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Luke Borchardt, BSN, RN, Laken Kittelson, BSN, RN, Rachel Holte, BSN, RN, and Rachel Jaeger, BSN, RN, graduate students enrolled in the University of North Dakota's Nurse Anesthesia Program, practice clinical skills at the Clinical Resource & Simulation Center on the University of North Dakota campus in Grand Forks, North Dakota.

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Management of Suspected Intraoperative Pulmonary Embolism

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Keywords: pulmonary embolism, thromboembolism, intraoperative complications

Acute intraoperative pulmonary embolism (PE) is a rare but life-threatening complication, with symptoms often obscured under general anesthesia. The incidence of PE ranges from 0.3% to 30% among various surgical populations, with the highest occurrence in orthopedic surgical patients.[1] PE associated with hemodynamic instability carries up to a 30% mortality risk.[2] No consensus treatment protocol exists for massive pulmonary emboli in the setting of ongoing surgery. Management of intraoperative pulmonary emboli requires rapid recognition and early intervention by the anesthetist.[3,4]

Case Report

A 73-year old, 72 kg, 162 cm female presented for open reduction and internal fixation (ORIF) of a left tibial plateau fracture, sustained after a mechanical fall two weeks prior. Her past medical history was significant for smoking and allergic rhinitis. Her medication history included oxycodone-acetaminophen 5 mg - 325 mg, albuterol inhaler, loratadine, and subcutaneous enoxaparin injections. Her past surgical history included a total splenectomy and oophorectomy. Her airway exam was unremarkable, though the patient reported she had been a difficult intubation in the past. An 18-gauge peripheral intravenous (IV) catheter was inserted, through which midazolam 2 mg was administered prior to transport to the operating room.

In the operating room, electrocardiogram, noninvasive blood pressure, bispectral index monitor, and pulse oximetry were applied. Inspired O_2 at 10 L/min was administered for 4 minutes, after which general anesthesia was induced via IV administration of lidocaine 100 mg, fentanyl 75 mcg, propofol 140 mg, and succinylcholine 100 mg. Video laryngoscopy exposed a grade 1 view and a 7.0 mm oral endotracheal tube (ETT) was atraumatically passed through the vocal cords, placement was confirmed with positive end-tidal carbon dioxide pressure ($ETCO_2$) and auscultation of bilateral breath sounds, and the ETT was secured. General anesthesia was maintained with sevoflurane 1.8% inspired concentration in a mixture of O_2 0.8 L/min and air 1.2 L/min, with boluses of fentanyl and rocuronium administered for analgesia and neuromuscular relaxation, respectively.

As plates and screws were being inserted for rigid internal fixation, a precipitous decline in $ETCO_2$ from 39 to 25 mm Hg was observed, accompanied by new onset sinus tachycardia of 115 to 120/min and hypotension with systolic blood pressure (SBP) of 80 mm Hg. The patient's SpO_2 did not drop below 95%. The patient was resuscitated with Lactated Ringer's solution 1000 mL and 5% albumin 250 mL in conjunction with a phenylephrine infusion, stabilizing the SBP to 100 to 110 mm Hg and maintaining a normal sinus rhythm throughout the rest of the case.

Upon completion of the procedure, the patient was observed to be diaphoretic, cool, and clammy with paroxysmal hypotension and return of sinus tachycardia. A decision was made to evaluate

the patient in the operating room prior to extubation. A transesophageal echocardiogram (TEE) was performed, revealing a severely enlarged and hypokinetic right ventricle (RV), severely underfilled left ventricle, and interventricular septal flattening. An internal jugular central venous catheter and arterial line were inserted, and arterial blood gas revealed a significant respiratory acidosis. The patient was subsequently transferred to the intensive care unit, intubated, on infusions of epinephrine at 0.07 mcg/kg/min, norepinephrine at 0.1 mcg/kg/min, and dexmedetomidine at 0.4 mcg/kg/min. Several hours later, computed tomographic pulmonary angiography scan revealed bilateral pulmonary emboli.

Discussion

Pulmonary embolism most often occurs due to the entry of thrombotic, fatty, gaseous, or detached tumor fragments into the pulmonary vascular system.[5] The incidence of intraoperative PE ranges from 0.3% to 30% in the various surgical populations, with the highest rates described in orthopedic surgical patients.[4] That surgical patients are at highest risk can be traced back to Rudolph Virchow's triad of factors implicating venous stasis, hypercoagulability, and endothelial injury in the formation of venous thromboemboli. Surgery engenders, among other risk factors, tissue injury leading to acute inflammation and clotting cascade activation, as well as reduced patient mobility.[6]

As the embolus lodges in the lungs, the resultant obstruction of blood flow increases physiologic dead space and reduces the cross-sectional area of the pulmonary vasculature. An increased alveolar-arterial gradient and right-to-left pulmonary shunting are common, as blood is diverted away from the occluded pulmonary artery (PA), resulting in overperfusion of the rest of the lung parenchyma and leading to edema, loss of surfactant, and alveolar hemorrhage.[1] Regional hypocarbia may cause localized bronchoconstriction, while the release of humoral vasoactive mediators (thromboxane, serotonin, histamine) can cause reflexive, generalized bronchoconstriction, further worsening any pre-existing areas of low ventilation/perfusion ratios. Without a corresponding increase in minute ventilation, an increased $PaCO_2$ should be observed, but hypoxia is more often seen in practice due to pulmonary changes. Hypocarbia manifests, as decreased cardiac output leads to systemic hypotension and tachycardia.[4]

The obstruction to forward flow may result in right ventricular (RV) dilatation, RV ischemia, and dysfunction and eventually, global cardiac dysfunction.[1] Electrocardiogram (ECG) changes include atrial arrhythmias, ST and T-wave abnormalities, and signs of acute cor pulmonale, such as $S_1Q_3T_3$ pattern, right bundle branch block, right axis deviation, t-wave inversions, or P-pulmonale.[7]

Rapid recognition is paramount to reducing morbidity but many of the classic presenting symptoms of PE are either obfuscated in the anesthetized patient or can be attributed to various causes in the perioperative setting. Sinus tachycardia and hypotension were observed in this patient but are nonspecific, while atrial arrhythmias and other ECG changes were not evident. No significant desaturations were noted the entire case. The most noteworthy change observed was a sudden and pronounced decrease of $ETCO_2$ at the time of hypotension. Changes in $ETCO_2$, though nonspecific, are associated with the earliest detection of intraoperative PE and lowest mortality.[3] In this case study, suspicion for PE did not remain high as initiation of a

phenylephrine infusion restored a normal sinus rhythm and normotension, and alteration of ventilator settings restored normocapnia. A TEE can be performed quickly and without interrupting the procedure, and will often detect the most common echocardiographic findings in PE- RV dilation, RV hypokinesis, and ventricular septal shift.

Treatment intraoperatively is supportive and though volume expansion is first-line in undifferentiated shock, fluid should be administered judiciously.[4] Fluid overload will increase RV preload, placing greater wall stress on a pressure-sensitive ventricle and potentially worsening any subendocardial ischemia.[4] Retrospectively, fluid resuscitation in the face of shock appeared to have been too aggressive, and earlier vasopressor administration should have been considered as suspicion for pulmonary embolism increased. Placement of a central venous catheter may reveal elevated central venous pressures, and though suspicion for air embolism was low in this case, can be used to aspirate air from the right atrium.[5] Though not present in this case, hypoxia may warrant the use of pulmonary vasodilators, such as inhaled prostacyclin or nitric oxide, to decrease PA pressures, and improve cardiac output and gas exchange without compromising systemic blood pressure.[4]

Based on the review of the evidence the following steps should be considered in the management of intraoperative pulmonary embolism causing significant hemodynamic compromise. Myocardial depressive effects of anesthetic drugs should be minimized. Nitrous oxide should be discontinued, not only to maximize fraction of inspired oxygen, but also to avoid an increase in pulmonary vascular resistance. Crystalloid administration should be limited to 500 mL and vasopressors considered early, particularly norepinephrine.[4] Norepinephrine's alpha-1 adrenergic effects will increase mean arterial pressure, RV perfusion pressure, and RV preload while its moderate beta-1 activity will augment contractility and cardiac output.[1] Alternative therapies include epinephrine and dopamine. Dobutamine may appear attractive due to its inotropic properties, but may cause undesirable peripheral vasodilation through its beta-2 effects.[4] Pulmonary vasodilators, such as nitric oxide or inhaled prostacyclin, may improve cardiac output, RV function and gas exchange by counteracting the vasoconstrictive neurohumoral response without significant systemic BP compromise.[1,4] Definitive treatment for hemodynamic decompensation with proven PE is thrombolysis or surgical thrombectomy.[4]

Overall, this case study aligns with much of the literature on both intraoperative PE manifestations as well as treatments. Pulmonary emboli occur with some frequency and improved outcomes rely on the anesthetist's high index of suspicion, rapid recognition, and prompt intervention.

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Central Venous Catheter Insertion and Pneumothorax

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Keywords: central line, central line insertion, central venous catheter, pneumothorax, mechanical complication of central line insertion

Each year, more than 5 million central venous catheters (CVC) are inserted with a complication rate of 15%.[1] One such complication is pneumothorax, representing 30% of all associated mechanical complications, with an overall incidence of up to 6.6%.[2-3] The literature indicates that pneumothorax as a result of CVC insertion has been associated with an additional 4.4 days of hospitalization and more than $17 000 in additional healthcare costs.[4] The risk for complication increases with clinical inexperience.[5] This case study will explore the circumstances surrounding a CVC insertion related pneumothorax caused by a novice clinician.

Case Report

An 83-year-old, 75.3 kg, 180 cm male presented for a transcatheter aortic valve replacement (TAVR) for aortic stenosis. His past medical history included: aortic valve stenosis, cardiomyopathy, coronary artery disease, hyperlipidemia, anemia, hypertension, and chronic kidney disease. The patient's medications included aspirin, lovastatin, metoprolol, cephalexin, coenzyme Q, vitamin B12, and iron. Preoperative cardiac catheterization revealed stenotic aortic valve area of 0.8 cm^2, a thermodilution cardiac output of 3.90 L/min, and nonobstructive, noncritical coronary artery disease. Preoperative echocardiogram revealed severe left ventricular dysfunction with an ejection fraction of 25-30%. Physical examination was unremarkable with the exception of an in situ 20-gauge peripheral intravenous catheter (PIV).

In the operating room, noninvasive monitors were applied and O_2 2 L/min was administered by nasal cannula with end tidal carbon dioxide monitoring ($EtCO_2$). A 20-gauge, right radial arterial line was inserted. The transduced arterial line demonstrated blood pressures in the range of 125-130/85-95 mm Hg. Once invasive hemodynamic monitoring was secured, oxygen was administered by face mask at 8 L/min. The patient received fentanyl 100 mcg and etomidate 20

mg for IV induction of anesthesia. Ventilation was established before administration of vecuronium 7 mg. The trachea was intubated with an 8.0 mm oral endotracheal tube (ETT). The patient remained on sevoflurane 1.5% inspired concentration and O_2 2 L/min after intubation. Mechanical ventilation with a respiratory rate (RR) of 10/min and tidal volumes (VT) of 500 mL was established. $EtCO_2$ measured 33-36 mm Hg.

After the airway was established, a right internal jugular (IJ) CVC was inserted utilizing the Seldinger technique under ultrasound guidance. The patient's right neck was prepped with chlorhexidine and a sterile drape was placed from head to toe. The patient was placed in the Trendelenburg position at 10° with the head turned to the left. The introducer needle was inserted at a 40° angle caudally toward the ipsilateral nipple while aspirating. When aspiration no longer revealed blood return the needle was slowly removed until blood return was reestablished. The CVC was inserted without resistance. All vital signs remained stable and $ETCO_2$ measured 30-34 mm Hg.

Within 7 minutes, the $EtCO_2$ decreased to 16 mm Hg with a dampened waveform. All other vital signs remained unchanged. The anesthesia professionals assessed the ETT and all connections from the ETT to the ventilator. There were no disconnections or leaks. The patient was easy to manually ventilate. The RR was decreased to 8/min and VT decreased to 450 mL resulting in no change to $EtCO_2$. An arterial blood gas revealed a PCO_2 of 28 mm Hg. The anesthesia practitioners requested a view of the patient's chest under fluoroscopy. The imaging revealed a small, right-sided pneumothorax.

A right-sided chest tube was placed by the surgeon. The patient's vital signs remained stable throughout the procedure. When the surgical procedure concluded, the patient was able to maintain VT > 500 mL with spontaneous ventilation and demonstrated purposeful movement. The patient was extubated without issue or complication. He was maintained on O2 4 L/min via simple face mask. The patient was transferred to the cardiovascular intensive care unit while his vital signs continued to be monitored. He remained hemodynamically stable throughout transport.

Discussion

Pneumothorax is one the most common complications of CVC insertion, representing up to 30% of all associated mechanical complications with an overall incidence of up to 6.6%.[2-3] Complications frequently associated with IJ and subclavian (SC) CVC insertion include infection, hematoma, and pneumothorax.[2] Other complications include pneumomediastinum, chylothorax, tracheal injury, injury to the recurrent laryngeal nerve, and air embolism.[6] The mortality of pneumothorax as the result of CVC insertion is estimated to be anywhere from 2-7%.[3-4] In 2012, The United States Agency for Healthcare Research and Quality found that pneumothorax was associated with an additional 4.4 days of hospitalization and more than $17000 in additional healthcare costs.[4]

The typical presentation of a pneumothorax includes respiratory distress, hypoxia, tachypnea, absent or distant lung sounds, tachycardia, and/or pulsus paradoxus.[5] This patient did not have a typical presentation for pneumothorax. The only noticeable change was the decrease in $EtCO_2$.

Despite the only appreciable change in the patient's status being an increased $EtCO_2$, this, along with the inexperience of the practitioner inserting the CVC, led to suspicion of a pneumothorax. Direct visualization of the pneumothorax was easily obtained due to the fact that the TAVR procedure was performed under fluoroscopy. It was important to respond to the hypocapnia caused by the pneumothorax so as not to put the patient at a greater risk for complications. Hypocarbia leads to decreased myocardial oxygen supply, increased myocardial oxygen demand, increased coronary vascular resistance, and an increased risk for coronary artery vasospasm.[7] This patient's history of aortic stenosis and coronary artery disease suggest that he would most likely not be able to tolerate a state of hypocarbia for long. Chest tube insertion is not necessary for all cases of pneumothorax, but the cardiothoracic surgeon felt that insertion was warranted for this patient due to his age and the culture of practice at this institution.[5-6]

Patient related risk factors for mechanical complications related to CVC insertion include underlying disease processes, abnormal anatomy, uncooperative behavior, or trauma to the area of insertion.[5] This patient did not have any significant patient related risk factors for complication. He was under general anesthesia for insertion and he was of normal body habitus with no underlying lung disease or abnormal anatomy. Equipment related risk factors for mechanical complication included the site chosen for insertion and the catheter type. Due to the anatomical location and closer proximity to the apex of the lung, SC insertion carries a greater risk of pneumothorax than IJ insertion, but that does not mean that IJ is without risk.[5] Further, a large bore CVC was placed, again increasing the risk for pneumothorax.

Practitioner associated risk factors for complications include clinical experience, previous catheterization attempts, and whether or not insertion was performed in an emergency situation.[5] Inexperience is a significant risk factor for CVC insertion complications. Central venous catheter insertion by a clinician who has performed 50 or more catheterizations is half as likely to cause a mechanical complication as compared to a clinician who has performed less than 50 catheterizations.[5] One of the most significant risk factors for mechanical complication of CVC insertion in this case study was the inexperience of the clinician. The SRNA inserting the central line was not the one to drape the patient. This resulted in the loss of visual landmarks that may have been helpful when inserting the introducer needle.[1] The introducer needle was then inserted past the point of being able to aspirate blood. It is recommended that the needle not go beyond a depth of 1-2 cm so as not to puncture the apex of the lung.[1] In this case, the needle was inserted beyond 2 cm as evidenced by the measurement markings on the needle. Despite the fact that ultrasound-guidance has been demonstrated to reduce the risk of complications, visualization of landmarks and an understanding of the anatomy is also beneficial for proper line placement.[1,3]

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Anesthetic Considerations for Submental Intubation in Maxillofacial Surgery

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Keywords: Submental intubation, panfacial fractures, maxillofacial surgery, facial trauma

Airway management for those with facial trauma requiring maxillofacial surgery presents unique challenges for the anesthesia practitioner. Submental intubation (SMI) is a less invasive, alternative method of airway management that was first described by Hernández Altemir in 1986.[1] Submental intubation provides a secure airway for those with complex midfacial fractures who cannot be intubated nasotracheally and do not require long term airway management a tracheostomy provides.[1-2]

Case Report

A 23-year-old, 75 kg, 175 cm male presented for open reduction internal fixation (ORIF) for mandibular fracture with maxillomandibular fixation and closed reduction of nasal fracture with SMI. The patient has no significant past medical history, no surgical history and no known drug allergies. Medications at the time of surgery included ibuprofen as needed (PRN), oxycodone PRN, amoxicillin-clavulanate 875-125mg and docusate sodium PRN.

Prior to arrival in the operating room, midazolam 2 mg and glycopyrrolate 0.2 mg were administered via an 18 gauge intravenous catheter. Upon arrival to the operating room, standard noninvasive monitors were applied to the patient. General anesthesia was induced with propofol 200 mg, sufentanil 10 mcg, rocuronium 80 mg. The trachea was intubated with a 7.5 cm oral Ring Adair Elwyn (RAE) tube via direct laryngoscopy. After confirmation of airway placement, total intravenous anesthesia was maintained with a propofol infusion 120mcg/kg/min, dexmedetomidine 0.3 mcg/kg/hr and sufentanil 0.2 mcg/kg/hr. 3 grams of ampicillin-sulbactam was infused over 30 minutes before surgical incision.

The maxillofacial surgeon made a 2 cm incision along the lingual border of the mandible creating a tract to the floor of the mouth. The adaptor of the RAE tube was removed. The RAE tube was passed from its' position in the oral cavity through the floor of the oral cavity and anterior floor of the mandible and out the anterior portion of the neck. The maxillofacial surgeons sutured the RAE tube to the skin. Dexamethasone 10mg was administered. 4mg of ondansetron was administered prior to emergence. The RAE tube was removed through the stoma with the patient awake and was transferred to the post anesthesia recovery unit with no complications observed.

Discussion

Anesthetic management for those with facial trauma presents unique challenges and requires effective communication and cooperation among anesthesia professionals and maxillofacial surgeons.[4] SMI is an alternative to tracheostomy in those with panfacial injuries and is preferred over tracheostomy in elective procedures due to morbidity associated with tracheostomy including pneumothorax, pneumonia, subcutaneous emphysema, tracheal stenosis, tracheomalacia and scar tissue at the stoma site.[1,2,5] SMI is performed by intubating the patient via the orotracheal route. The surgeon will make a 2cm incision medial to and parallel from the inferior border of the mandible. This facilitates passage of the orotracheal tube through the incision to be secured with nylon sutures.[3]

The choice of endotracheal tube (ET) for SMI is an important consideration for the anesthetist. A reinforced tube is preferred; however, most operating rooms possess reinforced tubes that have non-detachable connectors.[4] Lim and colleagues conducted a literature review of submental intubation over thirty years and determined armored, metallic tubes were used in 85.5% of patients undergoing submental intubation.[5] Samieirad and colleagues described modifications that can be made to an armored tube with a non-detachable connector. The most obvious approach would be to cut the tube at the level of the connector. Unfortunately, this exposes the internal wire of the tube and prevents an adequate connection when reattaching the connector. Another technique described by Samieirad and colleagues would be to remove the non-detachable connector with forceps and reconnect once the tube has passed through the submental incision. A loose connection can ensue leading to unacceptable ventilation for the procedure.[4]

Lim and colleagues noted a two-tube technique was used in 11.9% of patients undergoing submental intubation in their literature review.[5] The two-tube technique is performed by intubating the trachea via the orotracheal route. A second armored, non-detachable connector tube is passed through the submental incision. The first tube is removed and the second tube is passed through the trachea with Magill forceps.[1,4] This technique will negate the concern about non-detachable connectors but can be associated with airway trauma secondary to multiple laryngoscopy attempts.

The airway plan for the described patient included an oral RAE tube with a detachable connector. The decision for this tube as opposed to an armored tube with a non-detachable connector was made in concert with the maxillofacial surgeon. As described in the literature, our concerns were manipulating the connector on the armored tube and not having an adequate seal upon reconnecting to the anesthesia breathing circuit, leading to inadequate ventilation. The use

of the RAE tube did not lead to increases in peak airway pressure caused by obstruction of the RAE tube. There was no difficulty ventilating the patient at any point during the case.

Removal of the RAE tube was made through the submental incision. The SMI procedure describes removal of the ET tube should be done upon converting SMI back to an orotracheal position.[1-5] After discussion between the anesthesia team and maxillofacial surgeon, the decision was made to remove through the submental incision due to the degree of maxillary fixation performed. The concern for pulling the RAE tube through the submental incision would be introducing oral bacteria into the submental incision.[2] Antibiotic coverage was administered pre-incision and continued in the post-operative period.

Submental intubation is a safe, low morbidity technique for patients with complex facial fractures not requiring long-term airway management that tracheostomy provides. Available equipment and the surgical procedure dictated the approach to our patient. The unique challenges this technique presented was met and overcome with effective communication with our surgical colleagues.

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Coagulopathy Correction and Resuscitation in Hepatic Trauma

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Keywords: Trauma, transfusion, REBOA, ROTEM, coagulopathy

Severely injured patients experiencing hemorrhagic shock after trauma often require massive transfusion.[1] Coagulopathy has been shown to be present in approximately 25% to 35% of all trauma patients on admission to the emergency room. Viscoelastic methods that assess the speed

of clotting and quality of the clot, such as rotational thromboelastometry (ROTEM), have been successfully used to guide hemostasis and coagulopathy correction.[2] The adult liver, the largest organ in the body, accounts for 2% to 3% of overall body weight.[3] An uncontrolled bleed from the liver can lead to extreme blood loss.[3]

Case Report

A 26-year-old male with no known allergies and no known medical history presented to the emergency department (ED) status post motorcycle accident. The patient was wearing a helmet, suffered no loss of consciousness, and presented with a Glasgow coma scale score of 15. He also complained of numbness to all extremities, right sided chest tenderness, and diffuse abdominal tenderness. In the ED, the patient was found to be hypotensive with a systolic blood pressure of 50 mmHg. A massive transfusion protocol was initiated. The patient had a confirmed positive focused assessment with sonography for trauma (FAST) exam and was brought emergently to the operating room for an exploratory laparotomy.

The patient was transferred to the operating room table with log-roll technique and maintained neutral cervical alignment. The patient was then pre-oxygenated, with O2 10 L/min for 3 minutes. During the preoxygenation period 5 lead electrocardiography, a non-invasive blood pressure device, and a pulse oximeter were applied to the patient. A rapid sequence induction was performed with midazolam 2mg, etomidate 12 mg, succinylcholine 100 mg, and intubated with a 7.5 mm endotracheal tube using glideoscope assistance. A size four glidescope spectrum handle was used and the tube was secured at 23 cm at the lip. All airway manipulation was done while maintaining manual inline axis stabilization of C-spine.

Initial ventilator settings were: tidal volume 6 mL/kg (based on ideal body weight) and respiratory rate 12/min. Immediately after induction a right subclavian multi-lumen access catheter (MAC) and a right radial 4 French arterial line were inserted. Rapid volume administration was facilitated via the MAC catheter's introducer, 9 French, and 12-gauge lines. A baseline ROTEM was obtained to gauge fluid resuscitation status. Goal-directed coagulation treatment, in hemorrhaging patients, necessitates quick and reliable coagulation monitoring, and a targeted therapeutic approach according to the results.[2] Arterial blood gas samples were drawn every 5 minutes throughout the case to determine electrolyte, blood, and volume requirements.

Upon the surgeons entering the abdomen there was an extremely large rush of blood. The decision to obtain aortic control was made. To help limit blood loss and maintain hemostasis, a resuscitative endovascular balloon occlusion of the aorta (REBOA) device was placed. The patient was found to have an extensive right lobe of the liver laceration, which was 6 cm deep. The bleeding continued, a Pringle maneuver was initiated to decrease bleeding using a vascular clamp, and the REBOA was deflated.

After hemostasis was achieved, the surgical goal was to minimize the hepatic damage. The patient had received; PRBCs 56 units, FFP 50 units, platelets 11 units, cryoprecipitate 10 units, and factor eight inhibitor bypassing activity (FEIBA) 1,000 units. The patient had also received cell saved blood 4.2 L and plasmalyte 14 L. The estimated blood loss was 45 L. A wound vacuum was placed, and the patient was sent to interventional radiology for embolization of the

right hepatic artery. During the procedure, the patient also received: 8.4% sodium bicarbonate 14 amps, D50% 25 g, furosemide 10 mg, fentanyl 700 mcg, calcium chloride 17 g, hydrocortisone 100 mg and vasopressin 2 units. Systolic blood pressure at end of the procedure was in the 130s mm Hg and the heart rate was in the 90-110/min range. A ROTEM was sent at the end of the procedure to determine what the coagulation status of the patient was post massive transfusion.

Discussion

Coagulopathy represents a serious problem for major trauma patients and accounts for 40% of all trauma-related deaths.[2] It was important to verify that coagulation status had been stabilized. A vast majority of patients that survive their initial injury and reach the hospital are coagulopathic when they die.[5] It is estimated that nearly one quarter of all trauma admissions present in varying degrees of coagulopathy on admission. Once coagulopathy develops, patient morbidity and mortality drastically increase.[5] Massive injury can disrupt the clotting cascade.[5] Traumatic injury often requires massive resuscitation to replace blood volume and restore circulation.[5] Although required for initial resuscitation, crystalloid fluid dilutes coagulation factors and platelets and increases hydrostatic pressure. This leads to inadequate clot formation and nonsurgical bleeding.[5]

A baseline ROTEM, early in a trauma when massive blood loss is encountered, allows the anesthesia practitioner to determine what level of coagulopathy exists. A baseline ROTEM may also provide a product deficiency guideline. In the case study described above, the first ROTEM sent off intraoperatively indicated the patient needed more than just PRBCs. The patient also required clotting factors. The ROTEM sent at the end of the procedure showed that there was no postoperative coagulopathy present.

Acute coagulopathy occurs in approximately 25% of all severely injured patients. Patients with acute coagulopathy would benefit from a test that can quickly identify coagulation abnormalities.[6] The test itself has four assays that are run simultaneously: EXTEM (extrinsic pathway), INTEM (intrinsic pathway), FIBTEM (fibrinogen test), and APTEM (test for hyper fibrinolysis).[6] IA 2013 study regarding ROTEM analysis in trauma indicated that abnormalities in results are capable of identifying coagulopathy, predict the need for massive transfusion, and predict mortality.[6]

In trauma procedures, it is important for the anesthesia practitioner to be aware of some of the lifesaving equipment and maneuvers that can be performed by the surgical team to help achieve hemostasis. In this case a REBOA was deployed when it was deemed necessary to help achieve hemostasis. A REBOA is a resuscitative endovascular balloon occlusion of the aorta device.[4] It is a minimally invasive technique using a balloon catheter to temporary occlude large vessels in support of hemorrhage control.[4] Another technique used during this procedure of life-saving importance was the Pringle maneuver. The Pringle maneuver is clamping of the hepatoduodenal ligament and is primarily used in cases of hepatic trauma to control blood loss.[3] Temporary occlusion of the hepatoduodenal ligament that contains the main portal vein, hepatic artery, and common bile duct (Pringle maneuver) can be used in a liver resection to minimize blood loss.[3] The patient required two rounds of Pringle maneuver since there was bleeding from the right hepatic vein after the initial removal.

Throughout the patient's hospitalization, several surgical interventions were required due to the severity of the injury. The patient had recurring episodes of hypotension throughout the first few postoperative days along with lactic acidosis. These issues resolved over time with antibiotics, fluid administration, and intermittent vasopressors. Four days after admission, the patient required a right hepatectomy. Today, hepatic resections are performed with mortality rates of 5% or less.[3] Partial hepatectomy in normal, non-cirrhotic livers is associated with mortality rates of 1% to 2%.[3] When any significant blood loss was encountered during a procedure, a ROTEM was sent off to lab, and blood products were given in accordance to the results.

One week after the patient's admission, he was extubated and talking. Two days later the patient was walking with the assistance of physical therapy. This case shows the importance of a predetermined plan on how to manage a trauma patient upon arrival, management of coagulopathy and fluid administration, as well as establishing an open communication with the surgical team early and often. Such a plan, along with the collaborative efforts of the surgical team, led to a successful patient outcome.

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Ventilation Strategies for Obese Patients Undergoing Laparoscopic Procedures

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Keywords: Alveolar recruitment maneuver, obesity, intraoperative, abdominal surgery, laparoscopy

Laparoscopic procedures are commonly performed in the operating room (OR) for patients with a body mass index (BMI) greater than 30 kg/m^2. This obese population has an increased risk for perioperative respiratory complications that potentially leads to intraoperative ventilation management difficulty.[1] Recruitment maneuvers (RMs) with the addition of positive end-expiratory pressure (PEEP) can be useful tools when patients encounter problems with oxygenation. A RM provides positive airway pressure at 40 cm H_2O for approximately 40 seconds to potentially improve oxygenation and ventilation. It is essential for anesthesia professionals to appreciate and strategically plan for potential refractory oxygen desaturation unresponsive to providing a fraction of inspired oxygen (FiO_2) of 100% and optimizing patient position. Recruitment maneuvers and PEEP have been shown to be a viable option to improve oxygenation.[1]

Case Report

A 52-year-old male, 165 kg and 193 cm, presented for an emergent laparoscopic appendectomy. The patient's past medical history included obesity, obstructive sleep apnea, hypertension, gastric esophageal reflux, and an allergy to latex. He did not smoke and reported occasional alcohol use. Surgical history included a toe amputation and Achilles tendon repair with no anesthetic complications. Home medications included lisinopril-hydrochlorothiazide, naproxen, omeprazole, zolpidem, multiple vitamins, and probiotic. Lab results were all within normal limits. Findings of an abdomen/pelvis CT scan revealed appendicitis. The preoperative airway examination revealed a Mallampati class 3 airway with a thyromental distance of 6 cm.

Upon entering the OR, vital signs included a heart rate (HR) of 141/min, respirations of 20/min, blood pressure (BP) of 192/82 mm Hg, and SpO_2 98% on room air. Peripheral intravenous access was established and normal saline was infusing. The patient was pre-medicated with midazolam 2 mg and fentanyl 50 mcg. Non-invasive monitors were applied. The patient was pre-oxygenated with oxygen 8 L/min via mask for approximately two minutes, followed by rapid sequence induction with lidocaine 50 mg, fentanyl 100 mcg, propofol 200 mg, and succinylcholine 140 mg. Endotracheal intubation was performed using a Glidescope (Verathon Inc., Bothell, WA), size 4 blade, and an 8.0 mm endotracheal tube (ETT). ETT placement was confirmed with end-tidal capnography and auscultation of bilateral breath sounds. Following induction and intubation, the patient quickly desaturated to a SpO_2 70%. The anesthesia professional performed two RMs with a pressure 30 cm H_2O and held for 10-15 seconds each, followed by manual ventilation until the SpO_2 was greater than 90% after approximately 30 seconds. The patient was placed on volume auto-control mode with a tidal volume 650 mL, respiratory rate 16/min, FiO_2 at 100%, and PEEP 5 cm H_2O. General anesthesia was maintained with desflurane 6.5% inspired concentration in O_2 1 L/min throughout the maintenance phase.

During the intraoperative period, cefazolin 2 g, rocuronium 90 mg, ondansetron 4 mg, decadron 8 mg, and normal saline 1500 mL was given. Vital signs remained stable throughout the intraoperative phase. After placing the patient in Trendelenburg position, two more RMs were performed for a SpO_2 91%. The SpO_2 improved, and ventilator settings remained unchanged. Residual neuromuscular blockade was antagonized with glycopyrrolate 0.6 mg and neostigmine 4 mg. Estimated blood loss was 25 mL. The patient's trachea was extubated without incident. The patient was transported to the post anesthesia care unit (PACU), with oxygen 6 L/min via simple mask. The length of the procedure was 105 minutes.

Discussion

Both obesity and pneumoperitoneum used during laparoscopic procedures can independently reduce lung volumes, decrease lung compliance, and impair oxygenation. In those where obesity and pneumoperitoneum are encountered, the risk for respiratory complications is increased. Therefore, these consequences can lead to an increase in morbidity and mortality, length of hospital stay, and healthcare costs.[1]

There are multiple strategies to reduce perioperative respiratory complications, and one of these strategies is the use of intraoperative RMs with the addition of PEEP.[1] A RM is performed after a secure airway has been established and usually involves providing positive airway pressure around 40 cm H_2O for approximately 40 seconds. Both the pressure and time can be altered, and these maneuvers can be performed multiple times during the intraoperative period. The goal of the RM is to recruit collapsed alveoli, caused by the excess cephalad pressure on the diaphragm from the pneumoperitoneum, excess patient weight, and gastric contents found in obese patients in a supine or Trendelenburg position. Recruitment maneuvers also improve oxygenation and ventilation. After the RM, PEEP of 10 cm H_2O is applied to reduce the re-collapse of the recruited alveoli.[2]

RMs increase SpO_2, allowing the anesthesia professional to wean FiO_2 as the patient tolerates.[3] Strategies using RMs and PEEP demonstrated to be effective in improving intraoperative oxygenation, lung volume expansion, and decreasing atelectasis. The combination of RMs and PEEP is more effective compared to independently using a RM or PEEP.[4] Although RM and PEEP prove to be beneficial during the intraoperative phase, these results appear to be lost once the ETT is removed from the trachea.[5]

Although RMs and PEEP can be useful tools during the intraoperative phase, it is essential to be aware of potential complications associated with the use of this strategy. It is possible that hemodynamic changes may be encountered when performing a RM, so caution must be used in hemodynamically unstable patients.[6] In the case presented, an increase in oxygen saturation was noted after applying the RMs and PEEP, with minimal to no hemodynamic changes during the intraoperative or postoperative phases of care.

Using RMs and PEEP can be adventitious; however, it is unclear of when and how often to perform them.[7] A randomized controlled trial studied four groups: patients who receive PEEP, patients who receive a RM, patients who receive PEEP and RM, and patients who receive PEEP

and RM with repeated RMs every ten minutes.[7] Recruitment maneuvers in the study involved pressure of 40 cm H_2O held for 15 seconds, and PEEP was applied at 10 cm H_2O. The group in which RMs were performed every ten minutes, followed by application of PEEP, had the most improvement in intraoperative oxygenation and compliance. This result is thought to be caused by reducing alveolar collapse through repeated RMs and maintaining open alveoli with PEEP.[7]

Research evidence reveals there are multiple methods for improving oxygenation during the intraoperative phase using RMs and PEEP.[4] In the case report, two RMs were performed initially with a pressure of 30 cm H_2O held for 10-15 seconds. However, once the patient was placed in Trendelenburg position, the patient desaturated again. In retrospect, increasing the PEEP to 10 cm H_2O after the first two RMs may have prevented the need for further RMs.

Given that complication such as hemodynamic alterations and barotrauma can occur, the use of RMs and PEEP should be discussed with the operative team. Specific patient conditions in which this intervention may be contraindicated, should also be considered and discussed. Research has revealed using RM and PEEP is useful for improving intraoperative oxygenation. However, future research needs to be performed to explore whether prophylactic use is warranted in the obese population. In addition, future research should focus on which method for implementing RMs with the addition of PEEP is the most effective in improving oxygenation.

There is sufficient, high-quality evidence that supports the use of RMs with the addition of PEEP to treat problems with oxygenation during the perioperative phase of surgery for bariatric patients undergoing laparoscopic procedures. Therefore, anesthesia professionals should consider using this no-cost intervention, as the evidence has demonstrated it may improve intraoperative oxygenation in the obese population. Lastly, the RM and PEEP intervention may lead to better patient outcomes and prevent additional hospital costs, with minimal risk of complications.

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Robotic-Assisted Diaphragmatic Hernia Repair and Pneumomediastinum

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Key words: laparoscopic thoracic surgery, robotic-assisted surgery, diaphragmatic hernia, insufflation, pneumomediastinum

Diaphragmatic hernias (DH) are seen most commonly in the neonatal and early childhood age groups.[1] An incidental finding of this diagnosis in adults is typically asymptomatic and treated surgically to prevent further issues, including incarcerated bowel and pulmonary disease.[1,2] An open surgical approach is more common for DH repair; however, the laparoscopic approach has had better post-operative outcomes, such as shorter recovery times.[3] With an incidence of 18%, pneumomediastinum can occur after laparoscopic esophageal hernia repair.[4]

Case Report

A 68-year-old, 64 kg female was scheduled for a robotic-assisted diaphragmatic hernia repair and diaphragm plication. The patient had a medical history of chronic obstructive pulmonary disorder, asthma, hemiparalysis of the diaphragm, sleep apnea with continuous positive airway pressure (CPAP), and gastroesophageal reflux disease (GERD). The patient initially presented for a pulmonary consult after her GERD and reflux symptoms were worsening despite diet changes and pharmacological management, and supplemental oxygen (O_2) at 2 L/min for increased shortness of breath. Prior to surgery, the patient had a computed tomography scan done that found an esophageal hiatal hernia, and an esophagogastroduodenoscopy (EGD) was completed to assess the gravity of her reflux. Findings from the EGD included significant hiatal hernia with slight sliding on the left side. All of her preoperative vital signs, assessment, blood work, and cardiac work up were within normal limits except for diminished breath sounds on the left side related to her left sided diaphragmatic hernia.

The surgery consisted of three parts: diaphragmatic hernia repair, Toupet fundoplication with EGD, and left diaphragm plication. The patient was preoxygenated with 10 L/min O_2 and induced with a rapid sequence induction (RSI) including cricoid pressure with lidocaine 100 mg, propofol 150 mg, and rocuronium 60 mg. Anesthesia was maintained with a total intravenous anesthesia (TIVA). which included a propofol infusion initiated at 150 mcg/kg/min titrated according the bispectral index and patient hemodynamics.

Placement of the trocars for the robot limbs was completed laparoscopically. The patient was placed in steep reverse Trendelenburg for maximal surgical field exposure. After the fundoplication and EGD were completed, the ETT was exchanged for a 35 French double lumen tube (DLT) for the plication portion of the surgery. Placement was verified by fiberoptic bronchoscope.

During the plication portion of the surgery, the surgeon alerted the anesthesia practitioners that he accidentally insufflated carbon dioxide (CO_2) at a pressure of 15 mm Hg of into the thorax. Although the insufflation occurred for less than one minute, the side effects of the added volume in the thorax were evident by hemodynamic changes. The patient required phenylephrine boluses from 50 mcg to 100 mcg aliquots to maintain hemodynamic stability. The peak inspiratory pressure alarm was activated with peak pressures in the 40s and the $EtCO_2$ was elevated from 35 mmHg to 47 mmHg. After DLT placement was reconfirmed, the ventilator settings were changed from volume control to pressure control with an increased respiratory rate to alleviate the elevated $EtCO_2$. The patient was found to have subcutaneous emphysema in her neck and upper chest postoperatively.

The surgeon placed a pigtail chest tube at the end of the surgery and neuromuscular blockade was antagonized with neostigmine 5 mg and glycopyrrolate 0.8 mg. Despite spontaneous respirations and a train of four ratio greater than 0.9, the patient's tidal volumes were inadequate at 120 – 150 mL. The decision to keep the patient intubated in the post anesthesia care unit (PACU) was made. The DLT was exchanged for an oral 7.0 mm cuffed tube via ETT exchanger without incident. In the PACU, the patient was on a propofol infusion at 50 mcg/kg/min on the ventilator. An x-ray showed proper placement of the ETT and signs of pneumomediastinum.

Discussion

Diaphragmatic hernias are typically congenital and are due to inadequate closure of the diaphragmatic foramina.[1] Because they are rare outside of the neonatal and early childhood age range, diaphragmatic hernias are often an incidental finding in adults.[1] Most patients are asymptomatic; however if symptoms are present they involve the pulmonary and/or gastrointestinal systems.[1] This includes GERD, breathlessness, and other pulmonary issues.[1] The diagnosis of a DH requires urgent surgical repair to prevent exacerbation of symptoms. If left untreated, a DH can lead to hernia incarceration, bowel strangulation, or pulmonary issues.[1,2]

There is currently a lack of literature comparing robotic-assisted versus laparoscopic thoracic procedures. Although the open surgical approach has been more common, the laparoscopic hernia repair has been seen to have superior postoperative outcomes including shorter hospital stays.[3,5] However, laparoscopic surgery does not go without consequence. Laparoscopic pneumoperitoneum involves insufflation of at least 15 mmHg of CO_2 into the peritoneum to create adequate surgical site exposure.[6] This added pressure affects numerous organ systems. The anesthesia professional may see signs of decreased venous return including hypotension and narrowed pulse pressures due to added pressure on the heart, and high peak inspiratory pressures due to decreased lung expansion upon initiation.[5,6]

Secondary pneumomediastinum is a side effect that can occur with laparoscopic esophageal hernia repair. This phenomenon occurs when air enters the mediastinum, and is not limited to surgical cause.[4,7] The clinical presentation of pneumomediastinum in an awake patient includes chest pain, dyspnea, coughing, pneumothorax, and dysphagia (although these symptoms can be associated with other underlying causes).[7] Current literature shows that this complication is not unheard of with esophageal hiatal hernia repair from gas insufflation seeping through diaphragmatic defects.[4]

In this case, the thorax was insufflated accidentally with CO_2, causing direct entry of gas into the thorax. Perioperative symptoms of pneumomediastinum are similar to those of cardiac tamponade: decreased venous return and a narrowed pulse pressure.[7] The arterial line showed a narrowed pulse pressure and hypotension which was treated accordingly with phenylephrine boluses. Thorax insufflation can also prevent adequate lung expansion, which was evident by increased peak inspiratory pressures. Despite the changes in peak pressures and deceased lung expansion, the patient's oxygen saturation was not altered.

Current literature also suggests that pneumomediastinum generally has a good prognosis, and can be seen as a normal finding after fundoplication surgery.[4,7] Unless diagnosed as malignant, pneumomediastinum is treated conservatively as the air in the cavity eventually gets absorbed by the mediastinal tissues.[7] The insertion of the chest tube at the end of the case can also help remove any residual CO_2 from the insufflation.[7]

The anesthetic plan for this procedure was driven by the anesthesia practitioner's experience with thoracic procedures. TIVA was the anesthetic of choice due to surgeon preference. A Cochrane review comparing TIVA versus volatile agents showed that one technique is not superior over the other.[8] Given the location of the hiatal hernia and what current literature suggests, a small pneumomediastinum may not have been avoidable in this case. Communication between the surgeon and anesthesia practitioners was important in order to treat the accidental insufflation of the thorax. Although a pneumomediastinum occurred, the patient remained hemodynamically stable and only required small boluses of phenylephrine to maintain arterial blood pressure.

Due to inadequate tidal volumes, the patient was kept intubated in the PACU. Although difficult to determine the main cause, many factors could have contributed to the inability to extubate. Despite the completion of the diaphragm plication, the patient's history of diaphragm hemiparalysis could be one of the main causes. The patient also had a history of sleep apnea with CPAP use, which could increase the need for pressure support ventilation. Although the patient's neuromuscular blockade was fully antagonized with the maximum dose of traditional reversal agents, there was still the possibility of residual paralysis from rocuronium. The use of sugammadex was not a common practice at this facility as it was reserved for airway emergencies at the discretion of the anesthesiologist. Despite ventilation requirement, the patient was extubated after one hour in the PACU and was admitted to the pulmonary unit for observation. As previously mentioned, pneumomediastinum is treated conservatively unless diagnosed as malignant. The patient was discharged home on post-operative day three without complications.

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Anesthesia Considerations for Intraoperative Neurophysiological Monitoring

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Keywords: Neurosurgery procedures, intraoperative neurophysiological monitoring, anesthesia management, and evoked potentials.

Neurophysiological monitoring involves evaluating evoked potential waveforms that result from electrical stimulation, providing an indication of the integrity of the neurological pathways being assessed. Evoked potential waveforms are obtained, recorded, and compared to the baseline waveforms during surgery to determine potential injury to the neurological pathways being monitored. The monitoring technician compares the latency (time it takes the stimulus to generate a response), and the amplitude (voltage of the response) of the evoked potential waveforms.[1] If a change from the patient's baseline is noted by a 50% decrease in amplitude and/or a 10% increase in latency, the monitoring technician communicates this to the surgeon and anesthesia professional. Possible causes for a change from baseline include: hypotension/hypoperfusion, hypoxia, hypothermia, hypercarbia/hypocarbia, and volatile anesthetic agents.[1] Anesthesia professionals have the ability to make corrections and potentially avoid any new onset neurological deficit.

Case Report

A 65-year-old, 113.9 kg, 185.4 cm female presented for right sided anterior cervical discectomy and fusion of levels C4 to C7 due to cervical degenerative disc disease with severe stenosis and radiculopathy which included upper right extremity weakness, numbness, and tingling. Pertinent past medical history included hypothyroidism, lumbar degenerative disc disease, chronic thrombocytopenia, spondylosis of lumbosacral region, postoperative nausea/vomiting, gastroesophageal reflux disease (GERD), iron deficiency anemia, hyperparathyroidism, bipolar disorder, and chronic opioid use. Pertinent past surgical history included right L4-S1 facet injections under fluoroscopy. The patient reported allergies to bupropion. Home medications consisted of levothyroxine, ferrous sulfate, morphine ER, oxycodone, clonazepam, lamotrigine, calcium carbonate with vitamin D3, trazodone, omeprazole, vitamin D, tiagabine hydrochloride, furosemide, bismuth subgallate, polyethylene glycol, and fiber psyllium.

A preoperative airway evaluation revealed full neck range of motion with no increase in pain or numbness/tingling. Preoperative vital signs were within normal limits and included a blood pressure of 135/80 and a heart rate of 70/min. A 20-gauge peripheral intravenous (IV) line was inserted preoperatively and used for IV induction. The patient was pre-medicated with midazolam 1 mg and she was then transferred to the operating room (OR). Once positioned on the OR table, standard noninvasive monitors were applied, and vital signs were obtained. The patient was pre-oxygenated by mask with 100% O_2 at 10 L/min for 10 minutes. A 20-gauge left radial arterial line was established prior to intubation.

Induction of general anesthesia included lidocaine 100 mg, propofol 200 mg, succinylcholine 180 mg, ketamine 50 mg, and methadone 14 mg IV. Video laryngoscopy produced a grade I view and the trachea was intubated with a 7.0 mm endotracheal tube (ETT). The ETT was secured after bilateral breath sounds were confirmed and the patient was then placed on the ventilator to maintain appropriate oxygenation and ventilation. Electrodes for both somatosensory-evoked potential (SSEP) and transcranial motor-evoked potential (MEP) neurophysiological monitoring were applied by the monitoring technician and baseline waveforms for amplitude and latency for all extremities was obtained.

Maintenance of anesthesia was accomplished with an expired sevoflurane concentration at 0.75 minimum alveolar concentration (MAC). One MAC refers to the dosage of inhalational anesthetic at 1 atmosphere where 50% of patients will not move with surgical stimulation.[1] The patient also received an intravenous infusions of ketamine at 10 mcg/kg/min and lidocaine at 3 mg/min. Because MEPs were being monitored, no additional neuromuscular blockade was administered. The patient received cefazolin 2 g intravenously prior to incision. During the procedure, the patient's blood pressure and heart rate were kept as close to baseline as possible. Because of this, the patient received ephedrine 15 mg and glycopyrrolate 0.4 mg for bradycardia and hypotension. Continuous SSEP and MEP waveforms were monitored by the monitoring technologist throughout the entire procedure.

The ketamine infusion was discontinued 45 minutes prior to extubation. The patient received labetalol 10 mg for tachycardia and hypertension that occurred during emergence from anesthesia. The lidocaine infusion was continued at 3 mg/min until the patient was transferred to

the post-anesthesia care unit (PACU). Final neurophysiological monitoring waveforms indicated improved amplitude and latency in the right upper extremity as compared to baseline, all other evoked potentials were at baseline. The ETT was removed and the patient placed on O_2 8 L/min via simple mask. A simple neurological exam indicated that the patient was able to follow commands with baseline strength in all extremities after she was transported to PACU.

Discussion

Prior to the extensive use of intraoperative neurophysiological monitoring, the "wake up test" was the only way to assess for new onset neurological deficit during spinal procedures.[2(p.539)] The wake-up test had several limitations including not being able to detect neurological insults as they were occurring in real time. Intraoperative neurophysiological monitoring, including SSEP and MEP, allows for real time monitoring of the ascending sensory nerve tracts via the dorsal column medial lemniscus pathway and the descending motor nerve tracts via the corticospinal pathway.[2]

SSEP evoked potential waveforms are obtained by an electrical stimulus being applied to peripheral nerves such as the ulnar or median nerve for upper extremities and the posterior tibial nerve for lower extremities.[1] The selected nerves are stimulated by either surface electrodes that are above the nerve on the skin or by fine needle electrodes.[1] The action potential that is generated from the electrical stimulus can then be monitored and recorded at specific points.[3] Recording electrodes for SSEP monitoring are placed at sensory cortex, cervical spine, Erbs point, and popliteal fossa.[1] Transcranial motor-evoked potential waveforms are obtained by an electrical stimulus being applied via stimulating electrodes placed in the scalp over the motor cortext.[1] The action potentials are then recorded at specific points such as the innervated muscle, the spinal column and/or the peripheral nerve.[1]

Nearly all anesthetics result in a dose-dependent suppression of both SSEP and MEP waveforms, as evident by a decrease in the evoked potential amplitude and/or an increase in latency as compared to baseline evoked potential waveforms. MEPs are generally more sensitive to the effects of volatile anesthetic agents than SSEPs.[3] Halogenated inhalational agents are known to cause a significant decrease in amplitude in both SSEP and MEP monitoring. In fact, these agents are capable of making it impossible to detect or acquire any evoked potentials especially with a MAC greater than 1.[4] Desflurane and sevoflurane are more commonly used over isoflurane due to their low solubility which allows for both a rapid induction and recovery of general anesthesia.[5] Isoflurane also causes a greater degree of suppression in evoked potential waveforms and sevoflurane is more likely to produce MEP suppression as compared to baseline evoked potentials than desflurane.[3,5] The suppressive effects of inhalational agents increase as the MAC increases. Both SSEP and MEP are able to be obtained with a 0.5 MAC but as the MAC increases above 0.5, the evoked waveform potentials will start to show suppression.[2]
The intravenous anesthetics and anesthetic adjuncts that are used with intraoperative neurophysiological monitoring produce a varied effect on the evoked potentials. Some of the intravenous agents used include propofol, lidocaine, dexmedetomidine, ketamine, and opioids. The amount of depression that propofol produces in SSEPs and MEPs is less than those produced by inhalational agents.[2] Propofol plays a large role in intraoperative neurophysiological monitoring. It is used to either decrease the amount of inhalational agents that are used in a

balanced anesthesia technique, or it is used as one of the main components of the general anesthetic as with a TIVA technique.[2] Given propofol's rapid metabolism, the infusion can be quickly titrated down to allow for improved SSEPs and MEPs if needed.[6]

Lidocaine is reemerging as an adjunct to anesthesia and it most definitely has a place within intraoperative neurophysiological monitoring. When a continuous infusion of lidocaine is used, either in conjunction with a balanced anesthesia technique or with a TIVA technique, the total amount of propofol used is decreased, the amount of opioids required is decreased, and the MAC value of an inhalation agent is able to be reduced.[7] Intravenous lidocaine has no appreciated effect on either SSEPs or MEPs.[7]

When dexmedetomidine is used as a continuous infusion, it can decrease both the amount of propofol required for induction and the infusion rate.[8] Generally, dexmedetomidine has little to no effect on SSEPs and MEPs, but if a loading dose is given too fast and the depth of anesthesia is deepened too quickly, both SSEPs and MEPs will be adversely affected.[8] A suppressive cumulative effect of SSEPs and MEPs can sometimes be seen with the co-administration of dexmedetomidine and propofol, but again, this is most likely related to the speed and the amount of the dexmedetomidine loading dose.[8] Ketamine is also another helpful adjunct to anesthesia as it decreases postoperative pain based on its analgesic properties.[2,6] When ketamine is given as a continuous infusion, it has no effect on latency, but increases the amplitude of both SSEPs and MEPs.[6]

Opioids produce a very slight decrease in amplitude and increase in latency with SSEPs and MEPs.[2] Remifentanil, sufentanil, and fentanyl can all be independently used with propofol as continuous infusions to provide anesthetic for intraoperative neurophysiological monitoring.[2] The major benefit of remifentanil is its rapid metabolism, expediting emergence and allowing a more rapid postoperative neurological assessment.[2] With the case report that was presented, the balanced anesthesia technique utilized consisted of 0.75 MAC of sevoflurane, an intravenous ketamine infusion at 10 mcg/kg/min, and a lidocaine infusion at 3 mg/min. During this case, there was no SSEP or MEP suppression.

In conclusion, intraoperative neurophysiological monitoring of SSEPs and MEPs are important tools to help detect potential new onset neurological deficits with spine surgery. During administration of the anesthesia with planned evoked potential monitoring, specific anesthetic techniques are required to maintain consistent and reliable SSEP and MEP waveforms. Proper planning and communication with the neurophysiological monitoring technician, the surgeon, and the entire surgical staff is paramount to ensure accurate and reliable neuromonitoring data. If evoked potential suppression is detected, both surgical and anesthetic interventions can be implemented immediately to preserve the integrity of ascending and descending nerve tracts.

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Primary Adrenal insufficiency and Pregnancy

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Keywords: adrenal insufficiency, pregnancy, anesthesia, Addison's disease

Primary adrenal insufficiency, also known as Addison's disease, results from an inability to generate an adequate supply of adrenocortical hormones.[1] Addison's disease is considered a rare, life-threatening condition and can be especially dangerous during pregnancy.[2] The estimated prevalence of Addison's disease in the general population in western countries is estimated to be 120-140 per million.[2] This case report is about a parturient with preexisting Addison's disease.

Case Report

A 28-year-old female patient presented for induction of labor at 39 weeks gestational age. The patient was 93 kg, and 168 cm tall. Medical history included Addison's disease, hypothyroidism, current pregnancy and anxiety. Her obstetrical history included a gravida 2, para 1 with a prior uneventful vaginal delivery. The patient had no past surgical history and denied any known drug allergies. She had routine prenatal care with regularly scheduled office visits. Current home medication regimen included levothyroxine, hydrocortisone, and fludrocortisone, and these medications were continued throughout the hospital stay. In addition, hydrocortisone 25 mg was given intravenously (IV) every six hours during delivery, and a one-time dose of 25 mg was given IV at the time of delivery. The patient's most recently available

laboratory values were hemoglobin 13.9 g/dL, hematocrit 40.6%, platelet count 18.4 x 10^9/L, and white blood cell count 11.7 x 10^9/L.

The patient requested epidural analgesia for control of her pain which was 7/10 with contractions. At the time of epidural analgesia, her cervical dilation measured at 4 cm and effacement was 40%. After consenting for an epidural placement, a 19-gauge Tuohy needle and subsequent catheter were placed midline at the L3-4 vertebral interspace using the loss of resistance technique. After a negative test dose, the epidural catheter was dosed using 0.25% bupivacaine 5 mL and fentanyl 100 mcg. Approximately 20 minutes after the initial loading dose was given, patient-controlled epidural analgesia (PCEA) was initiated. The PCEA contained 0.2% ropivacaine without epinephrine, and the pump was programmed to deliver 8 mL/hr with an optional patient-controlled bolus of 6 mL every 30 mins for a total maximum hourly dose of 20 mL.

The duration of the labor approximated 8 hours before fetal delivery. The PCEA bolus feature was activated twice throughout the 8 hours, and a final clinician bolus of 0.25% bupivacaine 3 mL and 2% lidocaine 4 mL was given approximately 10 minutes before fetal delivery. During labor, the patient received a total of 3000 mL of lactated Ringer's solution, and her vital signs remained unremarkable throughout the course of labor and delivery. The neonate had 1- and 5-minute APGAR scores of 8 and 9 respectively.

Discussion

Adrenocortical hormones, including mineralocorticoid and glucocorticoids, have far-reaching physiologic utility. The actions include anti-inflammatory activities, carbohydrate, protein metabolism, fatty acid metabolism, maintenance of electrolyte, maintenance of fluid balance, facilitation of catecholamine synthesis/action, and it assists in maintaining normal vascular permeability, tone, and consequently, cardiac contractility.[3] In Addison’s disease, the adrenal glands are unable to produce sufficient quantities of adrenocortical hormones.[1] A lack of mineralocorticoid secretion decreases renal tubular reabsorption leading sodium ions, chloride ions, and water to be excreted in urine and a decreased excretion of potassium.[1] The loss of sodium, chloride, and water results in decreased extracellular fluid volume and diminished cardiac output.[3] The lack of potassium excretion leads to hyperkaliemia.[1] A lack of glucocorticoids, mainly cortisol, leads to an impaired physiological reaction to bodily stress and widespread metabolic impairment.[1] A person with Addison’s disease is highly susceptible to the effects of even minor types of stress and bodily stresses such as a mild respiratory infection can lead to death.[1]

Moreover, in a healthy pregnancy, there is activation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased glucocorticoid secretion.[4] Throughout gestation, maternal ACTH, cortisol, androgens, aldosterone levels, and plasma renin activity are increased.[2] The increase in maternal glucocorticoid secretion is essential to maintain fetal growth and development, as well as maternal volume expansion and blood pressure maintenance.[2] Prior to delivery increased HPA activation fosters fetal organ maturation and myometrial activity.[2] The pregnant patient with Addison’s disease is unable to increase glucocorticoid secretion to meet physiological needs during gestation. Furthermore, aldosterone deficiency results in

hyperkalemia, hyponatremia, and decreased excretion of free water by the kidney which can complicate any pregnancy.[2]

Anesthetic management of a non-parturient patient with Addison's disease includes maintenance and repletion of glucocorticoids and replacement of water and sodium deficits.[3] In addition, Addison's disease may cause substantial fluid volume deficits that are typically manifested as hemodynamic instability.[3] According to Wall, there are no preferred anesthetic agent(s) or technique(s) when managing patients with Addison's disease. [3] To further complicate the issue, the literature is even more scarce for the anesthetic management of the patient with Addison's disease during pregnancy. One case report was found in which a general anesthetic was given because the patient refused regional anesthesia.[5] In this case, no immediate anesthetic complications were noted using general anesthesia.[5] However, while the exact precipitating factor is not known, it should be noted that the patient in the case study was admitted to the ICU with an Addisonian crisis on the 39th day post-cesarean section.[5]

Since 1956, maternal mortality from Addison's disease has been almost nonexistent because of the introduction of glucocorticoid replacement therapy.[6] In this case, a multidisciplinary approach was taken including glucocorticoid replacement therapy. Prior to labor and delivery, this patient was followed by her primary endocrinologist, a maternal-fetal medicine specialist, as well as the obstetrician and seen by the anesthesia team. Continuation of the fludrocortisone 0.1 mg/day during the pregnancy was decided upon, and the hydrocortisone was increased during labor to 25 mg every six hours and at the time of delivery. However, due to the stress of labor, current guidelines suggest an increase in that dose to hydrocortisone 50 mg IV be given in the second stage of labor and in the case of vaginal delivery, an additional 25-50 mg of hydrocortisone is advisable.[2] In addition, early labor analgesia can minimize the physical and emotional stress that can occur from labor and delivery.

If a parturient with Addison's disease has maintained proper steroid replacement therapy and there are no apparent contraindications, neuraxial anesthesia is an adequate anesthetic technique for a vaginal delivery. Neuraxial anesthesia can attenuate some of the additional increases in physiological stress during the peripartum period, but the practitioner must be mindful of possible negative synergistic consequences of hemodynamic instability with the use of neuraxial anesthesia in the hypovolemic patient with Addison's disease. Given the lack of current literature, further research is needed to find the optimal anesthetic management and analgesic technique for the parturient with Addison's disease. The guidelines previously mentioned may provide a basis for a safe anesthetic course.

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Suspected Placenta Accreta

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Keywords: placenta accreta, placenta previa, cesarean section

Placenta accreta is a rare but potentially fatal complication of pregnancy arising from the diagnosis of placenta previa, usually accompanied with previous cesarean section or uterine scaring. The primary pathophysiological process involves the abnormal attachment of the placenta to the myometrium, making normal detachment difficult.[1] For accreta cases, cesarean section is warranted, and appropriate planning essential. Although fatality is quite high, proper preparation can successfully decrease the mortality rates drastically. This case study examines an incidence of suspected placenta accreta with subsequent planning and anesthetic course.

Case Report

A 28-year-old, 35 4/7 week gestation, gravida 3, para 1 with a history of cesarean delivery scheduled for repeat cesarean section. The patient was diagnosed with suspected focal anterior placenta accreta via ultrasound. Past medical history included mild childhood asthma, hypertension, anemia, cholelithiasis, depression, and anxiety. Past surgical history included a cesarean section and appendectomy. The patient had an uneventful obstetrics course, but reported preeclampsia in a prior pregnancy. The patient received a course of betamethasone for fetal lung maturation forty-five days prior. Current medications included prenatal vitamins, ferrous sulfate, aspirin, and albuterol. Social history included social alcohol use prior to pregnancy, no history of tobacco use, and was married.

Upon arrival, two large bore intravenous lines were inserted and blood was drawn for a complete obstetric panel. The laboratory values included hemoglobin and hematocrit 11.7 g/dL and 35.5%, platelet count 308 10^3/L, potassium 4.1 mEq/L, magnesium 1.9 mEq/L, and phosphate 3.7 mg/dL. These values were within normal range.Standard hemodynamic monitors were attached. A continuous lumbar epidural was placed at the L4-L5 interspace and a test dosed of lidocaine 30 mg and epinephrine 15 mcg was administered to confirm placement. After confirmation of the negative test dose, the epidural was dosed with 2% lidocaine with 1:200,000 epinephrine 10 mL. A sensory level of T9 was achieved. A Foley catheter was placed by the labor and delivery

(L&D) registered nurse (RN). The patient was transported to the interventional radiology suite with hemodynamic monitoring.

The interventional radiologist placed bilateral internal iliac artery balloons via femoral access. The balloons were tested in the suite and then deflated with appropriate reinflation instructions given to both the obstetricians and anesthesia professionals. Fetal heart tones were monitored continuously by the L&D RN during the procedure. The patient was transported to the operating room for cesarean section. An epidural sensory level was checked and noted to be at T10. The epidural was redosed with 2% lidocaine with 1:200,000 epinephrine 10 mL to achieve a T4 level for cesarean section. Upon arrival in the operating room, the presence of blood products and an autologous cell saver was confirmed. Tranexamic acid 1 g and cefazolin 2 were infused. The cesarean section was performed with a classical incision. Oxytocin was immediately infused ~~at~~ after delivery and the patient received a total of 30 units. No additional tocolytics were given.

Based on the patient's preference to retain fertility, obstetricians attempted to remove the placenta rather than perform a gravid hysterectomy. This was accomplished via hysterotomy and gentle traction. The uterine window was noted beneath the hysterectomy and estimated blood loss was 1046 mL. In addition to the lumbar epidural local anesthetics, the patient received epidural morphine 3 mg, and intravenous (IV) ketamine 30 mg, fentanyl 100 mcg, and midazolam 2 mg for analgesia and anxiolysis after delivery of the fetus. The neonate's Apgar scores were 8 and 9, with no intensive care required. The patient's husband was present during the course of the procedure.

The patient recovered from anesthesia in a standard post anesthesia recovery room. An interventional radiologist pulled the internal iliac artery balloons while in the recovery room. Bilateral transversus abdominus plane blocks and a patient controlled analgesia infusion of hydromorphone were implemented postoperatively due to unrelieved pain. The mother and neonate were discharged home on postoperative day 3.

Discussion

Mortality from placenta accreta is noted to be as high as 7%.[1] Incidence ranges from 0.3% for first cesarean section and up to 67% with greater than 6 cesarean sections.[1] These rates appear to be rising due to an increased number of cesarean deliveries and advanced maternal age.[2] Diagnosis is difficult with ultrasound, with a high incidence of false positives and false negatives. Placenta accreta is the most common cause of peripartum hysterectomy.[3] Planned delivery between 34 and 36 weeks gestation with or without hysterectomy is recommended.[3,4] Cesarean section should be planned at a suitable tertiary care center with an appropriate multidisciplinary care team.[4] Blood loss is reported to range from 2000 to 5000 ml, with frequent coagulopathies.[3,5]

Based on previous ultrasound results, the patient's anesthetic and surgical course was planned out by a multidisciplinary team of anesthesia, high-risk obstetrician, interventional radiologists, neonatologists, and obstetrical nursing prior to the cesarean delivery. There was also a plan in place for the patient in the event of arrival in labor prior to the scheduled cesarean delivery at gestation of 35+4/7 weeks. The plan in place for scheduled delivery included early admission at

35 weeks with insertion of two large bore IV lines, obtaining a full set of laboratory values, and type and cross matching for 4 units of packed red blood cells. The decision was made to perform the cesarean delivery in the main operating room versus the labor delivery operating room due to resource and equipment availability in the event of a massive blood transfusion situation. The four units of packed red blood cells were to be in a cooler in the main operating room and an autologous cell saver retrieval system setup for utilization during the case.

The cesarean section was to be performed by three high-risk obstetricians with preoperative insertion of bilateral internal iliac artery balloons in interventional radiology. The internal iliac artery balloons were only to be inflated in the event of hemorrhage. The anesthesia plan was for a lumbar epidural catheter to be placed in the specialty care obstetrics unit prior to transfer to interventional radiology. A consent was to be obtained for emergent hysterectomy in the case of hemorrhage, and the presence of the postpartum hemorrhage cart in the main operating room. The threshold for conversion to general anesthesia from lumbar epidural was low and prepared for by the anesthesia professionals.

The role of preoperative internal iliac artery balloons for these cases has been the subject of research.[2,4,5] Prophylactic insertion in this case, although never inflated, was a decision made by the high-risk obstetricians. The procedure for insertion carries few risks but can provide much needed hemorrhage control if necessary. The use of cell saver autotransfusion for cesarean section has been under scrutiny based on concern for fetal cellular debris and amniotic fluid.[2,3] Cell saver techniques were used in this procedure, however the blood collected was never transfused based on total blood loss. The decision to use regional verses general anesthesia was made days before the planned case. The threshold for conversion to general anesthesia was low and communicated to all members of the multidisciplinary team. Additional risks associated with general anesthesia were deemed unnecessary, although prompt conversion could be achieved in a very short period of time. Video laryngoscopy was present in the room as well as all equipment necessary for emergent tracheal intubation.

Placenta accreta can present many challenges for multidisciplinary teams from diagnosis to delivery. Planning and communication are imperative to provide the best and safest outcomes to both the parturient and baby. The outcomes in this case were improved based on proper recognition of a possible placenta accreta, appropriate and timely multi-disciplinary preoperative planning, and appropriate preoperative consent for both cesarean section and emergent hysterectomy. Additionally helpful actions included the appropriate use of specialized personnel and equipment, and the ability to successfully detach the placenta from the myometrium without excessive bleeding.

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Vagal Nerve Stimulator Implantation and Collagen Deficiency

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Keywords: Vagal nerve stimulator, COL4A1

Up to one third of patients with epilepsy may fail to respond to traditional antiepileptic medications and other treatments.[1] Patients who are deemed pharmacoresistant may benefit from surgical interventions, including vagal nerve stimulator (VNS) implantation.[1] At a large military medical facility, 30 VNS implantation cases were performed from April 2007 to April 2018, with 21 cases of these occurring in patients less than 12-years-old. Due to the rarity of this procedure, a review of perioperative complications and anesthetic preparation for a VNS is presented in this case report.

Case Report

A 4-year-old, 12 kg male presented for VNS implantation. Pertinent medical history included intractable seizure disorder, collagen type IV alpha 1 chain (COL4A1) gene mutation, intraventricular hemorrhage, spastic cerebral palsy, ventriculomegaly ex vacuo, cortical vision impairment, hyperinsulinemia, verbal developmental day, and gastrostomy tube dependent. Reported seizure history included multiple seizures per day, lasting up to 45 minutes and unresponsive to break through medications. Allergies included nystatin, nonsteroidal anti-inflammatory drugs, and cefazolin. Medications included levothyroxine, vitamin B6, diazepam, levetiracetam, and multi-vitamin, all administered via gastronomy tube. Past surgical history included gastrostomy with feeding tube insertion in 2016 with no anesthetic complications.

Midazolam 5 mg was administered preoperatively via gastrostomy tube. In the operating room general anesthesia was induced by inhalation via mask with 4% sevoflurane and 50% N_2O/ 50% O_2 at 6 L/min. After loss of consciousness, a 22 gauge intravenous line (IV) was placed in right forearm, rocuronium 5mg IV was given and the trachea was successfully intubated with 4.5mm cuffed endotracheal tube via direct laryngoscopy, using a Macintosh 2 blade, yielding a grade 1 view of vocal cords. Tracheal intubation was confirmed with auscultation and end title carbon dioxide. The endotracheal tube was secured and general anesthesia maintained with isoflurane 1.3% inspired concentration in a mixture of O_2 1 L/min and air 1 L/min.

The surgeon accessed the left vagal nerve via the carotid sheath. The VNS generator was placed in the left pre-axilla and the leads were connected via tunneling in a pocket over the left clavicle. Hemostasis was obtained and integrity verified by a Valsalva maneuver via positive-pressure breath hold. A generator test was performed directly on the implant before surgical closure via wireless device without hemodynamic complications. After surgical closure of the incisions, a second generator diagnostic test was performed on the outside of the chest. Both generator tests were positive for vagal nerve stimulation and negative for bradycardia and asystole.

During the case, the patient received a total of morphine 1mg IV, acetaminophen 180mg IV, glycopyrrolate 0.12mg with 0.6mg neostigmine 0.6mg IV to reverse any residual neuromuscular blockade. Intravenous fluid total was normal saline 60 mL of and D5NS 120 mL. Estimated blood loss was 10 mL. Urine was not measured, but the patient had a wet diaper on arrival to the pediatric intensive care unit.

Discussion

Patients with a history of profound seizure disorders refractory to multiple methods of medical treatment are candidates for VNS. Vagal nerve stimulators were approved in 2007 by the Food and Drug Administration for treatment of refractory epilepsy for children over 12 years and approved for children over 4 years of age in 2017.[2] The concept of vagal nerve stimulation started in the late 1800s when manual carotid massage was found to stop seizures. Throughout the next century, more studies were completed and in the late 1900s VNS insertion was approved for refractory seizures.[3]

The mechanism of action for VNS decreasing the number of seizures for refractory epilepsy is not fully understood, but evidence supports a decrease in the number of seizures following implantation. Refractory epilepsy poses many threats to patients including permanent structural damage to the central nervous system and brain, as well as depression, anxiety, negative social impacts, and increased mortality from vascular disease, pneumonia, or sudden death.[4]

The most common type of VNS is a programmable pulse generator device that creates an electrical charge to the vagus nerve, which may ultimately suppress seizures. The device is typically placed on the left side, as the right vagal nerve primarily mediates the cardiac receptors and bradycardia and asystole may be more common.[3] The anesthetist must be vigilant during periods of generator testing and be prepared to treat bradycardia with atropine or asystole with stopping the generator test and perform cardio-pulmonary resuscitation, as required.[3]

Potential perioperative complications present challenges for the anesthetist, requiring vigilance and close observation of surgical progression. Exposure of the carotid sheath may lead to massive bleeding from accidental puncture of the internal jugular vein or common carotid artery, as the vagus nerve is located deep within the carotid sheath. The patient can experience profound bradycardia or asystole from generator testing and manipulation of the vagus nerve. Damage to the recurrent laryngeal nerve may cause dysphagia or stridor post-operatively, possibly requiring immediate airway intervention or additional surgery. Significant pain caused by tunneling from the neck to the generator implantation site may require increased anesthetic depth and opioids.

The most common complication is infection of implanted pulse generator, which can result in surgical replacement.[5]

Omari, Et al retrospectively reviewed 30 consecutive patients with VNS implantation between 2007 and 2014 including seizure frequency, surgical complications, and device adverse effects. Results from a minimum of two years of follow-up appointments showed 30% to100% reduction in seizure frequency, except for one patient who experienced increase in frequency. The most common adverse effects were coughing and voice changes with mild intermittent shortness of breath in 33% of patients. Surgical complications included wound infection in 3% of patients. [6]

The subject of the case study also had a COL4A1 gene mutation, which presented additional anesthetic concerns. Collagen type IV alpha 1 chain provides genetic instructions for type IV collagen. Type IV collagen molecules are flexible proteins and are an essential component of basement membranes, especially in the vasculature. They also support cell migration, proliferation, and differentiation.[7] Disorders related to COL4A1 deficiency include small vessel brain disease, cerebral aneurysms, porencephaly, retinal disorders, cataracts, kidney dysfunction, cardiac arrhythmias, seizures, mental delays, and hemolytic anemia. Medical management includes supportive care for affected systems and prevention of head trauma and anticoagulant exposure.[8]

The anesthetist must be prepared for increased risk of bleeding due to type IV collagen deficiency. Vagal nerve stimulator insertion requires dissection into the carotid sheath for surgical lead placement which is in close proximity to the carotid artery and internal jugular vein. This patient is at potential increased risk for bleeding during exposure of the carotid sheath, tunneling, inadvertent vessel puncture, and surgical closure. Without additional research and understanding of COL4A1, the potential for bleeding due to collagen deficiency cannot be determined, therefore the response to a compromised vessel is unknown.[8] Close observation to heart rate, rhythm, and blood pressure throughout the case is essential and changes in hemodynamics should be promptly treated.

Preparation and knowledge of COL4A1-associated vascular risks, such as cerebral aneurysms, must be taken into account for patients presenting for surgery. Although the literature on surgery and COL4A1 is minimal, successful cases of general anesthesia have been reported. Over one third of patients with epilepsy experience refractory seizures and may present for VNS implantation.[1] Although this is not a commonly performed surgery, the anesthetist must be aware of potential surgical complications and anticipate steps of the surgical process and maintain vigilance throughout the case.

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Methylenetetrahydrofolate Reductase Deficiency

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Keywords: MTHFR deficiency, nitrous oxide, methionine synthase, atherosclerosis, hyperhomocysteinemia

Methylenetetrahydrofolate reductase (MTHFR) deficiency is a condition related to a number of gene variants that interfere with the creation of a cosubstrate required in the remethylation of homocysteine to methionine.[1] Any obstruction of this remethylation process can lead to increased plasma levels of homocysteine.[1] The use of nitrous oxide is associated with an acute increase in plasma levels of homocysteine, which is more prominent in patients with MTHFR C677T or A1298C gene variants.[2] Although controversial, elevated homocysteine levels are believed to increase a person's risk for cardiovascular disease.[1,2] Because nitrous oxide is a drug that is commonly accessible to many anesthesia practitioners, implications regarding its safety and use in this unique population merit consideration.

Case Study

A 38-year-old, 65 kg, 163 cm Caucasian female presented for a robot-assisted laparoscopic hysterectomy due to menorrhagia and dyspareunia. Her medical history included anxiety and methylenetetrahydrofolate reductase (MTHFR) deficiency with homozygosity for the C677T mutation. The patient expressed having previous anesthesia complications that involved prolonged emergence and an extended need for mechanical ventilation. According to the patient,

the cause of the prolonged mechanical ventilation was not investigated, but she believed it may have been related to a diagnosis of MTHFR deficiency.

In the preoperative area, the patient appeared anxious and was intravenously administered midazolam 2 mg prior to transferring to the operating room. Prior to induction, standard monitors and a bispectral index (BIS) monitor were applied to the patient. The patient was then intravenously administered additional midazolam 1 mg and fentanyl 50 mcg and an inhalation induction with sevoflurane 8% and fresh gas flows (FGF) of 8 liters per minute (L/min) ensued. Once the BIS monitor showed an adequate anesthetic depth with readings in the forties and the patient appeared well anesthetized, succinylcholine 100 mg was given intravenously. After noting muscle fasciculations, a Cormack and Lehane grade 1 view was observed during laryngoscopy and a size 7.0 endotracheal tube was placed without difficulty. Tube placement was subsequently confirmed via auscultation and appropriate capnography was noted.

During maintenance of anesthesia, dexamethasone 10 mg, famotidine 20 mg, and vecuronium 4 mg were administered intravenously. She was given glycopyrrolate 0.2 mg intravenously prior to insufflation in order to prevent bradycardia and she remained hemodynamically stable throughout the case. A total of fentanyl 100 mcg and hydromorphone 1 mg were intravenously administered in divided doses for pain control. In preparation for extubation, glycopyrrolate 0.4 mg, neostigmine 3 mg, and ondansetron 4 mg were intravenously administered while the sevoflurane was titrated from a maintenance dose of 2.5% in O_2 2 L/min. Once the volatile anesthetic was turned off the FGF increased to O_2 10 L/min. Subsequent spontaneous respirations were achieved without issue and the patient quickly regained consciousness. The patient remained calm throughout emergence and was extubated to face mask with oxygen 6 L/min without complication. Following extubation she was taken to the recovery area and later transferred to a hospital room for observation overnight. She received a total of normal saline 1,500 mL and the estimated blood loss was 50 mL. Total anesthesia time was approximately 2.25 hours. The course of her anesthesia was uneventful.

Discussion

MTHFR gene deficiencies are relatively common, with some variants as prevalent as 25% in Hispanics and 10-15% in North American Caucasians.[1] In the presented case, the patient had a more severe form of the gene variation, homozygosity for the C677T mutation, placing her at an increased risk of experiencing associated complications. This and another variant, A1298C, are relatively common, being present in 0-3% of African Americans and 9-11% of North American Caucasians.[3] Related risks and potential complications will be discussed.

During the methionine cycle, a sulfur-containing amino acid identified as homocysteine is formed.[1] Homocysteine is subsequently methylated to the essential amino acid, methionine, by the enzyme methionine synthase.[1,2] Along with vitamin B12, methionine synthase utilizes the biologically active form of folate, methyltetrahydrofolate (MTHF), as a methyl donor.[1,2] MTHF is obtained from folic acid by the enzyme MTHFR.[1,2] Gene variations of MTHFR have different enzymatic activity levels which can result in elevated levels of homocysteine.[3] Cases documented throughout anesthesia literature discuss vitamin B12 activity impairment due to

sustained exposure to nitrous oxide. Because of this, it was decided to avoid the use of nitrous in the management of this case. Although nitrous oxide reduces vitamin B12's cofactor ability in methionine synthesis in all patients, in MTHFR-normal (no gene variation) patients, its effects require prolonged exposure to high concentrations of the gas. Issues normally only arise in circumstances in which scavenging systems are inadequate, such as during recreational use or in dental offices.[4] As opposed to those who are genetically normal, patients with a MTFHR deficiency, such as the presented patient, are at a heightened risk for developing hyperhomocysteinemia, even when exposed to subtherapeutic doses of nitrous oxide.[2,4]

The main complication associated with MTHFR deficiency is the elevation of total homocysteine levels (between 4 and 15 μmol/L).[3-7] Although hyperhomocysteinemia is associated with various health issues including osteoporosis, neurological symptoms, and dementia, the main concern is how elevated total homocysteine affects the cardiovascular system.[4-7] Because the patient had no other known health issues, only a preoperative complete blood count and basic metabolic panel were ordered with all results returning within normal limits. Current literature has shown an increase risk in developing atherosclerosis, coronary artery diseases, and other vascular issues with higher plasma homocysteine levels.[2,5,6] Because of this association, homocysteine has been deemed an individual risk factor for the development cardiovascular disease.[2,5] Although the exact mechanism is unknown, studies have shown that homocysteine affects endothelial cell function and can influence coagulation.[2,5] Hyperhomocysteinemia is also associated with an increased risk for venous thrombosis formation due to an altered coagulation state.[2] This procoagulant state is thought to be due to increased platelet adhesion to the endothelium and increased prothrombic factors, thus facilitating thrombus formation.[2,7] Atherosclerosis can develop with hyperhomocysteinemia potentially due to remodeling of the vascular smooth muscle cells and ultimately the arterial walls.[2] This can lead to decreased flexibility of the vasculature and alter the function of the vascular endothelium.[2] Although the patient had no known atherosclerosis, the issue of hyperhomocysteinemia and vascular muscle cell remodeling may, with an unknown amount of exposure, become an issue for her in the future, if administered nitrous oxide.

Because of the unknown cause of the patient's prolonged mechanical ventilation and the anesthesia professionals' lack of knowledge of MTHFR deficiency, several anesthesia practitioners performed a rapid investigation using on-line resources to finding the best possible anesthetic plan. One less credible source said to avoid the use of propofol. Although no other source validated this, we decided to not include propofol in our plan. Because the anesthetic implications related to these gene variants stem from the augmented risk of developing hyperhomocysteinemia from nitrous oxide, its use was duly avoided in the patient's anesthetic plan.[7] The end result of our rapid investigation led us believe that we should opt for a simple anesthetic plan using an inhalational induction with just sevoflurane.

Although there was unsubstantial evidence to tie the patient's MTHFR deficiency and the complications she experienced during her prior anesthetic, a new anesthetic concern arose. The nature of the patient's surgical procedure predisposed her to an increased risk for developing deep vein thrombosis. Current evidence has shown that factors including prolonged surgery time and abdominal hysterectomy can increase the risk of venous thromboembolism events after hysterectomy.[8] A leg compression device was utilized during this case.

There is no consensus regarding which level of plasma homocysteine is required in order to induce a hypercoagulable state, however research has shown that avoidance of nitrous oxide in patients with MTHFR deficiency is best practice at this time.[2,7] Further research following the case showed no evidence relating the use of propofol and genetic disturbances caused by MTHFR deficiency.[7] If faced with a similar scenario in the future, the author would opt for an intravenous induction with propofol while continuing to avoid the use of nitrous oxide. In the setting of the author's unfamiliarity with the effect of propofol on a patient with a MTHFR deficiency, an inhalational induction was an acceptable alternative.

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Medialization Thyroplasty with Arytenoid Adduction

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Keywords: medialization thyroplasty**,** arytenoid adduction, vocal cord paralysis, dysphagia, dysphonia, phonation, recurrent laryngeal nerve injury

Medialization thyroplasty is a surgical technique that medializes a paralyzed vocal cord utilizing an implant inserted through the thyroid cartilage.[1-3] The main reason this procedure is performed is to decrease the risk of aspiration while simultaneously improving the quality of the patient's voice, which is often hoarse due to unilateral vocal cord paralysis from recurrent laryngeal nerve (RLN) injury.[2-7] This technique allows the paralyzed cord to make contact with the unaffected cord, improving phonation. It is unique in the sense that the patient needs to phonate for the surgeon to ensure proper placement of a small silicone implant intraoperatively.[1,2]

Case Report

A 49-year-old, 170 cm, 56.7 kg female with a body mass index of 19.6 kg/m^2 presented for medialization thyroplasty with arytenoid adduction. The patient reported several allergies including propofol, fentanyl, and hydromorphone. Her health history included dysphagia and dysphonia from previous prolonged intubations in the ICU due to a motor vehicle accident, chronic shoulder pain with daily opioid usage, anxiety, and depression.

The patient was administered midazolam 2 mg intravenously preoperatively followed by an additional dose of 1 mg on arrival to the operating room. Standard noninvasive monitors were placed, and the patient was pre-oxygenated with O_2 15 L/min for five minutes. The patient was induced with lidocaine 50 mg, etomidate 12 mg, ketamine 20 mg, and rocuronium 30 mg.

A video laryngoscope was utilized providing a Cormack and Lehane grade 1 view. This allowed a 5.0 mm cuffed microlaryngoscopy tube (MLT) to be placed with ease. Correct tube placement was confirmed with bilateral breath sounds and a positive end tidal CO_2 waveform. The MLT was secured at 19 cm at the lip. Respiration was controlled via mechanical ventilation on pressure control ventilation with volume guarantee. General anesthesia was maintained with an expired concentration of sevoflurane 1% in a mixture of O_2 1 L/min and N_2O 2 L/min. Cefazolin 2 gm was administered prior to incision.

At 20 minutes prior to emergence, a dexmedetomidine infusion was started at 0.3 mcg/kg/hr, morphine 1 mg, and ketamine 10 mg were administered intravenously, and the sevoflurane was discontinued. In order to perform intraoperative phonation, the dexmedetomidine infusion was also discontinued. Neuromuscular blockade was antagonized with sugammadex 100 mg. Ondansetron 4 mg and famotidine 20 mg were administered to help prevent post-operative nausea. As the patient was able to follow commands and was ventilating spontaneously, the MLT was removed and a nasal cannula was placed with O_2 6 L/min. The patient was successful in phonating for the surgeon.

The case proceeded as planned without complications. For patient comfort, the surgeon requested further sedation after successful implant; therefore, the dexmedetomidine infusion was restarted at 0.6 mcg/kg/hr. She was also given morphine 4 mg in divided doses. The patient remained sedated but arousable for the remainder of the procedure.

Upon case conclusion, the dexmedetomidine infusion was discontinued. At this time, the patient became extremely agitated and aggressive. On transfer to PACU, the patient started hitting herself in the head and intensely scratching at her arms despite efforts to stop her. Once in PACU, the patient was administered lorazepam 2 mg and diphenhydramine 25 mg IV. The medications along with guided imagery were successfully utilized to help calm her down. Minimal blood loss was reported. Her total anesthesia time was approximately 3.5 hours.

Discussion

Unilateral vocal fold paralysis (UVFP) is a condition that has the potential to cause impairment in laryngeal function affecting quality of life through dysphonia, dysphagia, dyspnea, poor cough efficiency. There is also an increased risk of aspiration caused by poor vocal fold adduction.[4,5,7] This patient reported that she had previously spent a week intubated in the ICU due to a motor vehicle accident. The prolonged intubation along with her numerous past surgeries were determined to most likely be the cause of her UVFP.

Unilateral vocal fold paralysis can result from an unsuitable endotracheal tube (ETT) position, compression, and/or from high pressure in the ETT cuff.[8] When the ETT cuff is inflated, it can compress the anterior branch of the RLN between itself and the lamina of the thyroid cartilage, resulting in injury to the RLN.[8] UVFP is increased two-fold in patients that are intubated for 3-6 hours, and 15-fold in patients that are intubated for six hours or more and can most often be attributed to nerve or mechanical injury leading to incomplete closure of the vocal cords.[5-8] After videostroboscopy, it was determined that right-sided vocal fold paralysis was present. This caused an incomplete closure of the glottic opening, dysphagia, and dysphonia.

Medialization thyroplasty is considered to be the gold standard treatment for UVFP. It provides a permanent solution to an insufficient glottic opening. It utilizes an implanted stent that approximates the affected vocal cord with the unaffected vocal cord.[2,3] Typically, the procedure is performed under local anesthesia with minimal IV sedation. It is imperative that the patient understands what to expect in the operating room to have their full cooperation during the operation.[1-3] A skin incision is made at the level of the vocal cords to expose the thyroid cartilage where a window through the cartilage exposes the inner perichondrium. [1,2] After the window is created, the patient will phonate as it helps the surgeon determine the size and shape of the stent to be implanted.[1,4] The patient's quality of phonation helps determine the degree of medialization needed to further improve the patient's voice.[1,4] For this specific case, the surgeon had requested general anesthesia at the initiation of the procedure due to the patient's inability to hold still because of her chronic pain and anxiety. Therefore, the patient was sedated and intubated while access to the vocal cords was achieved.

Medialization thyroplasty performed alone often fails to fully adduct the arytenoids posteriorly resulting in a persistent posterior glottic gap.[2,8] Without adduction of the arytenoid, the vocal fold

is unable to achieve the physiologic phonating position, resulting in a weak voice and vocal fatigue.[2,8] Successful adduction results in a stronger voice, less vocal fatigue, and improvements to swallowing ability.[2,3,5-8] The arytenoid adduction is performed to correct a persistent gap between the vocal folds posteriorly and to correct vocal fold height mismatch, both of which can persist by only performing a thyroplasty.[1,2,8] A suture is placed around the muscular part of the arytenoid cartilage helping to adduct the vocal folds.[1,2] The suture emulates the vector of force of the thyroarytenoid muscle which rotates the arytenoid vocal process medialinferior.[2,8] This results in the closing of the posterior glottic opening.[2,8] Intraoperative imaging of the vocal cords with a fiberoptic scope is utilized during phonation to ensure proper repair.[1,2]

This patient's allergies, history of chronic pain, chronic opioid usage, and psychological issues led to a difficult anesthetic delivery. The patient spent the night on the surgical floor without any further issues and went home the next day.

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Sphenopalatine Ganglion Block for Postdural Puncture Headaches

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Key Words: postdural puncture headache, sphenopalatine ganglion block, epidural blood patch

Neuraxial anesthesia is the preferred anesthetic for pregnant women undergoing vaginal delivery or cesarean section. Postdural puncture headache (PDPH) is a serious and debilitating complication of neuraxial anesthesia.[1] PDPH is caused by leakage of cerebrospinal fluid (CSF) from a dural puncture site. Compensatory vasodilation occurs to maintain constant volume within the intracranial vault, contributing to patient discomfort.[2] The epidural blood patch has long been the gold-standard treatment for PDPH.[2] More recently however, the sphenopalatine ganglion block has been considered a less invasive, and potentially equally effective treatment.

Case Report

A 29-year-old, 76 kg, 162 cm, gravida 2, para 1 female presented to the obstetrical operating room for a planned cesarean section. Her medical history included asthma. Her surgical history included cesarean section. All laboratory values were within normal limits. The patient had no known drug allergies and was prescribed an albuterol inhaler which she reported using less than twice per year. The patient reported no past surgical or anesthetic complications. There was no known family history of problems with anesthesia.

The patient was premedicated with administration of a non-particulate antacid, sodium citrate, histamine-2 antagonist, famotidine, a dopamine antagonist, metoclopramide, as well as a 1 L fluid bolus of crystalloid via an 18-gauge intravenous (IV) in the left hand. Upon entry into the operating room, standard noninvasive monitors and nasal cannula with end-tidal carbon dioxide monitoring were applied. An initial set of vital signs was obtained with subsequent continuous monitoring of ECG, SpO_2, end-tidal CO_2, and a blood pressure every three minutes. The patient positioned herself in the sitting position at the side of the operating room table, curling forward over her abdomen to assist with identification of spinal landmarks and access to the subarachnoid space. Spinal anesthesia was performed with straightforward insertion of a 22-gauge cutting spinal needle at L3-L4, and intrathecal administration of 12 mg of 0.75% bupivacaine, 20 mcg fentanyl, and 200 mcg of morphine. Immediately following the procedure, the patient was placed in a supine position with left uterine displacement, prepped, and draped for the procedure. The patient's blood pressure was intraoperatively managed with crystalloid administration and a 20 mcg/mL phenylephrine infusion administered intravenously and titrated to maintain the patient's blood pressure within 20% of her baseline. Oxygenation was maintained with O_2 2 L/min via nasal cannula.

Forty hours following the cesarean section while in the mother-baby unit, the patient reported to the unit nurse a headache, which became worse in the sitting position and improved while supine. Upon initial report of the headache, no conservative treatments for PDPH such as caffeine, fluid, or sumatriptan were offered by the unit staff. Within 8 hours following the initial

report of the headache, the patient subsequently reported photosensitivity and tinnitus. The on-call anesthesia team was then called to the bedside for consultation.

After assessment of the patient 48-hours postoperatively, a diagnosis of PDPH was made. The patient was offered an epidural blood patch or sphenopalatine ganglion block, with discussion of the benefits and risks for both treatment options. The patient chose to proceed with the sphenopalatine ganglion block. The patient was placed supine with the neck extended in the sniffing position. A 10 cm cotton tipped applicator soaked in 4% lidocaine was slowly advanced along the superior border of the middle turbinate until it reached the posterior wall of the nasopharynx. The applicator was left in place for 30 minutes while the patient was instructed to remain in the supine position.

After 30 minutes the patient reported her headache had resolved. The cotton-tipped applicator was removed from the nasopharynx. One hour following removal of the applicator she reported no headache and a resolution of all associated symptoms. The patient was discharged home within two hours following resolution of the headache with no signs of returning symptoms.

Discussion

PDPH is a common complication of neuraxial anesthesia. Spinal anesthesia and epidurals are the predominant and preferred forms of anesthesia administered to pregnant women undergoing vaginal delivery or cesarean section. PDPH is caused by leakage of cerebrospinal fluid (CSF) from the site of dural puncture during spinal or epidural anesthesia. Compensatory vasodilation occurs due to loss of CSF volume in an attempt to achieve hemostasis and maintain constant volume within the intracranial vault.[2] The pain experienced is a result of downward traction on pain fibers in the central nervous system due to depleted CSF volume.[2] The epidural blood patch (EBP) has been the gold-standard treatment for PDPH.[3] The EBP is hypothesized to work by creating a patch over the dural puncture and therefore restoring intracranial CSF volume and pressure.[3] More recently however, the sphenopalatine ganglion (SPG) block has been considered a less invasive, and potentially equally effective form of PDPH treatment.

The SPG is an extracranial parasympathetic ganglion with multiple neural roots located on each side of the mid-face.[4] The SPG is found within the pterygopalatine fossa, which is described as a small, inverted pyramidal space measuring approximately two cm high and one cm wide.[4] The maxillary division of the trigeminal nerve receives afferent projections that pass through the SPG and form the sensory component of the SPG. The SPG is thought to play a role in the activation of the trigeminal-autonomic reflex, which results in headache pain.[4] It is postulated that when the dura is punctured and there is a leakage of CSF and a drop of pressure within the intracranial vault, postganglionic parasympathetic fibers from the SPG, which innervate cerebral and meningeal blood vessels, are activated and release chemical mediators that cause vessel dilation and activation of the trigeminal-autonomic reflex.[4] This provides a nociceptive stimulus perceived as headache pain by the sensory cortex.[4] Given the proposed role of the SPG in headache pain, SPG blocks are performed to provide symptomatic relief from PDPH.

Literature recommends performing the SPG block with the patient in supine position with the neck extended in the sniffing position. A 10-centimeter cotton tipped applicator soaked in 4% lidocaine is then slowly advanced along the superior border of the middle turbinate until it reaches the posterior wall of the nasopharynx. The applicator should then be left in place for 20 to 30 minutes to allow for diffusion of local anesthetic across the mucosa to reach the SPG.[3] Relative contraindications of the SPG block are facial malignancies, infection, thrombocytopenia, coagulopathy, and those with varying complex facial or nasopharyngeal anatomy.[3] Following the procedure, it is recommended the patient be monitored for 40-60 minutes for epistaxis, facial numbness or weakness, double vision, fever, exacerbation of symptoms, or a new onset headache on the contralateral side.[3]

Portuguese anesthesiologists Cardoso et al. published a case study providing support for the SPG block as a treatment for PDPH.[5] Cardoso et al. explained the patient felt relief of PDPH symptoms within five minutes and was subsequently discharged home.[5] The patient was contacted the next day, as well as one week following, with no reports of pain at either time.[5] Anesthesiologists Nair and Rayani published an article in The Korean Journal of Pain supporting the use of the SPG block specifically for PDPH and emphasize the drawbacks of the EBP such as another inadvertent dural puncture, meningitis, seizures, and loss of hearing or vision. The SPG block had the reported benefits such as reduced visit time, adequate pain relief, and the avoidance of the EBP.[6]

Most recently, Cohen et al. published a 17-year retrospective study comparing the SPG to the EBP for PDPH treatment.[7] The study is believed to be the first-ever to compare the SPG block and EBP for PDPH. Finding were statistically significant for patients who received the SPG block experienced faster relief and no post-treatment complications as compared with their EBP counterparts.[7] Additionally, both groups experienced 100% relief of symptoms after one-week of receiving the treatment.[7] The patients who received the SPG block in this study also received the block a minimum of once and a maximum of three times within a three-day period.[7]
At this time, the SPG block is not always offered to patients as a treatment for PDPH. However, the SPG block can allow more patients to experience quick, safe relief without having to endure the potential complications of the EBP.

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Anesthetic Management of the Patient with Pheochromocytoma

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Pheochromocytomas are tumors that secrete catecholamines and most commonly arise from chromaffin cells in the adrenal medulla.[1] These tumors are able to produce, store and secrete their own catecholamines, mainly epinephrine and norepinephrine. Normal functioning adrenal glands secrete approximately four times more epinephrine than norepinephrine, while these tumors predominately secrete norepinephrine. In the majority of cases, it is difficult to accurately anticipate which catecholamine and concentration will be secreted.[1] The primary clinical manifestations of pheochromocytoma are paroxysmal hypertension, headache, sweating, and palpitations. The combination of diaphoresis, tachycardia, and headache in the hypertensive patient are the hallmark triad of symptoms for pheochromocytoma.[2]

Case Report

A 69-year-old, 104 kg female was scheduled to undergo a laparoscopic left adrenalectomy for a left-sided pheochromocytoma. The patient had an allergy to Naproxen, which caused generalized swelling. Her past medical history was significant for hyperlipidemia, hypertension, hypothyroid, rheumatoid arthritis, chronic obstructive pulmonary disease and type II diabetes mellitus. Past surgical history included abdominoplasty and spine surgery. The patient had a 30 pack-year smoking history and had smoked, as recently as, the morning of surgery.

Preoperatively, midazolam 2 mg was administered intravenously (IV), with another 1 mg given upon entering the operating room. Once in the operating room, the patient was transferred from the stretcher to the operating room table. Standard monitors were applied including a pulse oximeter, electrocardiogram leads, and non-invasive blood pressure cuff. A bispectral index (BIS) monitor was also applied. Once these monitors were applied, 2% lidocaine 1 mL was subcutaneously infiltrated around the right radial artery followed by successful placement of an arterial line.

The patient was pre-oxygenated with O_2 10 L/min for 5 minutes until the end-tidal O_2 was greater than 90%. Anesthesia induction was administered utilizing IV fentanyl 150 mcg, propofol 150 mg, rocuronium 50 mg, and 4% laryngotracheal administered lidocaine 4 mL. The trachea was intubated via direct laryngoscopy with a MAC 3 blade and placement of a cuffed 7.5 mm endotracheal tube was verified with positive $ETCO_2$, bilateral breath sounds, and chest rise. The patient was placed on mechanical ventilation using pressure control volume guarantee with general anesthesia maintained utilizing sevoflurane titrated to keep BIS between 40-60. The respiratory rate was maintained between 8 to 14/min in order to maintain $ETCO_2$ at 32 mm Hg with a tidal volume of 600 mL. Once the airway was secured, a second 18-gauge IV catheter was placed in the left wrist.

Prior to the surgical incision, the patient's mean arterial pressure (MAP) fell below 65 mm Hg. Phenylephrine boluses of 50 to 100 mcg were administered to maintain a MAP greater than 65 mm Hg. The patient received a total of 550 mcg phenylephrine and 1.3 L plasmalyte IV prior to surgical incision. During this time, an arterial blood gas (ABG) was drawn and showed an ionized calcium level of 4.4 mg/dL. The patient subsequently received 1000 mg calcium chloride IV. The patient was re-dosed with rocuronium 30 mg IV prior to incision as train-of-four (TOF) revealed there were two twitches present.

After incision, the patient received 50 mcg fentanyl IV and 5000 units of subcutaneous heparin per surgeon's request. Once the surgeon started to manipulate the tumor, the patient's MAP increased to 100 mm Hg. Nitroglycerin boluses of 20 mcg were administered IV to maintain MAP below 100 mm Hg. A total of 60 mcg NTG was given IV prior to removal of tumor. After the tumor removal, the patient became hypotensive and was administered 100 mcg phenylephrine and 500 mL of 5% albumin IV to maintain MAP above 65 mm Hg. Subsequent to this intervention, the MAP remained above 65 mm Hg. Prior to extubation, the patient had two twitches with the TOF, received 1 mg hydromorphone, 1000 mg IV acetaminophen, and was reversed with sugammadex 200 mg. The patient was extubated without incident and transported to PACU while waiting for an ICU bed.

Discussion

Proper anesthetic management of the pheochromocytoma patient begins well before the patient presents to the hospital on the day of their surgery. The patient should be optimized, which includes being started on an alpha antagonist a few weeks prior to surgery. The reported benefits of preoperative alpha blockade, include reduction of vasoconstriction, restoring intravascular volume, normalizing hematocrit, correction of regional wall motion abnormalities, symptom control, and reduction of intraoperative hemodynamic crises.[3] When starting patients on preoperative medications, it is imperative that alpha blockers are started prior to beta blocker administration. If this sequence is not followed appropriately, it can lead to unopposed alpha receptor stimulation resulting in a hypertensive crisis.[4] This patient had originally been prescribed phenoxybenzamine, but was switched to doxazosin due to cost considerations. The patient had been taking the doxazosin for over eight weeks prior to surgery. After the patient had been on doxazosin for three weeks, it was determined that the alpha blockade was sufficient and she was then started on propranolol.

There are three main areas of intraoperative consideration for the pheochromocytoma patient including intubation, tumor manipulation, and tumor removal.[5] The first two scenarios are critical as they can lead to uncontrolled hypertension. However, successful tumor removal may lead to hypotension as the remaining catecholamines are metabolized accompanied by downregulation of adrenergic receptors.[6] During intubation. the main goal is to reduce uncontrolled hemodynamic responses from excessive catecholamine release. This unintended response may be achieved with preoperative management combined with sufficient blunting of the sympathetic nervous system.[5] Fentanyl, remifentanil, and sufentanil can help mitigate hypertension and pain related to intubation making them an ideal choice for induction. Dexmedetomidine has analgesic, sedative, and sympatholytic properties and has been shown to reduce catecholamine release in pheochromocytoma patients. Dexmedetomidine acts on central alpha-2 receptors, which regulate norepinephrine though a negative feedback loop that inhibits its release.[7] After receiving only midazolam preoperatively, it was determined by the anesthesia practitioner that the patient was sufficiently sedated, and induction could proceed utilizing fentanyl, propofol, rocuronium, and lidocaine. The patient tolerated intubation well, but may have benefited from a dexmedetomidine infusion as there were hemodynamic instabilities prior to the start of surgery that required vasopressors.

After intubation, the next phase causing major hemodynamic changes included insufflation and tumor manipulation. Peritoneal insufflation can be responsible for initial hemodynamic changes as the tumor is compressed or blood flow to the tumor is altered.[6] As the tumor is dissected, there are surges in the release of epinephrine and norepinephrine that can cause labile hemodynamics. Vasodilators are the primary treatment for intraoperative hypertension, while beta blockers are used to treat tachyarrhythmias. Sodium nitroprusside (SNP) is a popular choice as it is a potent direct vasodilator that acts on venous and arterial smooth muscle.[1] Utilizing SNP is preferred for its effectiveness in managing hypertensive crises as it is short acting and can be adjusted to accommodate for sudden changes in blood pressure.[8] Phentolamine is a nonselective alpha antagonist that can be given as an IV bolus or continuous infusion. This medication was not readily available in the operative room during surgery but was available in pharmacy if needed during an emergency. Nicardipine, a calcium channel blocker, is useful for control of blood pressure, but was not needed in this case. Beta blockers, such as labetalol and esmolol are useful for tachycardia in addition to hypertension.[4] In this case, NTG was administered as it was more readily available, and the patient became hypertensive without arrhythmias. Overall, NTG is a potent vasodilator that acts on venous capacitance vessels and ultimately decreases preload. The patient was given 20 mcg boluses of NTG IV, in conjunction with incremental increases in sevoflurane, as these interventions proved to be sufficient to adequately lower blood pressure.

The final stage of major consideration occurs once the effluent vein is clamped and tumor removal begins. This process leads to hypotension resulting from decreased catecholamine release.[5] Hypotension is treated with fluid boluses to restore depleted intravascular volume and vasopressors. Phenylephrine, a direct alpha agonist is considered the medication of choice to treat hypotension once the tumor is removed. Ephedrine, an indirect alpha and beta agonist, should not be used as it can lead to excessive catecholamine release and uncontrolled hypertension.[2] Norepinephrine, a combined alpha and beta agonist, and vasopressin can also be used if phenylephrine is not effective in treating hypotension.[6] The patient responded well to phenylephrine and had a heart rate that was able to support its use.

Preparation and anticipation are two of the most important aspects when caring for the pheochromocytoma patient. There are no absolute guidelines for medication treatment throughout the surgery, which makes proper planning imperative for the anesthesia practitioner. Having a plan and medications available can make the difference between a smooth, uneventful surgery and one where the anesthesia practitioner is constantly attempting to manage the rapid variations in the patient's blood pressure.

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Effectiveness of Ketamine in Reducing Post-Operative Opioid Consumption

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Keywords: ketamine, postoperative pain, opioid consumption, preemptive analgesia, pain management

Introduction

Despite the availability of new treatments, guidelines, and protocols, up to 80% of patients experience moderate to severe pain after minor surgery.[1] Inadequate surgical pain management leads to a chronic pain condition referred to as persistent postoperative pain (PPP).[2] A cross-sectional survey of 12,932 patients, of whom 2,043 had undergone a surgical procedure greater than three months prior, found that 40.4% developed PPP.[2] PPP affects millions of patients every year, with pain lasting for months to years, resulting in undo patient suffering.[2] This raises the potential for significant impact on both patients and their families, which can cause quality of life to deteriorate. Development of PPP is a potentially devastating outcome from an otherwise successful procedure.

Opioids are frequently administered to manage postoperative pain, which often results in chronic use. Brummett et al. analyzed insurance claims of 36,177 adults to compare opioid consumption pre and post-operatively.[3] Six (6) percent developed chronic opioid use, defined as an opioid prescription filled greater than 90 days following a surgical procedure. This finding supports the fact that opioid use after elective surgery could lead to chronic opioid use.[3] The abuse of opioids and associated overdose deaths are well-known problems in the United States. The Center for Disease Control and Prevention estimates opioid overdose accounted for more than 33,000 deaths in 2015, with more than sixty percent involving prescription drugs.[4] Over the course of the last decade deaths resulting from opioid overdose have risen at an alarming rate. In 2017 the number of opioid overdose related deaths was six times higher than in 1999, with an average of 130 Americans dying daily from opiod overdose.[4] Thus, decreasing postoperative opioid consumption may curtail chronic opioid use and eventual mortality from opioid overdose.

A non-opioid multimodal approach has been suggested as an alternative to opioids for management of postoperative surgical pain. One non-opioid drug that is being used to manage postoperative pain and limit opioid consumption is ketamine, an N-methyl-d-aspartate (NMDA) receptor antagonist. At sub-anesthetic dosages, defined as 0.4 mg/kg or less, ketamine exerts its' profound analgesic effect with minimal psychological adverse effects.[5-6] Ketamine exerts its' potent analgesic effect primarily by blocking the NMDA receptors at the level of the spinal cord and midbrain, which attenuates afferent nociceptive impulse transmission to the brain.[5-7]

The purpose of this evidence-based project was to examine the current literature on the opioid-sparing effects associated with the use of low-dose ketamine in a multimodal analgesic approach for adults undergoing gastrointestinal (GI) and gynecological (GYN) surgical procedures. Specifically, we examined whether administration of low-dose ketamine significantly reduced

postoperative pain scores and opioid consumption. In addition, we investigated the effective dose of ketamine and the appropriate time of administration to achieve optimal efficacy.

Methods

Evidence-based Practice Model

Using the population, intervention, comparison, and outcome (PICO) format, the following clinical question was developed: In adult patients undergoing gastrointestinal or gynecological surgery (P), does the administration of low dose intravenous ketamine of 0.4 mg/kg or less (I) reduce the incidence of postoperative pain and decrease opioid administration (O)?

Search Methods

A thorough search of the empirical evidence was conducted using PubMed, CINAHL, and Google Scholar databases, with search terms including "ketamine AND postoperative pain AND analgesia". The term "opioid consumption" was then added to narrow down the number of results. Inclusion criteria include human clinical trials published between 2012 and 2018, written in English, and adults 18 years and older undergoing GYN and GI surgery.

Article Yield & Levels of Evidence

The initial search yielded 106 results. After including the additional search term "opioid consumption" the results were reduced to 29 articles in PubMed, 23 in CINAHL, and 22 in Google Scholar. Of these, 25 articles were eliminated as they did not involve GI or GYN surgery. According to the Joanna Briggs level of evidence, 4 prospective randomized controlled trials providing level II evidence were present and selected from the remaining articles for analysis.

Literature Analysis

Gastrointestinal Surgery

In 2015 Kaur, Samoa, and Aggarwal performed a randomized-controlled study to examine the influence of ketamine on postoperative pain in patients undergoing laparoscopic cholecystectomy.[8] Eighty patients of both male and female sex, ASA status I or II, ages 21-50 years old were included.. Forty patients received a ketamine bolus of 0.2mg/kg at the induction of general anesthesia followed by an infusion of 0.1 mg/kg/hr throughout the duration of the procedure, and forty received normal saline (NS) at a similar volume and rate.[8] The study found that the ketamine group reported less pain than the NS group six hours postoperatively, but at 12 and 24 hours postoperatively, there was no significant difference between the groups. On average, the ketamine group consumed less morphine. This difference was statistically significant ($P<0.05$). No participants experienced hallucinations, sedation, headaches, dizziness, or respiratory depression. The authors concluded that IV infusion of low-dose ketamine in the intraoperative period significantly reduced postoperative pain and analgesic requirements.[8]

In 2017, Jain and Kochhar perfomed a randomized-controlled trial to observe if the timing of ketamine administration played a significant role in the occurrence of acute postoperative surgical pain in patients undergoing abdominal surgery.[9] Ninety ASA status I & II patients, aged between 18 and 65 years undergoing abdominal surgery under spinal anesthesia were selected to

participate in the trial. Patients undergoing emergency surgery were excluded. Using a double-blinded approach, 90 participants were divided into 3 groups: each assigned a different time frame to receive a dose of 0.25 mg/kg IV ketamine, either pre-incision, pre-incision and during skin closure, or only during skin closure. Although the results of the study showed a reduction in postoperative pain based on a Visual Analog Scale (VAS) in all 3 groups, the greatest reduction in postoperative pain was seen in the group receiving ketamine both before skin incision and during skin closure.[9]

Gynecological Surgery

Haliloglu and colleagues performed a randomized, double-blinded, placebo-controlled study to examine the effect ketamine had on postoperative morphine consumption in adult women, ASA class I & II, undergoing cesarean section under general anesthesia.[10] Fifty-two patients were divided evenly into two groups: Group one received a 0.5 mg/kg bolus dose of ketamine with induction of general anesthesia followed by an infusion of 0.25 mg/hr throughout the surgery, while group two received identical volumes of saline. Overall, morphine consumption at 0-6 hour, 6-12 hour, 12-18 hour, and 18-24 hour intervals were all decreased for group one patients. Additionally, the ketamine group had a significantly lower cumulative morphine consumption at 24 hours postoperatively.

Suppa and colleagues performed a randomized, double-blinded, placebo-controlled study in women undergoing elective cesarean section.[11] The intervention group of participants received a 0.5 mg/kg bolus of IV ketamine ten minutes after delivery of the fetus, followed by 2 mcg/kg/min ketamine infusion for twelve hours. The control group received a placebo administered in the same manner. Ketamine use reduced morphine requirements needed for rescue analgesia up to 24 hours postoperatively. Additionally, three years after surgery, there was no differences in residual pain between the groups.

Dosage for Analgesia

The empirical evidence cite the effective intraoperative bolus dose ranges of IV ketamine to be 0.3 mg/kg to 1.2 mg/kg.[6-11] Using clinical data taken from observation of 1,264 cases over a 5 year period, Friedberg concluded that a single 50 mg IV bolus dose of ketamine administered 3 to 5 minutes prior to initial surgical stimulation effectively blocked 98-99% of NMDA receptors in the midbrain, and witnessed that adult patients remained motionless in response to surgical stimulation.[7] While this observational study is clinically relevant, the 50mg bolus creates a wide weight-based dosage variability. The author argued the adult brain weighs approximately 1.5kg and does not vary with adult body weight and the midbrain (which the NMDA is a very small portion) accounts for a small percentage of the overall brain.[5,7]

Ketamine administration before surgical incision blocks the NMDA receptors in the midbrain and prevents transmission of impulses to the cortex for interpretation, thus avoiding the "wind-up" phenomenon associated with the pain response cascade.[6-7] In simpler terms, the brain does not respond to surgical stimulation because it does not receive those inputs. Although Friedberg's method has not been confirmed by a large randomized controlled trial, the administration of a single dose of 50mg IV ketamine is informally known to anesthesia and pain management personnel as the "nifty fifty," and is said to block the most noxious stimulus to the

brain. Empirically, the 50mg dose equates to 0.35–1.2 mg/kg for adults weighing between 120 and 280 pounds.

Timing of Administration

Many studies have compared ketamine's analgesic effects related to the timing of administration relative to surgical incision. The reaserch supports that a single injection prior to surgical stimulation may be insufficient to achieve desired postoperative analgesia.[5] Research performed by Amaya and colleagues show that painful chemical mediators are released both during and after surgical stimulation.[12] Thus, a single injection of ketamine at the beginning of an operation will likely not provide effective analgesia to last into the postoperative period. On the other hand, Himmelseher and Durieux argue that the ideal dosing regimen should include a pre-incision bolus followed by additional dosing throughout the length of the case in order to maintain adequate plasma concentrations during all times of painful stimulation.[6] Current literature shows that receiving a bolus dose between 0.3 – 1.2 mg/kg of IV ketamine at multiple intervals provides the most effective postoperative pain relief.[7,9]

Table: Summary of literature on intraoperative ketamine

Author	Level of Evidence	Population	Purpose	Findings
Kaur et al.[8]	Randomized, double-blind controlled clinical trial; Level II	80 adult patients undergoing open cholecystectomy under general anesthesia.	To observe pain scores at different time intervals and cumulative morphine consumption over 24 hours	-The group receiving ketamine reported less pain 6 hours post-operatively, but there was no significance between the groups at 12 and 24 hours. -Additionally, the group receiving ketamine had a significant reduction in morphine consumption.
Jain et al.[9]	Randomized, double-blind controlled clinical trial; Level II	90 adult patients undergoing abdominal surgery under spinal anesthesia.	To identify how timing of ketamine administration effected postoperative pain scores. Doses were given pre-incision, pre-incision and during skin closure, or during skin closure only.	-Results showed reduced pain scores in all 3 groups. -The most significant reduction was found in the group which received doses both pre-incision and during skin closure.
Haliloglu,	Randomized,	52 adult women	To evaluate the effect	-The average 24-

et al.[10]	double-blind controlled clinical trial; Level II	undergoing elective Cesarean section under general anesthesia.	of pre-incision low dose ketamine on post-operative pain and analgesic consumption.	hour morphine consumption was lower in all patients whom received ketamine.
Suppa et al.[11]	Randomized, double-blind controlled clinical trial; Level II	56 adult women undergoing elective repeat Cesarean section with spinal anesthesia.	To evaluate the effectiveness of ketamine at inducing postoperative analgesia and preventing neuropathic pain.	-Morphine consumption was reduced at 4-8h, 8-12h, and 12-24h postoperatively. -Following 3 years, patients reported no residual pain along the T10 dermatome.

Conclusion

Current literature suggest that low-dose IV ketamine in the range of 0.3-1.2 mg/kg may be effective for pain management and reduce opioid consumption after GI and GYN surgery. Controlling postoperative pain significantly decreases the incidence of developing PPP and may decrease the likelihood of patients requiring opioids for prolonged periods.[1,2] Given the magnitude of the current opioid epidemic, ketamine has the potential to play a large role in reducing opioid administration, which could lead to a decreased risk for opioid abuse and dependence. This evidence based practice analysis report supports ketamine is most effective when administered both prior to surgical stimulation and repeated just before the time of skin closure.[7-9] Additionally, the findings of the project support dosages in the range of 0.3-1.2 mg/kg exhibiting the greatest analgesic benefit[5-11], which parallels the observational study which used a universal 50mg approach to administration of pre-incisional ketamine.[7] As more clinicians implement the use of ketamine in to their practice, postoperative pain will likely decrease, which will reduce the demand for opioids. With the ongoing opioid crisis it is imperative that anesthesia practitioners implement strategies to reduce postoperative opioid requirements. One approach is the use of multi-modal therapy with ketamine as a preemptive analgesic agent. Ketamine provides a reliable alternative to narcotic opioids in the field of acute pain management and could be a way for anesthesia personnel to limit the spread of the worsening opioid epidemic.

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Sphenopalatine Ganglion Blockade for the Treatment of Headaches

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Keywords: local anesthetic, lidocaine, bupivacaine, block, sphenopalatine ganglion, pterygopalatine, sphenopalatine fossa, intranasal, migraine, headache

Introduction

Headaches are a leading case of disability worldwide with a lifetime incidence of 93% in men and 99% in women.[1,2] Headaches are a primary complaint in 3-5% of all emergency department (ED) visits; 90% of these being chronic in nature.[2,3] Oral medications given in the ED to relieve these headaches often are only partially effective.[3] Intravenous medications have the potential for severe side effects, require intravenous access, and are susceptible to drug shortages.[3] The ideal treatment for chronic headaches would be effective in providing pain relief for an extended period of time, be fast acting, have minimal side effects and simple to administer. [3,4]

Sphenopalatine ganglion (SPG) blocks may meet these specifications thus offering a promising treatment for chronic headaches in this prevalent patient population.

Located under the maxillary branch of the trigeminal nerve within the pterygopalatine fossa, the SPG is the largest collection of neurons outside the brain.[5,6] The SPG is innervated by the maxillary division of the trigeminal nerve and contains sensory, parasympathetic and sympathetic components.[1,6] Activation of parasympathetic nerves within the SPG via trigeminal afferents is thought to be implicated in migraine development.[7] It has been proposed that stimulation of the SPG can cause release of neurotransmitters and vasoactive peptides which lead to cerebral vasodilation and neurogenic inflammation that activate the trigeminal nociceptors causing headache pain.[5,6] The purpose of this evidence-based practice analysis is to investigate the effects of local anesthetic applied to the sphenopalatine ganglion in the treatment of headaches.

Methods

Evidence-based Analysis Model
A population, intervention, comparison, and outcome (PICO) question was developed to provide a framework for the research and literature review process. "Do patients presenting with chronic migraine, cluster, or tension headaches (P) who are treated with local anesthetic (I) compared with normal saline (C) have reduced pain scores (O) when administered into the sphenopalatine ganglion?"

Search Methods
A literature review was conducted by searching the following databases: Cumulative Index to Nursing & Allied Health Literature (CINAHL), Cochrane Collection, EBSCO, Google Scholar, PubMed, Wiley Online Journal Library. Keywords utilized in the literature review included: local anesthetic, lidocaine, bupivacaine, block, sphenopalatine ganglion, pterygopalatine, sphenopalatine fossa, intranasal, migraine, and headache. Inclusion criteria were studies published in a peer-reviewed journal that examined the utilization of local anesthetics administered in the sphenopalatine ganglion to treat migraine, cluster, or tension headaches. All level I and II evidence articles published between 2010-2018 that were written in English and contained the keywords were included for analysis.

Levels of Evidence
Five articles were found that met the criteria for this review. All five articles were double-blinded randomized controlled trials which provided Level I evidence based on the Joanna Briggs Institute Levels of Evidence Hierarchy.

Literature Analysis

Barzegari et al. conducted a randomized, double-blind placebo-controlled trial that examined 100 patients between the ages of 15 and 55 years old who presented to the ED with the complaints of a primary migraine, cluster, or tension headache. Patients were randomly assigned to receive either 1 mL 2% intranasal lidocaine or 1 mL intranasal normal saline spray. In addition, patients in both groups were given 7.5 mg IV chlorpromazine. Pain scores were recorded using the visual

analog scale (VAS) at baseline, 5, 15, and 30 minutes after intervention. VAS scores were based on the Wong Baker Rating Scale. A zero represented no pain, five corresponded to moderate pain, and a ten indicated worse possible pain. Mean VAS scores at 5 minutes post-intervention were 4.56 for the lidocaine group and 5.30 for the placebo ($p=0.011$). At 15 and 30 minutes post-intervention, VAS scores were 3.86 and 2.94 for the lidocaine group ($p=0.001$) and 4.76 and 3.94 for the intervention group ($p=0.002$). Overall, patients who received intranasal lidocaine along with a 7.5mg dose of IV chlorpromazine experienced significantly higher rates of pain control at 5, 15 and 30 minutes after treatment when compared with a placebo group.[8]

A second randomized controlled trial by Cady et al. focused on examining the effects of local anesthetic on patients presenting with chronic migraine as defined by the International Headache Society. The 41 patients were randomized in a 2:1 ratio to receive either 0.3mL of 0.5% bupivacaine or 0.3mL saline. The rationale for this randomization ratio was not made clear by the authors. The medication was administered with a Tx360 device in a series of 12 SPG blockades over a 6-week period of time. This device was manufactured by Tian Medical for the purpose of delivering medication directly onto the SPG with increased accuracy via a small plastic tube that can be advanced into the pterygopalatine fossa. The SPG block was performed in each nostril with the patients being given a lemon candy as a taste distractor to assist with blinding. Baseline headache scores were taken utilizing a numeric rating scale (NRS) prior to each administration. Subsequent NRS scores were taken at 15 minutes, 30 minutes and 24 hours post-administration. Mean NRS scores at 15 minutes posttreatment were 2.53 for the bupivacaine group compared with 3.51 for the saline group ($p<0.001$). 30 minutes posttreatment mean NRS scores were 2.41 and 3.45 for the bupivacaine and saline groups, respectively ($p<0.001$). NRS scores at 24 hours posttreatment were similar with the bupivacaine and saline groups having mean scores of 2.85 and 4.20, respectively ($p<0.001$). Patients who received a SPG blockade with 0.5% bupivacaine administered via the Tx360 device have statistically significant improvement in NRS pain scores when compared with saline.[1]

Similar results were found in a third randomized controlled trial conducted by Mohammadkarimi et al. Patients between the ages of 15 to 72 years old who presented to the ED with a headache were divided into two groups: primary headaches which includes migraine, tension, and cluster or secondary headaches which were subcategorized as either traumatic or nontraumatic. The 90 patients who met study criteria were randomly assigned 1:1 ratio to either the lidocaine or normal saline group. A 1 mL puff of 10% lidocaine or normal saline was sprayed into each nostril. VAS pain scores were taken at baseline and 1, 5, 15, and 30 minutes postintervention. VAS scores at 1 minute were 4.31 for the lidocaine group and 6.35 for the normal saline group ($p<0.001$). The VAS scores for lidocaine versus normal saline at 5, 15 and 30 minutes were 4.2 and 6.1 ($p<0.001$), 4.2 and 6.35 ($p<0.001$), and 4.17 and 6.26 ($p<0.001$), respectively. Pain relief was achieved after one minute and the levels of relief did not significantly change over the following 30 minutes ($p<0.001$).[2]

Two studies found no statistically significant difference between intranasal local anesthetic and a placebo control. In a single-center, prospective, double-blind, placebo-controlled randomized trial, Avcu et al. examined 162 patients presenting with acute migraine attack as classified according to the International Headache Society criteria. Patients older than 18 years old who presented to the ED with acute headache were randomly assigned in a 1:1 ratio to receive either a

single intranasal dose of 10% lidocaine or normal saline solution administered in a pump spray solution. 1 puff of intranasal lidocaine was equivalent to 10mg. If the patient had a unilateral headache, the medication was delivered into the ipsilateral nostril. If the headache was bilateral, the medication was delivered to both nostrils, giving one puff in each. All patients received 10mg intravenous metoclopramide. Patients were asked to describe the intensity of their headache using an 11-point NRS prior to treatment and at 15 minutes, 30 minutes and 24-72 hours after treatment. Median reduction in NRS scores at 15 minutes was 3 for lidocaine group and 2 for saline group (Median difference= 1.0, 95% Confidence Interval (CI), -0.1-2.1). The median reduction in pain score at 30 minutes was 4 for the lidocaine group and 5 for the control group (Median difference= -1.0, 95% CI -2.1 to 0.1).[9]

Schaffer et al. evaluated the effects of administering bupivacaine to the SPG for acute anterior or global-based headaches. 87 patients between the ages of 18 to 65 years were randomly assigned in a 1:1 ratio to receive 0.3mL of either 0.5% bupivacaine or normal saline solution administered via the Tx360 device. VAS pain scores were assessed at baseline, 5 minutes, 15 minutes, and 24 hours postintervention. The primary endpoint assessed was a greater than or equal to 50% VAS reduction in headache severity at 15 minutes. This endpoint was unique among the studies examined. A 50% reduction in pain was achieved by 48.8% of bupivacaine group vs 41.3% of normal saline group (percent difference= 7.5%, 95% CI, -13% -27.1%). Thus, when looking at the primary end point, there was no significant difference between the two groups in achieving the assessment marker of a 50% reduction in VAS scores. A secondary endpoint of this study assessed median VAS scores at 15 minutes. Findings indicated a trend toward headache reduction with the bupivacaine group compared to the control group. However, findings were not statistically significant. Median VAS scores at 15 minutes were 34 for the bupivacaine group and 51.5 for the control group (percent of difference= 17.5%, 95% CI= -15.2 to 50.2). No p-value was given by the authors. Overall, 0.5% bupivacaine administered via a Tx360 device provided no statistically significant improvement in VAS scores in treating headache when compared with normal saline.[3]

Synthesis of Results

Three of the five randomized controlled trials examined found that local anesthetic provides statistically significant improvements in pain scores when administered the SPG to treat headaches.[1,2,8] Two studies found statistically insignificant differences between local anesthetic and placebo.[3,9] Shaffer et al. reductions found a 50% reduction in pain was achieved by 48.8% of bupivacaine group (20/41 pts) vs 41.3% of normal saline group (19/46), a statistically insignificant difference.[3] Avcu et al. likewise showed no improvement in pain scores when comparing 10% intranasal lidocaine with normal saline placebo.[9] Evaluation of the differences between studies with significant results and those with insignificant results is challenging as there is a great deal of heterogeneity between the studies.

The heterogeneity in the studies reviewed indicated that concentration, amount, and type of local anesthetic differed between the studies with varying results. Three studies utilized lidocaine at concentrations of either 2% or 10%.[2,8,9] Two of these three studies, one with 2% and one with 10% lidocaine found a significant decrease in pain scores.[2,8] The third study administered 10% lidocaine and found non-significant results.[9] The remaining two studies included in this review used 0.5% bupivacaine, with one reporting a significant decrease in pain scores while the other

did not.[1,3] Because each drug was equally efficacious in various studies examined, choice of local anesthetic for SPG blockade should be based on drug availability, cost effectiveness, and practitioner preferences. When utilizing the Tx360 device, 0.3 mL of 0.5% bupivacaine is recommended by the manufacturer due it is ability to deliver medication directly at the SPG.[1,3]

The inclusion criteria varied slightly between each study. With the exception of Schaffer et al., all studies analyzed utilized the International Headache Society classification system as inclusion criteria for patients presenting with headache. In two of these studies, the patients were required to meet the classification standard for migraine headaches.[1,9] Barzegari further expanded these criteria to also encompass all primary headaches which include migraine, cluster, or tension headaches.[8] Mohammadkarimi et al. studied patients with both primary as well as secondary (traumatic and nontraumatic) headaches.[2] Schaffer et al. did not reference the International Headache Society classification at all, instead the inclusion criteria were patients presenting to the emergency department with anterior or global-based headaches.[3] Pain scores were analyzed as the primary outcome in all studies, however, the scales utilized to measure these pain scores varied. Mohammadkarimi et al. and Schaffer et al. implemented visual analog scale (VAS) whereas Avcu et al., Cady et al., and Barzegari et al. all implemented the numeric rating scale (NRS).

Administration technique of the SPG block differed between authors with varying results. SPG blockade is commonly performed via hollow, cotton tip applicators soaked with lidocaine. All studies that met inclusion criteria in this review were performed using the spray technique, therefore the swab technique was not evaluated in this review. Cady et al. and Schaffer et al. administered the SPG block with a Tx360 device.[1,3] All other authors in this review utilized a local anesthetic puff spray to deliver medication into the nostrils.[2,8,9] Within these different techniques, laterality also varied. Avcu et al. utilized the spray technique and delivered the medication unilaterally if the headache was localized to one side of the head.[9] If patients presented with a bilateral headache, local anesthetic or normal saline was administered bilaterally.[9] Varying the application between unilateral and bilateral differed from every other study examined. With the exception of Barzegari et al. who did not specify laterality, all other authors utilized bilateral application techniques on all patients studied.[1-3,8] This could be one distinguishing factor that led Avcu et al. in finding no statistically significant difference in pain scores between SPG block with local anesthetic versus the placebo control groups.

Along with the differences in administration technique, there were two different patient positioning techniques utilized in these studies. Avcu et al. positioned the patients using the Barre method.[9] In this method, the patient lies supine with their head hanging over the edge of the bed and turned 30 degrees towards the side of the headache.[9] This position was held for 30 seconds after local anesthetic administration.[9] Cady et al. and Schaffer et al. utilized the Tx360 device to administer SPG blockade.[1,3] Both authors utilized the Tx360 manufacturing guidelines which specify that the patient is in the sitting position with neck slightly extended during administration of local anesthetic.[3] The remaining two studies examined in this review did not specify the patient's position while administering the SPG blockade. Further analysis is needed to determine if this positioning played a role in the nonsignificant findings.

Evidence Source [a]	N	Headache type	Variables [b]	Pain Scale Scores	Comments
Barzegari[8]	100	Primary migraine, cluster or tension	1 mL intranasal 2% lidocaine spray vs 1mL NS spray	VAS scores at 5 minutes were 4.56 for lidocaine group and 5.30 for placebo (p=0.011) At 15 minutes 3.86 vs 4.76 (p=0.001) At 30 minutes 2.94 vs 3.94 (p=0.002)	All patients received 7.5 mg IV Chlorpromazine
Cady[1]	38	Chronic migraine	0.3 mL 0.5% bupivacaine or 0.3 mL NS administered via Tx360 device bilaterally	15 minutes after treatment NRS 2.53 vs 3.51 (p<0.001) 30 minutes after treatment NRS 2.41 vs 3.45 (p<0.001) 24 hours NRS 2.85 vs 4.20 (p<0.001)	12 treatments given 2 times per week for 6 weeks. Individual results were analyzed after each administration.
Mohammadkarimi[2]	90	Migraine, tension, traumatic and nontraumatic	1 puff of 1 mL 10% lidocaine or 1 mL NS administered bilaterally	VAS at 1 minute 4.31 vs 6.35 (p <0.001) At 5 minutes 4.2 vs 6.1 (p<0.001) At 15 minutes 4.2 vs 6.35 (p<0.001) At 30 min VAS 4.17 vs 6.26 (p<0.001)	
Avcu[9]	162	Migraine	1 mL of 10% intranasal lidocaine puff spray vs 1 mL NS administered on side of headache (or both if bilateral)	Median reduction in numeric rating scale score at 15 minutes was 3 for lidocaine group and 2 for NS group (Median difference= 1, 95% CI= 0.1-2.1) Reduction in pain scores at 30 minutes was 4 for lidocaine group and 5 for saline group (Median difference= 1, 95% confidence interval 0.1-2.1)	All patients received 10mg metoclopramide
Schaffer[3]	87	Acute anterior or global-based headache	0.3 mL 0.5% Bupivacaine or 0.3 mL NS administered using the Tx360 device	50% reduction in pain was achieved by 48.8% of bupivacaine group (20/41 pts) vs 41.3% of normal saline group (19/46). Difference 7.5%, 95% CI= -13% to 27.1%. VAS scores at 15 minutes= 34 vs 51.5 (17.5% difference, 95% CI= -15.2 to 50.2) 24 hours median headache score o vs 1 (1% difference, 95% CI= -1.4 to 56.6)	

Abbreviations: mL, milliliter; mg, milligram; VAS, visual analog scale; NRS, numeric rating scale; NS, normal saline; IV, intravenous route

[a] Each study was randomized controlled trial design
[b] Each study was placebo controlled with blinding design

It is important to note that the side effect profile of SPG blockade is minimal. Avcu et al found that no serious adverse events, i.e. anaphylaxis, akathisia, dystonia and seizures were reported in either group.[9] One patient in the lidocaine group experienced-minor palpitations, but this was self-limited.[9] The most prevalent adverse event in the lidocaine group was local irritation which was present in 49.4% of patients compared to 11.1% of the normal saline group, a statistically

significant difference (percent difference= 38.3%, 95% CI= 23.9%-51.1%). [9] Cady et al. and Schaffer et al. found no statistically significant difference in adverse events between the intervention and control group.[1,3] No severe adverse events were reported but symptoms such as nasal dryness, runny nose, sore throat, congestion, mouth numbness, bad taste, and hoarseness were present in the bupivacaine group.[3] Nasal bleeding and a slight runny nose were found in the saline group.[3] Barzegari et al. and Mohammadkarimi et al. did not report on side effects seen for either the intervention or the control groups.[2,8]

Finally, other confounding variables may have impacted results. Barzegari et al. had statistically significant results when pairing the SPG block with 7.5 mg IV chlorpromazine.[8] Conversely, when Avcu et al. administered 10 mg of IV metoclopramide simultaneously with the SPG block, the pain scores did not significantly decrease.[9] Cady et al. gave each participant a lemon candy to serve as a taste distractor to further blind the participants, which was the only study included that performed blinding of the flavor of the treatment.[1] All studies included in the review utilized normal saline as a placebo.[1-3,8,9]

Conclusions

Due to its low side effect profile, noninvasive nature, and cost effectiveness, the efficacy of SPG block is an excellent option for the treatment of headaches. Although studies emphasize its usefulness for treatment of chronic headaches that are refractory to oral medications, it is also a viable primary treatment option.

The articles examined had varying results with both intranasal sprays and direct delivery devices. 0.3 mL of 0.5% bupivacaine and 1 mL of 2% to 10% lidocaine can be safely administered to the SPG via the Tx360 device or intranasal spray.[1,2,3,8,9] Routes of administration that allow for maximum contact between the nasal mucosa and the local anesthetic provide higher chances of success. The direct delivery of local anesthetic to the mucosa by devices compared to intranasal sprays favors their use. It is possible that the unilateral administration of the SPG for patients presenting with unilateral headaches and the Barre positioning may have attributed to the lack of significant improvement in pain scores found by Avcu et al[9], so bilateral administration should likely be performed to improve success rates. Further research is needed however to explore these methods in greater detail.

The optimal dose, optimal technique, and the potential benefit from combining local anesthetics with other IV adjuncts remain to be determined based on this critical review of the literature published on the subject. There is overall optimism that continued research on techniques, patient positioning, concentration, and type of local anesthetic will lead to improvement in results seen with SPG blockade.[5] Based on the benefits of this technique along with there being no major complication reported in any of the studies, current practice should incorporate intranasal local anesthetic administered around the SPG to patients presenting with migraine, tension, or cluster headaches that originate from SPG activation.

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Use of Neuromuscular Blocking Agents with Laryngeal Mask Airways

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Keywords: Laryngeal mask airway (LMA), neuromuscular blocking agents (NMBAs), insertion, function, complication.

Introduction

Laryngeal mask airways (LMAs) are tools commonly utilized for airway management during anesthesia. Although they are conceptually simple to use, varying patient and surgical circumstances can make insertion, fit, and utilization of these devices a challenge.[1] Ineffective

airway management related to LMA-specific issues such as obstruction, inadequate sealing pressures, excessive leakage volumes, or dislodgment may cause failure to ventilate or oxygenate a patient. Patients can also experience postoperative complications due to LMA use such as sore throat or nerve damage.[2]

Using increased induction doses of anesthetic agents is thought to facilitate LMA insertion by blunting patient responses such as moving, coughing, swallowing, and laryngospasm. However, researchers found that increased induction dosage of propofol alone could not control patient responses to insertion of LMAs.[3] Others studies concluded that increasing propofol doses to the extent needed to obtain adequate insertion conditions often leads to prolonged periods of hypotension, bradycardia, and apnea.[4] The effects of neuromuscular blocking agent (NMBA) administration on LMA insertion conditions, functionality, and postoperative complications has been investigated in multiple studies.[4-10] The purpose of this evidence-based practice analysis is to compare the ease of LMA insertion and rates of associated complications between adult surgical patients who receive NMBAs and those who do not.

Methodology

A PICO format guided the clinical question. In adult patients undergoing general anesthesia with an LMA (P), does the use of NMBAs (I) or no use of NMBAs (C) impact ease of LMA insertion and rate of complications associated with LMA usage (O)?

Scopus, PubMed, Medline, and Google Scholar databases were utilized to search current literature. Keywords used in combination or individually for search include supraglottic airway device (SAD), laryngeal mask airway (LMA), LMA Classic, LMA Unique, ProSeal LMA (PLMA), LMA Supreme, LMA Flexible (FLMA), neuromuscular blocking agents (NMBAs), paralytics, muscle relaxants, rocuronium, succinylcholine, mivacurium, cisatracurium, and atracurium. All relevant publications written in English and published between 2010 and 2018 were evaluated. Nine studies met inclusion criteria. Two of these studies evaluated SADs other than LMAs and were excluded. Seven studies remained and were selected for analysis. All selected studies were randomized control trials (RCTs), categorized as level I.c evidence in the Joanna Briggs Institute hierarchy of evidence.

Literature Review

Aghamohammadi et al.[4] conducted a double blind RCT to assess the effects of a mini dose of succinylcholine (0.1 mg/kg) in facilitating the insertion of an LMA. The study involved 60 patients of American Society of Anesthesiologists physical status (ASA PS) 1-3, 20-60 years of age, scheduled for urologic surgical procedures. All subjects received midazolam 0.01 mg/kg, fentanyl 1 mcg/kg, and propofol 2 mg/kg. Following induction of anesthesia, an LMA was inserted by a blind investigator thirty seconds (s) after saline (Group C) or succinylcholine (Group S) administration. The first attempt at LMA insertion was successful in 27/30 (90%) patients in Group S versus 14/30 (46.6%) in Group C (p=0.001). Additional propofol was required in 16/30 (53%) of Group C compared to 3/30 (10%) for Group S (p=0.001). An LMA was successfully inserted in all patients with subsequent attempts. Laryngospasm occurred in 11/30 (36.6 %) patients in Group C, and 0/30 (0%) in Group S (p=0.004). Postoperative myalgia

or sore throat occurred in 20/30 (66.7 %) patients in Group C, compared to 13/30 (43.3%) in Group S (p=0.06).

A RCT conducted by Chen et al.[5] investigated the use of NMBAs in 120 female patients undergoing gynecological laparoscopic procedures with a ProSeal LMA™ (Laryngeal Mask Co., Ltd., Henley-on-Thames, UK). Participants were ASA PS 1-2 between 18-55 years of age. Midazolam 2 mg, fentanyl 2 mcg/kg, and propofol 2-3 mg/kg were administered intravenously to induce general anesthesia. Group R received rocuronium 0.6 mg/kg and Group C did not. Insertion of the PLMA was successful in all participants. Respiration was controlled with a mechanical ventilator with a tidal volume of 10 mL/kg and respiratory rate adjusted to maintain end-tidal CO2 of 35-45 mmHg. Maximum sealing pressures with positive pressure ventilation were 32 ± 5.1 cm H_2O for Group R and 31 ± 5.1 cm H_2O for Group C (p=0.341). Lowest fresh gas flow rates which achieved full inflation of the ventilator bellows during expiration were 485 ± 291 mL/min in Group R and 539 ± 344 mL/min in the Group C (p=0.2). No difference was seen in the frequency of sore throats 12/60 (20%) Group R versus 13/60 (21.7%) Group C (p=0.28).

Fujiwara et al.[6] examined the effects of NMBAs on PLMA insertion efficacy and sealing pressures by conducting a RCT on 80 participants aged 20-85 years. Participants were either administered rocuronium 0.9 mg/kg (Group R) or not (Group C). Anesthesia was induced with propofol 1-2 mg/kg, fentanyl, 1 mcg/kg, and mask ventilation with sevoflurane 3-5% was administered by mask ventilation. PLMA was inserted after a BIS of < 60 (Group C) or 3 minutes (min) after administration of rocuronium 0.9 mg/kg in Group R. Insertion attempts for Group R were 1 attempt for 38 patients, 2 attempts for 1 patient, and 3 attempts for 1 patient. Insertion attempts for Group C were significantly higher with successful placement in 1 attempt for 28 patients, 2 attempts for 7 patients, and 3 attempts for 5 patients (p<0.001). Group R had higher initial sealing pressures (27.4 ± 5.4 cm H_2O) compared to Group C (21.2 ± 5.2 cm H_2O) during positive pressure ventilation (p<0.001). Leakage volume was significantly less in Group R (17.4 ± 29.1 mL) than the Group C (46.8 ± 45.5 mL) (p<0.001). The subjective rating of PLMA insertion difficulty on a Visual Analog Scale (VAS) of 0-100 was significantly lower in Group R (12.3 ± 23.1) than in Group C (39.4 ± 31.9) (p<0.001). Five patients reported pharyngeal pain in Group C, compared to 1 participant in Group R (p=0.08). Hoarseness was noted in one patient in Group C, and none in Group R (p=0.31).

George, Sahajanandan, and Ninan[7] compared the effects of succinylcholine 0.1 mg/kg (Group A), succinylcholine 0.25 mg/kg (Group B), and saline (Group C) on LMA insertion. The double-blind RCT included 283 patients of ASA PS 1-2, 20-65 years of age undergoing general anesthesia. All patients were given propofol 2 mg/kg and fentanyl 2 mcg/kg before receiving succinylcholine or saline. A LMA was inserted 60 s after drug or saline administration. Two insertion attempts were required for 8/95 (8.4%) patients in the Group C, 8/95 (8.4%) patients in Group A, and 2/93 (2.2%) in Group B (p=0.27). Two patients in Group C experienced partial laryngospasm, none occurred in Group A or Group B (p=0.136). In Group A, the overall insertion conditions were rated as excellent in 78/95 (82.1%), good in 6/95 (6.3%), poor in 4/95 (4.2%) and unacceptable in 7/95 (7.4%). Group B rated insertion conditions as excellent in 79/93 (84.9%), good in 11/93 (11.8%), poor in 1/93 (1.1%), and unacceptable in 2/93 (2.2%). In Group C, the insertion conditions were rated as excellent in 63/95 (66.3%), good in 18/95 (18.9%), poor

in 10/95 (10.5%), and unacceptable in 4/95 (4.2%) (p=0.003). Two patients in Group C experienced postoperative myalgia, versus 1 in Group A, and 0 in Group B.

PLMA insertion and pharyngeal morbidities were compared between paralyzed and non-paralyzed patients in a double-blind RCT.[8] The study included 160 participants of ASA PS 1-2, 18-70 years of age. All participants were anesthetized using midazolam 0.03 mg/kg, propofol target-controlled infusion at effect-site concentration of 4 mcg/mL, and remifentanil target-controlled infusion with effect-site concentration of 4 ng/mL. Group R received rocuronium 0.6 mg/kg before PLMA insertion. Group C received rocuronium 0.6 mg/kg after the PLMA was inserted. Bronchoscopic evaluation of PLMA placement was performed after insertion in both groups. First attempt insertion success was 65/80 (81.3%) in Group C and 63/80 (78.8%) in Group R (p=0.9). Amount of time for PLMA insertion was 20.3 ± 21.4 s for Group R and 17.9 ± 19.1 s in Group C (p=0.12). Sealing pressures were 25.9 ± 7.4 cm H_2O in Group R and 24.7 ± 7.3 cm H_20 in Group C. No statistically significant differences were found in fiberoptic bronchoscopic grade of PLMA placement (p=0.89). Incidence of postoperative pharyngeal discomfort was 11/80 (13.8%) in Group C versus 24/80 (30.0%) in Group R (p=0.02). Traumatic events occurred in 13/80 (16.3%) of Group C versus 26/80 (32.5%) of Group R (p=0.03).

A double-blind RCT evaluated ease of LMA placement, patient trauma, and quality of ventilation in patients receiving atracurium and those who did not.[9] The RCT was performed with 60 patients with ASA PS 1-2, 18-80 years of age. Midazolam 0.05mg/kg was given intravenously for pretreatment. After injection of either saline (Group C) or atracurium 0.15 mg/kg (Group A), general anesthesia was induced with lidocaine 1.5 mg/kg, fentanyl 1.5 mcg/kg, and propofol 2 mg/kg IV. A disposable LMA (Hitec Medical CO, Ltd., China) was inserted after loss of eyelash reflex. The LMA was correctly inserted in 29/30 (96.66%) patients in both groups on the first attempt. Insertion time was 5.06 ± 0.52 s in Group A versus 5.76 ± 0.67 s in the Group C. The incidence of easy LMA insertion was 30/30 (100%) in Group A versus 25/30 (83.3%) in Group C (p=0.001). No significant difference was found between the groups in blood around the LMA upon removal. Group C experienced coughing in the postanesthesia care unit (PACU) and 24 hours after surgery in 10/30 (33.3%) and 3/30 (10%) versus 4/30 (13.3%) and 0/30 (0%) in Group A (p< 0.05). The incidence of sore throat in Group C was 10/30 (33.3%) in PACU and 6/30 (20%) 24 hours postoperatively, versus 3/30 (10%) in PACU and 0/30 (0%) 24 hours postoperatively for Group A (p=0.05 PACU), (p=0.01 24hr after surgery).

Gong, et al.[10] conducted a single-blind RCT to investigate the incidence of ventilation leak with a FLMA™ (Laryngeal Mask Company Limited, Seychelles, Singapore) when rocuronium was utilized during radical mastectomy. Forty-five female ASA PS 1-2 patients of 25-67 years of age were included. All received midazolam 0.03 mg/kg, fentanyl 2 mcg/kg, and target-controlled infusion of propofol at an effect-site concentration of 3-3.5 mcg/kg IV. Rocuronium 0.4 mg/kg was given to Group R at induction; the Control group (Group C) received saline. The insertion time for group R was 21.4 ± 7.0 s, compared to 30.4 ± 13.6 s for Group C (p = 0.013). Peak airway pressure at 10, 20 and 30 min was significantly lower in Group R than those in Group C. Mean pressures at 10 min were 14.7 ± 2.8 versus 18.8 ± 5.5 cm H_2O (p =0.002), at 20 min 14.7 ± 2.3 versus 17.0 ± 4.2 cm H_2O (p=0.026), and at 30 min 14.8 ± 2.2 versus 17.8 ± 4.6 cm H_2O (p=0.035). Ventilation leak volumes at insertion, 10, 20, 30 minutes were lower in Group R.

Leak volumes at insertion were 32.0 mL versus 45.5 mL (p=0.04), at 10 min 35.0 mL versus 59.0 mL (p=0.002), at 20 min 41.0 mL versus 65.0 mL (p<0.001), 30.5 mL versus 52 mL (p=0.003). Oropharyngeal leakage pressure was comparable in group R (21.0 ± 5.1 cm H_2O) and Group C (19.6 ± 3.9 cm H_2O).

First attempt success ranged from 79 to 98% for groups receiving an NMBA, and from 47 to 97% for groups with no NMBA.[4,5,7-9] Insertion time in the NMBA groups ranged from 5 ± 0.5 to 21 ± 7 s compared to 6 ± 0.6 to 30 ± 14 s without NMBAs.[8-10] The incidence of postoperative trauma, coughing or discomfort ranged between 0 to 43% in the NMBA groups compared to 2 to 67% in the groups without NMBA.[4-9] Laryngospasm incidence was reported in two studies with no laryngospasm reported in the groups receiving the NMBA.[4,7] Aghamohammadi et al.[4] reported that 37% in their control group experience laryngospasm. They offered no explanation for this high number but also reported that 70% of the group moved their limbs during LMA placement.

Study	Sample/design	Ease of Insertion	Complications	Conclusion
Aghamohammadi et al., 2013[4]	Double blind RCT N= 60 ASA PS 1-3 20-60 years Urologic surgical procedures LMA classic Group S succinylcholine 0.1 mg/kg Group C normal saline	First attempt insertion success Group S 27/30 (90%) Group C 14/30 (46.6%) (p=0.001) All LMAs were successfully inserted upon second or further attempts in both groups	Laryngospasm Group S 0/30 (0%) Group C 11/30 (36.6 %) (p=0.004) Postop myalgia and sore throat Group S 13/30 (43.3%) Group C 20/30 (66.7%) (p=0.06)	Significantly higher first attempt success in Group S (p=0.001) Significantly lower rate of laryngospasm in Group S (p=0.004) No statistically significant difference in postop myalgia and sore throat (p=0.06)
Chen et al., 2013[6]	RCT N= 120 ASA PS 1-2 18-55 years Laparoscopic gynecological surgery ProSeal LMA Group R	Not evaluated, ProSeal LMA insertion was successful on all participants	Frequency of sore throats Group R 12/60 (20%) Group C 13/60 (21.7%) (p=0.28)	No statistically significant difference in frequency of sore throats (p=0.28)

	rocuronium 0.6 mg/kg Group C no NMBA			
Fujiwara et al., 2015[5]	RCT N= 80 20-85 years General anesthesia in supine position ProSeal LMA Group R rocuronium 0.9 mg/kg Group C no NMBA	Number of insertion attempts Group R 1 attempt: 38 2 attempts: 1 3 attempts: 1 Group C 1 attempt: 28 2 attempts: 7 3 attempts: 5 (p<0.001) VAS rating of insertion difficulty Group R 12.3 ± 23.1mm Group C 39.4 ± 31.9 mm (p<0.001)	Pharyngeal pain Group R 1/40 (2.5%) Group C 5/40 (12.5%) (p=0.08) Hoarseness Group R 0/40 (0%) Group C 1/40 (2.5%) (p=0.31)	Number of insertion attempts significantly less in Group R (p<0.001) VAS rating of insertion difficulty significantly easier in Group R (p<0.001) No statistically significant difference in pharyngeal pain (p=0.08) or hoarseness (p=0.31)
George et al., 2017[7]	Double blind RCT N= 283 ASA PS 1-2 20-65 years Classic LMA Group A Succinylcholine 0.1 mg/kg Group B Succinylcholine 0.25 mg/kg	Insertion attempts Group A 1: 87/95 (91.6%) 2: 8/95 (8.4%) Group B 1: 91/93 (97.8%) 2: 2/93 (2.2%) Group C 1: 87/95 (91.6%) 2: 8/95 (8.4%) (p=0.27)	Incidence of laryngospasm Group A 0/95 (0%) Group B 0/93 (0%) Group C 2/95 (2.1%) (p=0.136) Incidence of postop myalgia	Group A and Group B groups significantly better ratings of insertion conditions (p=0.003) No statistically significant difference in insertion attempts (p=0.27), laryngospasm (p=0.136), or postop myalgia

	Group C Normal saline	Insertion conditions Excellent(E) Good(G) Poor(P) Unacceptable(U) Group A E 78/95 (82.1%) G 6/95 (6.3%) P 4/95 (4.2%) U 7/95 (7.4%) Group B E 79/93 (84.9%) G 11/93 (11.8%) P 1/93 (1.1%) U 2/93 (2.2%) Group C E 63/95 (66.3%) G18/95 (18.9%) P 10/95 (10.5%) U 4/95 (4.2%) (p=0.003)	Group A 1/95 (1.1%) Group B 0/93 (0%) Group C 2/95 (2.1%)	
Na et al., 2015[8]	Double blind RCT N= 160 ASA PS 1-2 18-70 years Breast or inguinal hernia repair ProSeal LMA Group R rocuronium 0.6 mg/kg Group C normal saline	First attempt insertion success Group R 63/80 (78.8%) Group C 65/80 (81.3%) (p=0.9) Insertion time Group R 20.3 ± 21.4 s Group C 17.9 ± 19.1 s (p=0.12)	Postop pharyngeal discomfort Group R 24/80 (30.0%) Group C 11/80 (13.8%) (p=0.02) Incidence of traumatic events Group R 26/80 (32.5%) Group C 13/80 (16.3%) (p=0.03)	Postop pharyngeal discomfort significantly higher in Group R (p=0.02) Incidence of traumatic events significantly higher in Group R (p=0.03) No statistically significant difference in first attempt insertion success (p=0.9) or insertion time (p=0.12)
Nasseri., 2017[9]	Double blind RCT	First attempt insertion	Incidence of postoperative	Significantly increased

	N= 60 ASA PS 1-2 18-80 years Disposable LMA Group A Atracurium 0.15 mg/kg Group C Normal saline	Group A 29/30 (96.66%) Group C 29/30 (96.66%) Insertion time Group A 5.06 ± 0.52 s Group C 5.76 ± 0.67 s Incidence of easy LMA insertion Group A 30/30 (100%) Group C 25/30 (83.3%) (p=0.001)	cough Group A 4/30 (13.3%) in PACU 0/30 (0%) 24hr postop Group C 10/30 (33.3%) in PACU 3/30 (10%) 24hr postop (p<0.05) Incidence of sore throat Group A 3/30 (10%) in PACU 0/30 24hr postop Group C 10/30 (33.3%) in PACU 6/30 (20%) 24hr postop (p=0.05), (p 0.01)	incidence of easy LMA insertion in Group A (p=0.001) Incidence of postoperative cough significantly higher in Group C (p<0.05) Incidence of sore throat in PACU and 24hr postop significantly higher in Group C (p=0.05), (p=0.01) No statistically significant difference in first attempt insertion success or insertion time
Gong et al., 2015[10]	Single blind RCT N= 45 ASA PS 1-2 25-67 years Females Mastectomy Flexible LMA Group R Rocuronium 0.4 mg/kg Group C Normal saline	Insertion time Group R 21 ± 7.0 s Group C 30.4 ± 13.6 s (p=0.013)	Not evaluated in study	No statistically significant difference in insertion time (p=0.013)

Conclusion

Seven RCTs that evaluated the use of NMBAs with a LMA technique for airway management were analyzed. A variety of NMBAs were used in the studies, including rocuronium, succinylcholine, and atracurium. LMA versions include classic LMA, PLMA, and FLMA. Ease of LMA insertion was evaluated by comparing the number of insertion attempts, insertion time, the degree of insertion difficulty, and insertion conditions. The success or ease of LMA insertion was statistically significantly improved in five[4,5,7-9] of the seven RCTs when NMBAs were utilized. One study found no significant difference in first attempt insertion success[8] and two found no significant difference in insertion time.[8,10] Complications were evaluated in six of the seven studies. Included were laryngospasm, sore throat, myalgia, hoarseness, coughing, and traumatic events. Five studies[4-7,9] found complications to be less likely in groups that received NMBAs, two[4,8] reaching statistical significance. The Na et al[8] study was an outlier, finding a significantly higher incidence of traumatic events in the group receiving rocuronium. The authors hypothesized this was due to narrowing of the oropharynx with muscle relaxation.

The studies included in this evidence-based practice analysis vary in type of NMBA utilized, dosing, and type of LMA used. Future research comparing different NMBAs and doses may be useful for determining optimal drug selection and dosing. An unmentioned risk in many of these publications is that of aspiration. Most of these studies cite extensive exclusion criteria barring the participation of any subjects who may be at increased risk for aspiration. Further research may be needed to determine how NMBAs impact the risk of aspiration of gastric contents when using LMAs. Directly comparing NMBAs to other medications that can be utilized to facilitate LMA insertion and management may be another future topic of interest. Research investigating the impact NMBAs have on LMA functionality is also needed, as few studies in this analysis investigated objective parameters such as ventilation leakage volumes and oropharyngeal sealing pressures after LMA placement.

Recommendations for practice would include cautious, selective use of NMBAs with LMA use. The studies included in this analysis indicate that NMBAs may improve ease of LMA insertion and decrease associated complications. These findings may be most useful in a scenario of difficult LMA placement where avoiding an endotracheal tube would be beneficial for the patient. Use of NMBAs may be unwise in scenarios where loss of spontaneous ventilation would lead to difficulty ventilating, such as poor pharyngeal seal or reduced compliance. It cannot be recommended at this time to administer NMBA in order to improve seal quality of a poorly functioning LMA. Few studies in this analysis address the impact of NMBAs on LMA functionality.

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10. Gong Y, Yi J, Zhang Q, Zhang Q, Xu L. Effect of low dose rocuronium in preventing ventilation leak for flexible laryngeal mask airway during radical mastectomy. *Int J Clin Exp Med.* 2015;8(8):13616-13621.

Mentor: Sharon Hadenfeldt, PhD, CRNA

Editorial

"So many fascinating, current, and relevant topics for case reports. I truly hope many of these students continue their scholarship." I just wanted to share this comment made by one of our editors about this issue. It truly speaks to the mission of the journal, and serves as a reminder for why we do this. Thank you to ***everyone*** who contributes to the success of the ISJNA!

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 patient was intubated and put on a ventilator*. "The trachea was intubated and mechanical ventilation was initiated.
    d. *An IV drip was started.* "An intravenous infusion was initiated."
    e. Avoid the term "MAC" when referring to a sedation technique - the term sedation (light, moderate, heavy, unconscious) may be used. Since all anesthesia administration is monitored, pharmacologic, rather than reimbursement, terminology should be used.
14. Direct quotes are discouraged for reports of this length – please express in your own words.
15. Use the words "anesthesia professionals" or "anesthesia practitioners" when discussing all persons who administer anesthesia (avoid the reimbursement term "anesthesia providers").
16. Do not include ASA Physical Status unless it is germane to the report.
17. Do not use the phrase "ASA standard monitors were applied". Instead, "standard noninvasive monitors" is acceptable – additional monitoring can be detailed as needed.
18. References
    a. The **AMA Manual of Style must be adhered to** for reference formatting.
    b. All sources should be published within the past 8 years. Seminal works essential to the topic being presented will be considered.
    c. Primary sources are preferred.
    d. **A maximum of one textbook (must be most recent edition available) may be used as reference for case report submissions only**.
    e. All items cited must be from peer-reviewed sources – use of sources found on the internet must be carefully considered in this regard. URLs must be current and take the reader directly to the referenced source.

Heading – for all submission types (Case Report, Abstract, EBPA Report) use the following format.

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

Title

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

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

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
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