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Front Cover:
Texas Wesleyan University Nurse Anesthesia Program faculty instruct graduate students on ultrasound-guided central venous access placement, arterial line placement, and airway management skills in a simulated environment during their annual simulation symposium. Picture clockwise from top:

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Case Reports

Anesthetic Considerations for a Patient with Cerebral Palsy

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Keywords: cerebral palsy (CP), anesthetic management, neurological disorder, baclofen pump, laryngeal mask airway

Cerebral palsy (CP) is a collective term used to describe a diverse group of neurological disorders characterized by varying degrees of motor, sensory, and intellectual impairment. CP is caused by injury to or abnormal development of the immature brain.[1] Although CP is primarily a disorder of posture and movement, the more severe forms impact the patient's neurological, respiratory, gastrointestinal, musculoskeletal, and urological functions. Thus, the planning and implementation of an anesthetic plan for this patient population requires a multisystem approach.[1]

Case Report

A 23-year-old, 152 cm, 62 kg male presented for a baclofen pump replacement in the right lower quadrant of his abdomen. The patient's medical history consisted of spastic diplegic cerebral palsy, gastroesophageal reflux disease (GERD), and eczema. Functionally, the patient was able to independently perform activities of daily living and ambulate with a rolling walker. He had mild cognitive delays, was easily distracted, and exhibited mild slurred speech with excess oral secretions. Past surgical history included a previous baclofen pump revision with modification of the intrathecal catheter, resection of a benign fibromatosis, and hip subluxation repair, all without incident or anesthetic complications per patient and father. Current medications included ibuprofen and meloxicam as needed and omeprazole daily.

The patient was transported to the operating room (OR) and was positioned supine on the OR table. Warm blankets were applied preoperatively and after the patient was on the OR table. Standard monitors were placed and the patient was pre-oxygenated and de-nitrogenated to an end-tidal O_2 > 80%. Intravenous (IV) medications administered for induction consisted of fentanyl 100 mcg, lidocaine 40 mg, and propofol 180 mg. Glycopyrrolate 0.2 mg had been administered prior to arrival in the OR. A size four laryngeal mask airway (LMA) was placed atraumatically. LMA placement was confirmed via auscultation of airflow in the supraglottic region, bilateral chest rise, and presence of end-tidal CO_2 waveform. After LMA placement, an upper body forced-air patient warming blanket was applied and a nasal temperature probe was placed.

General anesthesia was maintained with isoflurane 1.2% inspired concentration in a mixture of O_2 1 L/min and air 1 L/min. Respirations were initially supported with synchronized intermittent mechanical ventilation (SIMV) with a respiratory rate of 12 breaths per minute and tidal volumes 6 ml/kg. Peak inspiratory pressure remained less than 20 cm H2O and end-tidal CO_2 was maintained between 35-45 mm Hg. Transient hypotension during maintenance was treated with two phenylephrine boluses of 120 mcg each. In anticipation of emergence, isoflurane was reduced to an end-tidal of 0.5% and a combination of N_2O and O_2 at 2 L/min

each. The patient was removed from SIMV and placed on pressure support (PS) after he had resumed spontaneous ventilation. Prior to LMA removal, N_2O was discontinued and O_2 increased to 10 L/min. A total of 800 mL of crystalloid was given for the 45-minute case.

Upon arrival to postanesthesia care unit (PACU), the patient had stable vital signs, maintained a patent airway with O_2 6 L/min via face mask, and had no complaints of pain.

Discussion

Patients with CP are likely to require multiple anesthetics throughout their lifetime due to various comorbidities associated with the disorder. In addition, many of the comorbid conditions and medical therapies can affect anesthesia management. Thus, an understanding of the multisystem effects specific to patients with CP will help the anesthesia practitioner anticipate and minimize perioperative complications.

CP is the most common cause of motor impairment in childhood.[1] Two-thirds of CP patients will have some degree of impaired intellectual and cognitive function, which may be difficult to determine because of problems with communication.[1] Communication difficulties may heighten the patient's perioperative anxiety and anxiolytic premedication should be considered. A caregiver's ability to facilitate communication can also help ease the patient's anxiety levels. [1] Upon meeting the patient and his father pre-operatively, the patient's father spoke for him, but the patient was affable and readily answered questions regarding his medical history. No premedication was required for the transfer to the OR.

Pulmonary complications are a common cause of death in cerebral palsy patients. Aspiration associated with GERD is the leading cause.[2] Complications can be prevented by verifying nil per os status prior to surgery, administration of antacids, and rapid sequence induction for those with concerns of uncontrolled GERD.[1] Patients with CP also have impaired ability to clear pharyngeal secretions leading to secretion pooling in the oropharynx. This is caused by hyperactive salivary glands and impaired swallowing.[3] Other airway concerns include poor dental hygiene, maligned and/or loose teeth, and temporomandibular joint dislocation secondary to muscle spasticity.[1] While the patient had a history of GERD, the patient stated he was not experiencing any symptoms the morning of surgery. The decision to use a LMA was made based on this finding. However, excessive secretions were noted during the pre-operative exam and glycopyrrolate 0.2 mg was given prior to surgery.

Anesthetic medications to address specifically include neuromuscular blocking and inhalational agents. While this patient did not require endotracheal intubation and/or muscle relaxation for his surgical procedure, knowledge regarding the use of neuromuscular blocking agents in the case of an emergency is prudent. Succinylcholine is not contraindicated. While some studies have demonstrated the presence of extrajunctional acetylcholine (ACh) receptors, other studies have demonstrated no significant difference in potassium release after succinylcholine administration.[1,2]

Minimal alveolar concentration (MAC) is reduced due to a decrease in inhibitory signals from upper motor neurons; this causes lower motor neurons to be more sensitive to inhalational

anesthetics. Thus, lower inhalational agent concentrations are needed to depress the motor response to painful stimulus.[2,5] With these considerations in mind, the patient's volatile anesthetic was maintained at 0.9 MAC throughout the maintenance phase. With the use of N_2O during emergence, the patient's emergence was timely and no complications noted post-operatively.

Postoperative concerns include the potential for hypoxia and hypothermia.[1] Hypoxia can result from a poor cough reflex and reduced respiratory drive.[6] Systemic and epidural opioids should be used with caution because they can accumulate and lead to over sedation, respiratory depression, and suppress the cough reflex in an already vulnerable patient group. Initially and throughout the duration of the surgical procedure, the patient was placed on SIMV while he recovered from the respiratory depressant effects of fentanyl given on induction in addition to inhalational agent being administered.[7] The LMA was uneventfully removed when the patient's unsupported spontaneous respirations were of regular rhythm and rate, tidal volumes 4-6 ml/kg, and laryngeal reflexes returned.

It should be noted that hypothermia, postoperative pain, and anxiety can all trigger acute muscle spasms. While patients with CP have normal responses to pain, communication difficulties may make postoperative pain assessment difficult.[1,2] To ensure the patient was euthermic peri-operatively, warm blankets were applied pre-operatively and after the patient was on the OR table. After intubation, an upper body forced-air patient warming blanket was applied and remained in place until replaced by warm blankets after extubation. The patient's temperature was monitored via nasal temperature probe throughout the duration of his anesthetic.

In summary, caring for a patient with CP requires an understanding of the disease process itself, the patient's comorbidities and medication regimen, and an understanding of the surgical procedure so that a safe anesthetic is provided.

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Anesthesia Management of the Goldenhar Syndrome Patient

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Keywords: Goldenhar syndrome, oculo-auricular-vertebral dysplasia, anesthesia

Goldenhar syndrome is a rare disorder of the first and second branchial arches that occurs during embryological development.[1] It is also known as oculauriculo-vertebral spectrum or OAV. Maurice Goldenhar, an ophthalmologist and general practitioner, first documented Goldenhar syndrome in 1952. The incidence is estimated to be 1:5,000, live births with an increased occurrence in males.[2] Manifestations include craniofacial abnormalities, which range from slightly asymmetrical deformities to severe maxillary, mandibular, auricular, and spinal-vertebral defects.[1] Approximately 40% of Goldenhar syndrome patients also have Klippel-Feil syndrome with corresponding short immobile necks, resulting in increased airway management concerns.[3] The low incidence of Goldenhar syndrome can lead to unfamiliarity for anesthesia practitioners of the various airway abnormalities and possible under appreciation for the inherent risks. Proper airway management protocols must be developed and utilized to protect this patient population.

Case Report

An 8-year-old, 32 kg female presented to surgery for dental restorations and extractions. The patient had no known drug allergies. The patient's medical history was significant for preterm birth at 32 weeks, Goldenhar syndrome, bilateral conductive hearing loss, ectropion of eyelid, cleft palate repair, and situational anxiety.

The preoperative assessment included micrognathia, hemifacial protrusion test III, a thyromental distance of less than 6.5 cm, reduced neck mobility, and a Mallampatti IV airway classification. Vital signs were within normal limits. The patient's mother stated that there was no history of previous anesthesia-related complications. Previous anesthesia records were reviewed to assist in the preoperative anesthesia plan. No previous complications or challenges were noted.

The difficult airway cart, including a video laryngoscope and flexible fiberoptic scope, was placed into the operating room in advance. The patient was transported to the OR, and a pulse oximeter, non-invasive blood pressure cuff, and electrocardiogram leads were applied. The patient was pre-oxygenated with 10 L/min of oxygen via facemask. Inhalation induction of general anesthesia was performed with an inspired concentration of 8% sevoflurane in a mixture of N_20 3 L/min nitrous oxide and O_2 2 L/min. Once the patient was assessed to be past stage 2 of anesthesia, a 22-gauge intravenous (IV) catheter was established in the right hand. Weight-based

IV doses of fentanyl 1 mcg/kg, acetaminophen 15 mg/kg, and rocuronium 0.3 mg/kg were administered. An oropharyngeal airway was placed in combination with a jaw-thrust maneuver, and two-person mask ventilation. Endotracheal nasal intubation was successful on the first attempt using a microlaryngoscopy tube loaded over a flexible fiberoptic scope utilizing an oral video laryngoscope to observe the fiberoptic approach to the cords. General anesthesia was maintained with an expired concentration of 2.3% sevoflurane in air 1 L/min air and $O_2$1 L/min. The patient was placed on volume control mode with a tidal volume of 6 mL/kg and a rate of 16/minute.

Following induction, weight-based doses of IV ondansetron 0.1mg/kg and dexamethasone 0.3 mg/kg were administered for nausea and vomiting prophylaxis. The surgery was subsequently completed without complication. After the return of regular spontaneous ventilation and adequate tidal volumes were noted the patient's neuromuscular blockade was then antagonized by administering neostigmine 0.08 mg/kg in combination with glycopyrrolate 16 mcg/kg. Also, ketorolac 0.3 mg/kg was administered IV for postoperative pain management. After a positive leak test was assessed at 20 cm H_20 and the patient met appropriate extubation criteria; the nasotracheal tube was removed with the patient fully awake. The patient was then transported to the postanesthesia care unit with O_2 8 L/min via facemask in stable condition.

Discussion

With the risk of airway compromise and difficult intubation at the forefront of patient safety, a thorough preoperative assessment is vital to determining an appropriate plan of action. Patient age must also be taken into consideration, as there is a direct relationship between the age of the Goldenhar syndrome patient and the degree of airway difficulty.[6]

If the anesthesia professional decides to implement neuromuscular blockade during the induction sequence, factors such as duration of action, available neuromuscular blockade antagonist agents, and potential side effects must be considered. Rocuronium was selected for this particular case due to the desire to avoid the side effects and potential risks associated with succinylcholine in the pediatric population.

Regarding preoperative airway preparation, various airway management techniques and advanced airway equipment may be considered. For example, the use of the I-gel supraglottic airway, which allows for passage of an endotracheal tube (ETT) and orogastric tube.[5] Additionally, the Airtraq optical laryngoscope might be considered due to the benefit of a 90-degree shape and a channel to help guide an ETT.[3] However, the gold standard for a known difficult airway is awake fiberoptic intubation. Conversely, awake fiberoptic intubations may prove challenging in patients that cannot maintain cooperation. Also, maintenance of spontaneous respirations with this patient population is preferred.[7] Although no adverse events occurred, performing an induction sequence that maintained spontaneous ventilations until tracheal intubation was established would have likely been a more ideal approach.

In addition to a thorough preoperative assessment, preoperative radiographic imaging should be considered. The gold standard for obtaining images in the Goldenhar syndrome patient is cone beam computed tomography (CBCT), which provides accurate and reliable three-dimensional

information of facial bones and related anatomical structures.[4] CBCT can prove useful for choosing the appropriate size of ETT on the initial intubation attempt. An undersized ETT can result in insufficient ventilation and increased aspiration risk while an oversized ETT may result in upper airway swelling.[4] Unfortunately, CBCT was not performed for this patient. However, the procedure took place in a pediatric institution where the occurrences of pediatric congenital craniofacial malformations are encountered relatively frequently. Nevertheless, a preoperative CBCT likely would have provided useful information that could have better-optimized anesthetic preparation for this particular patient.

Ultimately, Goldenhar syndrome is indicative of a difficult airway regardless of the severity of the condition.[3] Associated craniofacial abnormalities are of considerable importance to the anesthesia provider's airway management strategy. A thorough anesthetic evaluation and individualized planning are imperative.

Due to the low incidence of Goldenhar syndrome, additional research and case reports should be conducted to prepare better anesthesia professionals that are faced with the aesthetic challenges associated with this particular syndrome. Also, an evidence-based protocol regarding airway management of Goldenhar patients should be considered in facilities that care for pediatric patients with craniofacial anomalies.

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Vasoplegic Syndrome Predictors and Recommended Perioperative Practices

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Keywords: Vasoplegia, cardiopulmonary bypass, risk factors, complications, cardiac surgery

Vasoplegic syndrome occurs in up to 20% of all cardiopulmonary bypass cases and cardiac surgeries. It is recognized as systemic hypotension, a normal cardiac output and low systemic vascular resistance (SVR) unresponsive to vasopressors and volume resuscitation and is associated with an increase in morbidity and mortality.[1] Familiarity with risk factors, effective recognition of the syndrome and identifying appropriate treatments can significantly improve patient outcomes. This case study will focus on the risk factors, symptom identification and appropriate treatments available for vasoplegic syndrome.

Case Report

A 63-year-old male (180 cm, 79 kg, BMI 38 kg/m^2) was scheduled for a 3-vessel coronary artery bypass graft (CABG) secondary to coronary artery disease with increasing dyspnea on exertion over the last 2 months; he was now unable to climb two flights of stairs without shortness of breath. His past medical history includes gout, hypertension, and dyslipidemia. Home medications are lisinopril, rosuvastatin, calcium and allopurinol. The coronary angiogram from 3 days prior revealed 90% occlusion involving the left main artery and mid-proximal right coronary artery. A transesophageal echocardiogram performed at the same time demonstrated a left ventricular ejection fraction of 55%, with trace aortic valve regurgitation. Electrocardiogram revealed normal sinus rhythm (NSR) with a heart rate of 67/min. The patient's preoperative blood pressure was 121/63 mm Hg and laboratory values were hemoglobin 11.2 gm/dL and hematocrit 35%.

Preoperative sedation was achieved with intravenous (IV) midazolam 1 mg. Arterial line catheterization was performed in sterile fashion in the right radial artery using a 20 gauge catheter. The patient was preoxygenated with O_2 10 L/min for 3 minutes via a standard anesthesia mask. An intravenous induction commenced with fentanyl 250 mg titrated over a few minutes, lidocaine 100 mg, etomidate 18 mg, and succinylcholine 120 mg . Direct laryngoscopy revealed a grade I view and a 7.5 endotracheal tube was introduced into the trachea. Ventilation was mechanically controlled with settings in volume control mode: FiO_2 0.5, tidal volume 550 mL, respiratory rate 12/min, and positive end expiratory pressure 5 cm H_2O pressure.

General anesthesia was maintained with sevoflurane at 1 MAC in O_2 1 L/min and air 1 L/min. A multi-lumen 8.5Fr central venous catheter was introduced into the right internal jugular vein under sterile ultrasound guidance. A pulmonary artery catheter was inserted sterilely and positioned to 45cm in depth. A transesophageal probe was advanced into the esophagus for the echocardiogram examination; findings were congruent with the previous study. Pre-bypass vital signs were mean arterial pressure (MAP) greater than 55 mm Hg, pulmonary artery pressure 20's/10's mm Hg, cardiac index (CI) 2.2 L/min/m^2. Prior to incision vancomycin 1 g IV was administered. An aminocaproic acid 5 g IV bolus was administered followed by a continuous

infusion at 1g/hr. Once the veins were harvested and arteries were exposed, heparin 24,000 units IV was given in preparation for cardiopulmonary bypass (CPB). Cardiopulmonary bypass commenced when the activated clotting time was greater than 400 seconds. The total CPB time was 96 minutes and cross-clamp time was 45 minutes.

During discontinuation of CPB, epinephrine 12 mcg and phenylephrine 100mcg IV were administered. Residual heparin was reversed with protamine 240 mg IV given over 10 minutes. The cardiac rhythm was NSR with a heart rate of 70/min. Hemodynamic monitoring demonstrated: MAP less than 50 mm Hg, CI 2.6 L/min/m^2, SVR < 500 sec/cm.[5]A norepinephrine infusion was started at 3 mcg/min and increased to 8 mcg/min to treat the low SVR and MAP. Vasopressin 1unit IV boluses were also administered. Volume resuscitation was accomplished with 5% albumin 1250 mL, plasmalyte 2 L, and 1 unit of packed red blood cells. Estimated blood loss was 400 mL and total urine output was 1000 mL. The patient remained intubated and was transferred to the intensive care unit (ICU). The MAP remained <50 mm Hg and required the administration of a vasopressin infusion, methylene blue dose of 2mg/kg, and volume resuscitation with colloid and crystalloid in the ICU. The patient was extubated 2 days later and was discharged from the hospital after 7 days.

Discussion

Vasoplegic syndrome occurs in an estimated 20% of all cardiac surgeries and is linked with poor clinical outcomes.[1] Hypotension, normal or high cardiac output, and a low SVR with intractable or increasing requirement for vasopressors and volume resuscitation are the defining symptomatology.[2] It is associated with a longer ventilator requirement, increased length of stay in the hospital, increase in neurologic deficit, sternal wound infection, renal failure and mortality.[2,3] The ability to accurately identify this syndrome is vital to providing effective and timely treatment. There are multiple causes behind the pathophysiology of vasoplegia. Vasodilation is secondary to the upsurge in inflammatory mediators after CPB, endothelial dysfunction with the increase in nitric oxide synthase, and active ATP-dependent K^+ channels. Additional causes of vasoplegia include a lack of vasopressin due to a diminished baroreceptor response, vasopressin V1A receptor down-regulation, and nuclear factor KB stimulation.[3,4] Knowledge of the pathophysiology behind vasoplegia provides for a timely and effective treatment response for this syndrome.

Proper identification of vasoplegia risk factors can assist the anesthetist in anticipating those patients who may require treatment. Patient risk factors include increasing age, valvular surgery, heart transplant, ventricular assist devices, dialysis, perioperative blood transfusions, trauma, sepsis, and cardiopulmonary bypass. Medications used in the preoperative and perioperative period associated with an increased incidence of vasoplegic syndrome include ace inhibitors, diuretics, heparin, protamine, and amiodarone amongst others. There are conflicting studies in the setting of beta blockers defining it as a risk factor versus a preventative medication for vasoplegia.[1,4] For proper management of these patients it is imperative anesthesia providers understand the risk factors predisposing patients to vasoplegic syndrome.

The treatment for vasoplegic syndrome aims at targeting its different causes. Medication management for inotropic and vasopressor support is recommended with epinephrine,

norepinephrine, and vasopressin.[4] Ludhmila et al. compared the use of vasopressin versus norepinephrine in the setting of vasoplegia in a prospective, randomized, double-blinded study of 330 patients. They found a shorter length of stay in the ICU, and the hospital, along with a decrease in atrial fibrillation, renal failure, and duration of vasopressor support in the vasopressin group compared to norepinephrine. This suggests vasopressin as the superior vasopressor in the setting of vasoplegic syndrome.[2]

Vasopressin as a continuous low dose infusion (0.03 u/min) can be beneficial as a preemptive treatment in coronary artery bypass graft surgeries for patients on preoperative ace inhibitors. Papadolous et al. found a decrease in the incidence of vasoplegic syndrome with the early administration in high-risk patients. This study evaluated 50 patients and found a decrease in vasoplegic shock from 20% to 8% in patients on this infusion. It found higher postoperative hemodynamic values such as MAP, CI and ejection fraction, resulting in greater urine output over 24hrs post-surgery, less requirement for norepinephrine infusions and overall lower mortality in patients receiving vasopressin infusions.[5] Vasopressin is not only the superior vasopressor in the setting of vasoplegia it can also be used as a preemptive medication in decreasing the incidence of vasoplegic syndrome in high risk patients.

Other common therapies are methylene blue, hydroxocobalamin, K-ATP channel blocker, NF-kB inhibitor polyphenol, and indigo carmine. Methylene blue acts by reducing guanylate cyclase, decreasing the overproduction of nitric oxide. This inhibits vasodilation and increases vasoconstriction through cAMP.[4] Mehaffey et al. found in a retrospective study of 118 vasoplegia patients undergoing cardiac surgery that the early use of methylene blue in the operating room, versus the late use in the ICU, decreased the mortality rate from 29% to 10%.[6] The literature shows early management of vasoplegia, with correct medical therapy, is vital in improving patient outcomes.

Management of this case could have been ameliorated through a more proactive management of vasoplegic syndrome. There were several risk factors predisposing this patient to vasoplegia including: advancing age, CABG, CPB, blood transfusion, preoperative medication of lisinopril as well as the use of heparin and protamine.[1] Once this patient was identified as high risk, preemptive management techniques should have included selecting vasopressin as the primary vasoactive agent before norepinephrine or even starting a low dose vasopressin infusion. Coming off CPB, this patient exhibited classic signs of vasoplegic syndrome with hypotension, a normal CI and a low SVR. Although there was advancement in vasopressor support with norepinephrine and eventually vasopressin, aggressive therapy should have been initiated to treat the unstable hemodynamics. The anesthesia practitioner could have opted for earlier use of methylene blue at 2mg/kg. Having a strong understanding of what defines vasoplegic syndrome, its pathophysiology and recommended treatments are fundamental to improving patient outcomes in this patient population.

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Spinal Cord Protection for Anterior Cervical Discectomy

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Keywords: Langerhans cell histiocytosis, cervical spine surgery, spinal cord perfusion, hypotension

Langerhans cell histiocytosis (LCH) is a rare heterogenic disorder primarily found in children that results in the accumulation of dendritic cells in organ tissue and body systems.[1] LCH is classified as single or multisystem involvement with single system being the most benign and common.[1] Treatment is system dependent and may include surgery and chemotherapy. Eighty percent of cases involve the skeletal system and survival rates approach 100%.[1] This case study describes spinal cord protection in a pediatric patient with LCH presenting for cervical discectomy.

Case Report

A 6-year-old, 23.6 kg, 120.5 cm male presented for an anterior cervical discectomy with fusion of C2-C4, C3 corpectomy, and iliac crest bone grafting for a pathological fracture of C3. Before surgery, the patient complained of neck pain which was present at rest and worsened with movement. A computerized tomography scan of the patient's cervical spine revealed a lytic appearance of the C3 vertebral body. A magnetic resonance image demonstrated a pathological fracture of the C3 vertebral body with spinal canal stenosis and a prevertebral soft tissue mass that extended to the anterior arch of C1. A C3 vertebral body biopsy was performed and was diagnostic for LCH. The patient was admitted to the hospital and placed in eight pounds of halo traction before surgery.

The past medical history included a normal, full term, spontaneous vaginal birth, and appendicitis. The past surgical history was significant for an appendectomy, tonsillectomy, adenoidectomy, myringotomy, and tympanostomy with tube placement. The patient's preoperative medications included acetaminophen, hydrocodone-acetaminophen, and ibuprofen as needed for pain. Preoperative blood pressure, heart rate, respiratory rate and SpO_2 were 113/69 mm Hg, 73/min, 18/min and 99% respectively. A complete blood count and comprehensive metabolic panel obtained one month before surgery were unremarkable.

The patient presented to preoperative holding in halo traction. He was premedicated with 2 mg of intravenous midazolam and taken to the operating room. After preoxygenation with O_2 8L/min, general anesthesia was induced with fentanyl 15 mcg, lidocaine 30 mg, propofol 80 mg and succinylcholine 40 mg. A 5.5 mm oral endotracheal tube was placed using a Glidescope (GVL; Verathon Inc., Bothell, WA) with manual inline neck stabilization and halo traction in place. General anesthesia was maintained with sevoflurane at a minimum alveolar concentration of 0.5 with a mixture of O_2 0.7 L/min and air 1.3 L/min. Remifentanil 0.02-0.04 mcg/kg/min and propofol 200-300 mcg/kg/min were used as adjunctive anesthetic agents due to intraoperative neurophysiological monitoring. Intravenous Lactated Ringer's was infused at 60 mL/hr. Estimated blood loss was minimal, total urine output was 450 mL, and total volume of 690 mL of intravenous fluids were administered.

After the propofol infusion was initiated, the patient developed hypotension with a mean arterial pressure below 50 mm Hg. There was concern about spinal cord injury resulting from hypotension with the concurrent myelopathy. A target MAP of 70 mm Hg was set. A 250 mL bolus of albumin 5% was given and a dopamine infusion was initiated at 3-10 mcg/kg/min. Somatosensory evoked potentials (SSEP) and transcranial electrical motor evoked potentials (TcMEP) were monitored and remained normal throughout the case.

At the end of surgery, the patient was placed in a halo traction vest. During emergence, dopamine was gradually discontinued as the blood pressure returned to baseline. The patient was extubated and transferred to the post-anesthesia care unit. A neurological assessment was performed with no obvious neurological deficit. Analgesia was provided with incremental doses of intravenous morphine 1mg. The patient remained in a halo traction vest without neurologic deficits throughout recovery period and was discharged on postoperative day four.

Discussion

Patients undergoing cervical spine surgery with myelopathy are at an increased risk of spinal cord injury due to decreased spinal cord perfusion.[2] New onset postoperative neurological deficits after cervical spine surgery have been reported to be as high as 3.2%.[3] Recent studies conducted on the progression of cervical myelopathies suggest that oligodendroglia of the spinal cord may be hypersensitive to hypoperfusion caused by hypotension which predisposes the spinal cord to injury.[2] Therefore, it is imperative that anesthesia practitioners understand how to preserve spinal cord perfusion during cervical spinal surgery.

Spinal cord perfusion pressure is equal to the difference between MAP and cerebral spinal fluid (CSF) pressure.[4] Consequently, it is critical that MAP be maintained to adequately perfuse the spinal cord during surgery. There are no agreed upon limits for MAP during cervical spinal surgery. However, a MAP less than 60 mm Hg in patients without cervical myelopathies has been shown to produce a substantial reduction in the anterior spinal artery blood flow during doppler ultrasonograpy.[2] Mean arterial pressure should be maintained at or above baseline to ensure adequate spinal perfusion pressure.[2] In this case, a dopamine infusion was initiated to treat hypotension that developed as a result of anesthetic agents. Dopamine was chosen to maintain blood pressure based on the chronotropic profile and its ability to increase the patient's heart rate. The pediatric population relies on heart rate to increase cardiac output rather than stroke volume; therefore, dopamine was deemed appropriate. MAP was maintained above 70 mm Hg to ensure spinal cord perfusion.

Along with maintaining an adequate blood pressure, intraoperative neurophysiological monitoring (IONM) is another way to confirm spinal cord perfusion. Combined intraoperative monitoring of SSEP and TcMEP is highly effective means of detecting impending spinal cord injury.[3] SSEP monitor the posterior columns of the spinal cord that send somatosensory information to the brain. Insults to the posterior column will reduce the amplitude of SSEP signals in the brain.[3] The most common cause of SSEP changes intraoperatively is hypotension and once resolved the SSEP return to baseline rendering IONM a critical tool for ensuring spinal cord perfusion.[3] TcMEP monitors the motor pathway that is located in the lateral and ventral funiculi of the spinal cord. TcMEP activates the motor pathway by electrically stimulating the scalp which produces an electrical current in the motor cortex.[3] In this case, SSEP were monitored in the median and posterior tibial nerve and TcMEP were monitored in the bilateral upper and lower extremities. SSEP and TcMEP signals were unaffected by episodes of transient hypotension.

During IONM, the anesthetic regimen must be tailored to avoid interference with SSEP and TcMEP signals. Inhalation agents increase the latency of signals and decrease signal amplitudes for both SSEP and TcMEP in a dose-dependent manner.[5] TcMEP signals are more sensitive to the effects of inhaled anesthetic agents than SSEP.[6] As in this case, if inhalation agents are administered, concentrations should be maintained at less than 0.5 MAC. Inhaled agents are associated with higher rates of false-positive TcMEP readings.[7] A positive TcMEP is determined on amplitude alone and is considered when the baseline measurements decrease by 50%.[5] False-positive results increase the risk for complications because they may alter the surgical plan, prolong surgery, lead to the administration of unnecessary medications such as methylprednisolone, and the initiation of a Stagnara wake-up test.[7] Intravenous anesthetics such as opioids, benzodiazepines, and propofol**,** do not affect IONM to the same degree as inhalation agents.[5] As demonstrated in this case, infusions of remifentanil and propofol were used as adjuncts to allow for IONM. Anesthesia practitioners should use a short-acting depolarizing muscle relaxant to facilitate intubation and preserve motor responses. Nondepolarizing muscle relaxants have a longer duration of action and are avoided.[5] Accordingly, no nondepolarizing agents were used during this case and a regimen was used to avoid interference with IONM thus contributing to a successful outcome.

This unusual case involving cervical myelopathy in a pediatric patient with LCH illustrates the anesthesia practitioner's important role in spinal cord protection through blood pressure management and facilitation of IONM. Prior to the case, anesthesia practitioners should select agents that avoid interference with IONM and formulate a plan to manage hypotension. While there is no established safe lower limit for MAP in the presence of myelopathy, communication between surgeons, anesthesia practitioners, and neurophysiology technologists is important to formulate an effective anesthetic plan that will avoid spinal cord injury. Mean arterial pressure goals should be communicated by the surgeon to the anesthesia practitioner and neurophysiology technologist to avoid adverse outcomes associated with spinal cord hypoperfusion and injury.

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Anesthetic Management for Liver Resection

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Key words: liver resection, anesthesia management, fluid management, epidural, hepatic resection, hemodynamics

The liver is the only human organ capable of regenerating functional parenchymal tissue after resection.[1] Over the last few decades, research has led to a better understanding of the highly-

vascularized organ. Through improved research on patient selection, surgical and anesthetic techniques, perioperative mortality rates after hepatic resection have dropped to 3%.[2,4] Patients with a parenchymal liver disorder such as cirrhosis, however, continue to have elevated mortality rates.[2] Liver resection is utilized for donation in transplantation, hepatobiliary tumor resection, and liver trauma. For patients with colorectal cancer involving liver metastasis, hepatic resection remains the treatment of choice.[2] Patients undergoing hepatic resection require anesthesia practitioners that have a thorough understanding of the anatomy, physiology, and anesthetic implications of the liver.

Case Report

A 64-year-old male presented for an exploratory laparotomy, intraoperative liver ultrasound, partial liver resection, biopsy of hepatic lesion, biopsy of falsiform ligament, and ileostomy reversal. This procedure was scheduled after the patient had a liver biopsy which revealed metastatic adenocarcinoma. The primary lesion was found in his cecum. The patient had a medical port placed and chemotherapy was initiated. His past medical history was significant for cardiomyopathy, coronary artery disease, congestive heart failure, hypertension, automated internal cardiac defibrillator placement, smoking, chronic obstructive pulmonary disease, and an ileostomy placed post bowel perforation when the diagnosis of cancer was confirmed. He had no known drug or latex allergies. Current medications included amiodarone 200 mg, lisinopril 5 mg, metoprolol 25 mg, aldactone 25 mg, and warfarin 3 mg. Preoperatively, his laboratory work and vital signs were within normal limits. His height was 183 cm and weight was 102 kg. A prior echocardiogram showed an ejection fraction of 20%. A radial arterial line was placed pre-operatively, along with a thoracic epidural for pain management. The plan for a general anesthetic with an intravenous induction and endotracheal tube (ETT) placement was discussed with the patient. In the preoperative period, midazolam 2 mg was administered prior to arterial line and epidural placement.

Once the patient was transferred to the operating table, standard monitors were placed, and pre-oxygenation was started for 5 minutes with O_2 8 L/min. Anesthesia was induced with fentanyl 100 mcg, 1% lidocaine 100 mg, ketamine 50 mg, propofol 50 mg, and rocuronium 80 mg. The traches was intubated with size 7.5 mm ETT using a Miller 2 blade. Once placement of the endotracheal tube was confirmed with end tidal capnography and the presence of bilateral breath sounds, mechanical ventilation was initiated. An orogastric tube was inserted, and a second peripheral intravenous catheter was placed. The radial arterial line was monitored with a FloTrac^{TM} (Edwards Lifesciences, Irvine, CA) monitor. The baseline stroke volume variation (SVV) was 8%, cardiac index was 2.4 L/min/m^2, and the cardiac output was 4.8 L/min. A bolus of 4 ml of 0.125% bupivicaine was administered through the epidural catheter, prior to surgical incision.

General anesthesia was maintained with 0.8% inspired concentration of isoflurane in a mixture of air 0.6 L/min and O_2 0.5 L/min. Boluses of phenylephrine and a norepinephrine infusion were administered to manage hypotension. Additional crystalloid and colloid boluses were administered after observing increases in SVV. A total of 250 mL of 5% Albumin and 2,300 mL of Lactated Ringer's solution were administered. Additional rocuronium was administered during the case to a train of four count of 1-2 twitches. An additional dose of fentanyl 50 mcg

was given, along with dexamethasone 8 mg, and ondansetron 4 mg after induction, but prior to surgical incision. The patient remained in normal sinus rhythm with an SpO_2 of 100%. A systolic blood pressure of at least 110 mm Hg was maintained with vasoactive medications.

The surgeon started closure of the incision after approximately 5 hours. The patient was given an additional 0.125% bupivicaine 2 mL through the epidural catheter for postoperative pain management. Neuromuscular blockade was antagonized with neostigmine 3 mg and glycopyrrolate 0.4 mg. The patient began to spontaneously breathe and the oropharynx was suctioned. The ETT was removed without complications, and the patient was placed on O_2 4 L/min via nasal cannula and transferred to the post anesthesia care unit (PACU). Upon arrival to the PACU, the patient's vital signs were stable and his pain was well controlled.

Discussion

There are multiple goals when providing anesthesia for the patient with liver disease, including optimizing fluid blood volume, minimizing the use of vasoactive infusions, and improving encephalopathy, renal function, and coagulopathies.[1] Efficiently managing these complex patients is essential to having positive postoperative outcomes.

Initially, during the preoperative phase, the anesthetist should consider the overall surgical risk in the patient undergoing liver resection. Various scoring techniques have been used to measure perioperative risk. Risk factors accepted in this population include cardiopulmonary disease, elevated bilirubin levels, the magnitude of liver resected, length of surgical time, and the need for postoperative blood transfusions.[3,4] According to the age-adjusted Charlson comorbidity index, this patient scored a 6 on the scale, indicating his postoperative in-hospital mortality rate was 233% higher than patients with a score 0-1.[3] This case study highlighted a patient with multiple cardiac comorbidities. A retrospective study suggested that preoperative cardiac comorbidity is not directly associated with an increase in 30-day mortality after hepatectomy. It is also suggested that advanced age and hypoalbuminemia are independent risk factors for postoperative mortality and cardiac morbidity. Overall it is stressed that careful patient selection, rigorous preoperative cardiac evaluation and optimization, along with anesthesia practitioners with an expertise in cardiac and hepatic management is essential for anesthetic management.[3] Considering patient risk factors in the hepatic resection patient will assist the anesthetist in creating an individualized plan with any specific interventions.

Epidural placement prior to hepatic resection has been considered a protective measure in hepatic surgery.[4] Epidural placement has not been shown to significantly decrease the length of intensive care unit stay, but has greatly reduced the number of ventilator associated days and overall hospital stay.[7] The use of an epidural blunts the neuroendocrine and pain response, limiting the effects of surgical stress, opioid requirements. Decreased opioid use in pain management leads to increases in early mobility and gastric motility.[7] The coagulopathies associated with liver disease can limit which patients are able to receive epidural placement.[7] Also epidural placement may cause periods of prolonged hypotension due to the sympathetic blockade. This may result in excessive administration of intravenous fluid.[7] The patient mentioned in this case report had no contraindications to epidural placement prior to surgery, required minimal narcotics intraoperatively, and was able to be extubated immediately after

surgery. Hypotension after the initial bolus of local anesthetic was treated with vasoactive medications.

Overall, volatile anesthetics decrease hepatic blood flow.[5] The inhalation agents isoflurane and sevoflurane at 1 minimum alveolar concentration (MAC) decrease hepatic blood flow to a lesser degree.[1] Desflurane greatly decreases hepatic blood flow at 1 MAC. Animal studies have suggested that isoflurane is less likely to cause a disturbance in hepatic arterial blood flow and is preferred for patients with liver disease.[5] Isoflurane was used for this patient based on this information.

In end stage liver disease, serum albumin is decreased both qualitatively and quantitatively.[5] This decrease in serum albumin levels decreases the overall oncotic pressure, leads to the formation of ascites, and creates large fluid and electrolyte shifts. The goal for fluid management in patients with liver disease is controlled isotonic fluid administration to avoid further fluid shifts.[5] Monitoring for patients with end-stage liver disease typically includes routine noninvasive monitors, arterial pressure monitoring, and possible central venous pressure monitoring (CVP). One method for guiding fluid management and reducing blood loss is maintaining a CVP less than 5 mmHg.[6] Sustaining a low CVP is not limited to fluid restriction, but also involves nitroglycerin, morphine, milrinone, and furosemide.[6] Recent literature suggests that CVP monitoring may not be as advantageous as initially believed. Maintaining a low CVP increases the risk of air embolism, unnecessary hypoperfusion, and the associated risks involved with central venous catheter placement.[6]

Advances in arterial cannulation have allowed monitoring of cardiac output and stroke volume variation (SVV) with devices like the FloTrac™ (Edwards Lifesciences, Irvine, CA) monitor. The reliability of this monitoring has been questioned due to the hyperdynamic state many cirrhotic patients experience. They often have an increased baseline cardiac output, decreased peripheral vascular resistance, and a decreased response to physiologic, pharmacologic, and surgical stress.[5] However, a patient with hepatic metastasis may or may not respond in the same ways as a cirrhotic patient. Other literature has suggested that SVV is less invasive than CVP monitoring and is a sensitive indicator for fluid responsiveness in relation to preload status.[1,6] Utilizing a high SVV (11-13%) was associated with a decrease in blood loss. The SVV range of 11-14 was the goal when maintaining the fluid balance of this patient which was evidenced by his ability to maintain adequate urine output and minimal blood loss.

Numerous studies have stated that the use of synthetic colloids often lead to the need for renal replacement therapy, blood transfusions and lack clinical benefit.[6,8] Balanced crystalloid solutions, such as Lactated Ringers, remain the fluid of choice to maintain intravascular volume. Normal saline leads to many pathophysiologic changes including hyperchloremic acidosis.[6] Normal saline has also been linked to coagulopathies by diluting albumin and clotting factors.[8] This patient's intravascular volume was maintained primarily with Lactated Ringers along with a bolus of 5% Albumin.

The patient undergoing a liver resection often presents with a complicated medical history requiring a thorough understanding of pathophysiology and hemodynamics. Advances in research have established an evidence-based framework for providing the best anesthetic for

these high-risk patients. Providing optimum care for the hepatic patient begins in the preoperative period with understanding their surgical risk, obtaining a thorough health history, careful fluid management intraoperatively, and managing pain with an epidural postoperatively. The case study demonstrates the positive outcomes when an anesthesia provider utilizes evidence-based research to guide care for the hepatic patient.

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Pain Management of Adult Patient for the Nuss Procedure

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Keywords: Nuss procedure, anesthesia management, pectus excavatum

Pectus excavatum (PE) is a congenital chest wall abnormality that affects 1:400 children.[1] PE decreases pulmonary and cardiac function, causing reduced activity tolerance as well as damaging psychosocial effects.[2,3] The Nuss procedure involves placing metal bars under the skin fastened to the rib cage. This pulls the caved-in chest outward. While the Nuss is considered

minimally invasive, it remains a painful procedure.[4] Current research includes the use of both regional anesthesia and patient controlled analgesia for postoperative pain management. Benefits of adequate pain management include hemodynamic stability, minimizing physiologic and psychologic distress, and promoting healing.[5-7] This case study presents a 24-year-old male who underwent a Nuss procedure for repair of PE.

Case Report

The patient was a 24-year-old, 188 cm, 78.7 kg male with no other significant medical history. He had no known allergies, and took no prescription medications. He reported a brief history of social smoking and some occasional alcohol usage. He presented to his physician complaining of worsening dyspnea on exertion as well as dizziness. Electrocardiogram testing showed sinus bradycardia with left atrial enlargement and a right ventricular conduction delay. Preoperative lab testing was all within normal limits.

A 20-gauge intravenous (IV) catheter was started preoperatively and the patient was given a bolus of dexmedetomidine 0.5 mcg/kg IV over 20 minutes. A 20-gauge arterial line was placed in the left radial artery. Upon arrival to the operating room, the patient was given midazolam 2 mg IV. Standard non-invasive monitors were applied and the patient was pre-oxygenated while baseline vital signs were established. General anesthesia was induced with administration of fentanyl 100 mcg IV, lidocaine 100 mg IV, propofol 100 mg IV and rocuronium 40 mg IV. The patient was mask ventilated with O_2 10 L/min and sevoflurane 2% inspired concentration for 2 minutes then intubated with a 7.5 mm endotracheal tube. Mechanical ventilation was initiated at tidal volumes of 550 mL, respiratory rate of 10/min. Peak inspiratory pressures were initially 13 cm H_20 with positive end expiratory pressures of 4 cm H_20. Neuromuscular blockade was maintained at 1-2 twitches on train of four monitoring with rocuronium 0.1-0.2 mg/kg IV. Ongoing analgesia was provided with fentanyl 100 mcg IV boluses as well as dexmedetomidine 10 mcg IV boluses every 20-30 minutes. Ephedrine 5 mg IV and glycopyrrolate 0.4 mg IV were administered after induction to increase heart rate (HR) from 37-41 beats/min to 50-60 beats/min. Intraoperative sympathetic response to the passing of the sternal bars was controlled by bolus doses of esmolol 10mg IV and nitroglycerin 50 mcg IV to maintain a HR <100 beats/min and a systolic pressure of less than 140 mm Hg, respectively.

Before emergence, acetaminophen 1000 mg and toradol 30 mg IV were administered, as well as a final dose of dexmedetomodine 10 mcg IV. Neuromuscular blockade was antagonized with neostigmine 4 mg and glycopyrrolate 0.6 mg IV. Nausea prophylaxis included early administration of dexamethasone10 mg IV and ondansetron 4 mg IV. Following extubation, the patient was transported to the intensive care unit on a simple face mask with O_2 8 L/min. Post-operative evaluations were conducted by the anesthesiology service to monitor pain at 5, 20, and 24 hrs.

Discussion

Surgical repair for PE has become less invasive, no longer requiring the large chest incisions but there remain multiple anesthetic challenges for these patients. One of the main challenges is intraoperative and post-operative pain management.[6] This discussion will focus on a comparison

of the various methods that are being used to control pain for patients undergoing the Nuss procedure. The methods compared were thoracic epidurals (TE), subcutaneous (SQ) pain pumps, intercostal nerve blocks (ICNB), paravertebral blocks (PVB) and patient controlled analgesia (PCA) pumps.[4,5,6,7] There was no study that compared all methods simultaneously. Of the four studies chosen, one compared TE use with PCAs, one compared TE to PCAs and to PVBs, one compared TE to SQ pain pumps, and one compared ICNBs with PCAs. Only one study focused on adults and the others limited their scope to children between 3 and 18 years.

The use of a TE was well supported by research, and may offer better pain control than PCA pumps in the early post-operative period.[6] One of the concerns about TEs is that there can be increased pain after the epidural is removed, sometimes requiring an additional day at the hospital.[4,6,7] Additionally, epidurals are not always successful. Stroud et al[4] showed a 0-35% failure rate for epidurals, most often requiring the patients to switch to a PCA. Like TEs, ICNB and PVBs showed lower narcotic use in the first 24 hours postoperatively, but can be used without the limitations associated with central nerve blocks including coagulation and infection concerns.[4,5,7] It must be noted that none of the studies found a statistically significant difference between TE, PVBs, and PCAs related to pain control after the first 24 hours postoperatively.[4,6,7] Research from Shanghai[5] did show lower narcotic usage for patients who receive an ICNB as well as faster discharge from postanesthesia care unit and fewer analgesia-related side effects. However, it did point out that there is a lack of data on failure rates and complications with the use of ICNBs.[5]

For this case, the patient refused the TE and no other blocks were discussed. By using a multi-modal approach intraoperatively, adequate pain control without the negative side effects of a high narcotic anesthetic was achieved. There were no studies comparing the benefit of using adjunct medications like dexmedetomidine and esmolol in patients undergoing the Nuss procedure. A hydromorphone PCA pump was ordered and used by the patient for post-operative pain management. The patient reported sternal pressure and soreness but was able to ambulate and use the incentive spirometer with only mild to moderate discomfort. The numeric pain scale was used and the patient's goal was to maintain a score of 3 or less on a scale of 1-10. There were no reported analgesia-related side effects such as nausea, confusion, or respiratory depression. He was able to get up in a chair by the end of the operative day and was ambulating in the hall the next morning. He was discharged two days after the operation. While this patient had a successful outcome, there may have been greater benefit in using one of the peripheral nerve blocks that have been discussed. This patient wanted to avoid bedside procedures with needles while he was still awake. One advantage of the PVB is that it can be performed after the patient is under general anesthesia, which may have been more appealing than an epidural to this patient.

The results from most of the reviewed studies suggests comparable efficacy between multiple modes of postoperative pain control, allowing the provider and patient to choose the approach they find more appealing.[4,6,7] ICNBs did show improved outcomes, but further research needs to be done on the complications and risks of peripheral nerve blocks.[5] In addition, since the Nuss procedure is commonly performed in childhood, studies on adults are limited. More research needs to be compiled on adults undergoing repair of PE.

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Glycemic Control for Cardiac Surgery in the Non-Diabetic Patient

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Keywords: Non-diabetic, glucose management, insulin therapy, CABG

Hyperglycemia and insulin resistance are prevalent in the cardiac surgical patient with or without a pre-existing comorbidity of diabetes mellitus.[1] Hyperglycemia is an independent risk factor for cardiac surgery perioperative morbidity and mortality. Patients are prone to potential complications such as infection, stroke, delirium, coma, prolonged ventilator dependence, organ failure, and cardiac arrest.[1] Alternatively, there is a risk of post-operative hypoglycemic incidences with the interventions necessary to provide tight intra-operative glycemic control.[2] The purpose of this case report is to explore the benefits and risks of intra-operative glucose management in the patient undergoing coronary artery bypass grafting (CABG).

Case Report

A 69-year-old, 79.4 kg, 175 cm male presented for three vessel CABG due to symptomatic coronary artery disease. His history of present illness consisted of left sided chest pain, dull in nature, occasionally related to exertion of 5 to 20 minutes in duration. He had concomitant dyspnea, but otherwise denied any syncope, palpitations, orthopnea or leg edema. Other history included former smoker, trace mitral regurgitation, hyperlipidemia, hypertension, and peripheral artery disease. Electrocardiogram (EKG) was normal. An echocardiogram revealed a post-stress left ventricular ejection fraction of 54% with normal wall motion and normal wall thickening. However, due to the fact that he developed dyspnea, and with his other risk factors, he was referred for angiography. Angiography showed a heavily calcified left main with a distal 70% lesion that extends to the LAD. The left circumflex with a 50% ostial stenosis. Right coronary artery has a 70% calcified stenosis. Laboratory results were unremarkable. His home medications included Aspirin, Plavix, Losartan, Rosuvastatin, and Metoprolol.

In preoperative holding, the patient received midazolam 2 mg and fentanyl 50 mcg for an arterial line and central line placement. Once invasive lines were secure, the patient was transferred to the operating room. Appropriate monitors included a pulse oximeter, five lead EKG, arterial and central venous pressures. Neurologic monitoring was accomplished with cerebral oximetry. A pre-oxygenation arterial blood gas was sent for analysis. Baseline laboratory values were within normal limits. Oxygen was administered at 15 L/min via face mask until an expired O_2 concentration of greater than 85% was obtained. Induction of general anesthesia was accomplished with lidocaine 40 mg, fentanyl 250 mcg, etomidate 24 mg, and rocuronium 50 mg. Direct laryngoscopy was performed, and the airway was secured with an 8.0 mm endotracheal tube. Airway placement was verified via capnography and auscultation of bilateral breath sounds. A transesophageal probe was then placed for echocardiography.

Patient remained on inspired isoflurane 1.1% in O_2 0.5 L/min and air 0.5 L/min. Blood pressure was maintained in the appropriate range for venous and arterial cannulation with nitroglycerin and norepinephrine boluses. After administration of heparin 30,000 units, confirmation was made that the activated clotting time was at an acceptable range of greater than 400 seconds, and the patient was placed on the cardiopulmonary bypass circuit (CPB). Both hemodynamic monitoring and anesthesia were maintained by the perfusionist. Urine output and blood glucose (BG) were assessed every 30 minutes. The first BG on CPB was 198 mg/dL elevated from a baseline of 87 mg/dL. A regular insulin dose of 4 units was administered. A repeated BG revealed a sustained glucose level of 201 mg/dL. A regular insulin infusion of 2units/hour was initiated and titrated to achieve a BG range of 121 to 180 mg/dL. The insulin infusion continued for the duration of the procedure with a maximum rate of 5 units/h.

At the beginning of incisional closure, the insulin was discontinued with the patient's most recent blood glucose of 122 mg/dL. Report was given to the ICU nurse, including insulin administration and blood glucose level. Anesthesia was maintained for transfer to the ICU. Patient was extubated in the ICU two hours later, with no hypoglycemia or hyperglycemia noted.

Discussion

Hyperglycemia and insulin resistance are common during cardiac surgery and may lead to increased morbidity and mortality.[1,2,3,4,6] Stress situations, such as surgery and critical illness, induce counter-regulatory hormone release such as glucagon, norepinephrine, cortisol and growth hormone and exacerbate a hyperglycemic state.[3] Cardiac surgery with CPB produces significant surgical stress and marked elevation of blood glucose levels.[3] Hyperglycemia during cardiac surgery is not specific to diabetics alone; as 47% of non-diabetic patients undergoing CABG surgery have more than one consecutive glucose reading >250g/dL.[6] A postoperative serum glucose level of 250 mg/dL has been associated with a ten-fold increase in complications post CABG.[1,4] Some adverse consequences of hyperglycemia during and after cardiac surgery include impaired white blood cell function, deep sternal wound infection, worsened neurologic outcomes, critical illness polyneuropathy, bacteremia, inflammation, increased production of oxygen-derived radicals, decreased complement function, and activation of protein kinase C and nuclear factor kB.[3] Many studies demonstrated that glycemic control using insulin protocols reduce the risk of operative mortality, lowers operative morbidity, and improves long-term survival in non-diabetic patients undergoing cardiac surgery.[1,2,3,5]

Treating hyperglycemia intra-operatively is not without its risks. Studies have reported that the attempt to maintain normoglycemia during CPB with insulin therapy was associated with postoperative hypoglycemia.[6] Hypoglycemia presents its own risks including post-operative neurologic deficits, increases in length of stay, and increased morbidity and mortality.[6] Butterworth and colleagues studied the effects of intra-operative tight glycemic control in 381 patients without diabetes undergoing isolated CABG surgery.[4] In this study, intraoperative glycemic control failed to improve short-term or long-term clinical outcomes in a group of patients without diabetes.[4] The Society of Thoracic Surgeons (STS) encourages that caution should be exercised in initiating a continuous IV insulin infusion in non-diabetic patients.[4] This is because insulin requirements may decrease rapidly in the immediate postoperative period resulting in significant hypoglycemia.[4]

Though there is conflicting evidence, STS had enough middle to high level evidence to recommend maintaining a target BG range of 121 to 180 mg/dL for non-diabetic patients undergoing a CABG using an insulin infusion during the perioperative period.[1,4] Furthermore, the liberal group BG target range of 121–180 mg/dL in comparison to tight glycemic control, BG <126g/dL, had a quicker time to target BG range after admission to the cardiovascular ICU.[1,3,5] Maintaining BG within a specified target range, fewer patients had hypoglycemic events, and there was no difference between the groups on perioperative complications.[1,3,5]

The patient in the presented case was initially treated with a one-time bolus dose of 4units regular insulin for the initial BG of 198 mg/dl. The STS recommend that glucose levels of >180 mg/dL that occur in patients without diabetes only during CPB to be treated initially with a single or intermittent dose of IV insulin as long as levels remain less than 180 mg/dL. However, in those patients with persistently elevated serum glucose (>180 mg/dL) during CPB, a continuous insulin infusion should be instituted, and an endocrinology consult should be obtained.[4] The patient's repeated elevated BG required the use of an intraoperative insulin infusion to maintain his BG below 180 mg/dL. The presented case further followed the STS

recommendations to monitor the patient's BG every 30 min while receiving an IV infusion of insulin.[4] Additionally, it was recommended to have more frequent monitoring, as frequent as every 15 minutes, during periods of rapidly fluctuating sensitivity, for example, during the administration of cardioplegia as well as systemic cooling and rewarming.[4] The patient had no adverse outcomes reported and a non-eventful post-operative recovery.

The administration of an insulin infusion during cardiac surgery for non-diabetic patients is high risk and decisions require following a protocol or guideline to ensure no adverse events occur. Current evidence reports the risk that both hyperglycemia and hypoglycemia could have an effect on patient's recovery after cardiac surgery. All patients are at high risk for hyperglycemia during cardiac surgery and require constant monitoring and vigilance to ensure a safe and timely recovery.

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Insomnia Medications and Delayed Emergence during Anesthesia

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Keywords: insomnia, suvorexant, delayed emergence, orexin receptor antagonist, sleep, cataplexy

Insomnia is defined as difficulty maintaining or triggering sleep for at least one month.[1-2] Suvorexant, an orexin 1 (OX_1R) and 2 (OX_2R) receptor antagonist, was approved for treatment of insomnia.[1] OX_1R and OX_2R are G-receptors that promote arousal and consolidation of sleep and wakefulness cycles.[2] A potential adverse effect of OX_1R and OX_2R antagonist drugs is loss of muscle tone in parts of, or the entire body known as cataplexy.[2] Anesthesia practitioners may mistake orexin antagonist induced cataplexy as residual neuromuscular blockade or pseudocholinesterase deficiency.

Case Report

A 58-year-old, 101 kg, 177 cm female with a body mass index (BMI) of 39.1 kg/m^2 presented for a laparoscopic cholecystectomy for calculus of her gallbladder with acute cholecystitis. Her medical history included generalized anxiety disorder, severe recurrent major depression without psychotic features, coronary artery disease (CAD), hypertension, diastolic dysfunction, obstructive sleep apnea (OSA), and kidney stones. Surgical history included a breast lumpectomy, diagnostic laparoscopy, and dental surgery. The patient had allergies to amitriptyline, hydroxyzine, minocycline, mirtazapine, prochlorperazine, tetanus antitoxin, pramipexole, and ropinirole. The patient's home medications consisted of aspirin 81 mg, clonazepam 1 mg, lamictal 200 mg, metoprolol 50 mg, suvorexant 10 mg, and vilazodone 20 mg. Laboratory results were unremarkable. Following the pre-procedural time out, hydromorphone 0.4 mg was administered intravenously (IV).

The patient was transferred to the operating room where standard noninvasive monitors were applied. Initial vital signs were heart rate (HR) 70/min, blood pressure (BP) 155/108 mm Hg, SpO_2 96%, respiratory rate 18/min, and temperature 36.8°C. Oxygen was administered via facemask at 10 L/min until expired O_2 was greater than 96%. General anesthesia was induced with lidocaine 100 mg, hydromorphone 0.2 mg, propofol 200 mg, and rocuronium 40 mg IV. Video laryngoscopy was performed and the airway was secured with a 7.0 mm endotracheal tube (ETT). Airway placement was verified and an orogastric tube was placed. General anesthesia was maintained with Desflurane 5.25 – 6.4% inspired concentration in O_2 0.5 L/min and air 0.5 L/min. Volume control ventilation was utilized to maintain adequate tidal volumes and appropriate end tidal CO_2 levels. A 2% lidocaine infusion of 8 mL/hr was maintained for the duration of the procedure.

Trocar instruments were inserted into the patient's abdomen by the surgeon and CO_2 was used to inflate the peritoneal cavity for visual exposure. Dexamethasone 8 mg, ondansetron 8 mg and a total of 750 mL of crystalloid were administered during the procedure. Rocuronium and hydromorphone were not continued after induction.

Emergence was initiated by turning off the volatile anesthetic and increasing the O_2 to 10 L/min. A train of four count was checked to ensure adequate 4/4 twitch response. Neostigmine 3 mg and glycopyrrolate 0.6 mg was administered to antagonize the non-depolarizing neuromuscular blockade. Within 6 minutes, the patient aroused to name and was able to perform a sustained head lift. The patient had strong bilateral handgrip and was able to wiggle her toes to command. The ETT was removed and the patient was transferred to the post anesthesia care unit (PACU).

Once in the PACU, the patient was somnolent but could follow commands. She nodded her head in agreement to having trouble breathing. The patient was able to stick out her tongue to command but appeared very weak. She was unable to raise her arms and had a weak handgrip. Non-rebreather mask at 6 L/min was continued in the PACU and her end tidal CO_2 and vitals were monitored. Sugammadex 180 mg was administered IV for residual neuromuscular blockade. Roughly, three hours after the sugammadex was administered, she began to have increased strength in all four extremities and did not report having difficulty breathing.

Discussion

Sugammadex's complete TOF recovery occurs in 45 seconds, whereas neostigmine averages 16 minutes to reach a TOF ratio of 0.9.[3] Sugammadex is a gamma-cyclodextrin that encapsulates inactivates the steroidal neuromuscular blocker, The sugammadex-relaxant complex does not dissociate and 80% of the administered dose is excreted in the urine unchanged.[3] After the administration of sugammadex and no improvement in muscle weakness, the patient's medication list was further investigated. Her use of suvorexant was noted as treatment for insomnia due to her psychiatric condition and use of various antidepressant medications. Suvorexant enhances the patient's rapid eye movement (REM) and non-REM sleep by acting as an antagonist on the orexin receptors.[1] Orexins are produced by neurons in the lateral hypothalamus and are dormant during sleep but active during wakefulness; hence, orexin stimulates wakefulness.[1]

The side effects of suvorexant may explain the patients delayed recovery time after surgery.The patient's history of OSA, combined with the drug's sedative hypnotic effect, can adversely impact respiratory drive..[4] These respiratory side effects may explain the patient's sensation of breathing difficulty in the recovery room. Suvorexant administered at four consecutive nightly doses of 40 mg caused minimal and highly variable hypopnea and apnea scores in OSA individuals.[4] In 2014, the Food and Drug Administration (FDA) approved suvorexant at doses of 5, 10, 15, and 20 mg/day.[5] In phase III trials, the FDA did not approve suvorexant at 30 or 40 mg/day doses due to safety concerns particularly next-day driving impairments, sleep paralysis and hallucinations, unconscious nighttime behaviors, and narcolepsy-like events.[5] The loss of orexin neurons can result in narcolepsy with cataplexy, a disorder characterized by difficulty maintaining long period of wakefulness and rapid transitions into sleep.[6] The patient was experiencing cataplexy after surgery due to the antagonist effect on the orexin receptors from suvorexant.

The patient has a diagnosis of major depressive disorder which disturbs sleep and circadian rhythm.[7] The patient was prescribed suvorexant to control her insomnia and promote a healthy

circadian rhythm. Research suggests the circadian clock system plays a crucial role in preventing psychiatric disorders by controlling clock systems such as orexin.[7] Evidence reveals dysfunctional orexinergic activity is associated with the pathogenesis of depression.[7]

The most common adverse effect of suvorexant is daytime somnolence and fatigue.[8] No further interventions were indicated to speed the recovery process for the patient. Extended time in the PACU was necessary to evaluate end-tidal CO_2 levels and respiratory status. The patient was admitted overnight for observation and discharged the following day. Patients taking orexin antagonists are at an increased risk of cataplexy and somnolence post-surgery. When reviewing the patient's medications in the pre-operative setting, anesthesia providers should consider the adverse effects of orexin antagonists. These medications can present as residual neuromuscular blockade due to the cataplexy-like state and somnolence postoperatively and 12-hour half-life of suvorexant.[4] Oxygen therapy and patient reassurance are supportive measures until muscle strength is regained.

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Anesthesia for Fetal and Maternal Procedures

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Keywords: in-utero, fetal, myelomeningocele, maternal, spina bifida

Myelomeningocele (MMC) is a spinal cord defect diagnosed prenatally. Traditional treatment includes postnatal repair and closure, as well as management of primary functional deficits of lower limb paralysis, sensory loss, bladder and bowel dysfunction, and cognitive dysfunction.[1] Advancements in surgical technique have offered parturients prenatal intrauterine repair of fetal myelomeningocele (fMMC) as an alternative to postnatal repair with superior long-term outcomes.[2] Providing anesthesia during these procedures presents unique challenges. This case study and review of literature analyzes anesthetic implications and articulates safe management of general anesthesia for patients undergoing in-utero fMMC repair.

Case Report

A 28-year-old, 171 cm, 82 kg parturient presented at 23 weeks gestation for an elective in-utero fMMC repair. The patient's past medical and surgical histories were insignificant. The patient's only medication consisted of a prenatal multivitamin.

Upon arrival to the Special Deliveries Unit (SDU), an 18-gauge peripheral intravenous (IV) catheter was placedinserted. Blood specimens were collected and laboratory results reviewed. Two units of crossed, packed red blood cells for the patient, and a half unit for the fetus were stored in a cooler in the operating room. Cross-matched blood for mom and fetus was never given. ABORh status and fetal transfusion would be a strong consideration. Appropriate doses of epinephrine (10 mcg/kg), atropine (20 mg/kg), calcium gluconate (50 mg/kg), fentanyl (20 mcg/kg), and vecuronium (0.2 mg/kg) were prepared in syringes based on estimated fetal weight. A fetal IV micro drip was meticulously primed with Lactated Ringers (LR) and free of air bubbles.

The patient ambulated to the operating table and remained seated while noninvasive monitors were applied. Oxygen (O_2) was administered by nasal cannula (NC) at 4 L/min. An epidural catheter was placed and secured at L2-L3. The patient was positioned supine with left uterine displacement. Additional monitors for fetal heart rate (FHR) were applied, and baseline FHR was noted at 145/min. Pre-oxygenation was achieved with O_2 10 L/min via facemask until end-tidal O_2 was greater than 90%. A rapid sequence induction (RSI) with propofol 150 mg and succinylcholine 100 mg IV was performed with simultaneous cricoid pressure. The trachea was intubated orally with a 6.0 mm endotracheal tube (ETT) under direct laryngoscopy. Correct placement was verified by capnography and auscultation. The mechanical ventilator was set to pressure controlled ventilaton. Fresh gas flows were adjusted for a mixture of O_2 0.4 L/min and air 0.6 L/min, and 9% expired desflurane concentration. An orogastric tube (OGT) was placed for gastric decompression. Cefazolin 2 g IV was administered for antibiotic prophylaxis. Rocuronium 50 mg IV was administered for paralysis. A left radial 20-gauge arterial catheter

was placed under sterile technique and secured. A second 18-gauge peripheral IV catheter, urinary catheter, leg compression boots, and peripheral nerve stimulator were also applied.

Anesthesia and uterine relaxation were maintained with high-concentration of expired desflurane between 5-12%. A phenylephrine infusion was initiated at 0.1 mcg/kg/min and titrated to maintain maternal mean arterial blood pressure (MAP) above 65 mm Hg. Neonatal cardiologists monitored fetal status continuously via sterile intraoperative sonography and echocardiography, per routine protocol. Approximately half way into the procedure, intraoperative sonography and echocardiography revealed fetal bradycardia and decreased fetal cardiac function. Desflurane concentration was then reduced to 4% until improvement was noticed on echocardiography 15 minutes later. Nitroglycerine boluses of 20 mcg were administered 10 times until the surgeon verbalized adequate uterine relaxation. IV fluids were limited to 500 mL for the case.

Repair was completed without issue. During uterine closure, magnesium sulfate (6 g loading dose, then 4 g/hr infusion) was administered IV for tocolysis. Bupivacaine 0.25% 10 mL was administered through the epidural catheter for postoperative analgesia. Ondansetron 4 mg IV was administered. The peripheral nerve monitor elicited a 4/4 train of four response. Emergence and extubation occurred smoothly. The arterial line was discontinued, and a pressure dressing was applied. The patient was transferred to the SDU recovery room on oxygen at 2 L/min via NC. Tocolysis was continued by magnesium sulfate infusion for 24 hours postoperatively and then transitioned to oral administration.

Discussion

Fetal surgery necessitates an anesthetic plan that balances the unique physiologic needs of the parturient and fetus. Safe anesthesia care is essential throughout all stages of surgery: pre-induction, abdominal incision, hysterotomy, uterine closure, and postoperative recovery. More specifically, anesthetic management of intrauterine fMMC repair is a complex interplay of several factors: maternal anesthesia, fetal anesthesia, maternal hemodynamics, fetal hemodynamics and resuscitation, and uterine tone.

For maternal management, general ETT anesthesia with an epidural catheter for postoperative analgesia is associated with better outcomes for mom and fetus.[2] Mid-second trimester physiologic changes to maternal physiology are significant for increased airway difficulty and increased risk of aspiration.[3] For this reason, RSI was performed and an OGT was placed immediately following induction and set to low intermittent suction. After abdominal incision, maternal anesthesia recommendations are to maintain high minimum alveolar concentration (MAC) of volatile agents to allow for profound uterine relaxation, often exceeding two MAC. Adequate uterine atony is confirmed with manual palpation by the surgeon. If inadequate, nitric oxide donors, beta-adrenergic agonists, calcium antagonists, oxytocin-receptor antagonists, and halogenated inhaled anesthetics can be used to supplement myometrial relaxation.[4] Nitroglycerine, although associated with increased incidence of maternal pulmonary edema, is preferred for its fast-acting, short-lasting, and easy administration with no deleterious effects on the fetus.[4] The epidural catheter is dosed at the end of the case for analgesic coverage. This neuraxial technique allows for the avoidance of intravenous opioids or prostaglandin-inhibiting non-steroidal anti-inflammatory agents from affecting the fetus.[4]

Fetal anesthetic technique has been a highly controversial topic in light of studies on neuroplasticity and fetal perception of pain. Animal studies report that isoflurane exposure may cause neuronal apoptosis and degeneration.[3] However, a recent retrospective cohort trial of children under two years of age exposed to a single, short anesthetic did not have long-term cognitive implications.[3] Furthermore, scientists now accept that the fetus does experience pain through mechanisms differing from that of adults. [4] Until further human data is available, fetal anesthesia is primarily achieved by volatile anesthetics transferred from maternal circulation through the placenta.[3,5] Additionally, adequate analgesia can mitigate long-term maladaptive effects such as hormonal stress responses and behavioral issues. Intramuscular opioids, most commonly fentanyl, are commonly administered to the fetus under direct view.[5]

Another focus of anesthetic management for fMMC surgery is maternal hemodynamics. Profound anesthesia at 2-3 MAC may compromise maternal cardiac output, thereby depressing placental perfusion and fetal oxygenation by up to 30%.[3] Oxygen delivery to the fetus is critically dependent upon adequate uterine blood flow to the placenta. Thus, left uterine displacement in the supine position ensures placental blood flow and improves fetal perfusion by decreasing aortocaval compression.[6] Hypocarbia is also avoided to prevent umbilical vasoconstriction.[5] Furthermore, adequate perfusion is achieved by maintaining maternal MAP within 10% of baseline values, using vasoactive medications including phenylephrine or ephedrine as needed.[4,7] Maternal pulmonary edema was observed in 28% of subjects undergoing fetal surgery.[2] Therefore, fluid therapy has conventionally been restricted to 500 mL, despite a lack of evidence to show improved outcomes.

Likewise, fetal hemodynamics are constantly monitored throughout the procedure by ultrasound and echocardiography. Fetal temperature regulation is solely dependent upon the environment and hypothermia may lead to bradycardia.[5] Care is taken to maintain maternal euthermia and warm fluids for intrauterine irrigation. FHR is the primary determinant of cardiac output due to a fixed stroke volume. Thus, fetal bradycardia can rapidly deteriorate to circulatory collapse. If abnormalities in fetal heart rate or umbilical artery blood flow are noted on ultrasound or echocardiography, immediate measures are taken to improve fetal perfusion as discussed previously. In the case study patient, the cardiologist noted sudden significant cardiac depression on echocardiography. Desflurane concentration was subsequently lowered, uterine tone was instead relaxed with nitroglycerine, and vasopressors were used to optimize maternal MAP. Little improvement was noted following these adjustments. It was ultimately recognized that surgical compression on the splanchnic circulation was the cause. Once relieved, uterine perfusion was reestablished and fetal hemodynamics returned to normal/baseline. At least one peer-reviewed study suggests high concentration desflurane causes moderate to severe left ventricular systolic dysfunction in the fetus.[1] Other centers have found lower desflurane concentrations, supplemented by intravenous anesthesia to achieve uterine relaxation without the cardiodepressive effects that accompany volatile anesthetic levels of 2-3 MAC.[1] Oxygen partial pressure gradient, hemoglobin concentration, diffusion capacity, and acid-base status of fetal and maternal blood also have been shown to affect fetal hemodynamics.[3]

Uterine tone is maintained with magnesium sulfate therapy during uterine closure and 24 hours postoperatively. Tocolysis not only ensures suitable conditions for surgery, but also prevents (1)

compression of fetus or umbilical cord, (2) abruptio placentae, and (3) premature labor.[4] Magnesium sulfate has been implicated in prolonged neuromuscular blockade and increased incidence of pulmonary congestion. Thus, the parturient must be monitored throughout her recovery for these and other complications.

As fetal surgery techniques advance and increase in popularity, anesthetic techniques must also advance and adapt to current evidence. Safe maternal and fetal anesthesia care is essential for successful surgical outcomes during fMMC repair.

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Anesthesia Implications for Cardiac Ablation of Wolff-Parkinson-White Syndrome

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Keywords: Wolff-Parkinson-White Syndrome, radiofrequency catheter ablation, electrophysiology, bundle branch block, mitral valve injury

Wolff-Parkinson-White Syndrome (WPW) is a rare but potentially fatal condition in which both normal and accessory cardiac impulse pathways exist. The development of atrial fibrillation serves as a second, less common, pathway for tachycardia in the presence of WPW.[1,2] Patients with WPW can present asymptomatically or may exhibit. grave symptoms including unstable tachycardia, angina, and sudden cardiac death.[1] A hallmark in electrocardiograph tracings of individuals with WPW is the delta wave, characterized by a “slurred” QRS complex.[3]

Radiofrequency catheter ablation (RFA) is a treatment in symptomatic patients with WPW. This report describes management of RFA for a patient with WPW.

Case Report

A 24-year-old, 68 kg, 162 cm Caucasian female presented to the electrophysiology (EP) lab for RFA ablation of WPW. The patient's past medical history includes asthma, well-controlled with ipratropium bromide and albuterol sulfate inhaler, and anxiety for which she is prescribed 0.5 - 1 mg lorazepam prn. Pre-operative vital signs were temperature 36.5°C, heart rate, 98/min, blood pressure, 114/65 mmHg, and SpO_2 100% on room air. A baseline 12-lead ECG demonstrated both a shortened PR interval and a widened QRS complex, composing the delta wave. The patient reported multiple episodes of lightheadedness and reported a sensation of her heart beating out of her chest over the past 8 months.

Upon arrival to the EP suite, the patient was placed on standard non-invasive monitors and defibrillator pads were applied. General anesthesia was induced with midazolam 2 mg, fentanyl 100 mcg, lidocaine 60 mg, and propofol 100 mg IV. After mask ventilation was assured, dexamethasone 4 mg and rocuronium 40 mg IV were administered. The trachea was intubated with a size 6.5 endotracheal tube (ETT). The patient's ventilation was controlled using pressure support and general anesthesia was continued with sevoflurane 0.7 MAC and a remifentanil infusion of 0.02 mcg/kg/min. An arterial line was placed post induction and hemodynamic stability was maintained throughout the procedure.

The patient was prepped and draped by the EP team, the electrophysiologist obtained access via the femoral vein and heparin 7,000 units was administered with anticoagulation status monitored by Activated Clotting Time (ACT). The goal ACT was greater than 250. Transesophageal temperature was monitored closely. Three-dimensional mapping of the heart and subsequent ablation was performed. Following completion of the ablation, high dose isoproterenol at 20 mcg/min was administered via infusion to elicit any potential reoccurrence of arrhythmias. The isoproterenol was then discontinued once the procedure was deemed successful. Reversal of heparin was achieved with slow administration of protamine 70 mg IV.

Ondansetron 4 mg IV was administered 30 minutes prior to emergence. Upon meeting extubation criteria, the ETT was removed and the patient was transferred to the post anesthesia care unit (PACU) with O_2 6 L/min via facemask. The patient was admitted to a monitored bed for overnight observation.

Discussion

Incidence of WPW is reported at 0.13% to 0.25% of the general population.[2] The case described above illustrates a straightforward management of RFA ablation under general anesthesia with no subsequent complications. However, the broad array of clinical circumstances and relative infrequency in which providers may encounter these patients merits a discussion on the anesthetic considerations regarding perioperative management of and potential risks to patients with WPW undergoing cardiac ablation.

The topic of RFA ablation in the symptomatic versus the asymptomatic WPW patient is much debated. Malignant arrhythmia leading to sudden cardiac death has been found to be 2.4 per 1000 person diagnosed with WPW.[4] Recent literature highlights cardiac ablation for symptomatic patients while finding no difference in mortality between medical management and ablation among asymptomatic patients.[4,5]

Preoperative assessment and a thorough history may prove invaluable in detecting undiagnosed WPW in a patient with no abnormal ECG tracings.[2] Blunting of sympathetic outflow during periods of stimulation is vital, as any stimulus causing catecholamine release and hemodynamic stimulation can alter the electrical conduction system of the heart, thus potentiating arrhythmia.[2] This includes medications commonly used during anesthesia such as cholinergics, ketamine, and succinylcholine.[2] Phenylepherine is generally the preferred choice of vasopressor due to its tachycardia-limiting effect.[2]

There are three subcategories of WPW: Orthodromic atrioventricular re-entrant tachycardias (OAVRTS), antidromic atrioventricular re-entrant tachycardias (AAVRT), and atrial fibrillation or flutter.[2] Treatment of hemodynamic compromise hinges on the clinician's ability to differentiate between these three subtypes. The first-line treatment of OAVRT includes IV adenosine and subsequent IV verapamil, procainamide, and beta-blockers proving effective as second, third, and fourth-line therapies, respectively.[2] Amiodarone is the least effective treatment and should be reserved in the event that no other agent is successful in treating the tachycardia.[2] AAVRT and atrial fibrillation/flutter respond most successfully to procainamide as the first line of therapy, and amiodarone as a secondary treatment if procainamide is unavailable.[2] Cardioversion should be employed when the arrhythmia causes acute hemodynamic compromise and/or medications are proved ineffective.[2]

RFA ablation poses its own risks, with major complications reported to be between 3% and 4%.[6] Bundle branch blocks have been discovered status-post ablation for one of two etiologies: the block had been previously masked by WPW prior to ablation or unintentional ablation of areas within the conduction system.[7] Mitral valve injury is another complication of RFA ablation that could necessitate urgent treatment and surgical repair.[6] Other potential risks of RFA ablation include ischemia, pneumothorax, atrial/ventricle perforation, pericarditis, and complete heart block.[2] However, the risks should be weighed against the benefits as RFA ablation is found to be 90-95% curative upon first attempt and is considered the definitive treatment for WPW syndrome.[2]

In the aforementioned case, the patient underwent RFA ablation as treatment for symptomatic WPW syndrome with no apparent adverse sequelae. However, because of the infrequency with which WPW syndrome is encountered in the clinical environment, the anesthesia provider should be knowledgeable regarding the pathophysiologic considerations, pharmaceutical management of, and potential risks of RFA ablation in the WPW population.

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Mastocytosis in the Perioperative Setting

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Keywords: mastocytosis, anesthesia, perioperative, mast cells, inflammatory, management

In the perioperative setting, patients with mastocytosis are at increased risk for reactions associated with inflammatory mediator release, including anaphylaxis. Mastocytosis is a rare disorder characterized by proliferation and accumulation of mast cells (MCs) in various tissues, causing a variety of clinical manifestations resulting from the inappropriate release of inflammatory mediators.[1] It affects anywhere from 1:1000 to 1:8000 individuals with a slight female predominance.[2] General anesthesia and surgical stress are known triggers.[1] As described in this case report, anesthetists may encounter mastocytosis and should be knowledgeable on how to provide a safe anesthetic for these patients.

Case Report

A 35-year-old, red-haired, fair-skinned female presented for laparoscopic tubal sterilization after having triplets 11 years prior. Her reported height and weight were 170.18 cm and 73.481 kg respectively, with a BMI of 25 kg/m^2. She reported a non-anaphylactic intravenous (IV) contrast media allergy, as well as a 10 pack-year smoking history. Of significance was her past surgical history, which included eye surgery as a child for which she stated the surgeon was unable to complete. This was due to the development of cutaneous mastocytosis with symptoms of associated histamine release, including urticaria. The patient did not know specifics regarding this event; she did not report further episodes or follow-up with a specialist. Her only other surgical history was a cesarean section for which she received a spinal anesthetic without complication. She reported taking no home medications. A complete blood count and basal metabolic panel were normal except for a high absolute basophil count of 0.1 K/uL. A physical exam and pre-anesthesia evaluation revealed no abnormal findings.

The patient received midazolam 2 mg and was transferred to the operating room. General anesthesia was induced with fentanyl 100 mcg, propofol 120 mg, and vecuronium 6 mg, which was followed by successful tracheal intubation with a cuffed endotracheal tube (ETT). Cefazolin 2 g and acetaminophen 1000 mg were administered prior to incision. General anesthesia was maintained with sevoflurane 3% inspired concentration in a mixture of O_2 1 L/min and air 1 L/min. The patient's normothermia was maintained with an upper body convective air-warming system and the administration of warm IV fluids. Neuromuscular blockade with vecuronium was maintained. Ondansetron 4 mg and dexamethasone 10 mg were administered, and neuromuscular blockade was reversed with sugammadex 200 mg at the end of the case. The trachea was extubated without complication, and the patient was transferred to the post-anesthesia care unit. She was discharged to home later that day.

Discussion

Mastocytosis encompasses a group of heterogenous clonal disorders caused by a mutation in a proto-oncogene encoding for a tyrosine kinase receptor known as KIT that regulates cell division.[2,3] This mutation results in the abnormal proliferation and accumulation of mast cells, which inappropriately degranulate and release inflammatory mediators in response to various triggers. The inflammatory mediators include histamine, heparin, tryptase, prostaglandins (especially D2) and cytokines.[2,4] Cutaneous mastocytosis is primarily confined to the skin and most frequently presents in childhood, which was the case for this patient. On the other hand, systemic mastocytosis mainly affects adults and involves 1 or more extracutaneous organs (bone marrow, gastrointestinal tract, lymph nodes, and spleen), with or without skin involvement.[1] A somatic autoactivating point mutation at codon 816 of the KIT-receptor gene is the cause of most systemic mastocytosis cases.[1] Research surrounding mast cell disorders is scarce, mostly consisting of case reports.

The World Health Organization (WHO) has established criteria on the 7 variants of mastocytosis based on the identification of neoplastic MCs by their morphological, immunophenotypic, and molecular characteristics. According to WHO, mastocytosis can be classified as cutaneous mastocytosis, indolent systemic mastocytosis, systemic mastocytosis with associated

hematological non-MC-lineage disease, aggressive systemic mastocytosis, mast cell leukemia, mast cell sarcoma, and extracutaneous mastocytoma.[2] Cutaneous mastocytosis may be further subclassified as maculopapular, solitary, diffuse, or telangiectasia macularis eruptiva perstans, which is rare. This patient had a diagnosis of maculopapular cutaneous mastocytosis, otherwise known as urticaria pigmentosa.

A diagnosis of systemic mastocytosis is made according to a combination of WHO established major and minor criteria, specifically 1 major plus 1 minor or a minimum of 3 minor criteria.[2] The detection of multifocal dense infiltrates of MCs in bone marrow or other extracutaneous organs constitutes the only established major criterion, which is confirmed by tryptase immunohistochemistry. If more than 25% of MCs in the biopsied infiltrate are spindle-shaped, have atypical morphology, or are immature, a minor criterion is met. Other minor criteria include detection of Kit point mutation at codon 816 in bone marrow, blood, or other extracutaneous organs, MCs in bone marrow, blood or other extracutaneous organs that co-express antigens CD117 with CD2 and/or CD25, and serum total tryptase persistently >20 ng/ml. Tryptase is a marker of MC clonality, although it is nonspecific to mastocytosis.[1] This patient never had bone marrow biopsied, genetic testing, or serum tryptase levels analyzed, so the possibility of systemic involvement was unknown. At present, no firm predictors for pediatric mastocytosis to persist into adulthood exist.[2]

Clinical manifestations include pruritus, urticaria, flushing, angioedema, hypotension, dyspnea, coagulopathies, and anaphylaxis.[1,2] Other symptoms include nausea, vomiting, abdominal and musculoskeletal pain, reflux, diarrhea, weight loss, fatigue, headache depression, mood changes, and lack of concentration, as well as tachycardia and bronchospasm intraoperatively.[2] In rare cases, hypersplenism, pathologic bone fracture from osteopenia or osteoporosis, ascites, malabsorption, and cytopenia can result from end-organ dysfunction due to tissue infiltration by MCs. The severity of symptoms is independent of the mastocytosis form and is primarily triggered by non-IgE-mediated mechanisms.[4] The only clinical manifestation observed during the preanesthetic evaluation was urticaria.

Hymenoptera stings are the most frequent triggers, followed by food and drugs, including radiocontrast media and drugs used in general anesthesia.[1] This patient had an IV contrast dye allergy with reported hives and a history of cutaneous mastocytosis during general anesthesia. She did not know the specific drugs she received; her previous anesthetic record was unavailable. The risk of systemic reactions during general anesthesia can be reduced by assessing the patient's previous reaction to a drug or reaction during surgery. Known triggers include temperature changes and infusion of cold solution, both of which were avoided in this case. Additional triggers include surgery and tissue trauma, as well as friction, tourniquet use, and stress.[1]

A Nordic expert group consensus recommends a coordinated, multidisciplinary approach in hospitals equipped to manage this disease.[2] Premedication to reduce preoperative stress and anxiety is recommended,[2] as was done in this case with midazolam. For patients with systemic mastocytosis, Matito et al[5] recommends histamine 1 and 2 antagonists, benzodiazepines, and corticosteroids if there is a history of anaphylaxis, and/or montelukast 1 hour before surgery to decrease perioperative MC-mediator release. According to Konrad et al,[4] if the previous use of

NSAIDs or paracetamol cannot be established, they should be avoided; however, if the patient has previously taken NSAIDs without complication, they may be given to minimize prostaglandin D2 release.

Anesthetic drugs associated with histamine release, such as morphine (phenanthrene opioid), mivacurium (benzylisoquinoline) and succinylcholine, should be avoided. Other high-risk drugs include rocuronium, thiopental, lidocaine, and bupivacaine. To prevent MC mediator-associated symptoms, anesthetic drugs with the safest profiles should be selected, including ropivacaine (amide), aminosteroid nondepolarizers (pancuronium, vecuronium), cisatricurium (newer benzylisoquinoline), propofol, etomidate, ketamine, and atropine. Halogenated gases and nitrous oxide are considered safe. Phenylpiperidine opioids, such as fentanyl, sufentanil, remifentanil, and alfentanil, are synthetic and associated with a lower rate of allergic reactions. The use of low-risk drugs and "drug challenges under strict vigilance" is recommended,[5] meaning if a high-risk drug is to be given, it should be administered in decreased or incremental doses by an attentive anesthetist prepared to promptly treat a negative reaction. Anaphylaxis should be promptly treated with epinephrine.

Manifestations of MC-mediated reactions can occur up to 4 hours postoperatively.[3] Overnight stay is suggested, which was not done in this case due to the nature of the surgical procedure and the patient's history of cutaneous rather than systemic mastocytosis. The frequency of perioperative anaphylaxis is higher in mastocytosis patients compared to the general population,[5] putting these patients at risk for complications. Anesthetists should familiarize themselves with the management of mastocytosis in the perioperative setting.

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Adductor Canal Block as a Rescue Analgesic in Orthopedic Surgery

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Keywords: knee arthroscopy, adductor canal block, saphenous nerve block, rescue analgesia, opioids, pain

Advances in knee arthroscopic procedures led to a rise in ambulatory surgery cases.[1-2] Pain control in the perioperative orthopedic patient contributes to improved patient satisfaction, early mobilization, decreased length of hospitalization, and decreased costs.[1] Opioids have historically been used for perioperative pain management.[1-7] Large opioid doses are associated with adverse events. Peripheral nerve blocks (PNB) in orthopedic surgery have increased with the rise in the number of ambulatory surgical procedures performed.[2] The adductor canal block (ACB) as a rescue analgesic may alleviate pain without compromising respiratory status or mentation.

Case Report

A 22-year-old, 180 cm, 77 kg male presented for a left anterior cruciate ligament (ACL) reconstruction. The past medical history included gastroesophageal reflux disease. The patient had no past surgical history. The preoperative vital signs were within normal limits. The patient was consented for a rescue analgesic PNB if needed in the post anesthesia care unit (PACU). Intravenous (IV) midazolam 2 mg was administered in the preoperative holding area for anxiolysis.

The patient was transported to the operating room where standard monitors were applied and O_2 8 L/min was administered via face mask. Once end-tidal oxygen (EtO_2) of 85% was achieved, general anesthesia was induced with fentanyl 100 mcg, lidocaine 100 mg, propofol 200 mg, and succinylcholine 100 mg IV. The trachea was atraumatically intubated with a 7.5 mm cuffed endotracheal tube (ETT) and ventilation was delivered by a mechanical ventilator. General anesthesia was maintained with sevoflurane 2% inspired concentration in a mixture of air 1 L/min and O_2 1 L/min.

One hour after the tourniquet was inflated the patient became hypertensive, tachycardic, and tachypneic while breathing spontaneously. In response, fentanyl 200 mcg and hydromorphone 1 mg IV were administered over the course of an hour and half. The remainder of the intraoperative course was uneventful. At the procedure's end, sevoflurane and air were discontinued and O_2 flow was increased to 10 L/min. The patient was emerged. After extubation criteria were met, the ETT was removed without incident or complication.

Upon arrival to the PACU, the patient was somnolent, but responded to touch. The postoperative vital signs were SpO_2 94%, respiratory rate of 8 breaths per minute, heart rate 85/min and blood pressure 128/76 mm Hg. Within five minutes of transferring care to the PACU nurse, anesthesia practitioners were asked to evaluate the patient for a complaint of pain. The vital signs were SpO_2 88%, respiratory rate of 6 and shallow, heart rate 110/min and blood pressure 144/82 mm Hg. A simple facemask with an O_2 flow of 10 L/min was provided and the SpO2 increased to

94%. Periodically the patient would awaken and complain of severe pain at the surgical site. We decided to perform an ACB because additional opioid use would be unsafe.

A procedural time out was performed. Under sterile conditions, an ultrasound machine with a 12-5 MHz linear transducer (Flex Focus 400 Anesthesia, BK Medical) was placed over the anteromedial aspect of the left leg mid-thigh level in a transverse position. Deep to the sartorius muscle, the superficial femoral vessels were identified. The sides of the adductor canal were identified as the vastus medialis laterally and the adductor longus medially. A 5 cm 21-gauge needle was advanced in an in-plane technique from lateral to medial, targeting the hyperechoic saphenous nerve just anterior to the femoral artery. After negative aspiration was verified, 1-2 mL of plain bupivacaine 0.5% was administered via catheter to confirm needle placement and spread of local anesthetic around the nerve. Incremental doses of 2-3 mL of bupivacaine 0.5% were injected via catheter for a total of 10 mL. The needle was repositioned to facilitate the spread of local anesthetic around the nerve.

The patient was reassessed 15 minutes later and reported a significant decrease in surgical site pain. In addition, the patient had improved alertness, ventilation, and hemodynamics. No additional opioids were required and the patient was transferred to phase II PACU.

Discussion

Anterior cruciate ligament reconstruction can be a painful surgery. Judicious management of pain, following knee arthroscopy is important to improving patient outcomes, faster rehabilitation, and patient satisfaction.[1-7] Unimodal opioid therapy is frequently used for pain control following knee arthroscopy; however, the use of opioids alone generally results in suboptimal pain control.[5] Often, large doses of opioids are required to achieve adequate pain control, which can increase the incidence of adverse events such as somnolence, respiratory depression, and nausea..[5] Regional anesthesia can provide optimal pain relief, decreased opioid use, and lead to faster recovery.[2-8] Femoral nerve blocks (FNB) reduce quadriceps muscle strength, which is essential for mobilization. Because the ACB is predominantly a sensory block, it may be a superior rescue block in patients after knee arthroscopy.[3-7]

Kwofie et al. examined lower extremity muscle strength after ACB compared to FNB. Volunteers had an ACB placed in one leg, and a FNB in the other using ultrasound guidance with 3% chloroprocaine 15 mL for each block. Maximal voluntary isometric contraction of knee extension and hip adduction, and balance were assessed. Quadriceps strength and balance scores were similar to baseline following ACB. Following FNB, there was a significant reduction in quadriceps strength and balance scores compared with baseline. There was no difference in hip adductor strength.[6] These results demonstrate preservation of muscle strength and balance with ACBs compared to FNBs.

Abdallah et al. compared postoperative opioid use and muscle strength in patients undergoing ACL reconstruction. Patients were randomized to receive ACB or FNB with 0.5% ropivacaine with epinephrine 1:200,000 20 mL. The researchers found that ACB was superior to FNB in both morphine consumption (-4.8 mg) and area under the curve for pain scores (-71 mm h). Contraction force meaurement for ACB and FNB at 45 min were 26.6. pound-force and 10.6

pound-force, respectively. The authors concluded ACB offered better analgesia and preservation of quadriceps strength compared to the FNB.[7]

In a single blind randomized controlled trial study by El-Feky et al., 80 patients undergoing knee arthroscopy received either ACB or an FNB preoperatively. Both blocks were performed with 0.5% bupivacaine 15 mL. At one hour postoperatively, analgesic consumption and pain scores were not significantly different between ACB and FNB groups. A significant decrease in quadriceps strength was also observed in the FNB group.[8] These findings are consistent with the previously discussed research, supporting the use of ACBs in patients undergoing knee surgery.[6,7]

Common problems when providing analgesia with opioids are a lack of effectiveness and significant adverse events. When appropriate, anesthesia practitioners should select non-opioid analgesic techniques such as an ACB. In this case report, the patient was difficult to arouse and had respiratory depression in the immediate postoperative period due to repeated opioid administration. To avoid further respiratory depression and preserve motor strength and function, we performed an ACB. Current literature supports the use of ACBs as a reasonable option for maintaining muscle strength, and equal to FNB for pain management following knee procedures. While this patient benefitted from a postoperative ACB, patients undergoing arthroscopic ACL reconstruction should be considered for preoperative ACBs to improve analgesia and reduce total opioid requirements. While ACBs primarily provide a sensory nerve block, a limitation to preoperative administration can be the surgeon's desire to fully assess postoperative neuromuscular function of the extremity. In addition, ACB is ineffective in controlling thigh tourniquet pain.

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Dexmedetomidine as Primary Agent for Awake Fiberoptic Intubation

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Keywords: dexmedetomidine, awake fiberoptic intubation, difficult airway management

Many anesthetists consider awake fiberoptic intubation to be the gold standard technique for securing a predicted difficult airway.[1] A variety of sedative agents have been evaluated; however, most are associated with respiratory depression and potential loss of a patent airway which could be detrimental for a patient with a difficult airway.[2] Dexmedetomidine, a selective α_2 agonist, could be the ideal sedative agent for awake fiberoptic intubation, especially when used as part of a multimodal pharmacologic regimen.

Case Report

A 73-year-old male with a body mass index of 41 kg/m^2 presented for a total thyroidectomy. He had been recently evaluated for a sore throat, cough, and dyspnea on exertion. Pertinent past medical history included hypertension, coronary artery disease, sleep apnea, type 2 diabetes mellitus, and obesity. Relevant past surgical history included coronary angioplasty with the placement of 3 stents. The patient's medication regimen included amlodipine 5 mg, aspirin 81 mg, metformin 500 mg, metoprolol 50 mg, and valsartan 320 mg. The patient reported multiple medication allergies. A non-toxic, multi-nodular goiter causing thyroid enlargement and retrosternal space impingement of the left lobe was discovered by computerized tomography. In addition, the scan revealed 60% subglottic stenosis and a 7mm tracheal lumen, which is approximately 30% of its normal caliber. The preoperative assessment included documentation of an American Society of Anesthesiologists physical classification of 4, Mallampati classification III, a short and thick neck, and active inspiratory stridor. The anesthesia practitioners caring for this patient developed an anesthetic plan that included an awake fiberoptic intubation.

In the preoperative holding area, intravenous (IV) access was obtained, lactated ringers begun and midazolam 1 mg IV administered. Upon arrival to the operating room (OR), the patient was moved from the stretcher to the OR table and standard noninvasive monitors applied. Baseline vital signs included a blood pressure of 207/100 mm Hg, heart rate of 83/min, respiratory rate of 16/min, and SpO_2 of 94%. After reverse trendelenburg positioning, the patient was given nebulized 4% lidocaine 4 ml over approximately 10 minutes. A bolus dose of dexmedetomidine 100 mcg IV was administered over 15 minutes followed by a maintenance infusion of 0.6 mcg/kg/hour IV until endotracheal intubation was achieved. Ketamine 10 mg IV was administered 4 times during the initiation of sedation. An additional midazolam 1 mg IV was administered along with glycopyrrolate 0.1 mg IV prior to laryngoscopy.

Preoxygenation was achieved with O_2 8 L/min via mask as a flexible fiberoptic bronchoscope loaded with a 7.0 mm endotracheal tube (ETT) was prepared. Laryngoscopy was performed using a McGRATH MAC video laryngoscope (Medtronic, Minneapolis, MN). Upon visualization of the vocal cords, 4% lidocaine 4 ml was administered topically via a laryngotracheal topical anesthesia kit. The fiberoptic scope was advanced through the glottic opening as the tracheal rings were visualized. The ETT was advanced over the fiberoptic scope and through the vocal cords. The fiberoptic scope was removed and the ETT cuff was inflated to seal. Proper ETT placement was confirmed with bilateral breath sounds, chest expansion, the presence of $EtCO_2$ and ETT condensation. The patient's vital signs following intubation included a blood pressure of 185/88 mm Hg and a heart rate of 78/min. General anesthesia was achieved with propofol 100 mg IV, rocuronium 30 mg IV and isoflurane at 1.2% expired concentration. At this point, the dexmedetomidine infusion was discontinued. The patient remained stable throughout the thyroidectomy and was successfully extubated upon completion of the procedure.

Discussion

Although the decision to perform an awake fiberoptic intubation may often be a relatively easy clinical decision, the accompanying pharmacologic regimen may present a greater challenge. The ideal pharmacologic regimen to complement awake fiberoptic intubation is one that would provide hemodynamic stability, maintenance of a patent airway with spontaneous ventilation, and blunting of airway reflexes.[3] Additionally, it would be advantageous to both the patient and the anesthesia practitioner if the patient remained comfortable, cooperative, and amnestic during the procedure.[3] There are several medication regimens available for use during an awake fiberoptic intubation including benzodiazepines, propofol, opioids, and regional anesthetic techniques. However, these medications have limitations related to respiratory depression and maintenance of a patent airway.[2]

Dexmedetomidine is a newer medication being utilized either as the sole sedative agent or as part of a multimodal pharmacologic regimen during awake fiberoptic intubation. Dexmedetomidine supports natural sleep pathways and produces a sedated yet easily aroused patient with minimal respiratory depression.[2] Furthermore, dexmedetomidine has the advantage of containing anxiolytic, analgesic, and antisialagogue properties.[2]

There are proponents for administering dexmedetomidine as the sole sedative for awake fiberoptic intubation as well as claims that dexmedetomidine is best utilized in combination with

other agents. Some argue that there are times when using only dexmedetomidine is feasible and that it can provide desirable conditions for performing an awake intubation.[2] In contrast, proponents of supplementing dexmedetomidine with other agents argue that a multimodal approach may achieve better intubating conditions, hemodynamic stability, and sedation for awake fiberoptic intubation.[4] Researchers comparing dexmedetomidine alone with the combination of dexmedetomidine and ketamine concluded that the addition of low-dose ketamine to dexmedetomidine was favorable compared to dexmedetomidine alone.[4] The combination of dexmedetomidine and ketamine provides additive sedation and helps stabilize the cardiovascular system by offsetting the potential bradycardia and hypotension caused by dexmedetomidine.[4] Additionally, researchers explored the benefit of using dexmedetomidine as a sedative agent in combination with airway blocks compared with performing an airway block with no sedation. They concluded that dexmedetomidine used in conjunction with an airway block produced more favorable intubating conditions compared to the airway block alone.[5] By utilizing dexmedetomidine with an airway block, a higher patient satisfaction score related to sedation and comfort was noted as well as better hemodynamic stability.[5] Therefore, based on these researchers' findings, the benefits of dexmedetomidine appear to be greatest when utilized as the main pharmacologic agent in a multimodal regimen for awake fiberoptic intubation.

There are currently multiple pharmacologic options other than dexmedetomidine available for awake fiberoptic intubation.[2] Traditional medical management with opioids such as fentanyl are useful because of their ability to provide sedation, analgesia, and hemodynamic stability during awake fiberoptic intubation.[6] Benzodiazepines such as midazolam provide amnesia and patient comfort during the procedure.[6] Researchers are currently investigating the use of propofol and remifentanil in conjunction with target controlled infusion technology with the goal of providing a dependable sedation level for procedures such as awake fiberoptic intubation.[7] However, despite the potential advantages of these pharmacologic options, the risk of respiratory depression and associated airway compromise reduces the benefits of using these agents during awake fiberoptic intubation.[6]

In the case described above, an awake video laryngoscopy assisted fiberoptic technique was chosen because of the patient's significant subglottic stenosis. This method offered a better visualization of the supraglottic airway and passage of the fiberoptic scope through the vocal cords. A multimodal technique with dexmedetomidine as the primary pharmacologic agent was utilized. The combination of dexmedetomidine and ketamine allowed for additive sedation and hemodynamic stability, which was especially advantageous for this patient with significant preoperative hypertension. The use of nebulized and topical lidocaine decreased the risk of coughing during the procedure. Midazolam provided additional anxiolysis and glycopyrrolate assisted with decreased secretions and improved visualization of the airway.

There is evidence that dexmedetomidine alone is sufficient as the sole sedative agent for awake fiberoptic intubation.[7] However, supplementing dexmedetomidine with additional pharmacologic agents may provide better conditions for awake fiberoptic intubation. Additional research on drug choice, dose selection, and timing of administration of supplemental medications would be beneficial. Perhaps in the near future, a pharmacologic gold standard for awake fiberoptic intubation will include dexmedetomidine.

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Transcatheter Aortic Valve Replacement under Deep Sedation

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Keywords: transcatheter aortic valve replacement, awake TAVR, TAVR anesthetic management, aortic stenosis

The transcatheter aortic valve replacement (TAVR) procedure is the standard of care for patients with severe, symptomatic aortic stenosis and at high risk of complications related to conventional open heart procedures.[1] The TAVR procedure was first performed in 2002 under sedation as a last resort treatment for aortic stenosis.[2] General anesthesia (GA) with endotracheal intubation became the required anesthetic for these patients because of the extensive use of transesophageal

echocardiography (TEE) imaging.[2] The transfemoral (TF) approach to a TAVR is the most common technique used, which can be accomplished under moderate/deep sedation.[3]

Case Report

A 74-year-old male with a body mass index of 29 kg/m^2 presented for a TF-TAVR. His medical history included severe aortic stenosis, obstructive sleep apnea (OSA), congestive heart failure with an ejection fraction of 35%, severe dyspnea, atrial fibrillation, previous myocardial infarction, hypertension, peripheral vascular disease, stage III lung cancer, type II diabetes mellitus, hypothyroidism, and previous smoking. Past surgical history included cardiac catheterization, multiple coronary artery bypass grafts, and bilateral carotid endarterectomy. The patient's preoperative laboratory values included blood urea nitrogen 33 mg/dL, creatinine 2.2 mg/dL, estimated creatinine clearance 28.1 mL/min, glucose 404 mg/dL, and hemoglobin A1c 7.6%. Additional values were within normal limits. The patient's baseline SpO_2 was 93%, heart rate 85/min, and blood pressure 142/74 mm Hg.

The patient was interviewed in the preoperative holding area and the anesthetic plan for sedation was discussed. Noninvasive monitoring and O_2 2L/min via nasal were applied. The patient received midazolam 2 mg intravenously (IV) and a loading dose of dexmedetomidine 80 mcg IV over 10 minutes. Additional peripheral IV and radial arterial access were obtained. On arrival to the hybrid operating room, O_2 4L/min via nasal cannula with $EtCO_2$ monitoring was applied. The patient was given propofol 40 mg IV for insertion of a central venous line (CVL). Central venous pressure was monitored throughout the procedure. The patient's SpO_2 decreased to 55%. A nasal airway was placed and the SpO_2 increased to 92%. The patient was given regular insulin 10 units IV and a continuous IV infusion at 5 units/hr was begun. Dexmedetomidine 1mcg/kg/hr was infused throughout the procedure. Ketamine 10 mg IV and midazolam 2 mg IV were given in preparation for femoral cannulation.

After bilateral injections to the groin areas of 1% lidocaine 10 mL, the cardiologist performed a lithoplasty balloon dilation of the right common iliac artery to access the aorta. Right ventricular apex pacing wires were placed via the left femoral vein and tested at 170/min to insure loss of the arterial waveform. External pacing was available to initiate a rapid ventricular rate and rescue pacing at 80/min. Heparin 7,500 units IV was administered prior to valve deployment resulting in an activated clotting time greater than 250 seconds. At the completion of an aortic balloon valvuloplasty, ventricular pacing at 170/min was initiated. Once loss of the arterial waveform was confirmed, a 26 mm Edwards SAPIEN 3 (Edwards Lifesciences Inc., Irvine CA) transcatheter heart valve was deployed. The patient received propofol 10 mg IV and ketamine 10 mg IV for insertion of the TEE probe. The probe remained in place for 45 minutes with no additional sedation required. The new valve placement and gradient was assessed with TEE and the probe was then removed.

The valve placement was considered successful. The patient's right peripheral lower pulse was unable to be palpated or heard by ultrasound. The cardiac surgeon performed a right femoral artery angiograph. The patient received an additional heparin 2,000 units IV. The patient became bradycardic with a heart rate of 35/min. Treatment with glycopyrrolate 0.2 mg IV resulted in a heart rate of 45/min. A total of 100 mL of urine and 50 mL of blood loss were documented.

Arterial blood gases were collected every hour. While blood glucose gradually decreased, no treatment was necessary. The total procedural time was 2.5 hours and the patient required no vasoactive support. The patient was transported directly to the cardiac intensive care unit.

Discussion

An anesthetic plan with moderate/deep sedation was based on the patient's severe comorbidities. There is recent evidence that TAVRs can be safely and effectively performed with sedation. Sedation instead of GA can be advantageous for patients with severe lung disease because it eliminates risks associated with mechanical ventilation.[4] Sedation techniques are more often successful with a TF-TAVR approach than with other approaches.[3] However, contraindications to sedation techniques for patients undergoing a TAVR do exist. A detailed history and preoperative interview will help with determining whether or not the contraindications are classified as absolute or relative.

Contraindications to sedation techniques include a history of a difficult intubation, severe OSA, high risk of aspiration, inability to tolerate supine positioning, patient refusal, severe dementia, transapical or direct aortic approach, concurrent surgical procedures, or extensive TEE requirements.[2] There is evidence that the intraprocedural conversion rate from sedation to GA with TAVRs is 12%.[1] The most common reason for conversion is hemodynamic compromise, defined as arrhythmias, significant hypotension, or cardiac arrest.[1] Respiratory complications were the second most common reason reported for conversion to GA.[1]

There is conflicting evidence related to whether or not GA is required for TEE probe placement to evaluate a newly placed valve.[4] The use of a TEE during sedation usually requires a greater amount of sedation, which can lead to worsening obstruction or hypoventilation.[2] Advantages of TEE use versus transthoracic echocardiography (TTE) include significantly less total procedural and fluoroscopy time, and less procedural acute kidney injury.[5] Renal failure can be associated with the amount of iodine contrast utilized, whereas, with TEE, less contrast can be used.[5] Complications can be detected earlier with TEE imaging. However, TTE images can be obscured by the chest wall, tissue, or a hyperinflated lung.[5]

The advantages of using sedation techniques with a TAVR are significant and the number of TAVR procedures being performed with sedation is increasing.[3] The most significant advantages to sedation with TAVRs include shorter procedure time, minimal hemodynamic instability, less need for vasoactive support, early awakening, better ability to detect mental status change, faster recovery time, shorter length of hospital stay and lower hospital cost.[3] There are various sedation techniques described in literature and anesthetic plans should be individualized. Dexmedetomidine is gaining popularity for use in a multimodal pharmacologic approach for sedation with a TAVR.[6] Dexmedetomidine associated bradycardia is attributed to the decreased central sympathetic outflow caused by stimulation of alpha 2 receptors.[7] The risk of bradycardia increases when a loading dose of dexmedetomidine is given too quickly or when a maintenance dose greater than 0.7 mcg/kg/hr is utilized.[7] The bradycardia described in this case study could have been less profound or possibly avoided with a lower dexmedetomidine infusion rate. General anesthesia is recommended when a less experienced practitioner is performing the

TAVR.[3] The advantages of GA include more reliable patient immobility, less risk of airway compromise, and elimination of the risk of emergent conversion to GA.[3]

There is evidence supporting the use of less invasive monitoring for TAVRs with sedation.[3] The team discussed not placing a CVL but because lithoplasty dilation of the common iliac artery was required, the decision to place the CVL was made. There is also evidence that recovering TAVR patients in a post-anesthesia care unit contributes to lower overall costs.[8]

This case report includes the details of a TF-TAVR with sedation for a patient with significant comorbidities and increased risks related to GA. Weighing the risks and benefits of all proposed interventions and being aware of evidence based best practices are conducive to the creation of a safe, individualized plan of care. Although bradycardic and desaturation events occurred, conversion to GA with its associated risks was avoided. Moreover, the valve placement was successful and the patient was transferred postoperatively in a timely manner and remained in stable condition.

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Quadratus Lumborum Block for Postoperative Pain Management

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Keywords: Regional anesthesia, open ventral hernia repair, quadratus lumborum block, pain management

Truncal nerve blocks have been utilized for the management of postoperative pain for over 40 years. Their utilization became popularized in 2001 when the transverse abdominis plane (TAP) block was introduced for abdominal wall analgesia.[1] Prior to the advancement of ultrasound technology, these techniques were performed by anatomical landmarks only. Since the evolution from landmark based placement to ultrasound-guided technique, more complex regional blocks have been implemented to provide safer and more effective anesthesia and analgesia. The quadratus lumborum block (QLB) is one such variant that provides analgesia to both somatic and visceral areas of the abdomen.[1]

Case Report

A 62-year-old, 69 kg, 157 cm female presented for open retrorectus ventral hernia repair. Past surgical history consisted of an exploratory small bowel resection in 2013. The patient continued to have recurrent small bowel obstructions and underwent an additional exploratory small bowel resection in 2014. This was complicated by an incisional hernia that was repaired with mesh in 2016. The patient began complaining of increased mid-abdominal pain in April 2018, and was re-evaluated for an incisional hernia repair. Past medical history included hypertension, NASH, gastroesophageal reflux disease and previous bowel obstruction. This patient's medication regimen was comprised of alendronate 70 mg, diphenhydramine 25 mg, metoprolol 50 mg, and pantoprazole 40 mg.

The initial anesthetic plan included the placement of a thoracic epidural for postoperative pain management. As part of the institutional standardized preoperative order set, the surgical team ordered a dose of subcutaneous heparin to be administered preoperatively. The anesthesia team was not consulted on this order prior to administration, and the dose was administered by the preoperative nurse. Upon evaluation by the anesthesia team, it was decided that the subcutaneous heparin administered prohibited neuraxial catheter placement. In order to provide postoperative pain relief, the anesthesia team decided to perform a quadratus lumborum block.

While in the preoperative area, noninvasive monitoring was instituted and oxygenation was delivered at 4 L/min via nasal cannula. The patient was placed in the sitting position and the back was prepped in a sterile fashion. Ultrasound was used to visualize relevant anatomy and needle guidance. A 21-gauge blunt bevel non-stimulating needle was inserted using an in-plane technique. The needle tip was visualized and advanced with ultrasound guidance until the needle tip was seen in between the transversus abdominis and quadratus lumborum muscles. After negative aspiration, 0.25% bupivacaine 20 mL was injected. Frequent negative aspiration was performed during injection to insure that no local anesthetic was inadvertently delivered

intravenously. This procedure was repeated contralaterally to provide full analgesic coverage to the abdominal wall.

Upon arriving to the operating room, noninvasive monitoring was reapplied and O_2 15 L/min via facemask was delivered for 5 minutes. General anesthesia was induced with midazolam 2 mg, lidocaine 50 mg, fentanyl 100 mcg, and propofol 150 mg intravenously (IV). Successful mask ventilation was verified, followed by IV administration of succinylcholine 80 mg. Direct laryngoscopy using a Miller 2 blade was performed and a 7.0 mm endotracheal tube was placed. The patient was placed on volume controlled ventilation with a mechanical ventilator at a FiO2 of 50%, and 1.5% sevoflurane to maintain general anesthesia. Dexamethasone 4 mg and ondansetron 4 mg were then administered IV. Rocuronium 50 mg was administered IV in order to achieve complete paralysis. Muscle paralysis was maintained by administered rocuronium 10 mg in intermittent boluses in order to maintain 1 of 4 train-of-four twitches for the duration of the procedure. Upon completion of the procedure, neuromuscular blockade was successfully antagonized with sugammadex 200 mg IV. The procedure lasted five hours with a total of fentanyl 200 mcg being administered.

Once in the post-anesthesia care unit (PACU), monitoring was reinitiated. The patient maintained baseline vital signs throughout the duration of the PACU stay and had no complaints of nausea and no occurrences of vomiting. One dose of hydromorphone 0.4 mg was required 20 minutes into her stay in the PACU. Upon discharge from the PACU, the patient was transported to the medical-surgical unit and was placed on a hydromorphone patient controlled analgesia (PCA) pump with scheduled acetaminophen 975 mg and ketorolac 30 mg. The PCA settings were programed to allow the patient to receive 0.2 mg every 10 minutes with a lock out setting of 1.2 mg/hour. Over the next 24 hours the patient received a total of 1.4 mg of hydromorphone. After 48 hours, an additional 2.2 mg of hydromorphone was delivered IV and the PCA was discontinued. After 3 days post-operative stay as an inpatient in the hospital, the patient was discharged home with no complications.

Discussion

Thoracic epidurals are considered to be the gold standard in surgical procedures that involve an open abdomen. Recently, new trends are attempting to identify if less invasive techniques are available in order to achieve the same outcome. One of these methods is the QLB. The quadratus lumborum is a deep muscle located in the posterior abdominal wall that originates from the iliac crest and inserts onto the 12th rib and transverse processes of the first lumbar to the fourth lumbar vertebrae.[2-4] There are currently three approaches that are utilized in order to achieve analgesia; the quadratus lumborum 1 (QL1), quadratus lumborum 2 (QL2), and transmuscular quadratus lumborum (TQL). In each technique, local anesthetic is injected into the thoracolumbar fascia that encapsulates the muscles in the back. This allows the local anesthetic to spread in a craniocaudal direction that reaches the seventh thoracic to first lumbar dermatomes.[1,4-6]

Ultrasound guided quadratus lumborum blocks are a new option for truncal analgesia that the anesthesia provider can utilize. Current evidence does not suggest one approach to be superior to another. With that being said, it shares the same indications of use as the TAP block that include,

but are not limited to: large-bowel resection, open/laparoscopic appendectomy, cholecystectomy, cesarean section, open prostatectomy, renal transplant surgery, nephrectomy, exploratory laparotomy, and bilateral blocks for midline incisions.[1,2] There were three main reasons why the QLB was chosen over the TAP block in this particular case. First, in order to achieve maximum analgesic coverage over the abdomen, four injections are required with the TAP block compared to two with the QLB. Second, studies have demonstrated that patients who receive a QLB have analgesic coverage for a duration lasting as long as 24-48 hours.[1,8] While the TAP block has been demonstrated to be effective for 8-12 hours.[1,8] Lastly, the QLB has demonstrated evidence of providing analgesic coverage to both somatically and viscerally, as opposed to the TAP block which has only demonstrated somatic analgesic coverage.[1,4-6]

Evidence has also demonstrated that the QLB is an excellent approach to perioperative pain control. Blanco, Ansari and Girgis claim that patients have a pain reduction to 1 or 2 on the Visual Analog Scale (VAS), with functional analgesia lasting up to 24 hours. When the QLB is given in conjunction with a nonsteroidal anti-inflammatory drug and acetaminophen, patients have a significant reduction in opioid consumption. In one double blind, randomized controlled trial of 50 parturients after cesarean section; those receiving a QLB consumed 56% less morphine (10 mg) in the first 12 hours as opposed to those not receiving the block (23 mg). Blanco, Ansari, Raid and Shetty replicated the study once again, but this time compared the analgesic effects to patients receiving a TAP block. Their results concluded that the patients who received the QLB instead of the TAP block, consumed less morphine in the 12th, 24th, and 48th hour period.[8] This lead to decreased side effects such as nausea, vomiting and decreased gut motility. Improved pain control facilitated early ambulation, which is one of the leading measures in order to prevent deep vein thrombosis.[1,7]

In conclusion, the QLB, when combined with multimodal postoperative analgesia, has been shown to be an excellent method anesthesia providers can integrate into practice as a means to improve postoperative analgesia and decrease morbidity. In this specific case study, scheduled acetaminophen and ketorolac combined with the QLB helped reduce the need for opioid consumption of hydromorphone to 1.4 mg over the first 24 hours. Throughout postoperative day one, the lowest pain score the patient reported was 5. The QLB decreased pain scores to a tolerable level as verbalized by the patient. This allowed for early ambulation and no complications upon discharge.

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Serotonin Syndrome on Emergence

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Keywords: serotonin, serotonin syndrome, selective serotonin reuptake inhibitors, and SSRIs

Serotonin syndrome (SS) is an uncommon but potentially life-threatening condition that can be difficult to diagnose perioperatively. A case is presented here where a patient developed multiple episodes of fever, tachycardia, muscle rigidity, and agitation following emergence and continuing overnight. This case report discusses contributing factors, clinical presentation, and postoperative management of SS.

Case Report

A 52-year-old male was scheduled for a ventriculo-peritoneal-pleural shunt (VPPS) placement. The previous VPPS was removed 13 years ago secondary to infection. Since then, he had an endoscopic third ventriculostomy that failed, and his headache returned. A review of his previous anesthetic record revealed a history of post-operative nausea and vomiting. He had a medical history significant for hydrocephalus, seizures managed with oxcarbazepine 600 mg, with his last reported seizure approximately four months ago. His depression has been managed with paroxetine 25 mg and protriptyline 10 mg.

He was given transdermal scopolamine 1.5 mg and intravenous (IV) midazolam 2 mg preoperatively. Standard monitors were placed, and general anesthesia was induced using IV fentanyl 150 µg, lidocaine 50 mg, propofol 300 mg, and rocuronium 50 mg. Anesthesia was maintained with 2.3% inspired sevoflurane, oxygen 1 L/min., and air 1 L/min. Other intraoperative IV medications administered included acetaminophen 1000 mg, cefazolin 4000 mg, dexamethasone 8 mg, rocuronium 90 mg, fentanyl 100 µg, phenylephrine 600 µg, ephedrine 10 mg, ketorolac 30 mg, and ondansetron 4 mg.

At the end of the procedure, a train-of-four count of 4/4 was observed, and IV sugammadex 200 mg was given. Sevoflurane was discontinued, and O_2 flow was increased to 10 L/min. Once the patient was responsive and following commands, the endotracheal tube was removed. The patient was able to assist in moving onto a stretcher and placed on O_2 at 10 L/min delivered by simple face mask.

Prior to transport, clonus was observed in his upper extremities with arms elevated above his chest and elbows flexed. Unable to relax his arms, the patient was visibly agitated with a heart rate of 120/min. He was able to give a thumbs up on command, while his arms remained rigid. His arms relaxed immediately following IV administration of propofol 30 mg, and quickly regained control of his upper extremities. Upper arm rigidity returned within 5 minutes and IV midazolam 2 mg was given, but the dose administered was ineffective. Additionally, a second dose of propofol 50 mg was given and the patient regained control of his upper extremities. After the he remained asymptomatic for 5 minutes, the patient was transported to the post-anesthesia care unit (PACU).

Upon arrival to the PACU, the patient was tachycardic (120/min), afebrile, tachypneic, agitated, and the rigidity in both upper extremities returned. The patient received a second postoperative dose of IV midazolam 2 mg, which relieved his symptoms. The patient was transported for a cranial computed tomography (CT) scan to rule out hemorrhagic stroke, and no significant changes were identified when compared to prior CT scans. The patient was transported back to PACU and neurology was consulted.

The neurologist diagnosed the patient with SS, based on symptom presentation and medication history. Paroxetine, protriptyline, intraoperative fentanyl and ondansetron were thought to be primary contributors. He was admitted to the intensive care unit, remaining mildly febrile (101.6 °F), and tachycardic (low 100s/min) overnight. Serotonergic medications were avoided until the patient's symptoms resolved. He became asymptomatic on post-operative day two and he was transferred to the general surgical care unit.

Discussion

Serotonin syndrome may result when serotonergic medications are combined with other antidepressant medications, including selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), among others.[1] SSRIs and TCAs both increase serotonin levels by preventing its reuptake.[2] The combination of a SSRI and TCA with other serotonergic medications may have exposed the patient to abnormally high levels of serotonin in the central nervous system, thus leading to SS.[1]

Recent case reports have discussed the link between fentanyl and SSRIs causing SS.[1] Fentanyl and other phenylpiperidine opioids are both evidenced in the literature to augment the release of serotonin and cause minor serotonin reuptake inhibition.[1] While the incidence of SS in patients receiving both a serotonergic agent and fentanyl is low (0.09%), it is still higher when compared to patients on serotonergic agents without fentanyl administration (0.005%).[3] Morphine does not have serotonergic properties, so it should be an opioid of choice in this population.[4] Ondansetron, a 5-hydroxytryptamine type 3 antagonist, has been proposed to increase available serotonin. Such an increase may not be significant enough to cause toxicity, even when combined with other serotonergic agents.[5]

Serotonin syndrome can be mild, moderate, or severe.[6] Patients with mild symptoms may present mild hypertension, tachycardia, mydriasis, tremor, hyperreflexia, myoclonus, and diaphoresis, but without fever.[6] Moderate symptoms may include mild agitation, hyperactive bowel sounds, hyperthermia, ocular clonus, altered speech, and hypervigilance.[6] Severe symptoms may include greater hemodynamic instability, muscle rigidity, delirium, and hyperthermia (over 41.1°C).[6] Severe cases may progress to include rhabdomyolysis, metabolic acidosis, seizures, coma, myoglobinuria, renal failure, diffuse intravascular clotting, respiratory distress syndrome, and death.[6]

This patient's seizure history may have confounded the diagnosis of SS. The diagnosis of SS should be based on a review of current medications and symptoms since there are no laboratory tests that can be reliably used to diagnose it.[4] The Hunter Serotonin Toxicity Criteria is used to diagnose serotonin syndrome for patients exposed to a serotonergic agent. This tool has a sensitivity of 84% and specificity of 97%[7] SS Signs and symptoms objectively measured by this tool include spontaneous clonus, inducible clonus with agitation or diaphoresis, ocular clonus with agitation or diaphoresis, tremor with hyperreflexia, or hypertonic with temperature greater than 38°C or inducible clonus.[7]

Treatment for SS is focused on supportive management of the patient's symptoms. Immediate management should include IV fluid administration, cardiac monitoring, oxygen support, and stopping serotonergic medications.[1] Benzodiazepines are useful to control tremors and agitation,[1] but severe cases may need muscle relaxation and subsequent intubation.[6] Resolution of SS occurs within 24 hours after cessation of serotonergic medications in 60-70% of patients.[4] Cyproheptadine is a 5-hydroxytryptamine type 2A antagonist used to treat patients with moderate to severe SS, but is only available in oral form.[1] Chlorpromazine is a D2 dopamine receptor antagonist, that can be given intravenously for treatment of SS, but may exacerbate hypotension in volume-depleted patients.[4] Intralipid has also been proposed as a treatment for SS, by way of pulling serotonergic agents into the intravascular compartment.[4] Prevention is the best treatment of SS. Avoidance of serotonergic medications is important in patients concomitantly taking SSRIs and TCAs. The challenge for the anesthesia practitioner is to identify patients at risk for SS and to minimize agents that may trigger it.

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Tranexamic Acid in Postpartum Hemorrhage Management

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Keywords: tranexamic acid, TXA, post-partum hemorrhage, cesarean section, C-section

Introduction

Postpartum hemorrhage (PPH) is the most prevalent cause of maternal death around the world.[1] PPH is defined as an estimated blood loss greater than 500 mL following vaginal birth, greater than 1000 mL after cesarean section (C-section), or any blood loss that is sufficient to cause hemodynamic instability.[1] PPH is concerning as the incidence of C-section deliveries are increasing by 25-30% in many parts of the world.[2] C-sections compared to vaginal births have nearly double the expected blood loss and five times the rates blood transfusions (1% vs 5%).[2] During delivery, fibrinolytic activity increases when the placenta separates from the uterine wall. This fibrinolytic activity can lead to clotting deficiencies lasting 6-10 hours, and causing continued bleeding after delivery.[3]

Tranexamic acid (TXA) is a synthetic analog of the amino acid lysine. It works by competitively binding to plasminogen sites and acts as a potent antifibrinolytic agent thereby enhancing the patient's own hemostatic effectiveness.[3,4] TXA has been shown to reduce blood loss, mortality, and transfusion rates in major surgeries such as orthopedic and trauma surgeries.[5] The routine use of TXA in obstetric women is not universally agreed upon at this time.[6] Dosing of TXA in

research trials has ranged widely from 1 mg/kg to 100 mg/kg.[2] The purpose of this report is to review evidence for use of TXA in PPH.

Methods

The PICO (population, intervention, comparison and outcome) question developed for this topic is as follows: "Does administration of intravenous TXA significantly decrease blood loss in obstetric women presenting for delivery compared to those who do not receive TXA?" A literature search was performed through CINAHL and PUBMED. The article search was aimed to find studies within the last 8 years, in English, that were level II or higher regarding PPH treatment with TXA. Data was evaluated and analyzed through use of an evidence matrix.

Search terms: Post-partum hemorrhage, Tranexamic acid, C-section, TXA

Levels of evidence: Level II or higher

Literature Analysis

A randomized control trial by Ahmed et al. compared the use of 10 mg/kg TXA given over 5 minutes just prior to elective C-section versus no TXA.[6] Patients were treated with 10 units of oxytocin infused over 30 minutes and 1 mg methylergonovine intramuscular after delivery. Estimated blood loss was calculated by weight from placental delivery to the end of surgery and also from the end of surgery to two hours postoperatively. If additional uterotonics were needed after 2 hours postoperative, they could be given after estimated blood losses were totaled. Results showed that blood loss from placental delivery to closure of skin and also from skin closure to 2 hours postoperative loss was about 30% less (391 vs 597 mL) in the group that received TXA ($p<0.001$).[6] TXA significantly decreased blood loss in women with previous C-sections who were at higher risk for bleeding. There were significant differences in postoperative hemoglobin and hematocrit of 10.3 g/dL and 36.2% in the TXA group versus 9.2 g/dL and 34.5% in the control group (Hgb $p=0.001$ and Hct $p=0.001$).[6] None of the subjects experienced anaphylactic reactions or thromboembolic complications. No fetal complications or significant decreases in APGAR scores were noted. Only minor symptoms such as gastrointestinal upset were noted in the TXA recipients. In the control group, 3 patients did experience PPH 12-18 hours after surgery, but none in the TXA group. Limitations of this study include non-blinded care team members to TXA administration. Blood loss estimates were made objectively by the method of weighing sponges. The average blood loss decrease of the TXA group was 30% (206 mL)[6] and provides evidence supporting the use of TXA prior to elective C-section.

Goswami et al. performed a double-blind randomized control trial to observe the effects of different weight-based dosages of TXA versus placebo on measured blood loss.[2] Blood loss was measured by volume and weight from the delivery of placenta to 24 hours postoperatively. There were 3 intervention groups that included: 1) 10 mg/kg TXA; 2) 15 mg/kg TXA; and 3) placebo. TXA doses were administered intravenously 20 minutes prior to incision. Inclusion criteria for this study were patients with an ASA status 1-2, at least 18 years old, and hemoglobin 7-10 g/dL. Anesthetic technique for the study was subarachnoid block of 2-2.5 mL of 0.5% hyperbaric bupivacaine. After delivery of fetus, 20 units of oxytocin in 500 mL was administered at a rate of

8 mU/min. Blood loss was measured after delivery of placenta and continued for 24 hours. In order to exclude amniotic fluid, blood loss was calculated by weight. Results from the study showed the average blood loss reduction in the two TXA groups compared to control group were 146.34 +/- 56.32 mL (10 mg/kg) and 262 +/- 31.51 mL (15 mg/kg).[2] Blood loss in the group with a higher dose of TXA (15 mg/kg) was 115.66 +/- 24.81 mL less than the 10 mg/kg dose ($p<0.05$).[2] There were no statistically significant differences in the groups with regard to postoperative blood loss. Blood transfusions were needed in two patients in the control group and none in the two TXA groups ($p=0.02$).[2] Excluding nausea, there were no significant adverse effects in any of the groups. A limitation of the study includes blood loss not being measured until after the placental loss, which means total blood loss could actually be higher. The group with 15 mg/kg TXA had significantly longer surgical times, which could imply high variability in the skill and experience in the surgeon. Regardless, the 15 mg/kg group still had significantly lower blood loss than the 10 mg/kg and control groups. This study demonstrates reduced blood loss when using TXA at the time of delivery.

Mirghafourvand et al. performed a double-blind randomized control trial in 120 low-risk women presenting for vaginal birth.[7] The study compared administration of 1 gram TXA versus placebo with all subjects receiving 10 units oxytocin after delivery of the fetus. Blood loss was calculated from preoperative hematocrit levels and 12-24 hours after delivery. In addition to 10 units oxytocin, doses of TXA or placebo were administered over 10 minutes after delivery of the fetuses' anterior shoulder. All gowns, sheets, dressings and tampons were weighed before and after use. There was no significant difference in mean blood loss from delivery of the fetus to delivery of the placenta in the two groups ($p=0.523$).[7] There was a significant difference in the TXA group in the mean blood loss from delivery of the placenta to 2 hours postpartum (69 vs 108, $p<0.001$).[7] There was significantly less blood loss in the TXA group than the control group by an average of 140 mL ($p=0.036$).[7] The incidence of calculated PPH (EBL>1000 mL) was significantly lower in the TXA group (7%) compared to the placebo group (18%, $p=0.048$)[7]. Limitations of this study include a small sample size and differences in administration times. This study supports the use of TXA for vaginal births to reduce postpartum blood loss.

Gungorduk et al. conducted a randomized, double-blind placebo-controlled study including 660 women undergoing elective C-sections.[3] This study compared the administration of 1g TXA to placebo prior to C-section and estimated blood loss. TXA was administered 10 minutes prior to incision. After fetal delivery, all subjects were given a 5-unit bolus of oxytocin, and then 30 units in 500 mL lactated ringer's solution was infused at a rate of 125 mL/h. Blood loss estimates were calculated from hematocrit levels prior to surgery and also 48 hours postoperatively. Significantly fewer women in the TXA group reached PPH (EBL>1000 mL) (7 vs 19, $p<0.03$). The mean estimated blood loss was significantly lower in TXA group than the control group by about 100 mL (499.9 +/- 206.4 mL vs 600.7 +/- 215.7 mL, $p<0.001$).[3] No significant difference was found in the need for blood transfusions between the two groups ($p=0.28$).[3] Women in the TXA group needed fewer additional uterotonic agents than the placebo group (28 vs 48, $p=0.02$).[3] No subjects needed additional surgeries, such as hysterectomy, to control bleeding. Patients in the TXA group had significantly higher postoperative hemoglobin and hematocrit levels (Hgb 9.9 +/- 0.6 vs 9.7 +/- 0.5 g/dL, $p=0.001$; Hct 30.6 +/- 1.5 vs 30.2 +/- 1.1, $p<0.001$).[3] In the TXA group, 53 (16%) women experienced nausea vomiting or diarrhea. There were no differences in fetal outcomes. Thromboses did not occur in any women in the TXA group.

Limitations of this study include a relatively small sample size and the exclusion of patients at high risk for hemorrhage. This study supports the use of TXA to reduce PPH in women undergoing C-sections.

Xu et al. conducted a randomized, double-blind control trial of the effects of TXA in 174 primapara C-section women aged 22-34. Subjects were randomly assigned to receive either 10 mg/kg TXA IV over 10 or 20 minutes prior to spinal anesthesia or placebo. After delivery of the fetus 10 units of oxytocin and 0.4 mg methylergonovine were given IV. Blood loss was collected and calculated by weight at two different times (from the delivery of placenta to end of C-section and the end of C-section to 2 hours postoperative).[4] Blood loss was determined to have stopped if the rate was less than 50 mL of blood in 10 minutes. Threshold for transfusion for packed red blood cells was 8.0 g/dL. The difference in blood loss between the two groups in the time period between placental delivery and end of C-section did not differ (TXA 336.7 +/- 151.2 mL vs 368.5 +/- 156.4 mL, p=0.17).[4] A significant difference was found in total blood loss between the groups in the time period between end of C-section and 2 hours postoperative (397.2 +/- 160.1 mL vs 441.7 +/- 189.5 mL, p=0.02).[4] PPH ceased in 81 women who received TXA versus 65 in the placebo group (p<0.01).[4] The TXA group had a decreased risk of PPH during delivery of placenta to end of C-section (18 vs 27 in the placebo group)(p=0.04).[4] Fewer women in the TXA group met the threshold to receive blood transfusions (8 vs 19).[4] Mild transient side effects including nausea, vomiting, and phosphenes, were more likely in the TXA group. Severe side effects included two incidences of deep vein thromboses in each group. The authors discuss weaknesses of this study including how TXA was unable to decrease blood loss in the first period of delivery, and inquired if it should be given even earlier in future studies. The side effects of this study were mostly minor. Deep vein thromboses occurred equally in both groups. This study is consistent with previous studies on decreasing blood loss and provides further support for use of TXA compared to no TXA.

Study	**Dose/Timing**	**Population**	**Results**
Ahmed et al.[6]	Independent variable -10 mg/kg TXA 5 min prior to C-section -No TXA Dependent variable -EBL during surgery -EBL from end of surgery to 2 hrs post	N=124 -Singleton pregnancy -Full term -Elective CS	Average blood loss -TXA: 39 mL -No TXA: 597 mL (p=0.001)
Goswami et al.[2]	Independent variable -15 mg/kg TXA -10 mg/kg TXA -No TXA Dependent variable -Calculated blood loss by weight	N=90 -ASA 1 or 2 -18 y+ -Hgb 7-10 -Elective CS	Average blood loss -No TXA: 527.17 mL (+/-88) -TXA 10 mg/kg: 376.83 mL (+/-31) -TXA 15 mg/kg: 261.17 mL (+/-56) Difference between 10 mg/kg and 15 mg/kg was 115.66(±24.8 mL) (p<0.05)

Mirghafourvand et al.[7]	Independent variable -1 gram TXA -No TXA Dependent variable -Calculated blood loss -Measured blood loss From delivery of fetus to delivery of placenta and from placental delivery to end of second hour after birth	N=120 -18-35 y -Cephalic presentation -38-42 weeks -Normotensive (<140/90) -Vaginal birth	Calculated blood loss -TXA: 519 mL -No TXA: 650 mL (p=0.036) Measured blood loss from placental deliver to 2 hours postpartum -TXA 69 mL -No TXA 108 mL (p<0.001) Frequency of calculated blood loss>1000 mL -TXA 7% -No TXA 18% (p=0.048) No significant difference in blood loss from delivery of the fetus until placental expulsion in the two groups
Gungorduk et al.[3]	Independent variable -1 gram TXA 10 min prior to incision -No TXA Dependent variable -EBL (calculated) -EBL>1000 mL -Transfusion need	N=660 -38-weeks gestation -elective C-section	Mean EBL -TXA: 499.9 mL -No TXA: 600.7 mL (p<0.001) EBL>1000mL -TXA: 2.1% -No TXA: 5.8% (p<0.03) Additional uterotonics needed -TXA: 8.5% -No TXA: 14.5% (p=0.02)
Xu et al.[4]	Independent -10 mg/kg TXA 10-20 min before spinal anesthesia for C-section Dependent (EBL during 2 periods) -placental	N=174 -Primipara undergoing C-section	EBL end of CS →2h postpartum -TXA: 46.6± 42.7 mL -No TXA: 84.7±80.2 mL (p<0.01) Total quantity blood from placental delivery →2h postpartum -TXA: 379.2±160.1 mL -No TXA: 441.7±189.5 mL (p=0.02)

	delivery→end of C-section -from end of C-section→2 hours postpartum		<u>Blood loss from placental delivery→end of CS</u> -No difference between TXA and control group (p=0.17) <u>PPH Ceased</u> -No TXA: 65 (75.6%) -TXA 81: (92%) (p<0.01)

Conclusion

Blood loss

Blood loss can be difficult to measure accurately during vaginal birth and C-section. Visual estimation is notoriously underestimated by up to 571 mL and hematocrit levels can be overestimated by 2.1 times.[6] In the studies reviewed, administration of TXA leads to decreased blood loss by as much as 30%.[6] Interestingly, in the studies by Xu et al. and Mirghafourvand et al., TXA did not decrease blood loss during surgery but it did decrease the blood loss from end of C-section to 2 hours after surgery.[6,7] The average blood loss differences between the TXA and placebo groups in the included studies ranged between 100-250 mL. While this difference may not always be clinically significant, any intervention to decrease blood loss in high-risk patients would be of value. The study by Xu et al., showed TXA decreased the number of blood transfusions (8 vs 19) and, therefore, decreased the associated risk and cost.[4]

Timing

Several studies indicate the importance of prophylactic administration of TXA. A range of 5-20 minutes prior to incision was observed in the included studies. None of the studies were designed to compare administration timing differences. Hypotension is common with rapid injection and an infusion rate of 1 mL per minute is suggested by Ahmed et al.[6] Shakur et al. found that TXA should be given as early as possible when PPH is diagnosed since data showed no benefits when TXA is given after 3 hours.[1] This is due to early activation of fibrinolysis after birth which can last up to 6-10 hours after delivery and lead to increased blood loss.[3] Xu et al. observed that TXA did not decrease blood loss in the first period of delivery, and inquired if it should be given even earlier in future studies.[4]

Dosing

There was a wide range of TXA doses discussed throughout the literature search. Goswami et al. compared two doses for prophylactic treatment of anemic patients presenting for C-section.[2] They found that both 10 mg/kg and 15 mg/kg significantly decreased blood loss and blood transfusions, but 15 mg/kg was more effective without increases in side effects.[2] In most of the studies, 1 gram of TXA was given at the time of incision and effectively reduced blood loss with no significant increase in thromboembolic activity. The WOMAN study also used 1 gram TXA

and observed significantly decreased death rates.[2] Caution should be used with higher doses. Myles et al. conducted a study of 4,662 patients undergoing coronary artery surgery who were given TXA IV at high doses of 100 mg/kg.[8] Due to seizures in 15 TXA subjects versus 2 in the control group, the dose was reduced to 50 mg/kg during the study. Decreasing the dose did not decrease the number of seizures in this population. This study used very high doses of TXA; about 5 to 10 times higher than other studies.

Safety

Safety is a major concern in this population of women due to the hypercoagulable state that occurs during pregnancy and, also, the potential of harm from medications passing through the placenta to the fetus. These studies indicate TXA administration does not increase the risk of DVTs nor thromboembolic complications.[1-9] The most common side effects associated with TXA were minor and include nausea, dizziness, vomiting and diarrhea.[2-4] TXA crosses the placenta but concentrations are minimal and current literature does not provide any evidence of harm to the fetus. There was no variation in APGAR scores between the groups and, NICU admissions or length of stay for the infant did not increase.[3] Breastfeeding is also considered safe after receiving TXA since concentrations are 1/100th of the mother's blood concentrations.[9] Over 30 studies published have shown efficacy of TXA in reducing blood loss during delivery or after cesarean delivery with no significant increases in thromboembolic events.[9]

Limitations of this review include relatively small sample sizes in each of the studies. Most of the studies included only low risk subjects. Due to this limitation, a safety profile was difficult to determine with much confidence. The WOMAN study has a very large subject size of 20,021 and has determined TXA to be safe in this population.[1] The studies were not designed to determine the most effective timing but it appears that earlier administration is beneficial.[4] Future research should focus on improving accuracy of estimating blood loss during C-section and vaginal births. The level of evidence of the studies included are level II randomized control trials but higher level and larger studies would be preferred. TXA was used in combination with other uterotonics as is standard practice. Therefore, TXA should be used in combination to obtain the same results in these studies. The most common doses used were 1 gram, 10 mg/kg, and 15 mg/kg. The dose of 15 mg/kg was shown to be most effective without increasing side effects, but it is possible that a more effective dose exists.

Recommendations for current practice include early prophylactic administration of 15 mg/kg TXA IV in patients who are anemic or high risk for PPH. It is also recommended that patients who experience PPH after vaginal or C-section birth receive 15 mg/kg as early as possible to decrease further blood loss.

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Does Propofol TIVA Reduce Rate of Metastasis Following Tumor Excision?

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Keywords: TIVA, metastasis, cancer recurrence, propofol, inhalation anesthetics

Introduction

Surgical removal of a cancerous tumor is commonly used to remove cancer from the body. Although this method can remove most of the tumor, there is a risk that small pieces of the tumor can be disrupted and enter the blood stream and spread throughout the body. If this occurs during surgical stress when metabolic and neuroendocrine changes depress the immune system, small particles of the cancerous tumor can be transported elsewhere and result in metastasis postoperatively.[1] The choice of anesthetic during a tumor removal surgery has been found to be a factor in postoperative cancer metastasis occurrence. Inhaled anesthetic agents, like sevoflurane,

may promote cancer metastasis by inhibiting natural killer (NK) cell cytotoxicity and inhibiting t helper cell proliferation.[2] Propofol based total intravenous anesthesia (TIVA) promotes action of t helper cells and has anti-inflammatory properties.[2] Researchers are finding that a propofol based TIVA can decrease the risk of postoperative metastasis.

Methodology

As the framework for this evidenced based review, the population, intervention, comparison, and outcome (PICO) were identified to formulate a research question. In patients undergoing surgery to remove a cancerous tumor (P), does the use of a propofol TIVA (I) result in less cancer metastasis postoperatively (O) than the use of inhalation anesthetics (C)?

Online databases including the National Center for Biotechnology Information, Ovid, PubMed, and Science Direct were utilized for the literature review along with the academic anesthesia journal *Current Reviews*. Keywords used included anesthesia, cancer, and metastasis which yielded 890 responses. Adding the keyword propofol reduced the results to 67. Filters included English text, full text availability, scholarly peer reviewed journals, academic journals, and studies published between 2010 and 2018. Each of the articles selected were reviewed for relevance to the PICO question. Systematic reviews, literature reviews, retrospective analyses, and randomized controlled clinical trials (RCT) were included. Articles relating to regional anesthesia and blood transfusions were excluded. A total of 7 studies were analyzed for this review.

Literature Analysis

A summary of the literature analyzed for this report is presented below (see Table). Wigmore et al. performed a retrospective cohort study involving patients who presented for elective surgery to remove cancer over a period of 3 years at the Royal Marsden Foundation Trust in London.[1] Patients were divided into 2 groups based on whether they had received a general anesthetic with volatile agents or a propofol TIVA for excision of malignant tissue. After confirming that inclusion and exclusion criteria were met, 3,316 and 3,714 participants were assigned to the inhalation and TIVA groups, respectively. A Kaplan-Meier test was used to calculate overall survival rates in each group. The average survival rate at 1 year for participants in the propofol TIVA group was 94.1% and 87.9% for those in the inhalation group. After multivariate analysis, the hazard ratio for deaths in participants receiving a volatile anesthetic rather than a propofol TIVA was 1.46. These researchers concluded that participants who received an inhalation anesthetic had worse overall outcomes regardless of severity of surgery or metastasis than those who received a propofol TIVA.

Soltanizadeh, Degett, and Gögenur systematically reviewed patient outcomes after cancer excision surgery when the use of inhalation agents was compared to propofol TIVA.[2] PubMed, Scopus, EMBASE, and Cochrane Library were utilized. Animal studies, in vitro studies, and anesthetic interventions in combination with other simultaneous interventions were excluded. After reviewing 8 relevant studies, the researchers concluded that there was either evidence of increased risk of mortality with inhalation anesthesia or a decreased risk of mortality with TIVA. Findings from 1 study included evidence of decreased pulmonary complications following a

TIVA. While the researchers saw improved outcomes with propofol TIVA anesthetics, they suggested that a robust randomized clinical trial related to a specific type of malignancy be done to formulate more reliable conclusions.

Cassinello et al. systematically reviewed the effect of anesthesia on in vitro and in vivo cancer and post-surgical survival and recurrence.[3] Researchers utilized PubMed databased articles published before January 2014. The concept that cancer metastasis and surgery may be linked has been around for some time. The researchers cited a 1913 clinical trial by Tizzer involving surgery induced tumor growth in animals inoculated with malignant cells. Coussens and Werb found evidence that surgery can increase pro-inflammatory cytokine levels which promotes neoplastic progression.

Cassinello et al. also cites a 2003 clinical trial by Melamed et al. which is now considered seminal work in relation to the research question for this review. The Melamed group describes the effects of anesthetic agents on susceptibility to cancer metastasis in rats.[4] Anesthetics were administered to 344 rats between 13 and 16 weeks of age. Doses were titrated to maintain respiratory rates of 40/minute, which the researchers deemed equivalent to a lack of response to noxious stimuli. The rats were randomly assigned to the control group or 1 of 4 experimental groups based on the use of propofol, thiopental, ketamine or halothane. Blood samples were drawn to evaluate NK cell function 3.5 hours after exposures to anesthetic agents. The researchers found that in the rat models, inhaled anesthetics increased the risk of tumor metastasis by decreasing NK cell activity. They go on to explain how inhaled anesthetics promote immunosuppression and activate the inflammatory cascade while propofol promotes activation and differentiation of peripheral t helper cells, preserves cellular immunity and antitumor activity, and has anti-metastatic properties. The researchers conclude that propofol TIVA may prevent a decrease in immune cell function during and after surgery.[4]

Lee et al. retrospectively analyzed the records from 363 patients who had modified radical mastectomies for breast cancer with either propofol TIVA or a volatile anesthetic.[5] Overall 5-year survival rates and 5-year recurrence free survival rates were calculated. Patients received the same medications with the exception of some receiving volatile agents and some receiving propofol. Anesthetic agents were titrated to maintain BIS values of 40-60 with either sevoflurane 1.5 - 2.0% inspired concentration or effect-site concentration (Ce) propofol 1.5 – 4 mcg/ml. After meeting inclusion and exclusion criteria, 173 and 152 remained in the propofol TIVA group and the sevoflurane group respectively. Cancer recurrence was documented within 5 years in 20 of the 173 (11.6%) patients in the TIVA group and in 29 of the 152 (19.1%) patients in the sevoflurane group. Death occurred within 5 years in 9 of the 173 (5.2%) patients in the propofol group and in 11 of the 152 (7.2%) in the sevoflurane group. Based on Kaplan-Meier analysis, the propofol TIVA group had significantly longer recurrence free survival but overall survival was not statistically significant. The authors concluded that a propofol based TIVA significantly reduced the risk of cancer recurrence within the 5 years following breast cancer surgery when compared to a sevoflurane anesthetic. Their suggestions for future research include the need for prospective, multicenter studies to validate their findings.

In a randomized, controlled trial (RCT), Liu et al. studied 58 women between 30 and 65 years of age having laparoscopic surgery for excision of cervical cancer.[6] Propofol TIVA was

administered to half of the group, the other half received sevoflurane. Additional medications and treatments were controlled. Blood samples were collected from each participant 30 minutes pre-induction, at the conclusion of the procedure and 24, 48 and 72 hours postoperatively. The CD4+/CD8+ ratio is considered a reflection of immune system health. CD4+/CD8+ values were not significantly different between groups before induction, but the CD4+ levels were significantly lower in both groups following surgery and only returned to normal levels in the propofol TIVA group at 72 hours. There were no significant changes in CD8+ levels in either group but in the sevoflurane group, the ratio significantly decreased from the 24-hour postoperative level to the 48-hour postoperative level. CD3+, CD4+, T cells, and NK cell levels and the CD4+/CD8+ ratio were decreased postoperatively and were significantly lower in the sevoflurane group. Cell counts also took longer to return to preoperative levels in the sevoflurane group. This clinical picture suggests that the use of sevoflurane results in more postoperative immunosuppression. The limitations of this trial include that long-term effects of the decreased cell counts were not evaluated, and metastasis of cancer cells was not measured.

In another RCT, Zhou et al. studied the effects of propofol on NK cells in participants with esophageal squamous cell carcinoma (ESCC)[7]. Participants were diagnosed prior to onset of the trial but had received no treatment. Blood samples were drawn from 15 ESCC patients between 39 and 43 years of age. The NK cells were extracted from the samples and randomly assigned to the control or experimental group. The NK cells in the experimental group were incubated with propofol 50 μmol/L for 24 hours, the control group of cells received no intervention. After incubation, the researchers found that the percentage of NK cells in the propofol treated samples had increased when compared to the control group cells, indicating that innate immune response had increased. The researchers concluded that in patients with ESCC, propofol enhanced the activity of NK cells and improved NK cell function by increasing the expression of activating receptors. Propofol appeared to enhance the cytotoxicity of NK cells and promote proliferation of NK cells in vitro. The researchers concluded that propofol may have the potential to improve postoperative immunosuppression in patients with ESCC.[7]

Table. Recent Literature Related to Propofol Versus Volatile Agents in Patients having Tumor Excision Procedures

Authors Date	**Patient Groups**	**Level of Evidence**	**Outcomes**	**Key Results**	**Strengths and Weaknesses**
Wigmore et al., 2016	7,030 cancer excision patients with volatile anesthetic vs. propofol TIVA	Retro-spective Cohort Analysis, Level III evidence	Survival rate of 1 year after propofol TIVA: 94.1% Survival rate of 1 year after volatile anesthetic: 87.9%	Hazard Ratio of volatile to TIVA: 1.46	Strengths: Large sample size Studied long term effects of anesthetic choice Weaknesses: Lower level evidence Non-inclusion of cancer staging data
Soltan-izadeh et al., 2017	10,696 cancer excision	Systematic Review, Level IA	Inhalation anesthetics increased risk	Propofol TIVA decreases	Strengths: High inclusion criteria, high level evidence

	patients with inhalation vs. propofol TIVA	evidence	of mortality; propofol TIVA decreased risk of mortality.	mortality and complica-tions when compared to inhalation anesthetics.	Large sample size Weaknesses: Bias in 6 of 8 studies, 1 trial non- randomized, some participants required re-operation with sevoflurane use
Casinello et al., 2015	Postopera-tive cancer excision patients	Systematic Review, Level IA evidence	Volatile anesthetics can reduce NK cell activity and induce the inflammatory cascade.	Propofol provides protection against immune-suppression.	Strengths: Synthesized review of studies related to PICO question Included in vitro and in vivo studies High level evidence Weaknesses: PubMed database was only one used for review
Melamad et al., 2003	344 rats given propofol, thiopental, ketamine or halothane	RCT, Level I evidence	Thiopental, ketamine, halothane led to decreased NK cells; propofol did not reduce NK cells.	Propofol TIVA may prevent decreased immune cell function during and after surgery.	Strengths: Robust methods Variables highly controlled High level evidence Weaknesses: Non-human trial Only study agents administered
Lee et al., 2016	325 mastectomy patients receiving propofol TIVA vs. sevoflurane	Retro-spective Analysis, Level III evidence	5-year cancer recurrence: 20/173 in propofol group; 29/152 in sevoflurane group 5-year mortality: 9/173 in propofol group; 11/152 sevoflurane group	Propofol TIVA group showed longer recurrence free survival but overall survival not statistically significant.	Strengths: Large sample size Long term recurrence and survival rates studied Weaknesses: Uncontrolled and bias due to nature of trial Uncontrolled interventions
Liu et al., 2016	58 patients for cervical cancer excision with propofol TIVA vs. sevoflurane	RCT, Level I evidence	CD4+ only returned to normal with propofol. Sevoflurane: CD4+/CD8+ decreased between 24-48 hours.	Sevoflurane produces more postoperative immune-suppression than propofol.	Strengths: Robust methods Variables highly controlled High level evidence Weaknesses: No long-term outcomes measured

			CD3+, CD4+, T cells, NK counts lower and slower to return to normal, more postoperative infections.		
Zhou et al., 2018	15 ESCC patients with serum incubated with propofol vs. no propofol exposure	RCT, Level I evidence	Percentage of NK cells in propofol treated samples increased when compared to the control group.	Propofol enhanced the activity of NK cells in patients with ESCC.	Strengths: Robust methods with important findings for a specific patient population Weaknesses: Narrow age range Small sample size insufficient for comparing NK cell markers to metastasis

Conclusions

There is not yet enough evidence to consider the use of propofol based TIVA for cancer surgery a standard of care. However, this evidence-based review supports the concept that propofol TIVA can result in less cancer metastasis postoperatively in patients undergoing cancerous tumor excision when compared to inhalation anesthetics. Sevoflurane has been found to decrease lymphocytic activity and induce lymphocytic apoptosis while propofol has no significant effect on tumor metastasis and does not suppress NK cell activity.[8] Inflammatory cellular environments, such as those that result from surgical stress, promote tumor production and metastasis.[8] Researchers are calling for additional research, specifically high quality, RCTs focused on heterogeneous cancer sites and surgical interventions. Because propofol can reduce the risk of inflammation and immunosuppression, propofol TIVA could be the best anesthetic plan for patients presenting for cancer excision surgery.

References

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Mentor: Lisa Herbinger, DNP, CRNA

Editorial

This has been on my to-do list for quite some time, but it is my pleasure to announce that the ISJNA is now also posted on the IFNA website at https://ifna.site/international-publications/international-student-journal-for-nurse-anesthesia/. I am also proud to inform you that the ISJNA is now being translated into Chinese for dissemination by the Taiwan Association of Nurse Anesthetists in their newsletter.

I would like to welcome the following new Editorial Board Members:
Dawn Elizabeth Bent, DNP, MSN, CRNA
LCDR John Litchfield, PhD, CRNA, NC, USN

As often happens at our annual educator conference (the recently renamed Assembly of Didactic and Clinical Educators), several new individuals have joined our ranks as reviewers. I am always grateful and amazed at the willingness of these hard-working, busy CRNAs to commit their time and effort to the student journal – thank you for making the ISJNA a continued reality!

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, evidence-based practice project abstracts, 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 ^{o}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 **<u>AMA Manual of Style must be adhered to</u>** 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.

<u>Heading</u> – 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 . . .

Case Reports - 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 less than 100 words 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 not 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 your case noting how and why your case was the same or different 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 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 project 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)

Research Abstracts - 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)

Letters to the Editor - 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.

AMA MANUAL OF STYLE

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:
Kamangar N, McDonnell MS. Pulmonary embolism. *eMedicine*. http://www.emedicine.com/med/topic1958.htm. Updated August 25, 2009. Accessed September 9, 2009

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