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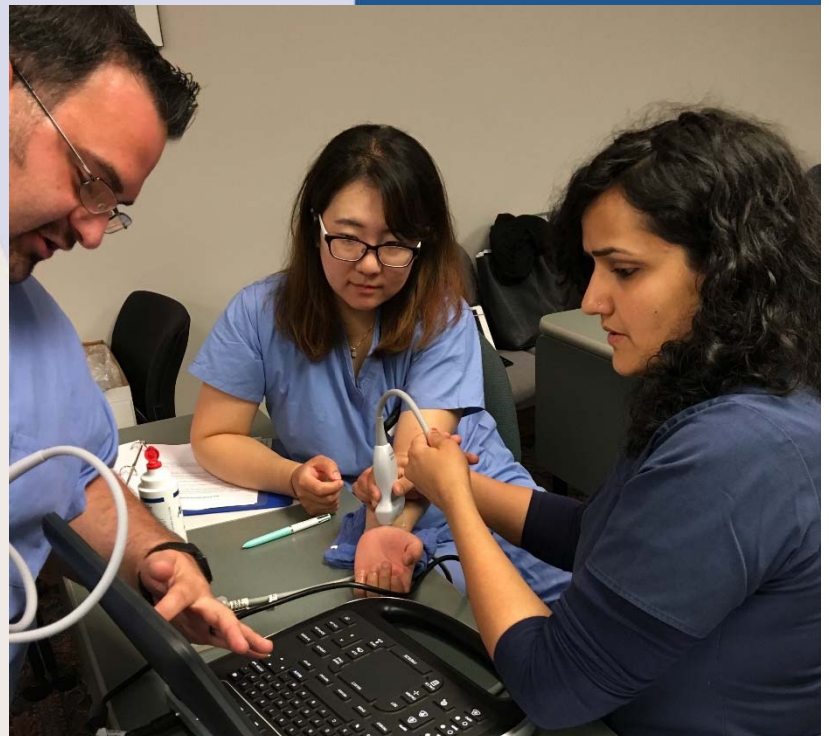
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Contributing Editors for this Issue

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Front Cover:

Virginia Commonwealth University (VCU) alumnus Andrew Metz, DNAP, CRNA instructs graduate students Ji Kim, BSN, RN and Meena Verma, BSN, RN on optimization of ultrasound images of the forearm at a hands-on workshop. The station is part of an intensive, four-day 'Anatomy Camp' event held on an annual basis at the Quillen College of Medicine, East Tennessee State University. The photographer was Michael Kammerman, Simulation Coordinator in the Department of Nurse Anesthesia at VCU.

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Propofol Administration in Patients with an Egg Allergy

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There has been a long-standing debate about whether propofol, commonly marketed as Diprivan, can be administered to patients with an egg allergy. Propofol warning labels vary from country to country regarding the administration of the drug in patients with egg allergies. Case reports of anaphylactic reactions to propofol lack evidence to suggest an egg allergy as the cause. [1-2] Conflicting statements and inconclusive evidence have resulted in confusion among clinicians. Anesthesia professionals refrain from administering propofol in patients allergic to eggs even though there is not definitive evidence confirming this is an absolute contraindication.

Case Report

A 29-year-old, 22 kg, 119 cm, male presented for surgical closure of an abdominal fistula. Past medical history included proportional dwarfism, anorchidism, moderate-persistent asthma, bronchopulmonary dysplasia, congenital lobular emphysema, hypospadias, and nephrolithiasis. Past surgical history included tracheostomy, gastrostomy, external auditory canal reconstruction, orchiopexy, hernia repair, right testicle removal, gastric fundoplication, and dental surgery. Current medications included mometasone furoate, cholecalciferol, budesonide, ipratropium-albuterol, epinephrine as needed (PRN), carbamide peroxide 6.5% PRN, docusate sodium PRN, and guaifenesin PRN. The patient's allergy list was extensive and included milk protein, latex, sulfamethoxazole/trimethoprim, egg white, egg yolk, erythromycin, and rocephin. No prior history of anaphylaxis was noted.

An inhalation induction was performed with N_2O 5 L/min and O2 3 L/min, and sevoflurane 2.0% expired concentration. After intravenous (IV) catheter insertion, the patient was given fentanyl 50 mcg IV and propofol 50 mg IV. Intubation with an ETT utilizing the tracheostomy site was unsuccessful due to strong resistance with advancement. A size 2.5 LMA was successfully inserted and a patent airway was confirmed. Vancomycin 350 mg IV was infused over 60 minutes prior to surgical incision. Propofol 20 mg IV and fentanyl 25 mcg IV were given after incision due to symptoms of pain and agitation. The patient required a total of 125 mcg IV phenylephrine, given in incremental doses throughout the case. Dexamethasone 4 mg IV and ondansetron 3 mg IV were administered prior to emergence. The LMA was removed uneventfully with the patient awake and then a stable transfer to the post-anesthesia recovery unit was achieved. He did not exhibit any signs of an allergic reaction throughout his perioperative experience and was discharged home from phase II without incident.

Discussion

Incidence of anaphylaxis during anesthesia is rare, occurring in 1 in 10,000 cases.[3] Propofol was specifically designed with allergic reactions in mind.[2] The egg lecithin, a highly-purified phosphatide, which can be found in propofol comes from egg yolk, but egg white contains the

most allergy containing proteins.[5] Propofol has two possible components that can cause an allergic reaction, a phenol group and a di-isopropyl side chain. Reactions, although rare, are often credited to the di-isopropyl group if reported on the first exposure and due to the phenol molecule if reported after repeated exposure.[3,4] The patient in the case report exhibited moderate hypotension following induction, a common side effect of propofol and fentanyl. However, he did not exhibit any other signs of a possible allergic reaction. The research on propofol administration in patients with an egg allergy explains why giving propofol to this patient was a safe and effective choice.

A randomized controlled trial was completed to determine the safety of using propofol in patients with allergic diseases and/or bronchial asthma. They found that the incidence of wheezing and bronchoconstriction after propofol administration was higher in this patient population. All patients with egg allergies were excluded from this study, yet severe reactions still occurred.[6] There have not been any conclusive case reports of anaphylactic reactions to propofol in patients who have egg allergies. Instead, in case reports presented by Koul et al. and You et al. they cite the cause of the allergic reactions as being the phenol or isopropyl group.[3,4]

A retrospective study was completed on two cohorts to ascertain if the practice of avoiding propofol in patients with egg, soy, or peanut allergies is evidence-based. Study A included patients who had a peri-operative allergic reaction and were exposed to propofol, while Study B included patients who had an IgE-mediated egg, soy, or peanut allergy. In study A 4 out of 153 patients had positive allergy tests to propofol. Only 1 of these 4 patients showed a possible IgE-mediated allergic reaction to propofol, evidenced by a positive skin test and elevated serum tryptase. None of these 4 patients stated they had an egg, soy, or peanut allergy and they all had negative specific IgE tests completed on egg or soy. Study B found that the 99 patients who had IgE-mediated egg, soy, or peanut allergies had no allergic reaction when given propofol. The authors of these studies concluded that propofol can be safely administered in patients allergic to egg, soy, and peanuts.[1] A retrospective observational study was conducted to assess the safety of propofol administration in patients with both eosinophilic esophagitis (EoE) and an egg, soy, legume, or peanut allergy. In this study 18 patients had an allergy and the other 52 patients had a sensitization to one of these foods. No allergic reactions were reported in any of the cases. Some of the patients in this study received propofol for the first time while the others had received propofol multiple times before. This study concluded that propofol could be safely administered to patients with an egg, soy, or peanut allergy.[5]

The literature regarding the use of propofol in pediatric patients with an egg allergy is less straightforward. IgE-mediated egg allergies most commonly occur in the pediatric population, but are often outgrown by adulthood. Interestingly, 75% of children who are allergic to eggs tolerate egg yolk without incidence and the amount of egg yolk in egg lecithin is highly unlikely to produce an allergic reaction.[7] Wisken et al. completed a study to determine if propofol administration in children with either non-IgE or IgE-mediated eggs, soy, or nut allergies is safe. Although 13 undesirable events occurred, none were accredited to propofol, so it was concluded that it is likely safe to administer propofol to children with egg or soy allergies.[8]
A retrospective case review regarding the safety of propofol administration was completed on children with IgE-mediated allergies to egg or soy. Within this sample, 42 out of 43 patients received propofol with no reaction, including one child with a severe history of egg anaphylaxis.

Another child with a history of egg anaphylaxis developed a nonanaphylactic reaction after receiving propofol for the first time. A skin allergy test for propofol was positive, but testing for the 10% Intralipid component was not completed. Therefore, it was undetermined if the reaction was due to residual egg allergens or the isopropyl/phenol components of propofol. A conclusion was made that propofol can be safely administered in most pediatric patients with egg allergies. However, since the study only included 2 children who have had an anaphylactic reaction to eggs it was deduced that propofol should be avoided in children with a history of egg anaphylaxis until further research is completed.[7]

The patient described in the initial case report was allergic to both egg white and egg yolk, yet he did not have an allergic reaction when given propofol.   The case report described coincides with the current research that states adult patients with an egg allergy can safely be given propofol. Although it is certain that propofol can cause allergic reactions, the cause of these reactions is inconclusive, but decidedly unrelated to egg allergies in the adult population.   Although research also shows that children with moderate egg allergies can be safely given propofol, more studies need to be completed before conclusions can be undoubtedly made on the use of propofol in the pediatric patient with a prior anaphylactic reaction to eggs

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Mentor: Amber Johnson, MS, CRNA

Continuous ST Segment Monitoring in the Operating Room

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The early detection and treatment of myocardial ischemia is crucial in reducing postoperative mortality related to cardiac complications.[1] Delivering anesthesia to patients in the operating room with increased cardiovascular risk factors requires increased vigilance and the appropriate monitoring tools for the earliest detection of myocardial ischemia. The electrocardiogram (ECG) monitor has been used for decades to monitor the heart rate of patients, but by assessing the ST segment of the ECG we can more specifically monitor the heart for ischemia.[1] Accurate lead selection and electrode placement can lead to an increased sensitivity in the identification of ST segment changes.[1]

Case Report

A 69-year-old female with a history of renal cell carcinoma presented for an open, right radical nephrectomy for a urinary fistula after partial nephrectomy. The patient's height was 147 cm and weight was 76 kg, with a calculated body mass index (BMI) of 35 kg/m^2. Allergies included cephalexin, morphine and sulfamethoxazole/trimethoprim. Past medical history included asthma, hypertension, dyslipidemia, diabetes mellitus type 2, atrial fibrillation, and chronic pain. Surgical history included a cholecystectomy, lumpectomy, lithotripsy, and orthopedic surgeries. The patient reported no personal or family history of anesthetic complications. The patient's medication regimen included amlodipine 10 mg, aspirin 81 mg, lisinopril 2.5 mg, alprazolam 0.25 mg, cyclobenzaprine 5mg, levothyroxine 100 mcg, metformin 500mg, and simvastatin 10mg. The last dose of these medications were taken the day prior to surgery.

She was referred pre-operatively for cardiology clearance due to her multiple risk factors. The consultation note addressed the fact that the patient's metabolic equivalent (MET) was less than 4 with fatigue being her predominant symptom. An ECG was completed and demonstrated normal sinus rhythm with no ST segment abnormalities. A transthoracic echocardiogram was also performed and showed an ejection fraction of 65% with no other significant abnormalities. She was classified as an intermediate cardiovascular risk due to her multiple risk factors and the proposed surgery itself. No further pre-operative studies were recommended. The day of surgery, a thorough preoperative examination included stable vital signs and laboratory data that were within normal limits. Her airway assessment was unremarkable.

When the patient entered the operating room, standard monitors were placed. The 5-lead ECG was placed in the normal position on the chest, with the V lead placed in the V5 position (fifth intercostal space, midway between the midclavicular line and the midaxillary line). Continuous ST segment monitoring was initiated, a baseline J point was established and an ECG strip was printed prior to induction.

Induction medications were given as follows: fentanyl 100 mcg, propofol 150 mg and rocuronium 50 mg. The trachea was intubated and correct placement was confirmed with bilateral breath sounds and presence of an end tidal carbon dioxide wave form. The 7.0 mm endotracheal tube was secured at 21 cm while the patient was placed on volume control ventilation. General anesthesia was maintained with sevoflurane 3% inspired concentration in a mixture of O_2 1 L/min and air 1 L/min. An arterial line was placed in the left radial artery and an additional 18 gauge intravenous catheter was placed in the right forearm.

The case lasted three hours and was complicated by blood loss totaling 1100 mL. The patient was given a total of 2500 mL of lactated ringers and 500 mL albumin. A hemoglobin of 8.8 g/dL was obtained when blood loss totaled 750 mL. The patient received 2 units of red blood cells (RBCs) prior to the end of the case. The patient's vital signs remained within 20% of baseline, requiring only 3 doses of phenylephrine 100 mcg. Throughout the case she remained in sinus rhythm and her ST segments deviated minimally (0.1-0.3 mm) from baseline.

At the end of the procedure, neuromuscular blockade was antagonized with glycopyrrolate 0.6 mg and neostigmine 3 mg. Antiemetics included dexamethasone and ondansetron. After suctioning the airway, the endotracheal tube was removed with the patient awake. Oxygen was administered at 3 L/min via nasal cannula. The patient was then transferred to the post-anesthesia care unit. Her hemoglobin the next day was 10.5 g/dL, she was discharged home 4 days later without complication.

Discussion

During the perioperative period, the decision of which ECG leads to monitor the patient in is based on their history and pre-operative 12-lead ECG. The ST segment of the ECG is measured from the J point, the point at which the QRS segment ends and the ST segment begins, and ends at the beginning of the T wave.[2] This segment should be isoelectric as it represents ventricular repolarization.[2] When calculating the ST segment for deviation, it is compared to the preceding PR segment as an isoelectric reference.[2] When the ECG is first connected to the patient, a baseline specific to that patient is established per the manufacturer's algorithm or can be set manually by the anesthesia provider. From this point on, subsequent ST segments will be compared to this baseline and displayed on the monitor as a positive or negative numerical value.[1] The four limb leads will always allow for continuous ST segment monitoring of leads I, II, III, AVF, AVR and AVL.[1] The decision to be made is which precordial (or V lead) is going to show the earliest ST segment changes specific to the patient and their history. Improper selection of this V lead can result in unrecognized myocardial ischemia or infarction.[2] If the patient has a pre-operative 12-lead ECG that has ST segment changes in a specific lead, known as the ST fingerprint, than that lead should be monitored throughout the case. Also if the patient has known coronary artery disease in a specific vessel, or recent coronary intervention, the selected lead should correspond with that coronary artery distribution.[3]

The debate and change in practice is with patients that do not have documented coronary artery disease or a remarkable pre-operative 12-lead ECG. Leads II and V5 are commonly monitored in the OR, but detect only 80% of significant ST changes.[4] The previous studies that recommended leads II and V5 were based on information gained from Holter monitoring in the

outpatient setting and they used absolute versus relative ST segment deviation.[4] More current literature has found that lead V3 most frequently (86.6%) demonstrates ischemia and is the earliest to show changes, followed by V4 (78.9%) and V5 (65.8%). For patients that experience perioperative infarction, V4 was the most sensitive and earliest in detecting ischemia (83.3%), followed by V3 and V5 (75% each).[5] The overall sensitivity in the detection of ischemia was 94.7% when either V3 or V4 was combined with the limb leads, compared to 76.3% when V5 was combined with the limb leads.[5]

Perioperative myocardial infarction (PMI) can occur from either plaque rupture leading to acute coronary syndrome (total occlusion) or from an imbalance in oxygen supply and demand.[8] Similarities found in these studies support the idea that the majority of PMI occur due to an imbalance in oxygen supply and demand (depicted by ST depression), rather than plaque rupture (depicted by ST elevation).[6-8] In these studies, perioperative cardiac events were rarely (<2%) or never, preceded by ST segment elevation.[6,7] They found a strong association between long duration ST segment depression (>20 minutes) and progression to postoperative complications including myocardial infarction and death.[6,7,8] The longer the duration of ST segment depression, the higher the postoperative trend of troponin levels.[7] Another similarity in the studies was that each episode of ST segment depression was preceded by tachycardia (ranging from 90-120bpm). In the 2001 Landesberg[7] study, patients were monitored using 12-lead ECG prior to induction through 72 hours post-operatively. According to this study, the episodes of "long duration" ST segment depression occurred during the emergence phase of anesthesia, when oxygen supply and demand can be imbalanced from an increase in heart rate, blood pressure and sympathetic discharge. Eight of the patients who suffered PMI (68%), had their longest episodes of ST depression during emergence.[7] None of the patients had significant ischemia (defined as greater than 10minutes in duration) during induction.[7] Landesberg's[6] prior study in 1993 highlighted a similar connection between ST depression and tachycardia, but this study found that the majority of "long duration" ST depression occurred in the postoperative period but shorter episodes were identified during high demand, low supply periods in the OR (intubation, emergence and extubation). The importance of preventing and having a low threshold for treatment of tachycardia is essential. Both studies noted that the ST depression was transient in all episodes. Since these episodes of ST depression were transient, choosing the most sensitive leads for its detection, will allow the anesthetist to more rapidly identify and treat ischemia, limiting the time of ST depression and hopefully decreasing the incidence of post-operative myocardial complications.

In retrospect, the case study discussed was a good example of a typical patient with increased risk factors for heart disease presenting for surgery. Her preoperative ECG was noncontributory but her METs less than 4 due to fatigue was concerning. The ability to do continuous ST segment monitoring in the operating room was a valuable, simple and cost effective tool for this patient. Assuring that the ECG leads were placed in the appropriate positions for the most accurate data capture, establishing a baseline for the J point, identifying that the ST segment alarms were on and set to alarm with 1mm of elevation or depression were important steps in correctly monitoring for ST segment changes. An area for improvement was the selection of V5 for the chest lead. Evidence suggests that monitoring the patient in V5 is based on outdated literature and is not the most sensitive chest lead in the detection of ST segment changes. Since

this patient did not have documented coronary artery disease, V4 would have been the more appropriate and sensitive chest lead for monitoring.

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Opioid Free Total Intravenous Anesthesia for Laparoscopic Sleeve Gastrectomy

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Keywords: opioid free anesthesia, total intravenous anesthesia, laparoscopic sleeve gastrectomy, bariatric surgery, obstructive sleep apnea

Opioid abuse has reached epidemic figures in the United States. In 2015 there were 33,091 opioid related deaths, approximately half of which were attributed to prescribed narcotics.[1,2] As the primary prescribers and administrators of perioperative medications, anesthesia practitioners play a critical role in the exposure of patients to opioids during the surgical period. Opioid free anesthesia (OFA) reduces reliance on postoperative opioid prescribing for pain, minimizing opioid exposure.[3-6] This case demonstrates that a multimodal approach of an OFA total intravenous anesthesia (TIVA) is a safe and effective alternative to a traditional anesthetic with opioids and inhalational agents.

Case Report

A 41-year-old female (height: 158 cm, weight: 118 kg, body mass index: 47.3 kg/m^2) presented for a laparoscopic sleeve gastrectomy. Her medical history was significant for morbid obesity and obstructive sleep apnea (OSA) requiring nighttime continuous positive airway pressure. The patient's surgical history included a hysterectomy with severe postoperative nausea and vomiting (PONV). There was no known family history of adverse response to anesthesia. The patient had no known drug allergies and her only medication was a daily multivitamin. All laboratory values were within normal limits. Midazolam 2 mg was administered intravenously (IV) in the preoperative area.

Upon arrival to the operating room, standard noninvasive monitoring was instituted and pre-oxygenation was completed with O$_2$ 10 L/min delivered via facemask for 5 minutes. General anesthesia was induced with lidocaine 100 mg and propofol 200 mg IV. Successful mask ventilation was verified, followed by IV administration of rocuronium 10 mg and succinylcholine 120 mg. Direct laryngoscopy using a Miller 3 blade was performed and a 7.0 mm endotracheal tube was placed. Volume controlled ventilation was initiated with a mechanical ventilator with a mixture of O$_2$ 1 L/min and air 1 L/min. General anesthesia was maintained with propofol initially at 200 mcg/kg/min IV, then titrated to a final rate of 125 mcg/kg/min during the case. Ketamine 35 mg IV was also administered along with dexemedetomidine 50 mcg IV over a 10 min period (10 mcg every 2 minutes) and magnesium sulfate 2 g IV administered over 30 minutes. A lidocaine infusion of 0.5 mg/kg/hr was maintained throughout the procedure.

The patient was positioned supine with arms supported on padded arm boards at 75 degrees. Prior to incision, cefazolin 2 g was administered IV. Ondansetron 4 mg, dexamethasone 10 mg, and acetaminophen 1 g, were also administered IV intraoperatively. Neuromuscular blockade was maintained with intermittent IV boluses of rocuronium, for a total of 40 mg. A phenylephrine infusion was titrated with an average rate of 80 mcg/min to maintain a mean arterial pressure greater than 65 mm Hg. A total of Lactated Ringer's 1 L was administered intraoperatively.

Surgery was completed in 2 hours, after which IV infusions were titrated down and discontinued in correlation with decreasing levels of surgical stimulation. Dexmedetomidine 50 mcg IV was administered over 10 minutes and neuromuscular blockade was antagonized with IV glycopyrrolate 0.6 mg and neostigmine 3.5 mg. After local anesthetic and surgical dressings were applied to the operative sites by the surgical team, oxygen flow was increased to 100% O$_2$ at 10 L/min. Once the patient was maintaining an average tidal volume of 500 mL, respiratory rate of at least 12/min and following commands, the ETT was removed and the patient was taken to the post-anesthesia care unit (PACU) on O$_2$ 4 L/min via nasal cannula where she denied pain, discomfort, or recall. No postoperative opioids were administered prior to discharge from the PACU.

Discussion

This case describes a successful use of an opioid free, total intravenous anesthetic for a laparoscopic sleeve gastrectomy in an obese patient with OSA and history of severe PONV. The patient denied significant postoperative pain and was discharged from the PACU without the need for opioid administration.

This multimodal approach is a safe and effective alternative to commonly practiced anesthetic techniques, which utilize opioids and inhalation agents. OFA TIVA reduces opioid exposure and limits the incidence of PONV associated with opioids and inhalation agents, which was of concern for this patient.[6,7] Hypnosis, amnesia, analgesia and immobility were successfully maintained with this multimodal approach. Suppression of the sympathetic system was achieved with ketamine, lidocaine, magnesium, propofol, and dexmedetomidine. Analgesia was ensured with ketamine, magnesium, acetaminophen and dexamethasone.[8] Hypnosis and amnesia were attained with ketamine, propofol, and dexmedetomidine. Immobility was maintained with succinylcholine and rocuronium. This multimodal opioid free approach allowed for adequate blockade of the patient's autonomic responses to surgical stimulation while avoiding the serious risks and side effects related to opioids.

Opioids are among the most consistently effective modulators of a wide range of painful conditions, from acute perioperative pain to the agony of chronic cancer and metastases. Unfortunately, opioids are also associated with significant risks and adverse effects. The most disconcerting effects include addiction, induction of tolerance and respiratory depression, the combination of which proves fatal in nearly a hundred occurrences per day in our communities.[2]

Clearly, the useful properties of opioids make them indispensable under the appropriate conditions and, without safer replacements, they will likely continue to be prescribed. However, it is incumbent on all medical professionals to use these medications judiciously and with forethought in light of America's opioid crisis. A recent editorial in the AANA Journal stated "CRNAs have a moral and professional obligation to help patients and families affected by opioid misuse in any way possible."[9]

Recognizing these factors, it is imperative that anesthesia practice be expanded to include multimodal techniques that optimize intraoperative and postoperative pain management.[10,11] OFA can reduce reliance on opioid prescribing for postoperative pain and limit opioid exposure to help combat this public health crisis.[11] Avoidance of opioids is preferred in patients who are obese and those who have known or suspected OSA.[12] A multimodal technique that does not rely on opioids can also be useful in managing chronic pain patients for whom opioid tolerance makes achieving sufficient analgesia challenging. In addition, OFA is important for patients requesting avoidance of these medications due to current or past opioid addiction or with tendency for opiate induced nausea and vomiting, or constipation and urinary retention.

While a direct correlation between perioperative opioid use and subsequent chronic consumption awaits further elaboration, available data do suggest that caution is advised. In a 2016 retrospective review of insurance claims of patients who underwent 11 of the most common types of surgical procedures, it was revealed that 0.5% became chronic opioid users.[13] With

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approximately 30,500,000 surgical hospital admissions per year in the US,[14] a 0.5% at risk group would calculate to a consequential figure of 150,000 patients. Even if some patients underwent multiple procedures each year, the numbers of increased chronic opiate users is significant. As noted in the retrospective review, anesthesia professionals may be able to mediate long-term risk by using replacements for opioids whenever possible.[11,13] These statements are consistent with those from the AANA, although additional training and continuing education may be necessary for anesthesia providers to successfully incorporate OFA into their anesthesia armamentarium.

A review of available resources for anesthesia professionals interested in OFA research and implementation include a general PubMed search for "opioid free anesthesia" which yields 638 articles as of February 2018. The Society for Opioid Free Anesthesia (SOFA), a nonprofit organization that promotes opioid free pain management techniques and research is another valuable resource for anesthesia providers. Anesthesia professionals are in a unique position in the medical community to assist in mitigating and perhaps limiting the devastation experienced by patients and families as a result of America's deadly opioid epidemic, by reducing the amount of perioperative opioid exposure and postoperative opioid requirements.

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Mentor: Nicole Damico, PhD, CRNA

Intraoperative Pneumothorax: A Case Study

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Intraoperative pneumothorax can occur in up to 2% of all laparoscopic procedures and upwards of 10% in Nissen fundoplications for large hiatal hernia repairs.[1-3] Early detection of an intraoperative pneumothorax by anesthesia practitioners is imperative because small entry points may not always be obvious to the surgeon.[2] Signs that might be appreciated are paradoxical ballooning of the hemi-diaphragm, increased airway pressures and end-tidal carbon dioxide ($EtCO_2$), decreased breath sounds and oxygen saturation as measured by pulse oximetry (SpO_2).[1,2] Hemodynamic changes such as a decrease in systolic blood pressure (SBP) and an increase in heart rate (HR) can also be seen.[2]

Case Report

A 164 cm, 109 kg, 46-year-old female with a BMI of 40.5 kg/m^2 and no known allergies was scheduled for a laparoscopic Nissen fundoplication due to a history of refractory gastric esophageal reflux disease (GERD) and the presence of a hiatal hernia. Medical history included: hypothyroidism, GERD, smoking, morbid obesity, and depression. Surgical history included: thyroidectomy, cholecystectomy, and esophagogastroduodenoscopy (EGD). The patient's oral home medications included: omeprazole, levothyroxine, pantoprazole, and ranitidine. Preoperative lab values were all unremarkable.

During the pre-operative interview the patient confirmed the presence of active GERD so 10 mg of metoclopramide and 20 mg of famotidine were administered intravenously (IV). The patient was also given 2mg of IV midazolam as a pre-op sedative prior to entering the operating room (OR). In the OR, the patient was pre-oxygenated with O_2 12L/min via face mask and standard noninvasive monitors were applied. A rapid sequence intubation was performed due to the patient's active GERD, hiatal hernia, and obesity. Cricoid pressure was applied and anesthesia was induced with fentanyl 100 mcg, propofol 300 mg, lidocaine 100 mg and succinylcholine 140 mg IV. Tracheal intubation was performed without difficulty. Anesthesia was maintained with 7% desflurane along with a mixture of air 1 L/min and O_2 1 L/min to maintain a 60% inspired oxygen concentration. Return of muscle twitches was confirmed and surgical paralysis was initiated with rocuronium 50 mg to a level of 1 out of 4 twitches prior to incision.

Introduction of the trochanters and insufflation of the abdomen proceeded without complication. Thirty minutes after induction, as the surgeon dissected the tissue where the esophagus passes through the diaphragm, in an attempt to mobilize the esophagus and fundus of the stomach, he abruptly notified the anesthesia practitioner that he had created a large tear in the parietal pleura. The patient was placed on O_2 15 L/min and abdominal insufflation was ceased. The patient's SpO_2 decreased from 97% to 88%, peak inspiratory pressure increased from 29 to 42 cm H_20 and the SBP dropped from 110 to 70 mm Hg. Breath sounds were found to be nearly absent on the right chest. A 750 mL Lactated Ringers fluid bolus and 100 mcg boluses of phenylephrine were administered to maintain at SBP of 90 mm Hg. Hemodynamic stability improved so it was thought deemed appropriate to get a AP chest film to confirm the diagnosis which ended up showing a large right pneumothorax.

After consultation between the anesthesia team and surgical team the decision was made to place a right chest tube. Under the guidance of the Certified Registered Nurse Anesthetist (CRNA) the senior Student Registered Nurse Anesthetist (SRNA) prepared to place the chest tube. The right chest wall was prepared and draped. The second intercostal space was located and anesthetized with 1% lidocaine. A 2-cm incision parallel to the intercostal space was created and curved forceps were used for blunt dissection at the level just above the third rib to avoid any neurovascular injury. The pleural space was found to be free of adhesions. A 32-French chest tube was placed in the apical direction and put to water seal. The incision was covered with petroleum gauze and foam tape. At this point, the pneumothorax appeared to resolve, with rapid improvement in hemodynamics and respiratory status. The patient's SpO_2 increased from 87% to 98%, peak inspiratory pressure decreased to 28 cm H_20 and the SBP increased from 90 to 130 mm Hg.

After the insertion of the chest tube, the patient remained stable and the decision was made to complete the surgery. The surgery was then converted to an open approach and completed without any further complications. Following the procedure, the patient remained intubated and was taken to the intensive care unit (ICU) for close observation.

Discussion

The incidence of pneumothoraces has been documented in the literature in both intraperitoneal and extraperitoneal procedures.[4] The incidence has been documented to be the highest in

fundoplication surgeries due to the dissection of the peritoneum in a mediastinal direction and can be a potentially life-threatening complication.[1,4] A pneumothorax that occurs during abdominal insufflation is classified as a tension pneumothorax. The pathophysiology associated with the creation of a tension pneumothorax in this case was due to an inadvertent tear in the pleura created during tissue dissection, leading to the progressive accumulation of carbon dioxide under pressure in the pleural cavity.[4,5] A pneumothorax secondary to carbon dioxide from abdominal insufflation has also been termed a capnothorax.[3,4] Other causes of pneumothoraces could be an undiagnosed congenital diaphragmatic communication between the abdominal cavity and the plural space or the rupturing of a bullae of an emphysematous bleb.[2,5] One of these causes is unlikely as the surgeon recognized the creation of a plural tear.

Clinical signs that the anesthesia practitioner might see during a tension pneumothorax are related to the compression of other anatomical structures within the chest.[1,5] These signs are variable but most common signs that could be seen are hypotension, hypoxemia, tachycardia, increased airway pressures, and absence of breath sounds on the affected side. [1,5] A tension pneumothorax can also lead to decreased venous return, cardiac disturbances and an increase in central venous pressure.[1,5]

Diagnosis of a pneumothorax is confirmed by chest radiography. As in the case report described above, if a clinically significant tension pneumothorax is suspected the primary treatment is to discontinue abdominal insufflation immediately and place a chest tube to decompress the chest cavity.[1] Literature has also described the use of positive end-expiratory pressure (PEEP) to decrease the pressure gradient between abdominal and pleural cavities leading to a mechanical seal of the tear.[1] If only a small pneumothorax is detected and no respiratory or hemodynamic compromise is present, a more conservative approach can be followed where the patient can be monitored without intervention.[3,4] A CO_2 pneumothorax can resolve rapidly due to the high solubility of carbon dioxide and may not reoccur once the pneumoperitoneum is released.[3,4] If the patient remains stable, insufflation can be resumed and the surgery continued.[3] In our case, an open approach was chosen to better visualize anatomical structures since the patient had a large body habitus.

Literature has suggested that there is a higher incidence of pleural trauma leading to pneumothorax during laparoscopic surgery if the patient smokes cigarettes, is elderly, has an $EtCO_2$ greater than 50 mm Hg, has a large hiatal hernia, or had a prior operation in that area.[2,4] The incidence also increases if the surgery is longer than 200 minutes or the surgeon is less experienced.[2,4]

Overall, the initial anesthesia plan for this patient was well prepared and thought out. Up until the creation and identification of the pneumothorax, it was an uneventful anesthetic. Once the complication was identified, it was effectively communicated by the surgical team to the anesthesia practitioner ensuring a prompt response leading to a successful patient outcome. The CRNA knew where the emergency chest tube insertion trays were and how to manage an intraoperative pneumothorax. His advanced level of experience allowed him to be comfortable teaching a SRNA how to perform a chest tube insertion. Extra staff and anesthesia practitioners were readily available.

An alternative to chest tube placement described in some literature is the aggressive application of PEEP.[2] This could have sealed the tear and avoided the placement of a chest tube. However, the placement of a chest tube was seen as the definitive treatment and thus undertaken. Good communication between staff, knowledge of complications associated with laparoscopic surgeries and knowing the location and usage of emergency equipment helped lead to a successful outcome. After being admitted to the ICU, the patient was extubated in 6 hours without complications. Her chest tube was removed the following day and she was discharged to home on post-operative day three without sequelae.

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Anesthesia Implications for Patients with Left Ventricular Assist Devices

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Key Words: noncardiac surgery, left ventricular assist device, continuous flow device, intraoperative management

Left ventricular assist devices (LVAD) provide mechanical cardiac support to patients diagnosed with heart failure that has failed to respond to all other medical management treatment options. LVADs are now approved as destination therapy to prolong life, which indicates healthcare facilities will be treating these patients more frequently than ever before.[1] As nearly 50% of LVAD patients return to the hospital for minor surgical procedures within 6 months of implantation, they provide unique challenges to the anesthesia professionals in regards to monitoring SpO_2 and blood pressure in the presence of non-pulsatile flow.[2]

Case Report

A 25-year-old, 83 kg, 163 cm female presented for hysteroscopy with dilation and curettage (D&C) due to active uterine bleeding. The patient had undergone a D&C two month prior to this encounter for an abortion of pregnancy and had experienced intermittent bleeding since that time. Significant medical history included end-stage systolic heart failure secondary to peripartum cardiomyopathy, pulmonary hypertension, essential hypertension, iron deficiency anemia, and status post HeartMate II continuous flow LVAD implantation eight months prior. Prior to LVAD implantation, her ejection fraction was estimated between 25-30%. The patient's active medications included aspirin 81 mg, carvedilol 6.25 mg, digoxin 0.125 mg, gabapentin 300 mg, iron polysaccharides 150 mg, lisinopril 5 mg, magnesium oxide 400 mg, sildenafil 20 mg, tramadol 50 mg, and warfarin 2 mg. Pre-operative vital signs were temperature 36.8^0C, heart rate 90/min, blood pressure 101/68 (86) mm Hg, and SpO_2 99% on O_2 2 L/min via nasal cannula. Baseline 12-lead electrocardiogram revealed sinus rhythm with ST and T wave abnormalities in leads V3-V6, II, III, and aVF suggesting possible new onset anterolateral and inferior wall cardiac ischemia. Following pre-operative administration of two units of packed red blood cells and two units of fresh frozen plasma, significant abnormal lab values included: hemoglobin 9.4 g/dL, hematocrit 27.0%, prothrombin time 21.7 seconds, and international normalized ratio 2.13.

The ventricular assist device (VAD) coordinator was met in the pre-operative holding room and remained with the patient throughout the perioperative period. Midazolam 1 mg was administered intravenously in pre-operative holding. Once in the operating room, O_2 6 L/min was administered via facemask. Monitoring devices included 5-lead continuous electrocardiography, continuous end tidal CO_2 monitoring, non-invasive blood pressure (NIBP) cuff monitoring every two minutes, and continuous SpO_2 monitoring which maintained a strong signal throughout the case indicating presence of pulsatile flow through LVAD. Another dose of midazolam 1mg was administered intravenously prior to procedure start. A cervical block was placed by surgeon prior to initiation of procedure. The patient was lightly sedated with a total of ketamine 80 mg and propofol 220 mg via intravenous boluses intermittently throughout the two-hour case. Patient received a total of 800 mL of lactated ringers, no vasopressor therapy was required. Vital signs remained stable. Upon completion of procedure, patient was transported to the inpatient post anesthesia care unit for post-operative monitoring. The patient remained stable with no pain or nausea and maintained adequate respirations and SpO_2 on O_2 2 L/min via nasal cannula.

Discussion

Peripartum cardiomyopathy is idiopathic heart failure that occurs during the last month of pregnancy or in the first 5 months postpartum.[3] Peripartum cardiomyopathy occurs in the absence of any determinable heart disease and is characterized by an ejection fraction of < 45%.[2] As with any heart failure patient, when all medical management options fail to provide adequate heart function, mechanical support will be required. Due to approval of LVAD use not only as bridge to candidacy, or bridge to transplantation, but as a destination therapy (used to prolong life), institutions can expect to care for an increasing number of LVAD patients requiring noncardiac surgery.[1] As nearly 50% of LVAD patients return to the hospital for minor

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procedures within 6 months of implantation, they provide unique challenges to the anesthesia personnel in regards to monitoring SpO$_2$ and blood pressure in the presence of non-pulsatile flow.[2] Current research on this topic seeks to determine appropriate facility resource utilization in terms of proper monitoring and presence of specialized cardiac trained anesthesia practitioners.[2]

Newer LVADs provide better patient outcomes with the use of continuous flow technology, as compared to the older pulsatile flow devices.[2] Patient's with continuous flow devices have a narrow pulse pressure that may result in a non-palpable pulse. If this pulsatile flow is lost due to inadequate intravascular volume or insufficient pump settings, NIBP and SpO$_2$ are inaccurate.[4] Current research supports the use of NIBP monitoring in procedures where no large volume shifts or excessive blood loss are expected, and frequent blood gas analysis is not required.[4] If pulsatile flow in a continuous flow device is maintained via adequate fluid loading, NIBP is sufficient.[4] The LVAD patient population requires more frequent invasive BP monitoring than the general population, but it is not recommended as a standard of care in routine procedures.[5] If unreliable NIBP monitoring is noted, a Doppler with a manual BP cuff can be utilized to obtain more accurate pressure readings. [5] Doppler based Korotkoff sounds at the brachial artery, in conjunction with manual blood pressure cuff, will accurately determine mean arterial pressures (MAP) in 94% of the cases when an automatic cuff fails to provide an adequate reading.[4] Goal MAP should be 70-80 mm Hg to maintain adequate tissue perfusion.[1] For this case, although traditional NIBP monitoring provided accurate pressure readings, a Doppler and manual blood pressure cuff were available.

If pulsatility is lost, traditional SpO$_2$ monitoring will not be accurate.[4] Hypovolemia and vasodilation can quickly result in the loss of pulsatility, particularly with induction of anesthesia or in the event of significant blood loss.[4] Therefore, continuous cerebral oximetry is routinely recommended for patients with LVAD.[4] Cerebral oxygenation monitoring is reliable in the absence of pulsatile flow and can provide adequate indications of oxygenation status until pulsatility is restored with fluid resuscitation.[4] Although the SpO$_2$ remained accurate throughout this case, cerebral oximetry should be made available for all future LVAD cases.
Another anesthetic consideration for patients with LVADs is the risk of bleeding and coagulation disorders. LVAD patients require long-term anticoagulation to prevent ischemic stroke secondary to increased risk for clot formation.[6] Anticoagulation is maintained with a goal INR of 1.5-2.5 and daily aspirin for antiplatelet therapy.[6] These patients frequently develop an acquired vonWillebrand deficiency due to destruction of vonWillebrand factor by the LVAD pump.[1] These issues contribute to chronic anemia and frequent hospital admissions for GI bleeding related issues.[1] In this case, the patient remained on her coumadin with an INR of 2.0 and required red blood cell and platelet transfusions prior to the start of the procedure.

A concern for many institutions in regards to the growing number of LVAD patients presenting for noncardiac surgery is resource allocation of trained staff.[4] While a survey of current institutions reveals that most facilities are still utilizing a cardiac anesthesiologist to manage LVAD patients, even for minor procedures, studies performed by other institutions reveal that anesthesia care can be safely provided by noncardiac trained anesthesia professionals.[2,4] The greater reliability of the newer LVAD devices provides superior hemodynamic stability such that specialty trained anesthesia personnel are no longer necessary.[4] However, if the patient is not

hemodynamically stable, requires pharmacologic support, or large fluid shifts are expected, use of a cardiac trained anesthesia professional is recommended.[4] The facility should provide training on alarms and basic mechanics of LVADs, as well as a review of how to optimize basic hemodynamics.[4] A ventricular assist device (VAD) coordinator was present in the operating room throughout the conduct of this case, which is in accordance with standard practice recommendations for all noncardiac surgical procedures.[4] The VAD coordinator is responsible for managing the power sources, monitoring function and assisting with troubleshooting, interpreting alarms as encountered, and making device setting changes intraoperatively as needed.[4]

The number of patients with LVADs presenting for non-cardiac surgery will continue to increase. Anesthesia for these patients can be safely provided using routine, non-invasive monitoring by noncardiac trained anesthesia professionals in the presence of VAD coordinator. As with any patient, it is imperative to evaluate the LVAD patient's co-morbidities and develop an anesthetic plan that is safe based on that patient's specific needs.

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Postoperative Serotonin Syndrome in the Presence of a Denervated Heart

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Serotonin syndrome is a rare but potentially lethal condition that affects the central nervous system (CNS).[1] Increased serotonergic activity in the CNS is most commonly caused by selective serotonin reuptake inhibitors (SSRIs) and medications that work synergistically with SSRIs.[2] Serotonin syndrome presents with a spectrum of neurologic, autonomic, and neuromuscular changes.[1,2] Since common anesthetic medications can potentiate SSRIs and mask the symptoms of serotonin syndrome, anesthesia practitioners must readily diagnose and treat the condition. This report describes a case of serotonin syndrome that developed following the administration of remifentanil to a patient with a denervated heart taking citalopram.

Case Report

A 61-year-old, 73 kg, 168 cm caucasian female presented for a bronchoscopy with bronchial-alveolar lavage. History of present illness included a persistent cough and right upper lobe infiltrate due to aspiration pneumonia. Past medical history included peripheral neuropathy for which the patient took citalopram daily and light chain amyloidosis. The patient was one-year status post heart transplant and reported a history of postoperative nausea and vomiting. The preoperative assessment included a blood pressure of 118/74 mm Hg, a heart rate of 118/min, and neurologic function within normal limits.

Induction of anesthesia was achieved with midazolam 2 mg, fentanyl 100 mcg, propofol 200 mg, and succinylcholine 100 mg. The trachea was intubated and respiration was controlled by a mechanical ventilator. General anesthesia was maintained with propofol 70 mcg/kg/min and remifentanil 0.4 mcg/kg/min. Dexamethasone 4 mg and ondansetron 4 mg were administered. Ephedrine 10 mg and phenylephrine 200 mcg were used to maintain the mean arterial blood pressure greater than 60 mm Hg.

Forty-five minutes after induction, the heart rate increased to 140/min and the blood pressure increased to 170/110 mm Hg. Esmolol 20 mg and labetolol 20 mg were administered. The patient did not regain consciousness after cessation of the propofol and remifentanil infusions. Nerve stimulation demonstrated four out of four twitches and sustained tetany without fade. Blood glucose levels were within normal range. Naloxone 0.2 mg and flumazenil 0.9 mg were administered.

One hour after cessation of anesthesia, the patient demonstrated spontaneous eye opening with ocular clonus and myoclonus. The agitated patient did not follow commands. The patient was transferred to the post anesthesia care unit (PACU) while endotracheally intubated and with respirations assisted by a mechanical ventilator. The patient's blood pressure was 159/105 mm Hg and heart rate was 108/min.

One hour after arrival in the PACU, the patient's neurologic status had not improved. A computed tomography (CT) scan of the head revealed an acute ischemic infarct in the left frontal lobe. The patient was admitted to the medical intensive care unit (MICU) with a Glasgow Coma Scale (GCS) of 5. A subsequent magnetic resonance imagining (MRI) study revealed no infarct, indicating that the initial CT scan was interpreted erroneously. The patient was administered cyproheptadine 12 mg by orogastric tube and regained full neurologic function. The patient was then transferred from the MICU to a medical floor with a GCS of 15 and discharged at baseline neurologic status the next day.

Discussion

In the case described above, the patient developed serotonin syndrome due to a combination of serotonergic agents. Serotonin syndrome is a pathologic neurological condition caused by increased serotonergic activity, specifically by the stimulation of 5-HT1A and 5-HT2A postsynaptic receptors in the CNS.[2] This increased serotonergic activity results from medications that increase the release of serotonin, such as amphetamines; by medications that impair reuptake of serotonin, such as SSRIs; by medications that inhibit serotonin metabolism, such as monoamine oxidase inhibitors (MAOIs); and by medications that directly agonize serotonin receptors, such as phenylpiperidines.[1]

The increasing therapeutic use of SSRIs in the treatment of depression, anxiety, and neuropathy indicates that more patients will be susceptible to increased perioperative serotonergic activity.[1,2] While serotonin syndrome may follow administration of a single serotonergic medication, it commonly develops due to the summative serotonergic effect of a combination of these medications administered simultaneously.[2] Historical speculation once theorized that 5-HT3 antagonism by ondansetron increased the amount of serotonin available in the synapse and contributed to serotonin toxicity, but recent data suggest that this effect is negligible.[3,4] Phenylpiperidine opioids, such as fentanyl and remifentanil, are among the most commonly administered agents in anesthesia. These drugs have the potential to potentiate serotonin reuptake inhibition, release, and receptor agonism.[1,5] This patient's use of citalopram, an SSRI, made her vulnerable to an increase in serotonergic activity.[1,2] Although ondansetron's antagonism of 5-HT3 receptors likely caused no significant increase in serotonergic activity,[3,4] the fentanyl and high-dose remifentanil infusion, in conjunction with the patient's baseline inhibition of serotonin reuptake, caused a serotonin toxicity.[1,5]

In this case, multiple misdiagnoses led to delayed treatment and several unnecessary interventions. The classic presentation of serotonin syndrome includes a spectrum of mental status changes, neuromuscular hyperactivity, and autonomic hyperactivity.[1,2] Neurologic symptoms include agitation, delirium, and restlessness. [1,2] Neuromuscular symptoms include ocular clonus, myoclonus, and hyperreflexia. [1,2] Autonomic symptoms include hypertension, tachycardia, hyperthermia, and diaphoresis. [1,2] These symptoms may range from mild to severe, and while mild cases often resolve with supportive measures within twenty-four hours after cessation of the causative agent, severe cases may lead to death and require treatment with serotonin receptor antagonism. [1,2]

Unfortunately, the cardinal signs of serotonin syndrome are relatively nonspecific. In the presence of excessive serotonergic activity, more common complications of anesthesia may distract from the true cause. For example, this patient's tachycardia and hypertension was interpreted as a normal sympathetic response to stimulation instead of autonomic instability and treated with sympatholytics. The patient's postoperative altered mental status was attributed to delayed emergence and treated with opioid and benzodiazepine antagonists after neuromuscular blockade and hypoglycemia were ruled out. When these agents failed to produce a return to baseline function, the patient's agitation and neuromuscular hyperactivity was misdiagnosed as a cerebrovascular accident. Only once diagnostic imaging ruled out an acute infarct was the patient properly diagnosed with serotonin syndrome and administered a serotonergic antagonist, ciproheptadine.

Even in the presence of a transplanted heart, serotonin syndrome still produced hemodynamic changes in this patient, although they were less pronounced than they may have otherwise been due to the physiology of the denervated heart. The transplanted heart lacks parasympathetic innervation, and thus, acetylcholine exerts no cholinergic influence over it.[6] As a result, the denervated heart has an elevated baseline heart rate of 90 to 110 beats per minute.[6] The transplanted heart also lacks sympathetic innervation.[6] Therefore, the CNS cannot initiate a rapid, direct sympathetic response in the denervated heart.[6] The denervated heart does, however, contain alpha- and beta-adrenergic receptors, and serotonin stimulates the adrenal gland to release catecholamines.[6,7] Despite the baseline tachycardia and reliance on a delayed catecholamine response characteristic of denervated hearts, increased serotonergic activity eventually initiated sympathomimetic effects of tachycardia and hypertension in this patient.

Fortunately, this patient made a full recovery. Had the anesthesia providers in this case accurately diagnosed the serotonin syndrome in the operating room or PACU, the patient could have been spared several ineffective treatments, unwarranted tests, and nearly twenty-four hours of mechanical ventilation and sedation in the MICU. This case exemplifies the necessity for anesthesia providers to vigilantly recognize and treat serotonin syndrome.

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Angelman Syndrome

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Angelman syndrome is a rare genetic disorder caused by a mutation on chromosome 15.[1] This syndrome is characterized by severe developmental delays, seizures, ataxia, craniofacial abnormalities and a "happy demeanor".[1,2] The gamma-aminobutyric acid (GABA) system in the central nervous system is directly affected by the chromosomal mutation.[2] This mutation causes varying responses to anesthetic agents. [3] Angelman syndrome patients may also have increased vagal tone, difficult airways, and peripheral weakness which are challenges to anesthesia practitioners.[3]

Case Study

A 10-year-old girl with Angelman syndrome was scheduled for dental restoration due to dental caries. Her history was significant for developmental delay, nonverbal communication only, hyperactivity, aggressive behavior, anxiety, constipation, prematurity, unsteady gait, incontinence, difficulty sleeping, and obesity. Her current medication regime included melatonin, risperidone, and polyethylene glycol.

She arrived preoperatively with her custodial grandfather. They were shown a quiet, removed room to reduce her anxiety. She was alert, rocking and flapping her hand upon exam. Her weight was 64 kg and, height 152 cm. She had prognathism, a large mouth, wide spaced teeth, and a large tongue. No attempts were made for awake IV access and a mask induction was planned. She was fully cooperative and rode in a wagon to the operating room. Once inside the room, she was lifted out of the wagon to the operating tabling. She did not resist positioning, the anesthesia mask or monitors. Her preoperative vital signs were blood pressure 104/52 mm Hg, SpO2 95%, and heart rate 74/min in sinus rhythm. Anesthesia was induced with 6% inspired sevoflurane in O2 5 L/min. A 22 gauge intravenous (IV) catheter was placed in her right hand. Her nares were prepped with oxymetazoline hydrochloride spray and lubricant. Propofol 60 mg and fentanyl 30 mcg were given IV prior to nasal intubation. A Cormack and Lehane grade 2 view was obtained

during laryngoscopy with a curved blade. A 6.5 mm cuffed nasal endotracheal tube was placed without difficulty.

During maintenance of the anesthesia, dexamethasone 4 mg and ondansetron 4 mg IV were administered. She received lactated ringers 300 mL. She maintained spontaneous breathing with pressure support. She remained hemodynamically stable throughout the case. The anesthesia gas was changed to desflurane within the last 10 minutes of the case to facilitate an awake extubation. She received additional propofol 40 mg and fentanyl 25 mcg IV prior to extubation.

Her dental restoration consisted of treating 11 caries and 1 extraction. At the conclusion of the dental restoration, anesthesia gases were stopped. The patient's consciousness returned quickly. She remained calm and was extubated. She was transferred to the recovery area and later discharged to the care of her grandfather. Her total anesthesia time was approximately 1.25 hours. Her anesthesia course was uneventful.

Discussion

Angelman syndrome was first described in the 1960's as "happy puppet syndrome" by pediatrician Harry Angelman.[3] This genetic disorder is characterized by severe developmental delay, seizures, hyperactivity, uncontrollable laughing and smiling, ataxia, speech delays, and sleeping disorders.[4] Phenotypical characteristics that are a concern for anesthesia include microcephaly, craniofacial abnormalities, protruding tongue, sucking and swallowing disorders, prognathism, drooling, obesity, scoliosis, cardiac abnormalities and peripheral atrophy.[4] Although reaching adulthood is rare, gastroesophageal reflux is severe in adults with Angelman syndrome.[4] The incidence of Angelman syndrome is 1:10,000 to 1:40,000.[2,4]

The pathogenesis of Angelman syndrome rises from a partial chromosomal deficit on chromosome 15.[3] This is known to happen in 4 different ways. The most common and most severe phenotype type is caused by deletions in the 15q11.2-q13 region, followed by paternal uniparental disomy, imprinting defects and mutations in the ubiquitin-protein ligase E3A gene (mUBE3A). All mechanisms result in the non-functioning of UBE3A. Ten percent of Angelman syndrome patients have no genetic abnormality. UBE3A is responsible to encode a ligase that degrades intracellular proteins.[3,5]

Gamma-aminobutyric acid A (GABA-A) receptor subunits are also affected by deletions on chromosome 15.[2] The deletions result in alternations of GABA synthesis, release and GABA receptors. Hypo and hyperfunction of the GABA system result. Alterations in β3 subunit are thought to be responsible for seizures and movement disorders in patients with Angelman syndrome.[3]

Patients' with Angelman syndrome require anesthesia even for simple procedures because they lack the ability to cooperate.[1] The most common reasons for anesthesia include non-invasive procedures, dental, ear, nose, throat, and orthopedic procedures.[3] Developing an anesthesia plan for Angelman syndrome patients is difficult because deficiency of the GABA-A receptor subunit β3 makes intravenous anesthesia drugs unpredictable.[2] Many common anesthesia medications activate GABA receptors: midazolam, propofol, etomidate, anti-seizure medications and volatile

anesthetic agents.[1,6] Case reports and studies reveal variable patient reactions to GABA stimulants. A retrospective review performed by Landman et al. found no exaggerated responses to GABA stimulating drugs.[6] A dental case study reported delayed emergence after benzodiazepine administration.[3] Unresponsiveness to benzodiazepines was reported in an open cholecystectomy of a 36-year-old female with Angelman syndrome.[7] Insensitivity to propofol and etomidate, or reduced duration of action have been observed with Angelman syndrome patients.[3] In our case, the patient did not appear to have resistance or be oversensitive to GABA stimulating agents. Anesthesia practitioners should be aware that this is a possible complication and be prepared to switch anesthesia agents and support exaggerated responses as needed.

Bispectral index monitoring is a reasonable adjunct to use in monitoring a patient with Angelman syndrome to help determine the level of consciousness. In our case, this was not available. Patients with Angelman syndrome have been found to have increased vagal tone that predisposes them to bradycardia and asystole.[3] It is hypothesized that changes in intrathoracic pressure during periods of uncontrolled laughter can cause bradycardia and syncope.[3] One case study reported asystole that was resistant to treatment during exploratory laparoscopy.[3] Avoiding laparoscopic procedures, pretreating with vagolytics and avoiding anticholinesterases are suggested to protect patients from vagal hypertonia.[2,3] In our case, paralytics were not required, so we avoided them for intubation and therefore avoided anticholinesterases. Our patient remained hemodynamically stable without treatment with anticholinergics.

Most patients with Angelman syndrome have a history of a seizure disorder or are likely to develop one. Their seizures are typically resistance to treatment.[2,3] Patients who take seizure medication should continue it through surgery, and medications that stimulate seizures should be avoided; specifically, ketamine should be avoided.[3]

Peripheral muscle atrophy is common in patients' with Angelman syndrome.[3] These patients may be more sensitive to muscle relaxants than other patients and should be given a lower dose and titrated to effect.[3] Depolarizing muscle relaxants should be avoided if muscle atrophy is present. Anticholinesterases should be considered when paralysis is no longer needed to ensure residual weakness does not occur. Anticholinesterases may also predispose the patient to hyper-vagal response and caution is warranted with their use. In our case, we avoided paralytics for intubation and anesthesia management.

Angelman syndrome can be associated with craniofacial abnormalities, specifically microcephaly and prognathia, as well as excessive drooling and difficulty swallowing.[3] Ensuring mask ventilation before paralytics, when possible, and having emergency airway equipment available is prudent. During our case, the mask induction allowed for control of her airway and an oral airway helped keep her large tongue out of the way. Emergency airway equipment was readily available.

Angelman syndrome is a rare genetic disorder that has implications for anesthesia practitioners. Insensitivity to anesthesia agents and hypersensitivity have been reported which makes developing a treatment plan difficult. Anticipating that each may occur and having alternatives prepared is necessary to care for a patient with Angelman syndrome. Preparing for difficult airway scenarios and the potential for vagal hypertonia is necessary. Having appropriate

medications available and communication with the surgical team are essential for providing the best care.

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Pulmonary Hypertension Secondary to Congenital Heart Defect

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Keywords: Atrial septal defect, pulmonary artery hypertension, chest lung venous return repair, partial anomalous pulmonary vein, left-to-right shunt

Pulmonary hypertension is defined hemodynamically as a mean pulmonary artery pressure of more than 25 mmHg at rest.[1] Pulmonary hypertension is commonly classified into five groups each with different pathophysiologic causes.[1] Pulmonary hypertension due to congenital heart defect (CHD) is classified as pulmonary artery hypertension (PAH).[1] Partial anomalous pulmonary venous connection is a congenital anomaly that occurs when one or more of the pulmonary veins drain into the right atrium instead of the left, creating a left-to-right shunt.[2] The following report demonstrates the anesthetic management of PAH owing to CHD.

Case Report

A 40-year-old, 177 cm, 73 kg male presented to the emergency department with acute chest pain and a previous diagnosis of anomalous drainage of the right superior pulmonary vein and an unrepaired atrial septal defect (ASD). The patient was scheduled for a chest/lung venous return repair in the month to follow, but was immediately rescheduled for the following day, as the patient was demonstrating severe signs of worsening PAH despite efforts to control it with medications. The patient's previous cardiac workup included an echocardiogram that reported right ventricular hypertrophy and an ejection fraction of 45%. The electrocardiogram demonstrated normal sinus rhythm with right axis deviation and a right bundle branch block. A chest x-ray documented enlargement of the pulmonary arteries. Diagnostic labs demonstrated normal values. Lung sounds were diminished in the base of both lungs upon auscultation.

The patient received his morning dose of sildenafil prior to surgery upon request by the anesthesia team. The patient was transported from the intensive care unit (ICU) with a 20 gauge radial arterial line in place to the operating room (OR). An intravenous (IV) induction for general anesthesia with cardiopulmonary bypass was planned. Upon application of standard monitors, all vital signs were within normal limits. A single dose of nitric oxide 20 parts per million was made available in the OR. After five minutes of denitrogenation, proper end-tidal CO_2 waveform, and an oxygen saturation of 100%, general anesthesia was induced intravenously. A slow and controlled IV induction included lidocaine 50 mg, etomidate 5 mg, phenylephrine 100 mcg, fentanyl 250 mcg, midazolam 5 mg and rocuronium 50 mg. The patient was placed on mechanical ventilation with a programmed tidal volume of 350 ml and a respiratory rate of 14 breaths per minute with no added positive end expiratory pressure (PEEP).

The patient was prepped and draped for a left subclavian central line. The line was placed successfully with an initial central venous pressure reading of 12 mmHg. A transthoracic echocardiograph (TEE) was performed after the surgery was successfully started. The TEE demonstrated a prominent left-right shunt due to anomalous drainage of the right superior pulmonary vein. The patient remained stable and maintained a MAP greater than 70 mm Hg with no added vasopressors for support. Upon discontinuation of cardiopulmonary bypass, a dopamine infusion was started at a rate of 5 mcg/kg/min. The patient was on bypass for approximately one hour and forty-five minutes during which, the surgeon was able to reroute the patient's pulmonary venous flow into and through the ASD back in to the left atrium. The patient was administered midazolam 5 mg before transporting to the cardiac ICU with ventilatory support. Vital signs remained stable during transport.

Discussion

Congenital heart defects affect approximately eight in one thousand live births.[4] A partial anomalous pulmonary vein is reported to be right sided in 90% of cases and is twice as common in females as in males.[2] ASD associated with partial anomalous pulmonary vein is the most common misdiagnosis for PAH due to the fact that there are multiple causes of PAH and this specific CHD can easily go unseen on magnetic resonance imaging or TEE if an expert in CHD is not diagnosing the scan.[3] In the presence of both a partial anomalous pulmonary vein and an ASD, a left-to-right shunt of cardiac blood flow occurs with both defects due to a higher-pressure

gradient on the left side of the heart over the right.[4] The increased pressures on the right side of the heart begin to damage the small pulmonary arteries and arterioles ultimately increasing the pulmonary vascular resistance (PVR).[4] With an increasing PVR, PAH will ensue.[4] As the patient increases in age the risks for arrhythmia, heart failure, valve regurgitation, and PAH worsen.[4]

After a confirmed diagnosis of partial anomalous pulmonary vein and ASD causing secondary PAH, there are multiple treatment options.[3] Some of the possible options include surgical repair of the defect with continued therapy, maintenance of advanced therapy, or combination therapy.[3] Many patients diagnosed with PAH and this specific CHD undergo a "shunt reversal" which occurs when pressures on the right side of the heart exceed the pressures on the left and a previous left-to-right shunt becomes a right-to-left shunt.[3] "Shunt reversal" is a contraindication for surgical repair owing to rapid desaturation on induction of anesthesia.[3] The patient presented above was considered a candidate for surgery as he had not yet undergone a shift from left-to-right to right-to-left. Fear of the occurrence did potentiate the need for immediate surgery before the shift could take place. If PAH is too severe for repair of the CHD, right ventricular assist devices may be utilized.[1]

Before inducing a patient with PAH due to CHD it is vital that the anesthesia provider have a strong understanding and background knowledge of PAH and the effects of anesthesia on the disease state. A detailed preoperative evaluation will help guide the anesthetic plan for the patient and determine the severity of the PAH.[5] All medications being taken for pulmonary vasodilator therapy should be continued on the day of surgery.[1,5] Monitoring for PAH patients should include arterial lines along with central venous access in order to quickly react to acute changes in pulmonary artery pressures caused by anesthesia.[5] Care must be taken when placing the central line to avoid creating arrhythmias.[1] Hypoxia, hypercarbia, and acidosis must be aggressively controlled as these states increase PVR drastically.[1,5] Inhaled nitric oxide, a potent pulmonary vasodilator, was made available in the OR for the patient both as an emergency medication and a preventative medication to help decrease PVR.[1,5] Other pulmonary vasodilators include milrinone, nitroglycerin, or prostacyclin.[1] Appropriate medications for hypotension and decreases in systemic vascular resistance include phenylephrine, vasopressin and norepinephrine.[5] When inducing a patient with PAH, the most crucial thing to consider is a very slow and titrated induction.[1] By slowing the induction sequence this will limit the amount of hemodynamic changes that occur.[1] Euvolemia is the goal for fluid therapy as not to induce or aggravate right ventricular dysfunction.[5] Ventilator management should be aimed towards a lung protective strategy that will prevent a decrease in venous return.[1] Minimal PEEP, if any at all, and small tidal volumes with increased respiratory rate will help decrease atelectasis and hyperinflation.[5]

This report discussed a case of PAH secondary to CHD undergoing a chest/lung venous return repair. Adequate anesthetic management of a PAH patient must be well understood in order to have favorable outcomes for this patient population.[1] The management of this anesthetic closely mirrored the literature review performed above. This patient's PAH was assessed thoroughly preoperatively which helped guide an anesthetic plan and an emergency plan specific to the patient.[5] The patient remained on a pulmonary vasodilator the morning of surgery to help decrease PVR when undergoing induction of anesthesia.[5] Proper monitoring for the PAH patient was utilized in this case and helped guide hemodynamic stability while also maintaining an

appropriate anesthetic level for surgery.[5] A TEE was utilized intraoperatively to assess the patient's congenital anomaly and confirm pathophysiology before starting surgery.[5] Inotropic assistance was required at the end of the case to maintain an adequate MAP. The patient underwent successful chest/lung venous repair with a favorable postoperative outcome for decreasing PAH. Over preparation of case management and a strong clinical knowledge are two important factors for providing positive patient outcomes involving PAH.

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Magnesium for Management of Postoperative Pain

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Keywords: magnesium sulfate, postoperative pain, analgesia

Magnesium is the fourth most common cation in the body and it plays an important role in many physiologic activities in the body, one of which is thought to be the reduction of pain. It is an antagonist at N-methyl D-Aspartate (NMDA) receptors and calcium channels, which is the mechanism of action behind pain control in the body. Magnesium can cause analgesia through its blockade of voltage-dependent block of the NMDA receptor.[1] However, it is not a primary analgesic itself. Magnesium is considered more of an adjuvant to more traditional analgesics (fentanyl, morphine, hydromorphone, etc.) because it is believed to enhance the effects of those medications.

Case Report

A 47-year-old, 170 cm, 90 kg, Caucasian male presented for left total hip arthroplasty for arthritis. His past medical history included hypertension, hypercholesterolemia, obesity, and

former smoker (10-pack-years). His current medications included amlodipine, atorvastatin, and multi-vitamins. Preoperative vital signs were within normal limits. Pertinent labs included hemoglobin 14.1 g/dL, hematocrit 43%, platelets 244 K/uL, sodium 140 mEq/L, potassium 4.3 mEq/L, glucose 78 mg/dL, creatinine 1.03 mg/dL, prothrombin time 12 seconds, and international normalized ratio 1.1. An electrocardiogram showed sinus rhythm, and chest x-ray was negative for any acute process.

Spinal anesthesia along with a propofol infusion was discussed and agreed upon by the patient, surgeon, and anesthesia practitioners. General anesthesia was an alternative plan if neuraxial anesthesia was not effective. Once the patient entered the room, he was placed in a sitting position for insertion of a subarachnoid block. The proper interspace was located via palpation of the superior iliac spine bilaterally then going toward midline to the spine. The interspace was at a level of L3-L4 and was marked accordingly. The 20-gauge introducer was placed midline, perpendicular to the back at an angle of 15-degrees cephalad. A 25-gauge pencil point spinal needle was advanced for return of CSF. Injection of 0.75% bupivacaine 0.5 mL was injected into the subarachnoid space; however, the patient moved and return of free-flowing CSF was lost. Aseptic technique was performed throughout the procedure.

The patient was then placed supine and initial testing of sensory blockade indicated a level of T10. Propofol bolus of 20 mg was administered and an infusion was started at 100 mcg/kg/min. Upon incision, the patient moved his leg and his blood pressure and heart rate increased. General anesthesia was subsequently induced with 100 mg of propofol to facilitate placement of a LMA for maintenance of the inhalational anesthetic agent—sevoflurane. Pharmacologic agents used to minimize postoperative pain were ketamine 30 mg, hydromorphone 1 mg, and magnesium sulfate 2 g. Vital signs remained stable throughout the case with no fluctuations over 20% from baseline vital signs. Prior to closure of the operational incision, the surgeon administered 0.5% bupivacaine 30 mL as a field block surrounding the surgical site. The LMA was removed while the patient exhaled 0.1 minimum alveolar concentration of sevoflurane with spontaneous ventilations of 6-8 mL/kg. The patient maintained a patent airway and was subsequently transported to the recovery unit without complications.

Postoperatively, upon emergence the patient complained of no pain and vital signs remained stable. The patient's initial experience of pain occurred 3-hours later in the post anesthesia care unit. Pain was adequately controlled from a 6/10 to 1/10 on a visual analogue pain scale with a single dose of fentanyl 50 mcg. No additional opioid was required until 2 hours later when ambulation with physical therapy was performed. At that time an additional 50 mcg of fentanyl was adequate to reduce pain levels from 7 /10 to 2/10 during ambulation.

Discussion

A recent systematic review and meta-analysis of perioperative administration of magnesium for postoperative pain showed a clinically significant reduction in opioid consumption and pain scores in the first 24-hours post-operatively in various types of surgeries studied.[2] This finding is consistent with those of the patient in this case study, however, the patient also received a field block of local anesthetic at the incision site along with other pain medications such as ketamine and hydromorphone intraoperatively. While pain was controlled for the first 3-hours

postoperatively, it is more likely due to residual subarachnoid blockade along with the administration of intraoperative opioids, and less likely from a low one-time dose of magnesium. However, magnesium is known as an adjuvant drug that enhances the effectiveness of other analgesics; therefore, the patient may require less overall analgesic within the first 24-hour postoperatively compared to patients who did not receive magnesium. This is consistent with another systematic review and meta-analysis done at Johns Hopkins University by Murphy et al. which suggested that a magnesium infusion during surgery resulted in an overall reduction of postoperative morphine requirement by 28%.[3] Magnesium, while not an opioid, can prevent the proliferation of nociceptive receptions that occur during hyperalgesia and reduce the requirement of pain medication in the first 24-hours postoperatively.[3]

Magnesium plays an important role in the inhibition process of central sensitization of pain. A recent study evaluating a single-dose of intravenous magnesium for inguinal surgery concluded that 50 mg/kg of magnesium infused over 30-minutes prior to induction patients required less postoperative pain medication than those who did not receive magnesium during surgery.[4] When the inhibition of NMDA receptors and calcium channels occur prior to a noxious stimulus, central sensitization also becomes inhibited which results in a reduction in pain perception. This results in less narcotic requirements in the post-operative period.[4] This is thought to be related to the analgesic action caused by the blockade of calcium channels which results in an increased nociceptive threshold which prevents the influx of calcium that is required for the release of nociceptive and inflammatory neurotransmitters.[4]

There are some safety concerns with the administration of magnesium, such as hypermagnesia. Normal range of magnesium in plasma is 0.7-1.1 mmol/L. Hypermagnesia is rare unless the patient has impaired renal function. When plasma concentrations of magnesium reach 4.5 mmol/L, loss of deep tendon reflexes and dizziness can occur. At higher concentrations, respiratory arrest (> 6mmol/L) or cardiac arrest (>8 mmol/L) can occur. At doses of 30-50 mg/kg followed by a maintenance dose of 6-20 mg/kg/h infusion, magnesium toxicity rarely occurs unless the patient has renal insufficiency. The patient in this case report only received magnesium 2 g as a one-time bolus and there was a noted decrease in overall pain and opioid requirements in the 1st 24-hour postoperatively.[5]

In conclusion, NMDA is an amino acid receptor and is involved in excitatory synaptic transmission. The NMDA receptor has positive binding sites for glutamate and negative binding sites for magnesium and ketamine for the modulation of pain perception. In addition, it is also coupled with K and Ca ion channels. Intraoperative magnesium administration can reduce pain and overall narcotic requirement in the first 24-hours postoperatively. The mechanism of action is thought to be antagonism at the NMDA receptor and calcium channels. This results in an inhibition of central sensitization of pain. Magnesium is not a primary analgesic, but rather an adjuvant to traditional intraoperative opioids. It enhances the effects of other analgesics when given as a multimodal analgesic drug. At traditional dosing of magnesium at 30-50 mg/kg, there are few documented reports of adverse reactions and this dosing is considered safe when administered to a patient without renal impairment.

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The Role of Intravenous Magnesium Sulfate in Preventing Postoperative Pain

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Keywords: intravenous magnesium, magnesium sulfate, pain, analgesia, postoperative, surgical pain

Introduction

Postoperative pain is caused by the inflammation of tissues and direct damage to nerve cells. Pain control in the postoperative period is critical to preventing patient discomfort and improving morbidity and mortality after surgery. Postoperative pain control is necessary to optimize surgical patient outcomes by contributing to early ambulation after surgery, increasing patient satisfaction, and reducing the cost of hospitalization by shortening length of stay.[1] Several modalities are used to prevent and treat postoperative pain. One common pain-relieving option is opioid analgesics, which act on the mu receptors in the central nervous system. Opioids are effective at treating pain but they have an array of side effects including nausea, vomiting, sedation, and respiratory depression. Both tolerance and dependence can occur with chronic opioid use.[2] Due to the adverse effects associated with opioid use and current investigations on pain pathophysiology, there has been an emphasis on multimodal management of pain, specifically the incorporation of non-opioid analgesics.[3]

Painful stimulation leads to the release of neurotransmitters such as glutamate and aspartate, which bind to pain receptors in the body. One of these receptors is the N-methyl-D-asparate (NMDA) receptor, which causes calcium and sodium influx upon activation leading to central sensitization and wind up phenomenon.[4] Magnesium regulates calcium into the cell and acts as an NMDA receptor antagonist. Magnesium also antagonizes the expression of inflammatory mediators such as histamine, serotonin, and cytokines in peripheral tissues.[5] Not only has magnesium shown promising results in the prevention of postoperative pain and the reduction of postoperative opioid consumption,[6] it also decreases the incidence of sore throat due to tracheal intubation.[7]

Methodology

A PICO format guided the clinical question for search criteria. The PICO parameters include: P (patient population) = patients undergoing a surgical procedure, I (current intervention) = intravenous magnesium sulfate in the perioperative period, C (comparison) = no intravenous magnesium sulfate, O (outcome of interest) = prevention of postoperative pain and reduction of opioid consumption in patients undergoing general anesthesia with endotracheal intubation (GETA).

The purpose of this review is to examine the administration of intravenous magnesium sulfate for the prevention of postoperative pain and the reduction of opioid consumption in the postoperative period after GETA. The clinical questions that guide this evidence based practice analysis include: Is intravenous magnesium sulfate effective at preventing postoperative pain in the surgical patient? Does perioperative use of intravenous magnesium sulfate reduce opioid consumption in the postoperative period?

The search terms include: "intravenous" "magnesium" "magnesium sulfate" "pain" "postoperative" "perioperative" "surgical pain". An electronic database search was performed using PubMed, Cochrane library, EBSCOhost from years 2011-2016, for articles published in English. A total of four prospective randomized controlled trials (level 2 evidence) along with a systematic review (level 1 evidence) were selected for analysis. Melnyk and Fineout-Overholt's level of evidence classification was used to categorize the research.[8]

Literature Analysis

A systematic review and meta-analysis by Albrecht, Kirkham, Liu, and Brull assessed the role of perioperative intravenous magnesium sulfate on reduction of postoperative pain. This review examined twenty-five randomized control trials comparing magnesium to a placebo. Throughout the trials, perioperative magnesium reduced morphine consumption 24 hours postoperatively and numeric pain scores at rest and on movement. The authors concluded that perioperative intravenous magnesium reduces opioid consumption and pain scores in the first 24 hours postoperatively without any serious adverse effects. The data supports a single bolus dose of magnesium sulfate 40-50 mg/kg without infusion. The limitations of this meta-analysis were the wide variability in trial methods and outcomes measured. For instance, only eight studies out of twenty-five evaluated the incidence of adverse effects with intravenous magnesium.[6] Also, several of the trials examined magnesium in concurrent use with paracetamol. Because of this, it

is difficult to decipher if the effect of magnesium on opioid consumption is additive to paracetamol.[9] The strength of this meta-analysis is the high level of evidence it contributes to this practice analysis and the body of literature as a whole.[8]

Demiroglu, Ün, Ornek, et al. conducted a randomized control trial to investigate the effect of systemic and regional use of magnesium sulfate on postoperative tramadol consumption in lumbar disc surgery. This trial randomly assigned 75 patients to three groups: to receive magnesium intravenously, to receive magnesium injected in the intramuscular operative site, or to be in the control group. The intravenous group received 50mg/kg of magnesium sulfate in 150mL of saline over 30 minutes. The intramuscular group received 50mg/kg of magnesium sulfate in 30mL of saline. The control group received 30mL of normal saline injected intramuscularly. The results showed that nausea and vomiting occurred more frequently in the control group. This was attributed to increased tramadol use postoperatively in this group. Tramadol consumption in the intramuscular group was significantly lower than the other two groups. The intravenous magnesium group used less tramadol compared to the control group at the 1 and 24 hour postoperative mark; however, the results were only statistically significant for the 24 hour postoperative period. This led the authors to conclude that magnesium injected in the intramuscular operative region is more effective for postoperative analgesia than systemically administered magnesium. The strengths of this study are the comparison of two different routes of administration for magnesium. A limitation of this trial is that serum magnesium levels were not measured, which could have provided useful information to supplement the findings.[5]

The positive results of magnesium sulfate are not consistently displayed among trials. A randomized double-blind controlled clinical trial by Ghaffaripour, Mahmoudi, Eghbal, and Rahimi studied the effect of intravenous magnesium sulfate on postoperative analgesia during laminectomy surgery. This study divided 40 patients into two groups: those who would receive intravenous magnesium during surgery and those in the control group. The case group received a loading dose of magnesium sulfate (30mg/kg) within five to ten minutes followed by a maintenance dose of 10mg/kg/hr until the end of surgery. The study outcomes showed no significant difference between the two groups in the amount of morphine consumed 24 hours after surgery, pain intensity, and the time it took for patients to use their patient-controlled analgesia (PCA) pump. These outcomes led to the conclusion that the infusion of intravenous magnesium sulfate had no significant effect on patients' pain and opioid requirement during the first 24 hours after surgery. The lack of statistically significant findings contribute to the limitations of this study. This trial only examined patients undergoing laminectomy surgery. This surgery itself often relieves the chronic pain that patients experience and could have been the reason why there was no difference in pain scores between the two groups. Also, the trial took place in Iran where pain perception can be influenced by a variety of cultural factors.[1]

Magnesium can play a role in supplementing existing pain-relieving medications. The effect of magnesium with ketamine in reducing morphine consumption was explored after scoliosis surgery in a randomized double-blind study by Jabbour, Naccache, Yazbeck, et al. Fifty patients undergoing scoliosis repair were divided into two groups: those that received ketamine and magnesium during surgery and those that received only ketamine. The ketamine and magnesium group received an intravenous bolus of ketamine 0.2mg/kg and magnesium 50mg/kg after induction of anesthesia, followed by continuous infusion of ketamine (0.15mg/kg/hr) and

magnesium (8mg/kg/hr) until extubation. The ketamine only group received an intravenous bolus of ketamine 0.2mg/kg followed by a continuous infusion of ketamine (0.15mg/kg/hr) along with a bolus and continuous infusion of normal saline. The results showed the average cumulative morphine consumption was significantly lower in the ketamine and magnesium group compared to the ketamine only group. Visual analog pain scores were not statistically different between the two groups, however quality of sleep and satisfaction scores were better in the ketamine and magnesium group. The authors concluded that the ketamine and magnesium regimen reduces postoperative morphine consumption after scoliosis surgery. Additionally, it provided better sleep quality and improved patient satisfaction scores.[3]

A double-blind clinical trial by Jarahzadeh, Harati, Babaeizadeh, Yasaei, and Bashar examined the effect of intravenous magnesium sulfate on reduction of pain after abdominal hysterectomy surgery under general anesthesia. This trail placed 60 patients into two groups: a control group and those receiving intravenous magnesium sulfate. The study group received 50mg/kg of magnesium sulfate in 500mL of Ringer's serum over 20 minutes while the placebo group received only 500mL of Ringer's serum. The results showed mean pain scores immediately after surgery and at 1, 2, 6, and 12 hours after surgery were lower in the intravenous magnesium group compared to the control. Narcotic consumption was higher in the placebo group. There were no significant differences in the two groups in adverse effects. These results led to the conclusion that intravenous magnesium sulfate can reduce pain, reduce morphine consumption and reduce side effects of morphine in patients after abdominal hysterectomy surgery.[2]

Author(s), Date	Patient Groups	Level of Evidence	Study Outcomes	Key Results	Strengths and Weaknesses
Albrecht, Kirkham, Liu, Brull, 2013[6]	Twenty-five randomized control trials evaluating: IV magnesium bolus v. placebo (n=6) IV magnesium bolus + infusion v. placebo (n=15) IV magnesium infusion v. placebo (n=4) <u>Total subjects</u> n=1461: Perioperative IV magnesium, n=732 Placebo Group=729	Quantitative systematic review and meta-analysis; Level 1[8]	*Primary* -Morphine consumption at 24 hours *Secondary* -Pain scores at rest/motion at 24 hours -Early Morphine consumption at 6 hours -Early pain scores at rest/motion -Time to first analgesic request -PONV/ Pruritis *Additional* -Adverse effects -NM blockade -Mg levels	-Decreased morphine consumption by 24.4% (p<0.00001) 24 hours postoperatively -Decreased numeric pain score at rest and movement by 4.2 (p<0.0001) and 9.2 (p=0.009) out of 100, respectively -No difference in sedation and hypotension between the magnesium and placebo groups. Bradycardia was more prevalent in the magnesium group but responded to first line therapy	*Strengths* -High quality level 1 evidence -Statistically significant p values *Weaknesses* -Wide variability in the methodology of the studies examined -Not every study included adverse effects in their outcome measurements

| Demiroglu, Ün, Ornek, et al., 2016[5] | ASA 1-2 surgical patients presenting for lumbar disc surgery, n=75

IV Group, n=25: 50 mg/kg MgSO4 given IV

IM Group, n=25: 50 mg/kg MgSO4 given IM to surrounding muscles

Control, n=25: saline injected to surrounding muscles

All MgSO4 given at time of closure | Prospective randomized control trial, Level 2[8] | *Primary*
-Postoperative analgesia consumption in IV vs. IM MgSO4 groups

Secondary
-Hemodynamic changes
-Demographic data
-Duration of anesthesia and surgery
-Pain scores (NRS)
-Ramsay sedation score (RSS)
-Nausea and vomiting
-Potential side effects | -Tramadol consumption in the first hour: IM Group < IV Group & control, (p<0.05); IV group < control, no statistical significance

-Tramadol consumption in the first 24 hours: IM Group < IV Group < control, with statistical significance between the groups (p<0.5)

-Varied, no statistical difference in pain scores among groups

- PONV: Present in control > Groups IM and IV (p<0.05) | *Strengths*
-Two different routes of administration of magnesium were compared to each other and a control group
-Statistically significant p values

Weaknesses
- Use of Numeric Pain Rating Scale instead of Visual Analog scale Unable to directly compare pain score reduction results to other studies
-IV magnesium was not as effective as reducing pain scores compared to IM |
| Ghaffaripour, Mahmoudi, Eghbal, Rahimi, 2016[1] | ASA 1-2 patients undergoing elective laminectomy, n=40

Group Mg, n=20: loading dose 30 mg/kg IV with maintenance dose 10 mg/kg/h, until the end of surgery

Control, n=20: patient received normal saline IV bolus and drip | Randomized double-blind controlled clinical trial; Level 2[8] | *Primary*
Amount of Morphine consumed in the first 24 hours after surgery

Secondary
-First time using the PCA pump
-Pain intensity score | -Amount of morphine consumed 24 hours after surgery: Group Mg (0.59 mg/kg) < control (0.7 mg/kg); No statistical significance, p=0.23

-First time to use PCA (mean time): Group Mg, 3.61 hours v. control, 3.73 hours; no statistical significance, p=0.79

-Pain intensity scores: varied, no statistical significance | *Strengths*
-Double-blind to reduce risk of bias
-ethic review board approved

Weaknesses
- No statistically significant results
-Type of surgery examined
-Cultural implications of pain reporting
-Small sample size |

Jabbour, Naccache, Yazbeck, et al., 2014[3]	Patients undergoing scoliosis surgery, n=50 Group K+Mg, n=25: ketamine 0.2mg/kg bolus followed by 0.15mg/kg/h infusion and magnesium 50mg/kg bolus followed by 8mg/kg/h infusion Group K Control, n=25: ketamine 0.2mg/kg bolus followed by 0.15mg/kg/h infusion and Normal Saline 50mg/kg bolus followed by 8mg/kg/h infusion	Prospective randomized double blind study; Level 2[8]	*Primary* -Morphine consumption 48h postoperatively *Secondary* -Visual Analog Scale (VAS) pain scores 48h postoperatively -Occurrence of side effects 48 h postoperatively -Sleep Quality -Patient Satisfaction	-Morphine consumption was significantly lower in the ketamine and magnesium group compared to the ketamine only group (p<0.05). The relative difference in postoperative morphine consumption was 29.5% between the two groups. -Visual analog pain scores were not statistically different between the two groups -Quality of sleep and patient satisfaction scores were better in the ketamine and magnesium group (p=0.027 and p=0.016, respectively).	*Strengths* -Statistically significant p values -Magnesium examined in conjugation with ketamine to show synergistic effects -Double-blind to reduce risk of bias *Weaknesses* -Small sample size -Unable to determine effects of intravenous magnesium alone -VAS pain scores not statistically significant
Jarahzadeh, Harati, Babaeizadeh, Yasaei, Bashar, 2016[2]	Patients undergoing abdominal hysterectomies under general anesthesia, n=60 Group Mg, n=30: 50mg/kg magnesium sulfate in 500mL Ringer's serum over 20 minutes Control, n=30: 500mL Ringer's serum over 20 minutes	Double-blind randomized clinical trial; Level 2[8]	*Primary* -Visual Analog Scale (VAS) pain scores immediately after surgery and at 1, 2, 6, and 12 hours postoperatively *Secondary* -Narcotic consumption immediately after surgery and at 1, 2, 6, and 12 hours postoperatively -Drug complications	-VAS scores at 1,2,6, and 12 hours after surgery were lower in the intravenous magnesium group compared to the control (p<0.05). -Narcotic consumption was higher in the placebo group at the time intervals (p<0.05). -No significant differences between the two groups in drug complications	*Strengths* -Statistically significant p values -Double-blind to reduce risk of bias *Weaknesses* -Small sample size -Patient population diversity limited by gender

Conclusions

Due to the adverse effects of opioid analgesics, the use of multimodal medications to control postoperative pain is gaining popularity amongst anesthesia providers. The use of intravenous magnesium sulfate is an effect non-opioid analgesic and can play an essential role in the

multimodal regimen. In the studies examined, several benefits of intravenous magnesium sulfate were revealed including decreased postoperative pain scores and reduced opioid consumption in the postoperative period. With limited number of side effects reported, the use of intravenous magnesium is considered safe for clinical use. In current practice, magnesium sulfate is often used for electrolyte replacement and obstetric anesthesia. This practice analysis supports an additional use for this medication in the prevention of postoperative pain.

Intravenous magnesium sulfate should be considered as an adjuvant medication for postoperative analgesia. Although some variability exists in the dosing regimens of intravenous magnesium, the most common dose administered amongst the studies and the dose recommended by the systematic review is a single bolus dose of 50 mg/kg of magnesium sulfate administered over 20-30 minutes without infusion.[2,5,6,9] Magnesium is effective if administered as a bolus after induction of anesthesia.[1,5,9] Common side effects seen with intravenous magnesium use were bradycardia and hypotension.[4,6,10] Less common adverse effects of intravenous magnesium include sedation, nausea and vomiting, increased serum magnesium levels, and potentiation of neuromuscular blockade.[2,5,6]

Magnesium is effective at preventing pain and decreasing opioid requirements in the postoperative period. Two studies showed the effect of intravenous magnesium sulfate in reducing pain scores after surgery.[2,6] Four studies showed a decrease in analgesic requirements in the postoperative period when patients received magnesium during surgery.[2,3,5,6] In dissecting the meta-analysis, nineteen studies demonstrated the reduction of intravenous morphine consumption postoperatively and fifteen studies showed decreased pain scores with perioperative intravenous magnesium use.[6] Other benefits of magnesium sulfate were better sleep quality and improvement in patient satisfaction scores.[3] Only one study reviewed did not show any statistically significant improvements in patients' pain and opioid requirements after surgery. This study examined patients who underwent laminectomy surgery.[1]

The use of magnesium when injected intramuscularly into the operative site was proven to be more effective at preventing pain in comparison to intravenous magnesium in one trial.[5] This analysis only focused on intravenous administration of magnesium sulfate in preventing postoperative pain in the patient undergoing GETA. It would be beneficial to conduct another review on alternative routes of administration of magnesium sulfate during surgery in preventing postoperative pain and reducing analgesic medication requirement.

A limitation of this analysis is the lack of level 1evidence.[8] Only one systematic review and meta-analysis was found in examining the role of magnesium in surgical pain.[6] The rest of the studies analyzed were randomized control trials with small to medium study participation. More research is needed with larger sample sizes to more effectively investigate the role of magnesium in the prevention of postoperative pain. Another limitation of this analysis is that many studies showed the effects of magnesium in conjunction with other pain medications. Because magnesium was used in combination with other pain-relieving modalities, it is difficult to delineate the effects of magnesium alone in comparison to the additive effects of other medications. However, when incorporated into practice, intravenous magnesium sulfate will most often be used synergistically with other non-opioid medications to enhance the multimodal

regimen. In general, more research is needed to explore the potential benefits of magnesium sulfate in preventing pain for the surgical patient.

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Mentor: Susan Krawczyk, DNP, CRNA

Editorial

I am very pleased to announce the release of our updated Author Guidelines! Notable changes and additions include:

1. addition of a new submission option for the Evidence Based Practice Project Abstract.
2. an increase the word count for the research abstract to 600 (to match the new EPB Project Abstract), with a maximum of 5 references for both types of abstracts (previous language discouraged use of references)
3. a reduction to 1 textbook allowable as a reference for case reports (must be the most recent edition). Textbooks are not accepted as references for other submission types.
4. a change to the subject heading for submissions – ISJNA Submission_submission type_author last name_mentor last name (e.g. ISJNA Submission_CaseReport_Smith_Jones).
5. addition of language on academic integrity.

I would also like to welcome the following individuals as new Editorial Board Members:

Terri M. Cahoon, DNP, CRNA, Samford University
Terri D. Kane, DNAP, CRNA, Texas Wesleyan University
Brian T. Koonce, DNAP, CRNA, Texas Wesleyan University
Stephanie B. Woodruff, DNP, MSN, CRNA, Cedar Crest College

All of these individuals started their ISJNA 'career' as reviewers, and I am grateful for their hard work and desire to take on additional responsibility for student journal. I truly appreciate all of the time and effort the editorial board members and reviewers commit to sustaining the ISJNA – it would not exist without you! Have a wonderful summer everyone!

Sincerely,

Vicki C. Coopmans, PhD, CRNA
Editor

*"**The International Student Journal of Nurse Anesthesia** is produced*
exclusively for publishing the work of nurse anesthesia students. It is
intended to be basic and introductory in its content. Its goal is to introduce
the student to the world of writing for publication; to improve the practice of
nurse anesthesia and the safety of the patients entrusted to our care."

INTERNATIONAL STUDENT JOURNAL OF NURSE ANESTHESIA

GUIDE FOR AUTHORS

MISSION STATEMENT

The International Student Journal of Nurse Anesthesia (ISJNA) is produced exclusively for publishing the work of nurse anesthesia students. It is intended to be basic and introductory in its content. Its goal is to introduce the student to the world of writing for publication; to improve the practice of nurse anesthesia and the safety of the patients entrusted to our care.

ITEM PREPARATION & SUBMISSION

Case reports, research abstracts, evidence-based practice (EBP) analysis reports, and letters to the editor may be submitted. These items must be authored by a student under the guidance of an anesthesia practitioner mentor (CRNA or physician). Case and EBP analysis reports must be single-authored, while abstracts may have multiple authors. Submissions may list only one mentor. **Mentors should take an active role** in reviewing the item to ensure appropriate content, writing style, and format prior to submission. The mentor must submit the item for the student and serve as the contact person during the review process. Items submitted to this journal should not be under consideration with another journal. Authors and mentors should critically evaluate the topic and quality of the writing – multiple reviews of the item by the mentor, faculty, and peers (fellow graduate students) prior to submission is recommended. If the topic and written presentation are beyond the introductory publication level we strongly suggest that the article be submitted to a more prestigious publication such as the *AANA Journal.*

The journal is committed to publishing the work of nurse anesthesia students. The review process is always initiated with the following rare exceptions. We are conservative in accepting reports where the patient has expired, realizing that you can do everything right and still have a negative outcome. Submissions that report a case demonstrating failure to meet the standard of care (by any practitioner involved in the case) will not be accepted. Unfortunately, while the experiences in these cases can offer valuable insight, these submissions will not be accepted for review due to potential legal risks to the author, journal, and anyone else involved in evaluating the report.

It is the intent of this journal to publish items while the author is still a student. In order to consistently meet this goal, all submissions must be received by the editor **at least 3 months prior** (4-6 months recommended) to the author's date of graduation. Manuscripts must be submitted by the mentor of the student author via e-mail to **INTSJNA@aol.com** as an attachment. The subject line of the e-mail should use the following format: ISJNA Submission_submission type_author last name_mentor last name. The item should be saved in the following format – two-three word descriptor of the article_author's last name_school abbreviation_mentor's last name_date (e.g. PedsPain_Smyth_GU_Pearson_5.19.09)

REVIEW PROCESS

Items submitted for publication are initially reviewed by the chief editor. If the chief editor does not acknowledge receipt of the item within two weeks, please inquire to ensure receipt. Upon receipt, the chief editor will review the submission for compliance with the Guide to Authors. If proper format has not been followed, the item will be returned to the mentor for correction. This is very important as all reviewers serve on a volunteer basis. Their time should be spent ensuring appropriate content, not making format corrections. It is the mentor's responsibility to ensure formatting guidelines have been followed prior to submission.

All accepted submissions undergo a formal process of blind review by at least two reviewers. After review, items may be accepted without revision, accepted with revision, or rejected with comments. Once the item has been accepted for review the chief editor will send a blinded copy to an editor, who will then coordinate a blinded review by two reviewers who are not affiliated with the originating program. The editor will return the item to the chief editor, who will return it to the mentor for appropriate action. Every effort is made to complete the process in an efficient, timely matter. Again, the goal is for all articles submitted by students to be published while the author is still a student. If an item is not ready for publication within 6 months after the student author has graduated it will no longer be eligible for publication. Mentors will be listed as contributing editors for the issue in which the item is published.

PHOTOS

Photos of students for the front cover of the Journal are welcome. Please contact the chief editor at intsjna@aol.com to submit photos for consideration. Only digital photos of high quality will be accepted. If the photo is accepted, consent forms must be completed and returned by all identifiable individuals in the photo, and the individual who took the photo.

ACADEMIC INTEGRITY

Issues of academic integrity are the responsibility of the author and mentor. Accurate and appropriate acknowledgement of sources is expected. The two most common breaches of academic integrity that have been identified in submissions to this journal are (AMA 10th ed., p. 158):

1. Direct plagiarism: verbatim lifting of passages without enclosing the borrowed material in quotation marks and crediting the original author.
2. Paraphrase: restating a phrase or passage, providing the same meaning but in a different form without attribution to the original author.

Please note that changing one or two words in a reference source passage (e.g. 'of' for 'in', or 'classified' for 'categorized') and then citing it as a paraphrase or summary is also not appropriate, and still falls within the definition of direct plagiarism. If plagiarism in any form is identified, review of the item will be suspended and it will be returned to the mentor. Repeated instances of plagiarism will result in rejection of the item.

Plagiarism detection software (TurnItIn, PlagScan, SafeAssign, etc . . .) can be used to analyze the document prior to submission to ensure proper citation and referencing, but is not required.

"Plagiarism is the presentation of someone else's ideas, writings, or statements as one's own. Plagiarism is a serious breach of academic integrity, and anyone who is found to have committed plagiarism will be subject to disciplinary action. Paraphrase is the act of putting someone else's ideas into one's own words. The use of paraphrase can be an acceptable practice under some circumstances if it is used sparingly and if the original text is properly acknowledged. Unacknowledged paraphrase, like plagiarism, is a serious breach of academic integrity. Any improper use of sources may constitute plagiarism. Every quotation from another source, whether written, spoken, or electronic, must be bound by quotation marks and be properly cited. Mere citation alone is not sufficient when a scholar has used another person's words. Similarly, every paraphrase or summary (a more concise restatement of another's ideas) must be properly cited."
https://sites.google.com/a/georgetown.edu/gsas-graduate-bulletin/vi-academic-integrity-policies-procedures

GENERAL GUIDELINES

Items for publication **must adhere to the** *American Medical Association Manual of Style* (AMA 10th ed., the same guide utilized by the *AANA Journal* and such prominent textbooks as *Nurse Anesthesia* by Nagelhout and Plaus). Page numbers are provided for easy reference in the AMA Manual of Style throughout this document. The review process will not be initiated on items submitted with incorrect formatting and will be returned to the mentor for revision. Please note the following:
1. Use complete sentences.
2. Acronyms/Initialisms (p. 379) - spell out with first use, do not capitalize the words from which the acronym/initialism is derived unless it is a proper noun or official name. If you are using the phrase only once, do not list the acronym/initialism at all. Avoid beginning sentences with acronym/initialisms.
3. Abbreviations (p. 441)
4. Use *Index Medicus* journal title abbreviations (p. 472, http://www.ncbi.nlm.nih.gov/nlmcatalog/journals)
5. Always provide units of measure (p. 521 & 795). In most cases The International System of Units (SI) is used. Abbreviations for units of measure do not need to be spelled out with first use. Report height in cm, weight in kg, temperature in $^{\circ}$C, pressure in mm Hg or cm H_2O. Report heart and respiratory rate as X/min (e.g. the patient's heart rate increased to 145/min).
6. In general, first use of pulmonary/respiratory abbreviations should be expanded, with the following exceptions: O_2, CO_2, PCO_2, $PaCO_2$, PO_2, PaO_2, $EtCO_2$, N_2O. Please use SpO_2 for oxygen saturation as measured by pulse oximetry.

7. Use the nonproprietary (generic) name of drugs (p. 568) - avoid proprietary (brand) names. Type generic names in lowercase. When discussing dosages state the name of the drug, *then* the dosage (midazolam 2 mg).
8. Use of descriptive terms for equipment and devices is preferred. If the use of a proprietary name is necessary (for clarity, or if more than one type is being discussed), give the name followed by the manufacturer and location in parenthesis (p. 583, e.g. a GlideScope (Verathon Inc., Bothell, WA) was used) Please note, TM and ® symbols are not used per the AMA manual.
9. Infusion rates and gas flow rates:
    a. Use mcg/kg/min or mg/kg/min for infusion rates. In some cases it may be appropriate to report dose or quantity/hr (i.e. insulin, hyperalimentation). If a mixture of drugs is being infused give the concentration of each drug and report the infusion rate in ml/min.
    b. Report gas flow of O_2, N_2O and Air in L/min (not %) and volatile agents in % as inspired or expired concentration (e.g. General anesthesia was maintained with sevoflurane 3% inspired concentration in a mixture of O_2 1 L/min and air 1 L/min.)
10. Only Microsoft Word file formats will be accepted with the following criteria:
    a. Font - 12 point, Times New Roman
    b. Single-spacing (except where indicated), paragraphs separated with a double space (do not indent)
    c. One-inch margins
    d. End the sentence with the period before placing the superscript number for the reference.
    e. Do not use columns, bolds (except where indicated), or unconventional lettering styles or fonts.
    f. Do not use endnote/footnote formats.
11. Do not use Endnotes or similar referencing software – any embedded formatting must be removed prior to submission.
12. Remove all hyperlinks within the text.
13. Avoid jargon and slang terms. Use professional, scholarly, scientific language.
    a. *'The patient was reversed'* - Did you physically turn the patient around and point him in the opposite direction? "Neuromuscular blockade was antagonized."
    b. *The patient was put on oxygen.* "Oxygen 2 L/min was administered via face mask."
    c. *The <u>patient</u> was intubated and put on a ventilator.* "The trachea was intubated and mechanical ventilation was initiated.
    d. *An IV drip was started.* "An intravenous infusion was initiated."
    e. Avoid the term "MAC" when referring to a sedation technique - the term sedation (light, moderate, heavy, unconscious) may be used. Since all anesthesia administration is monitored, pharmacologic, rather than reimbursement, terminology should be used.
14. Direct quotes are discouraged for reports of this length – please express in your own words.
15. Use the words "anesthesia professionals" or "anesthesia practitioners" when discussing all persons who administer anesthesia (avoid the reimbursement term "anesthesia providers").
16. Do not include ASA Physical Status unless it is germane to the report.
17. Do not use the phrase "ASA standard monitors were applied". Instead, "standard noninvasive monitors" is acceptable – additional monitoring can be detailed as needed.
18. References
    a. The **AMA Manual of Style must be adhered to** for reference formatting.
    b. All sources should be published within the past 8 years. Seminal works essential to the topic being presented will be considered.
    c. Primary sources are preferred.
    d. **A maximum of one textbook (must be most recent edition available) may be used as reference for case report submissions only**.
    e. All items cited must be from peer-reviewed sources – use of sources found on the internet must be carefully considered in this regard. URLs must be current and take the reader directly to the referenced source.

Heading – for all submission types (Case Report, Abstract, EBPA Report) use the following format.
    1. **Title** is bolded, centered, 70 characters (including spaces) or less
    2. Author name (academic credentials only) and NAP are centered, normal font,.
    3. *Graduation date and email address* are centered, italicized, and will be removed prior to publication)
    4. **Keywords** is left-justified, bolded – list keywords that can be used to identify the report in an internet search

Title

Author Name
Name of Nurse Anesthesia Program
Anticipated date of graduation
E-mail address

Keywords: keyword one, keyword two, etc . . .

<u>**Case Reports**</u> - The student author must have had a significant role in the conduct of the case. The total word count should be between 1200 – 1400 words (references not counted). Case reports with greater than 1400 words will be returned to the mentor for revision prior to initiation of the review process. The following template demonstrates the required format for case report submission.

Heading (see above)

A brief introductory paragraph of <u>less than 100 words</u> to focus the reader's attention and interest them to continue reading. This may include historical background, demographics or epidemiology (with appropriate references) of the problem about to be discussed. It is written in the *present tense*. Although it is introductory, the heading word '*Introduction'* is <u>not</u> used. Be certain to cite references in this section, especially statistics and demographics.
[space]
Case Report (bold, 400-600 words)
[space]
This portion discusses the case performed and is written in the *past tense*. Do not justify actions or behaviors in this section; simply report the events as they unfolded. Present the case in an orderly sequence. Some aspects need considerable elaboration and others only a cursory mention. Under most circumstances if findings/actions are normal or not contributory to the case then they should not be described. Events significant to the focus of the report should be discussed in greater detail. The purpose of the case report is to set the stage (and 'hook' the reader) for the heart of your paper which is the discussion and teaching/learning derived from the case.
- Give dosage and schedule only if that information is pertinent to the consequences of the case.
- **Significant** laboratory values, x-rays or other diagnostic testing pertinent to the case. Give the units of measure after the values (eg. Mmol/L or mg/dL).
- Physical examination/pre-anesthesia evaluation - **significant** findings only.
- Anesthetic management (patient preparation, induction, maintenance, emergence, post-operative recovery).
[space]
Discussion (bold, 600-800 words)
[space]
Describe the ***anesthesia*** implications of the focus of the case report citing current literature. Describe the rationale for your actions and risk/benefits of any options you may have had. This section is not merely a pathophysiology review that can be found in textbooks. *Relate the anesthesia literature with the conduct of <u>your</u> case noting how and why your case was the <u>same or different</u> from what is known in the literature.* Photographs are discouraged unless they are essential to the article. Photos with identifiable persons must have a signed consent by the person photographed forwarded to the editor via first class mail. Diagrams must have permission from original author. This is the most important part of the article. In terms of space and word count this should be longer than the case presentation. End the discussion with a summary lesson you learned from the case, perhaps what you would do differently if you had it to do over again.
[space]
References (bold)
[space]
A minimum of 5 references is recommended, with a maximum of 8 allowed. One textbook may be used as a reference – it must be the most recent edition. All references should be no older than 8 years, except for seminal works essential to the topic. This is also an exercise in searching for and evaluating current literature.
[space]
Mentor: (bold, followed by mentor name and credentials in normal text)
E-mail address: (normal text, will be removed prior to publication)

EBP Analysis Reports - Evidence-based practice analysis reports are limited to 3000 words. Please do not include an abstract. The report should provide a critical evaluation of a practice pattern in the form of a focused clinical question about a specific intervention, population, and outcome. The manuscript should:

1. Articulate the practice issue and generate a concise question for evidence-based analysis. A focused foreground question following either the PICO or SPICE format should be used.
2. Describe the methods of inquiry used in compiling the data.
3. Critically analyze the quality of research reviewed and applicability to different practice settings.
4. Draw logical conclusions regarding appropriate translation of research into practice.

The same general format guidelines apply with the exception of the section headings as below. Textbooks and non-peer reviewed internet sources may not be used, and sources of reference should be less than 8 years old unless they are seminal works specifically related to your topic of inquiry. A maximum of 16 references is allowed.

Heading

Introduction (bold)
[space]
Briefly introduce the reader to the practice issue or controversy, describe the scope or significance or problem, and identify the purpose of your analysis. Describe the theoretical, conceptual, or scientific framework that supports your inquiry.
[space]
Methods (bold)
[space]
Include the format used for formulating the specific question you seek to answer, search terms and methods used, and levels of evidence.
[space]
Literature Analysis (bold)
[space]
Analyze and critique the literature relevant to your question, determining scientific credibility and limitations of studies reviewed. Your synthesis table is included in this section. Your review and discussion of the literature should logically lead to support a practice recommendation. Subheadings may be used if desired.
 [space]
Conclusions (bold)
[space]
Summarize the salient points that support the practice recommendation and make research-supported recommendations that should improve the practice issue, while also acknowledging any limitations or weaknesses
[space]
References (bold, 16 maximum)
[space]
Mentor: (bold, followed by mentor name and credentials in normal text)
E-mail address: (normal text, will be removed prior to publication)

Evidence Based Practice Project Abstracts - Evidence-based practice abstracts are limited to 600 words.
References do not impact the word count - a maximum of 5 are allowed. Note that the abstract is different from a project proposal. The following format should be used:

Heading

Introduction (bold)
[space]
A brief introductory paragraph including purpose (what change is intended) and rationale (why change is needed/evidence to support the change) here.
[space]
Design and Methods (bold)

[space]
Include population, intervention, and measures
[space]
Outcome (bold)
[space]
Present results from statistical analysis – do not justify or discuss here.
[space]
Conclusion (bold)
[space]
Discuss results (implications). Optionally include limitations, suggestions for future projects/research.
[space]
References (bold, 5 maximum)
[space]
Mentor: (bold, followed by mentor name and credentials in normal text)
E-mail address: (normal text, will be removed prior to publication)

<u>**Research Abstracts**</u> - Research abstracts are limited to 600 words. References do not impact the word count - a maximum of 5 are allowed. Note that the abstract is different from a research proposal. The following format should be used:

Heading

Introduction (bold)
[space]
A brief introductory paragraph including purpose and hypotheses.
[space]
Methods (bold)
[space]
Include sample and research design
[space]
Results (bold)
[space]
Present results from statistical analysis – do not justify or discuss here.
[space]
Discussion (bold)
[space]
Discuss results (implications, limitations, suggestions for future research)
[space]
References (bold, 5 maximum)
[space]
Mentor: (bold, followed by mentor name and credentials in normal text)
E-mail address: (normal text, will be removed prior to publication)

<u>**Letters to the Editor**</u> - Students may write letters to the editor topics of interest to other students. Topics may include comments on previously published articles in this journal. Personally offensive, degrading or insulting letters will not be accepted. Suggested alternative approaches to anesthesia management and constructive criticisms are welcome.
The length of the letters should not exceed 100 words and must identify the student author and anesthesia program.

<u>**AMA MANUAL OF STYLE**</u>
The following is brief introduction to the *AMA Manual of Style* reference format along with some links to basic, helpful guides on the internet. The website for the text is http://www.amamanualofstyle.com/oso/public/index.html. It is likely your institution's library has a copy on reserve. Some helpful websites are listed below:
https://guides.nyu.edu/amastyle
https://owl.english.purdue.edu/owl/resource/1017/01/

Journal names should be in *italics* and abbreviated according to the listing in the PubMed Journals Database. The first URL below provides a tutorial on looking up correct abbreviations for journal titles; the second is a link to the PubMed where you can perform a search.
http://www.nlm.nih.gov/bsd/viewlet/search/journal/journal.html
http://www.ncbi.nlm.nih.gov/pubmed

The International Student Journal of Nurse Anesthesia (ISJNA) is not listed in the PubMed Database. For the purpose of citing the ISJNA *in this Journal* use "**Int Student J Nurse Anesth**" as the abbreviation.

Journals - A comma is placed after the first initials until the last author, which has a period. If there are six or less authors **cite all six**. If there are more than six authors **cite only the first three** followed by "et al." Only the first word of the title of the article is capitalized. The first letters of the major words of the journal title are capitalized. There is no space between the year, volume number, issue number, and page numbers. If there is no volume or issue number, use the month. If there is an issue number but no volume number use only the issue number (in parentheses). Page numbers are inclusive - **do not omit digits** (note - some online journals do not use page numbers). Some journals may be available both as hard copies and online. When referencing a journal that has been accessed online, the DOI (digital object identifier) or PMID (PubMed identification number) should be included (see example below).

Journal, 6 or fewer authors:
Han B, Liu Y, Zhang X, Wang J. Three-dimensional printing as an aid to airway evaluation after tracheotomy in a patient with laryngeal carcinoma. BMC Anesthesiol. 2016;16(6). doi:10.1186/s12871-015-0170-1.

Journal, more than 6 authors:
Chen C, Nguyen MD, Bar-Meir E, et al. Effects of vasopressor administration on the outcomes of microsurgical breast reconstruction. *Ann Plast Surg*. 2010;65(1):28-31. PMID: 20548236.

Elayi CS, Biasse L, Bai R, et al. Administration of isoproterenol and adenosine to guide supplemental ablation after pulmonary vein antrum isolation. *J Cardiovasc Electrophysiol*. 2013;24(11):1199-1206. doi: 10.1111/jce.12252.

Electronic references - Only established, peer-reviewed sources may be referenced. Please do not reference brochures, fact sheets, or informational websites where a peer-review process cannot be confirmed. The URL must be functional and take the reader directly to the source of the information cited. The accessed date may be the only date available.

Author (or if no author, the name of the organization responsible for the site). Title. *Name of Website*. Year;vol(issue no.):inclusive pages. URL. Published [date]. Updated [date]. Accessed [date].

Examples:
1. Kamangar N, McDonnell MS. Pulmonary embolism. *eMedicine*.
   http://www.emedicine.com/med/topic1958.htm. Updated August 25, 2009. Accessed September 9, 2009.
2. Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, et al. SEER Cancer statistics review, 1975-2012.
   National Cancer Institute. http://seer.cancer.gov/csr/1975_2012/. Published April 2015. Updated November 18, 2015. Accessed February 29, 2016.

Textbooks - There are two types of books – 1) those that are fully authored by one or more individuals, and 2) those that are edited by one or more individuals, with chapters authored by different individuals. Edited textbooks give primary credit to the chapter authors, who are listed first, and the inclusive page numbers of the entire chapter are provided at the end. Textbooks that are authored do not have different chapter authors and the chapter titles are not listed, but the inclusive page numbers where the information was found are provided, unless the entire book is cited.

Authored text:
Shubert D, Leyba J, Niemann S. *Chemistry and Physics for Nurse Anesthesia*. 3rd ed. New York, NY: Springer; 2017:405-430.

Chapter from an edited text:
Pellegrini JE. Regional anesthesia. In Nagelhout JJ, Elisha S, eds. *Nurse Anesthesia*. 6th ed. St. Louis:Elsevier; 2017:1015-1041.

SUBMISSION CHECK LIST

___ **Adheres to AMA Manual of Style and all other format instructions**
___ Total word count not exceeded (1400 for case report, 600 for abstracts, 3000 for EBPA report)
___ The item is one continuous Word document without artificially created page breaks
___ All matters that are not common knowledge to the author are referenced appropriately
___ Generic names for drugs and products are used throughout and spelled correctly in lower-case
___ Units are designated for all dosages, physical findings, and laboratory results
___ Endnotes, footnotes not used
___ Jargon/slang is absent

Heading
___ Concise title less than 70 characters long
___ Author name, credentials, nurse anesthesia program, graduation date and email are included
___ Three to five **Keywords** are provided

Case Report
___ Introduction is less than 100 words.
___ Case Report section states only those facts vital to the account (no opinions or rationale)
___ Case report section is 400-600 words and not longer than the discussion
___ Discussion section is 600-800 words
___ Discussion of the case management is based on a review of current literature
___ Discussion concludes with lessons learned and how the case might be better managed in the future

Abstracts
___ The 600 word count maximum is not exceeded
___ Appropriate format used depending on type of abstract (research vs. EBP project)

EBPA Report
___ The 3000 word count maximum is not exceeded
___ A critical evaluation of a practice pattern in the form of a precise clinical question about a specific intervention, population, and outcome is presented
___ A focused foreground question following either the PICO or SPICE format is used
___ Includes Introduction, Methodology, Literature Analysis (with synthesis table), and Conclusion sections

References
___ Adheres to AMA Style format
___ Reference numbers are sequenced beginning with 1 and superscripted
___ References are from anesthesia and other current (within past 8 years) primary source literature
___ Journal titles are abbreviated as they appear in the PubMed Journals Database
___ Number of references adheres to specific item guidelines (1 textbook allowed for case reports only)
___ Internet sources are currently accessible, reputable, and peer reviewed

Transmission
___ The article is sent as a attachment to **INTSJNA@AOL.COM**
___ The file name is correctly formatted (e.g. PedsPain_Smyth_GU_Pearson_5.19.09)
___ Item is submitted by the mentor
___ Subject heading format - ISJNA Submission_submission type_author last name_mentor last name