarely. Case reports like this one serve to remind us to crank up our index of suspicion when fever and nausea begin in the second or third week following an inhalation anesthetic; even a desflurane anesthetic.

Michael Fiedler, PhD, CRNA
CARDIOPULMONARY BYPASS, HEMOLYSIS, AND NITROPRUSSIDE-INDUCED CYANIDE PRODUCTION

Anesth Analg 2007;105:29-33

Cheung AT, Cruz-Shiavone GE, Meng QC, Pochettino A, Augoustides JA, Bavaria JE, Ochroch EA

Abstract

Purpose The purposes of this study were to: 1) quantify the amount of red blood cell lysis and free hemoglobin that occurs in adults during cardiopulmonary bypass (CPB) and 2) correlate plasma free hemoglobin levels with free cyanide following exposure to sodium nitroprusside (SNP) (Nitropress®).

Background Cyanide toxicity is a known potential complication of SNP administration. Normally, the cyanide released during SNP administration is converted to thiocyanate and eliminated renally. Cyanide toxicity associated with SNP administration has been previously linked to prolonged infusion, out of date solutions, or excessive dosing. Nevertheless, cyanide toxicity has been reported following administration of doses within the recommended range and, occasionally, even fairly short duration infusions.

While the pathway of SNP metabolism has not been firmly established, SNP has been shown to generate free cyanide in a reaction with sulfhydryl groups found on hemoglobin. In vitro studies have shown that free cyanide production increases by between 5 and 8 times when SNP is allowed to react with free hemoglobin rather than hemoglobin contained inside an intact red blood cell membrane.

CPB has been identified as a risk factor for cyanide toxicity following SNP administration. The incidence of cyanide toxicity has been reported to be 2.4% in cardiac surgery patients. Since hemolysis is known to occur during CPB, cardiac surgery patients may be at increased risk of cyanide toxicity following SNP administration.

Methodology This observational study included a convenience sample of 25 patients undergoing CPB. The study included both an in vivo and an in vitro component. Blood samples were taken after heparinization, every 30 minutes during CPB, and at the end of bypass. Patients who received SNP before or during the study period were excluded from data collection. Each sample was analyzed for free hemoglobin by spectrophotometry. The samples were then incubated in vitro with a known concentration of SNP and free cyanide measured by spectrophotometry.

Result Data was collected from 8 female and 17 male patients ages 37 to 86 (mean age 65 years). CPB time ranged from 75 minutes to 322 minutes with an average CPB time of 186±15 minutes. A total of 172 samples were collected.

Maximum free hemoglobin levels ranged from 30 mg/dL to 240 mg/dl and averaged 94±11 mg/dL. Free hemoglobin increased as CPB time increased (P<0.001). In follow up laboratory testing, cyanide levels were directly related to the concentration of free hemoglobin (P<0.001). When the free hemoglobin concentration was held steady, the generation of cyanide was directly related to the concentration of SNP present over a wide range of SNP concentrations (r² = 0.906) (P<0.001). Cyanide levels were independent of patient age, weight, or gender. Cyanide levels were also independent of baseline hemoglobin concentration, type of surgery, minimum patient temperature during CPB, or volume of cell saver blood.

Conclusion CPB was associated with hemolysis and increased levels of free hemoglobin that correlated with the duration of CPB. Free hemoglobin increased the generation of cyanide in the presence of SNP. For a given concentration of free hemoglobin, cyanide generation increased as SNP concentration increased.

Comment

Sodium nitroprusside does things that no other drug does. While other drugs can be used to reduce systemic vascular resistance, no other drug that I am aware of: does so to the exclusion of almost any other pharmacologic effect, is as reliable and dose dependent, has an onset as fast or a duration as short. But, the Achilles heal of nitroprusside has always been cyanide toxicity. Concerns about cyanide toxicity have played a variable role in clinical decision making over the years. After some study, the conventional wisdom has been that nitroprusside was generally safe as long as a fresh infusion solution was used (less than 24 hours old), the infusion solution was protected from light, moderate doses were used, and the total infusion time / dose was limited.
Assuming that collecting a blood sample causes no hemolysis, the normal free hemoglobin level is <0.6 mg/dl. Since some hemolysis often occurs during sample collection and processing, a pathologic level of free hemoglobin has been established as >20 mg/dl. All patients in this study had a maximum free hemoglobin level in excess of 20 mg/dl, on average it was 94±11 mg/dl. And in follow up lab tests, as the level of free hemoglobin increased, more cyanide was produced when nitroprusside was added to hemolyzed samples.

The investigators correctly identified an important limitation of this initial study. Because actual plasma concentrations of SNP during clinical use are not known and because the cyanide testing was in the lab \textit{(in vitro)} rather than in actual patients \textit{(in vivo)} cyanide generation may have been over or under estimated. Despite this limitation, this well conceived study still teaches us two things:

1. The more free hemoglobin that is circulating in a patient, the more cyanide that can be produced during SNP administration.
2. At any given free hemoglobin concentration, the amount of cyanide that can be produced during SNP administration is directly related to the dose of SNP over a wide range of SNP concentrations.

This study adds substantively to our understanding of cyanide toxicity during nitroprusside administration. And while CPB does result in progressively greater hemolysis as time goes on, the real message has to do with hemolysis, not simply CPB. We can use this knowledge clinically when we decide whether or not to use SNP and to adjust our index of suspicion for cyanide toxicity when SNP is in use.

Michael Fiedler, PhD, CRNA
Regional Anesthesia

SPINAL PERNAL BLOCK: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND COMPARISON WITH SPINAL SADDLE BLOCK

Anesth Analg 2007;104:1594-1596

Wassef, MR, Michaels EI, Rangel JM, Tsyrlin AT

Abstract

Purpose The purpose of this study was to compare the effectiveness of 1.5 mg spinal bupivacaine with 6 mg spinal bupivacaine for perirectal surgery.

Background Attempts have been made to target specific nerve roots with spinal anesthesia for particular surgical procedures and to allow a reduction in local anesthetic dose and faster recovery. Few investigations have attempted to further reduce the local anesthetic dose for rectal or perineal surgery.

Methodology This prospective, randomized, double-blind study included 80 ASA class I and II patients scheduled for elective perianal surgery with subarachnoid block anesthesia. While sitting, dural puncture was performed at L4-5 or L5-S1 with a 24 gauge Sprotte needle. The opening of the Sprotte needle was faced caudad for the injection of either 1.5 mg or 6 mg of bupivacaine. Editor’s note: while not specified by the investigators, the local anesthetic appeared to have been a hyperbaric solution. Sensory and motor function was assessed before and after surgery.

Result The surgical procedures performed included hemorrhoidectomy, perianal fistulectomy, perianal lesion excision, chondylomata excision, and anal mass biopsy.

Block set up time sufficient for the surgical procedure took an average of one minute longer in the 1.5 mg group than the 6 mg group (P<0.01). Bupivacaine 1.5 mg produced a median and maximum block up to the S-4 dermatome. Bupivacaine 6 mg produced a median block height of S-1 and a maximum height of L-4 (P<0.01). Bupivacaine 1.5 mg produced no motor block discernable by modified Bromage criteria while the 6 mg dose produced some motor block (P<0.01). Regression of the block below the S-4 level took an average of 76 and 153 minutes in the 1.5 mg and 6 mg groups respectively (P<0.01). Time to ambulation was 33% faster and time to discharge was 49% faster in the 1.5 mg group (P<0.01).

Conclusion Spinal bupivacaine 1.5 mg may be useful for selected perianal surgical procedures.

Comment

I’m glad someone was motivated to try a dose this low because I don’t think I ever would have. For selected procedures, this 1.5 mg hyperbaric bupivacaine spinal technique appears to hold some real promise. Regional anesthesia effectively reduces the risk of PONV. But regional anesthesia has long been underused in outpatient settings, in part because of concerns about having to wait longer to discharge patients. But in this study the 1.5 mg bupivacaine group was ready for discharge in an average of 126 minutes after the block was injected. In the outpatient setting I work in, this is comparable to general anesthesia discharge times, when measured from induction to discharge. I will be interesting to see if other researchers or clinicians can reproduce these results.

Michael Fiedler, PhD, CRNA