

**Magnesium Sulfate as an Anesthesia Adjunct:
Establishing Opportunities for Enhancing Outcomes of Care**

by

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Dedication & Acknowledgements

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Abstract

Magnesium sulfate can be utilized as an analgesic adjunct for patients undergoing surgery. It can lead to decreased postoperative pain scores, improved patient outcomes, better perioperative care, and it can curb the current opioid crisis. When administered as an analgesic adjunct, the sole reliance on opioids to manage perioperative pain is reduced therefore the associated adverse effects of opioids are also minimized. Magnesium Sulfate effectively provides pain relief for a multitude of different surgical populations, is relatively easy to administer, and is inexpensive. It works as an analgesic by noncompetitively blocking NMDA receptors as well as acting as a calcium channel blocker. A formal educational webinar was provided to Certified Registered Nurse Anesthetists (CRNAs) that are members of the Michigan Association of Nurse Anesthetists (MANA). The purpose of the webinar was to inform providers of the mechanism of action, efficacy, and benefits of intravenous magnesium sulfate as an opioid sparing analgesic adjunct in select surgical scenarios. A post-webinar evaluation was distributed to webinar attendees and their respective responses were evaluated. Overall, CRNAs responded positively and provided comments that the webinar was extremely informational permitted a greater understanding of the benefits to enhance patient care outcomes.

Background & Significance

Anesthesia services are a key component of the perioperative and peri-procedural arena; Certified Registered Nurse Anesthetists (CRNAs) are professional providers of anesthesia services. The responsibilities of the CRNA are vast. As licensed and credentialed advanced practice nurses who are experts in anesthesiology, CRNAs exercise independent professional judgment within their scope of practice. CRNAs are accountable for their services and actions and for maintaining individual clinical competence. The scope of an individual CRNA practice is determined by education, licensure, and certification.

Nurse anesthesia practice may include but is not limited to preoperative and pre-procedure anesthesia-related care, intraoperative and intra-procedure anesthesia care, postoperative and post-procedure anesthesia-related care, and pain management services. Quality improvement processes and participation in the ongoing review and evaluation of anesthesia care to assess quality and appropriateness to improve outcomes is clearly outlined in The American Association of Nurse Anesthesiology Standards for Nurse Anesthesia Practice and is a key responsibility of the CRNA (Standards of Nursing Anesthesia Practice, 2014).

Surgery itself necessitates anesthesia; the type of anesthesia and the method of delivery is dependent on a host of patient-related factors such as the preoperative diagnosis, preexisting comorbidities, current comorbid state, medication history, planned surgical procedure, and the planned recovery process. Traditionally, the anesthesia plan for most procedures includes the administration of opioid narcotics for the purpose of minimizing the inherent pain response associated with surgery. Opioids, however, are associated with numerous adverse effects such as respiratory depression, hypercarbia, postoperative nausea and vomiting, increased hospital length of stay, pruritus, and decreased gastrointestinal motility. In addition, there is a predisposition for

progression to chronic postoperative pain, especially when acute postoperative pain is not managed effectively.

Opioids act via specific receptors (mu, delta, kappa) on the cell membrane in the peripheral, spinal, and supraspinal regions of the nervous system. They alter the ion channel conductance within the cell to mediate an analgesic effect. For example, post synaptic activation of opioid receptors open potassium channels and hyperpolarize the neuron, thus exhibiting a post-synaptic inhibition process. In the presynaptic junction, activation of opioid receptors inhibits the release of neurotransmitters involved in pain, such as substance P and glutamate (Neuropathology of Drug Addictions and Substance Misuse, 2016). Additionally, when opioids bind to mu, kappa, and delta receptors, a large volume of the neurotransmitter dopamine is released by the cell. There is an accumulating body of evidence that delineates dopamine's role in the regulation of chronic pain pathways within the brain and its vital role in pain modulation (how the body alters and interprets a transmitted pain signal). D2-like receptors along the descending dopaminergic pathway are said to elicit an antinociceptive effect. They are one of several dopamine receptors found to have analgesic properties (Li et al., 2019). This entire sequence of minimizing nociception potentiates the desire for continuing opioid use; the experience therefore is often repeated even when not necessary, leading to narcotic misuse and abuse.

As previously stated, when opioids are prescribed as the sole method for postoperative pain management there is potential for developing tolerance, dependence, misuse, abuse, and progression to a chronic pain state (when acute pain is not managed satisfactorily). Poorly controlled acute postoperative pain is associated with increased morbidity, functional and quality-of-life impairment, delayed recovery time, prolonged duration of opioid use, and higher

health-care costs. Furthermore, the presence and intensity of acute pain during or after surgery is consider a risk factor for developing chronic pain.

Currently there exists a global opioid crisis. In 2017, more than 47,000 Americans died of opioid overdose, and an estimated 1.7 million suffered from substance abuse disorders related to prescription opioid painkillers. In addition, prescription opioid misuse in the United States costs approximately \$78.5 billion per year due to the costs of treatment for addiction, and criminal justice involvement (National Institute on Drug Abuse, 2019).

Due to the known adverse effects of opioids, which have contributed to the global opioid crisis, their routine administration as the sole perioperative analgesic has undergone intense scrutiny. In response, CRNAs are utilizing adjunctive medications to provide perioperative opioid-free or opioid-sparing anesthesia/analgesia to decrease the reliance on opioids as the sole method to manage perioperative pain.

Opioid-free anesthesia (OFA) is a technique where no intraoperative systemic, neuraxial, or intracavitary opioid is administered in conjunction with other anesthetic agents. Avoiding opioids throughout the perioperative period has benefitted specific patient populations undergoing various surgical procedures (Sultana et al., 2017). In contrast, opioid-sparing anesthesia (OSA) is a less restrictive technique that utilizes opioids as part of an anesthetic regimen, but in very small quantities and doses. Both opioid-sparing and opioid-free anesthesia methods rely on non-opioid adjuncts such as IV ketamine, lidocaine, and dexmedetomidine as well as regional methods such as peripheral nerve blocks. These adjuncts act on different receptors within the cell, have altered pharmacokinetic profiles and mechanisms of action, and provide analgesia via different neurologic pathways than opioids. When non-opioid analgesics are administered in conjunction with low-dose opioids, adequate antinociceptive coverage can be

provided for the perioperative period. A reduction in the total amount of opioids administered can minimize their previously noted adverse effects (Siu & Moon, 2020).

There are several different classes of adjunct medications available for providing opioid-sparing anesthesia and analgesia including acetaminophen, antiarrhythmics, anticonvulsants, antidepressants, antipsychotics, benzodiazepines, alpha 2 agonists, beta adrenergic blocking agents, calcium channel blockers, central nervous system stimulants, corticosteroids, local anesthetics, N-methyl-D-aspartate (NMDA) receptor antagonists, and nonsteroidal anti-inflammatory drugs, to name a few.

Intravenous magnesium sulfate is an NMDA receptor antagonist. Magnesium competes with calcium at the motor end plate to reduce acetylcholine release and concomitantly halt cellular excitation. Essentially, it acts as an endogenous calcium channel antagonist at the neuronal synapses, which is what is thought to prevent the activation of the NMDA receptors by excitatory neurons such as glutamate. When magnesium blocks these voltage-gated calcium channels on the receptor, it does not allow the cell to excite, and therefore results in an antinociceptive effect (Shin et al., 2020). Current evidence supports the efficacy of magnesium sulfate as an opioid-sparing anesthesia and analgesia adjunct in select patient scenarios.

Literature Review

The Cumulative Index of Nursing and Allied Health (CINAHL), the Cochrane library, PubMed, UpToDate, and Google Scholar were queried using a comprehensive list of article titles and keywords. Keywords included magnesium, intraoperative, pain, postoperative pain, analgesia, and adjunct. More than 882 articles matched the key work search criteria. Parameters such as publication year and human and peer-reviewed journals were determined. The inclusion criteria for the selection of publications included: written in the English language, publication

dates 2015 to 2021, evidence of use of the visual analog scale (VAS) or other pain assessment modality for evaluating efficacy, intravenous route of magnesium administration, surgical procedure time greater than one hour, adults only, and patient ASA classification score of I-III. Articles were excluded if the patient ASA score was greater than or equal to four, subjects included in the study had pre-existing severe cardiovascular comorbid states, and subjects who were chronic opioid consumers. The following literature review is organized into several subsections:

- a. The role of magnesium in the human body
- b. Therapeutic uses of magnesium
- c. The mechanism of action of magnesium sulfate as an analgesic adjunct
- d. The pharmacokinetic profile of intravenous magnesium sulfate
- e. The use of magnesium sulfate in the perioperative setting
- f. Magnesium Sulfate as an opioid sparing agent - Reports of clinical trials and respective

patient outcomes

The Role of Magnesium in the Human Body

In the human body, magnesium typically occurs as the Mg^{2+} ion and has notable physiologic importance. It is an essential mineral nutrient for human life and one of the most abundant cations in the intracellular compartment. The cation serves as a cofactor in more than 300 enzyme systems that regulate diverse biochemical reactions including protein synthesis, muscle and nerve function, blood glucose control, and blood pressure regulation. In addition, magnesium is required for the synthesis of DNA, RNA, and the antioxidant glutathione (National Institute of Health, 2022).

Laguipo (2019) discussed that magnesium is also required for energy production, oxidative phosphorylation, and glycolysis. It contributes to the structural development of bone, which is where most of it is found in the body. Magnesium aids in the conduction of nerve impulses, heart rhythms, and muscle contractions by regulating electrolyte balances and assisting the body in producing, generating, and using adenosine triphosphate (ATP). ATP is the energy stored in the body's cells that is an important factor in actions such as cell reproduction and transportation of substances across a cell barrier (Laguipo, 2019). Simply put, without the presence of magnesium sulfate, the human body would not be able to functionally operate and support life's demands.

Therapeutic uses of Magnesium

There are many therapeutic uses for Magnesium Sulfate. One such use is for the treatment of bronchospasm and bronchospastic disorders; bronchospasm is characterized by the loss of the protective reflex of the tracheobronchial tree. When the protective reflex is no longer present, extensive lower airway irritability and airway constriction results. Bronchospasm is defined as the activation of a vagal-reflex mediated constriction of bronchial smooth muscle and results in increased airway resistance and inability to ventilate (Miller & Cohen, 2019). This can be a life-threatening event if it occurs acutely and cannot effectively be managed. Magnesium sulfate relaxes the smooth muscle in the trachea and bronchial tree by blocking the influx of calcium and prevents calcium binding at respective calcium binding sites, therefore producing bronchodilation. Magnesium also blocks the influx of calcium into the cell and decreases the release of acetylcholine from the neuromuscular junction (NMJ) of cholinergic nerves. This too alleviates bronchospasm because acetylcholine can trigger the release of histamine from mast cells. Less acetylcholine within the NMJ leads to a reduction in histamine-induced airway spasm

and the ultimate result of bronchodilation with overall resolution of bronchospasm (Miller & Cohen, 2019).

Magnesium and its use in obstetrics

The second therapeutic use for magnesium is in obstetrics. It is deemed the first-line treatment for the prevention of primary and recurrent eclamptic seizure disorders, it aids in prophylactic treatment for severe preeclampsia, and it is used to help prevent preterm labor. Because magnesium competitively blocks the entry of calcium at the synaptic junction, there is a reduction in neuromuscular transmission. This in turn increases the threshold for seizure activity. According to Norwitz (2021), magnesium's ability to oppose calcium also promotes cerebral vasodilation. Calcium-dependent arterial vasospasm causes the constriction of cerebral vessels, and the administration of magnesium can negate this effect, thereby reducing cerebral barotrauma and stabilizing the central nervous system membrane. Additionally, Norwitz (2021) mentions that magnesium's antagonistic effects on NMDA receptors also promote an increase in the seizure threshold.

Tocolysis is a procedure carried out to delay the delivery of a fetus and prolong gestation by slowing down or halting uterine contractions. This is often done by administering medications that inhibit contractions of uterine smooth muscle, also known as tocolytics, such as magnesium sulfate (Mayer & Apodaca-Ramos, 2021). Tocolytics block calcium-mediated uterine contractions and relax the smooth muscles of the uterus to delay preterm labor.

Magnesium and its role in the cardiovascular system

There is a pharmacologic role for magnesium in the treatment of specific conduction disturbances of the heart. For example, magnesium sulfate is efficacious in the treatment of torsade de pointes and atrial fibrillation (AF) as described by Baker (2016). Magnesium

decreases Ca^{2+} activity and halts the arrhythmia of torsade de pointes. It also controls the ventricular response in patients with AF and triggers the conversion of AF to a normal sinus rhythm. Additionally, therapeutic use for magnesium has been postulated related to its physiologic effect of promoting vasodilation, reducing vascular resistance, and lowering systematic and coronary artery resistance. In the myocardium, magnesium antagonizes Ca^{2+} activity during myocardial ischemic events. This can limit infarction size and reduce coronary artery vasospasm, reducing post myocardial infarction oxidative damage (Baker, 2016).

The Mechanism of Action of Magnesium Sulfate as an Analgesic Adjunct

Magnesium has been established as an N-methyl-D-aspartate (NMDA) receptor blocker; this is the proposed mechanism of action for its analgesic effects (George, Condrey, & Wilson, 2018). NMDA receptors are proteins located in post-synaptic membranes of neurons in the central nervous system. They are glutamate-gated cation channels that play an important role in the human body and are associated with neuropathic pain, hyperalgesia, and reduced functionality of opioid receptors. NMDA receptors are embedded in the membrane of nerve cells that receive signals across the synapse from a previous nerve cell. They are involved in signal transduction via controlling the opening and closing of ion channels, and they have been studied extensively for their role in the initiation and maintenance of central sensitization. The Institute for Chronic Pain defines central sensitization as a condition of the nervous system associated with developing and maintaining a chronic pain state (Institute for Chronic Pain, 2017). This is thought to result from a suppressed reuptake or increased release of excitatory neurotransmitters associated with pain such as glutamate, aspartate, and substance P. In addition, they are associated with neuropathic pain. Neuropathic pain is the result of increased spinal neuron sensitization that leads to a heightened level of pain.

The hypothesized analgesic mechanism of action of magnesium is due to its competitive and noncompetitive NMDA antagonism as well as its ability to act as a calcium channel blocker (Siu & Moon, 2020). Magnesium appears to prevent central sensitization and produce analgesia. Specifically, magnesium sulfate blocks the flow of sodium, potassium, and calcium ions in a voltage-gated manner within the channel of the NMDA receptor. Although the receptor is the same, this mechanism of action and site of action is different from other noncompetitive antagonists, such as Ketamine. Magnesium also plays a role in reducing catecholamine release with sympathetic stimulation. This leads to decreased peripheral nociception and a decreased stress response to surgery (Haryalchi, Taheri, Ghanaie, and Arejan, 2015). Considering magnesium and ketamine have differing effects on the same receptor, these two medications can be administered simultaneously to produce a synergistic effect and increase the analgesia produced.

In contrast, the mu, kappa, and delta opioid receptors are the primary site of action of opioids. These receptors are located in the dorsal root ganglion, the spinal cord, periphery, and in supraspinal regions that are associated with pain modulation (Vanderah, 2010). When these receptors experience a decrease in efficiency due to sensitization of signaling pathways, opioid-induced hyperalgesia (OIH) and acute opioid tolerance can occur. This results in the escalation of opioid requirements to manage pain as well as the development of hypersensitivity to painful stimuli. Weber, Yeomans, & Tzabazis (2017) determined that the best strategy to combat opioid-induced hyperalgesia is to prevent its occurrence by utilizing a multimodal analgesic approach. A multimodal approach involves the usage of different drugs to achieve the various dimensions of anesthesia such as: opioids to produce antinociception, propofol or another hypnotic to maintain unconsciousness, and additional agents with specific central nervous system targets such as

dexmedetomidine and/or ones with less specific targets, such as magnesium. Choosing a combination of agents that act at different targets in the nociceptive system can be used to control nociception intraoperatively and pain postoperatively. (Brown, Santa Cruz & Subramanian, 2019). These authors also provided evidence that stimulation of NMDA receptors can precipitate OIH. Since magnesium acts as an NMDA receptor antagonist, it makes sense that is can minimize OIH.

Magnesium is a naturally occurring ion in the human body and the intravenous form (Magnesium Sulfate) is associated with a favorable benefit/risk profile in select clinical case scenarios when given as an analgesic adjunct. There have been numerous research studies (Altıparmak et al., 2018; Haryalchi, Taheri, Ghanaie, and Arejan, 2015; Mendonca et al., 2020; Benevides et al., 2021, etc.) demonstrating reduced postoperative pain scores when magnesium is given in concurrence with lidocaine, ketamine, low-dose opiates such as fentanyl and morphine, and other analgesic adjuncts. It has shown to be most beneficial for gynecologic, thoracic, orthopedic, bariatric, and endoscopic ENT procedures.

The Pharmacokinetic Profile of Intravenous Magnesium Sulfate

Magnesium sulfate is administered either intravenously, intramuscularly, or orally, but the focus of this project involves the intravenous route. It is widely distributed throughout the body, 30% being protein bound and only 1-2% being extracellularly distributed and not metabolized. The unbound magnesium ions can diffuse into extracellular spaces and cross the placenta where they are rapidly taken up by fetal tissue (The Electronic Medicines Compendium, 2019).

The onset of intravenous magnesium sulfate is typically immediate, but can be up to thirty minutes, and the duration of action is between three and six hours. Normal blood

concentration levels are 0.7 to 1.05 mmol/l (1.4 to 2.2 meq/l or 1.7-2.4 mg/dL) (Surana, 2016 & Medscape, 2021). Magnesium homeostasis is largely controlled by the kidney and 120mg of magnesium is excreted in the urine each day. The remainder is reabsorbed in the ascending limb of the loop of Henle. This should be taken into consideration when administering magnesium to those with impaired kidney function (Surana, 2016 & Medscape, 2021). Individuals with impaired renal function should receive a decreased dose of magnesium to avoid hypermagnesemia.

The Use of Magnesium Sulfate in the Perioperative Setting

Opioid-sparing and opioid-free anesthesia techniques are one method to combat the nation's opioid crisis. There are several classes of medications that effectively manage perioperative pain with the goal of minimizing opioid administration. These analgesic adjuncts include non-steroidal anti-inflammatory agents (NSAIDs), acetaminophen, gabapentinoids, dexmedetomidine, ketamine, and magnesium.

It appears that magnesium sulfate is not being used to its greatest potential in individualized anesthesia plans; this may be due to a lack of exposure and a lack of evidence-based information. Described below are numerous clinical trials and respective patient outcomes when magnesium sulfate was incorporated in an anesthesia plan.

Magnesium Sulfate as an Opioid-Sparing Agent

Magnesium sulfate in OB/GYN surgery

Sousa, Rosado, Neto, Guimarães, and Ashmawi (2016) compared the analgesic effects of perioperative intravenous magnesium sulfate and ketorolac infusions for laparoscopic gynecological surgeries. Subjects were randomly divided into three groups: a magnesium group, a ketorolac group, and a placebo (saline) group. General intravenous anesthesia was induced

with target infusions of remifentanyl and propofol. Self-reported pain scores, pain intensity, and consumption of analgesics were measured postoperatively and compared between the three groups: K (ketorolac), M (magnesium sulfate) and S (saline). Patients that received ketorolac or magnesium had significantly lower overall morphine consumption compared with patients who received the saline solution. Patients in group K consumed 2.3mg of morphine after 60 minutes and 6.7 mg within 24 hours; group M consumed 3.38 and 5.7 mg of morphine, and group S consumed 5.7 and 12 mg of morphine after 60 minutes and 24 hours, respectively. In groups K and M, morphine consumption was significantly lower than in group S. The time to first morphine dose in PACU for group K was 10 min, group M was 5 min and group S was 5 min. Morphine consumption in PACU for group K was 2.31, 3.38 for group M, and 5.7mg for group S. The average pain score on a VAS from 0-100 for patients in group K after 60 min was 17.5, 10.0 for group M, and 30.0 for group S. The average pain score on a VAS from 0-100 after 24 hours for patients in group K was 0, 0 for group M, and 10 for group S. Although the ketorolac group experienced similar results compared to the magnesium group, nonsteroidal anti-inflammatories (NSAIDs) like ketorolac are contraindicated in some patients such as those with moderate to severe asthma, coagulation disorders, and renal disease, thus ketorolac has contraindications to its use unlike magnesium.

The efficacy of low dose intravenous magnesium sulfate to reduce postoperative pain in women undergoing total abdominal hysterectomy (TAH) was studied by Haryalchi, Taheri, Ghanaie, and Arejan (2015). Women were randomly divided into two groups: a saline group and a magnesium group. All patients underwent a standardized general anesthetic without any premedication. Each patient was induced with sodium thiopental 5mg/kg, fentanyl 1 μ g/kg, and succinylcholine 1mg/kg. The maintenance period was conducted utilizing a balanced mixture of

50% oxygen, 50% nitrous oxide, and 0.5% isoflurane. Atracurium 0.5mg/kg was utilized to maintain muscle relaxation, and fentanyl 1 μ g/kg was administered if there were signs of lacrimation, sweating, or a 20% increase in heart rate or blood pressure. The magnesium group received IV magnesium sulfate 50 mg/kg in 100mL of normal saline solution 15 minutes prior to induction of anesthesia. The control group received 100mL of 0.9% sodium chloride solution at the same time. Pain scores were evaluated using the Numeric Rating Scale (NRS) at postoperative hours 0, 6, 12, and 24. The consumption amounts of pethidine, a synthetic opioid comparable to meperidine (Demerol) in the United States, was also documented. Pain scores were lower in the magnesium group at postoperative hours 6, 12, and 24 ($p < 0.05$), and pethidine requirements were reduced in the magnesium group throughout 24 hours after surgery ($P = 0.0001$). This study concluded that magnesium sulfate use during the intraoperative period decreases the consumption of postoperative opioids and results in lower pain scores for those undergoing TAH surgery.

A double-blind randomized control trial conducted by Altiparmak et al. (2018) found that magnesium sulfate given intraoperatively decreased postoperative Visual Analog Scale (VAS) scores in patients undergoing cesarean sections utilizing general anesthesia. In this study, patients were divided into four groups dependent upon the inhalation agent used and whether intravenous magnesium sulfate was administered. The groups were labeled as follows: S (sevoflurane), D (desflurane), S-M (sevoflurane with magnesium), D-M (desflurane with magnesium). Group S and Group D were considered the control groups. Pain scores were measured at one, two, and 24 hours postoperatively. The magnesium groups (S-M and D-M) had significantly lower pain scores at all three-time intervals ($p < 0.001$). At the one-hour mark, group S relayed a VAS score of 8.1 compared to group S-M's score of 7.1. At the two-hour mark,

group S members relayed an average VAS score of 5.1 while group S-M only expressed a score of 3.5. At 24 hours, group S and group S-M VAS scores were 4.0 and 3.0, respectively. Group D and D-M yielded similar results with group D-M expressing significantly decreased pain scores at all three time intervals when compared to Group D ($p < 0.001$). While cesarean sections are not performed with general endotracheal anesthesia ‘electively’ in the United States, emergent and/or urgent cesarean sections are performed using this method. When patients must have a cesarean section under general anesthesia in an emergent situation, this study provides valuable information regarding the efficacy of magnesium as an opioid alternative. This study did not measure placental transfer effects of magnesium on the fetus.

Although not considered gynecologic surgery, Mendonca et al. (2020) studied magnesium for its efficacy as an analgesic adjunct on patients having mastectomy procedures with standard general endotracheal anesthesia. A total of 120 patients were randomly divided into four groups: group one received an intravenous infusion of remifentanyl (0.1 mcg/kg/min), group two received lidocaine (2mg/kg bolus followed by 3mg/kg/h infusion), group three received magnesium (50mg/kg bolus followed by 15mg/kg/h infusion), and group four received a combination of both lidocaine and magnesium in the same doses as groups two and three. Intravenous bolus of alfentanil was administered for intraoperative analgesia to the participants of any of the four groups who experienced an increase in mean arterial pressure (MAP) or heart rate (HR) greater than 20% of the patient’s baseline value. It was found that group four, those who received a combination of both magnesium and lidocaine, consumed the least amount of alfentanil during surgery. The magnesium and lidocaine group consumed an average of 150µg, the remifentanyl group 261.1µg, the lidocaine only group 688.3µg, and the magnesium sulfate only group 1,005µg. Postoperatively, only two patients, or 6.7%, who were in the combined

lidocaine and magnesium sulfate group needed rescue opioids in PACU ($p < 0.001$). This difference was significantly lower when compared with those who received remifentanyl and magnesium sulfate alone, 76.7% and 70.0% of whom required rescue opioids in PACU, respectively. These findings illustrated that a combined lidocaine and magnesium sulfate infusion was efficacious in reducing both intraoperative and postoperative opioid administration in patients undergoing elective mastectomy.

McKeown, Seppi, and Hodgson (2017) conducted a systematic review specific to the efficacy of intravenous magnesium in patients undergoing cesarean sections with either general endotracheal or neuraxial anesthesia. After inclusion and exclusion criteria was applied, a total of seven studies were analyzed that involved either an intravenous magnesium bolus dose preoperatively compared to placebo (control). A Visual Analog Scale (VAS) scoring process was used to assess postoperative pain scores. Patients who received the magnesium sulfate bolus had lower VAS scores, however, the time intervals differed between the trials. For example, some studies measured VAS scores at one hour, six hours, 12 and/or 24 hours. More specifically, VAS scores were lower at 24 hours ($p < 0.05$) while others studies resulted in VAS scores being lower at 6 or 12 hours ($p < 0.05$). However, regardless of the time interval, preoperative intravenous magnesium sulfate administered by a bolus dose was shown to decrease analgesia requirements in patients following caesarean section without any serious adverse events reported.

In a randomized, controlled, double-blind study by Benevides et al. (2021), 86 patients undergoing a total abdominal hysterectomy were randomly placed into two computer-generated groups: Group Mg who received a 50mg/kg bolus of intravenous magnesium sulfate over 15 minutes followed by a 15mg/kg/h infusion, and a control group who received the same dose of normal saline. Both groups received a spinal anesthetic after their bolus dose of either

magnesium sulfate or normal saline. The intrathecal dose contained 100µg of morphine added to 3.5mL of 0.5% hyperbaric Bupivacaine and was administered over 30 seconds. Just prior to administration of the spinal anesthetic, patients received a bolus of 0.03mg/kg of midazolam and 0.25µg/kg of fentanyl for sedation. Postoperative pain scores were assessed for the groups using the Visual Analog Scale (VAS), with 0 representing no pain and 10 representing worst pain imaginable. The control group who received a normal saline infusion was noted to have higher postoperative VAS scores after 6 hours than Group Mg, 3 and 2, respectively ($p = 0.02$). This study also concluded that magnesium sulfate did not cause any notable adverse patient effects.

Magnesium sulfate use in bariatric surgery

The efficacy of magnesium sulfate as an analgesic adjunct during sleeve gastrectomy procedure was studied by Kizilcik and Koner (2018). Participants in this study were randomized into two groups: an intravenous magnesium group (group M) and a control group that received normal saline as a placebo (group C). The intravenous magnesium group was given a 30mg/kg bolus of magnesium sulfate 30 minutes prior to the induction of general anesthesia; the placebo group was administered the same volume of normal saline as a replacement. The Visual Analogue Scale (VAS) was used to record pain scores at 30 minutes, 90 minutes, and 2, 4, 6, 12, and 24 hours postoperatively for both groups. Patients were each provided with a patient-controlled analgesia (PCA) with IV morphine, and the total amount administered by patients was also recorded at these times. The average VAS score at 30 and 90 minutes and hours 2, 4, 6, 12, and 24 was 4.5 for group C and roughly 2.5 for group M ($p < 0.01$). The total morphine consumption after 30 minutes for group C was 8.78mg and 6.63mg for group M. After 60 minutes, group C's total consumption was up to an average of 12.65mg while group M's was

9.50mg. After 2 hours total morphine consumption for group C was 14.90mg and 12.95mg for group M. Finally, at 24 hours postoperatively, group C had consumed an average total of 26.5mg of morphine while group M had only consumed 21.13mg. At every time interval measured in this study, the group that received magnesium sulfate (group M) had a significantly reduced consumption of morphine when compared to the control (group C) ($p < 0.001$).

In 2021, Filho et al. published their research findings specific to the effectiveness of intraoperative magnesium sulfate use as an analgesic for patients undergoing bariatric abdominoplasty. Subjects were randomized into two groups: an intravenous magnesium group (MSG) that received a magnesium sulfate infusion during the surgical procedure at 10mg/kg/hour, and a remifentanyl group (RG) that received an infusion of remifentanyl during the procedure at 0.2mcg/kg/min. Total intravenous anesthesia (TIVA) was the anesthetic technique utilized for both groups in the form of a 1.5mg/kg bolus of Lidocaine followed by a propofol infusion with administration rates determined utilizing the Bispectral Index (BIS). To achieve an appropriate anesthetic plane, a BIS of 40-60 was the proposed target range. A 1.0 mcg/kg bolus of intravenous fentanyl was used as a rescue analgesic for all participants. The affirmed rescue analgesic was only administered when a patient's blood pressure (BP) remained 20% above their baseline for greater than two minutes after the infusion dose of magnesium sulfate or remifentanyl had been doubled. All continuous infusions were discontinued upon completion of the procedure. The amount of fentanyl administered intraoperatively was significantly greater in the magnesium group, with the RG receiving no fentanyl and the MSG receiving an average of 49.48 mcg ($p < 0.004$). A Verbal Numeric Scale (VNS) from 0-10 was used to assess patients' pain postoperatively. At postop hour six, the two groups displayed statistically similar pain scores with the RG average score being 0.79 and MSG being 0.86. Patients were then followed

up for three days after their procedure to assess pain scores. There was no statistically significant difference between the two groups at any of the postoperative timepoints analyzed. While this study reveals that magnesium sulfate is not an appropriate sole intraoperative analgesic, it illustrates that magnesium can in fact produce similar postoperative pain scores with a reduction in overall postoperative opioid consumption. Of the 23 patients in the MSG, only 8 required opioid supplementation, and fentanyl was administered at a low dose of only 1-3mcg/kg. The 20 participants who were part of the remifentanyl group all received opioids perioperatively. This means that 100% of RG received opioids while only 34.8% of those in the MSG received opioids. Magnesium may not be able to completely omit the use opioids, but this study shows that it can decrease the number of patients we administer them to.

Magnesium sulfate use in orthopedic surgery

Intravenous magnesium sulfate has also been studied as an analgesic adjunct in the orthopedic surgery patient population. A total of 44 patients participated in a randomized controlled clinical trial conducted by Shin et al. in 2016. Patients having staged bilateral total knee arthroplasty (TKA) procedures were enrolled for participation.

For the first and second TKA procedure, all participants received a subarachnoid block utilizing 2.0–2.5mL of 0.5% hyperbaric bupivacaine with an added 10-20µg of fentanyl, a continuous femoral nerve block with 0.2% ropivacaine administered at 5mL/h to be continued via catheter for 50 hours after surgery, and a postoperative intravenous PCA pump (regimen: 2000µg of fentanyl for patients 60–70 years of age and 1500µg for patients >70 years of age in 0.9% saline, total volume of 100mL; no basal infusion, bolus 1mL, lockout time of 10 min). Patients also received 650mg of oral acetaminophen, 200mg of celecoxib, and 75mg of pregabalin every 12 hours after surgery along with 50mg of IV ketoprofen as needed as a rescue

analgesic and 10mg of IV metoclopramide as needed for nausea/vomiting. Patients were randomized into two groups: the magnesium group and the control/placebo group. The magnesium group received magnesium sulfate, 50 mg/kg in 100mL of isotonic saline over 15 minutes during the beginning of the procedure. This loading dose was followed by a continuous infusion of magnesium sulfate at 15 mg/kg/h for the duration of the procedure. The control group received a loading dose as well as continuous infusion of normal saline at equivalent fluid volumes as the magnesium group. The Visual Analog Scale (VAS) was used to assess pain at 24 and 48 hours postop with 0 being no pain and 100 being the most severe pain imaginable. Scores were higher in the control group than in the magnesium group after both the first and second TKA at both assessed times. The second TKA also proved to be significantly more painful for the control group with VAS scores 24 hours postoperatively being 29 after the first TKA and 44 after the second ($P<0.001$). For the magnesium group, there was no significant difference in pain levels at postop hour 24 between the first TKA compared to the second. The average VAS score for this group was 19 after the first TKA and only 20 after the second. At 48 hours postop, the control group average VAS score was 33 and 43 after the first and second surgeries, respectively. At this time, the magnesium group presented with VAS scores of 24 after the first surgery and 25 after the second surgery, which were significantly lower than those of the control group ($p=0.001$ and $p<0.001$, respectively). Overall, the magnesium group presented with lower VAS scores when compared to the control group after both the first and second surgery and at both time frames measured.

In addition, patient-controlled analgesia (PCA) use was significantly greater in the control group compared to the magnesium group 48 hours postoperatively after both the first and second surgeries. The control group had a PCA consumption of 525 μ g of fentanyl after the first

surgery and 870µg after the second. The magnesium group had a consumption of 300µg after the first surgery and 495µg after the second surgery. When compared to the control group, the magnesium group required a significantly lower dose of fentanyl after the first and second surgery ($p=0.014$ and $p=0.001$, respectively). This study demonstrated that magnesium sulfate administration not only effectively attenuates postoperative pain, but also decreases pain in situations where there is an elicited increase in pain intensity, such as staged bilateral total knee arthroplasty.

Magnesium was also studied by Dehkordy et al. in 2020 for its efficacy in patients having posterior lumbar spinal fusion surgery. A randomized controlled clinical trial was conducted comparing 50 mg/kg of IV magnesium in 100mL of saline over 15 minutes administered prior to the induction of anesthesia followed by a continuous 15mg/kg/h infusion for the duration of surgery, to a placebo. A standardize anesthetic was performed for both groups: induction was performed with IV propofol at 2mg/kg, atracurium 0.5mg/kg, and was maintained with IV fentanyl 5µg/kg, midazolam 0.02 mg/kg, 40% O₂, 60% N₂O, and isoflurane at 1–2 MAC. Pain scores were measured postoperatively via the Visual Analog Scale (VAS) scoring method: 0 being no pain at all and 100 being the worst pain ever felt. Participants were assessed at 1, 6, 12, 24, and 48 hours postoperatively. The VAS scores at 1, 6, 12, and 24 hours after the surgery were significantly lower in the magnesium group. At the 1-hour mark, the control group had an average VAS score of 18 and the magnesium group 16.8 ($p = 0.08$). At 6 hours postop, the control group's VAS score was 45 and the magnesium group's score was only 32.7 ($p < 0.001$). After 12 hours, the control group recorded a score of 38 while the magnesium group's was only 26.7 ($p = 0.042$), and at postop hour 24 the control group had an average VAS score of 32.8 and the magnesium group had a score of 23 ($p = 0.022$). Morphine consumption via PCA was also

measured for 48 hours after surgery and was significantly lower in the magnesium group compared to the placebo group. At 6 hours, the morphine consumption for the control group was 17mg, which was significantly less compared to only 13mg for the magnesium group ($p = 0.037$). After 12 hours, the control group consumed 31.5mg of morphine PCA and the magnesium group 21mg ($p = 0.046$). At 24 hours postop, the control group was at 53mg total while the magnesium group was at 38mg ($p = 0.02$). Lastly, at 48 hours postop, the control group's PCA consumption was totaled at 78mg, and the magnesium groups was 53mg ($p = 0.015$). In this study, magnesium sulfate lessened the amount of morphine required and appeared to enhance patient comfort.

Tsaousi et al., 2020 studied lumbar laminectomy patients and their response to magnesium sulfate as a perioperative analgesic adjunct. In this randomized controlled trial, the magnesium group received intravenous magnesium sulfate as a 20mg/kg bolus diluted in isotonic saline to a volume of 100mL over 15 minutes. It was administered prior to the induction of general anesthesia and followed by a continuous infusion of 20mg/kg/h until surgery end. The control group received normal saline in the same volume bolus and infusion. All patients received a general anesthetic and were induced with 1-2mg/kg of propofol, 2mcg/kg of fentanyl, and 0.2mg/kg of atracurium. Desflurane was administered at 5-6% to keep the patients anesthetized along with a remifentanil infusion with plasma target concentrations of 1.5-3 μ g/ml. Remifentanil was titrated to manage an increase in heart rate or mean arterial pressure 20% above the patients' baseline value. All infusions were discontinued upon surgery end. Pain scores were measured via the VAS scale postoperatively at hours 1, 2, 4, 6, and 24. The magnesium group's VAS scores as well as morphine equivalent consumption were lower at all assessed time periods, however, not all differences were significant. At postop hour 4, the magnesium group's

morphine equivalent was about 3ml, which was significantly less than the control groups, which was 8ml ($p = 0.002$). At postoperative hour 6, the magnesium group had consumed an average total of 5ml of morphine equivalent while the control group had consumed an average total of 12ml ($p = 0.000$). At the 24-hour postoperative timeframe, the magnesium group had again required a significantly less total morphine equivalent than the control group - 6ml and 14ml, respectively ($p = 0.000$). At postoperative hours 2, 4, 6, and 24, the magnesium group also had significantly lower VAS scores than the control group ($p \leq 0.005$ for all). Of note, the magnesium group experienced less overall need of remifentanyl intraoperatively compared to the control group. The magnesium group consumed 44.2 μ g/hour while the control group required an average of 196.9 μ g/hour ($p = 0.000$). This study demonstrated that the use of magnesium sulfate as an analgesic adjunct reduced postoperative morphine equivalent consumption by an average of 63.4% in the first 24 hours after lumbar laminectomy, and it can serve as a beneficial, safe component to a multimodal anesthetic approach.

Peng et al. 2018, conducted a systematic review to evaluate the efficacy of magnesium sulfate for postoperative analgesia during orthopedic surgery. Eleven randomized control trials met the inclusion criteria using the PRISMA guidelines. It was concluded that intraoperative magnesium sulfate administered intravenously as a bolus, an infusion, or both, significantly reduced postoperative analgesic consumption following orthopedic surgery procedures. Bolus doses varied between 30-50mg/kg and infusion rates ranged between 8-10mg/kg/hour. The studies included a wide range of orthopedic procedures including arthroscopic knee surgery, knee or hip arthroplasty, lower extremity osteotomy, posterior spinal fusion surgery, and laminectomy. Nine of the 11 studies measured pain intensity via the VAS scoring system, one study used the numeric assessment scale (NMS), and one used the 'faces' pain scale-revised

(FPS-R). The timeframe for pain measurements varied from the immediate postoperative period to 48 hours post-procedure. Six of the 11 studies revealed a significant decrease ($p < 0.05$) in postoperative pain scores when magnesium was administered compared to controls. In 3 of the studies, mean pain intensity scores (utilizing one of the three scales previously mentioned) were decreased in the magnesium group compared to the control at the 24-hour postop mark by 53% and at postop hours 4, 6, and 12 by 55%, 41%, and 45%, respectively. Two of the 11 studies assessed postop pain at hours 1, 2, 3, and 8, and demonstrated decreased scores in the magnesium group compared to the control group at all measured times. In these studies, the magnesium group's scores were 56% lower at postop hour 1, 52% lower at postop hours 2 and 3, and 45% lower at postop hour 8.

Of the 11 studies, eight revealed a significantly decreased dose in overall analgesics consumed by patients who received magnesium sulfate than those who were part of a control group ($p < 0.05$). Analgesics utilized in these eight studies included morphine, tramadol, pethidine, piritramide, and fentanyl, and their cumulative administration was assessed at 24 hours postoperatively in all studies. Cumulative morphine consumption was reduced by 38% and 57% in two studies, tramadol consumption was reduced by 16%, pethidine consumption was decreased by 33%, and cumulative piritramide and fentanyl consumption were reduced by 38% and 85%, respectively. This systematic review provided evidence that intraoperative magnesium sulfate administration is efficacious in providing analgesia for orthopedic surgeries, and it can decrease pain scores as well as postoperative analgesic consumption (Peng et al., 2020).

Magnesium sulfate in thoracic surgery

In 2017 Sohn et al. studied intravenous magnesium sulfate administration for analgesia in patients undergoing video-assisted thoracoscopic surgery (VATS). In this randomized, double-

blind, controlled trial, a total of 62 patients participated and were randomly placed into two groups: a magnesium sulfate group and a normal saline group. General anesthesia was induced and maintained with continuous propofol and remifentanyl infusions. Rocuronium was administered at 0.6mg/kg to facilitate intubation of a left-sided double-lumen tube. The magnesium group was then given a magnesium sulfate bolus of 50mg/kg intravenously over 10 minutes followed by a continuous infusion of 15mg/kg/hour for the duration of the procedure. The control group was given equal bolus and infusion volumes of normal saline. Throughout the procedure, the remifentanyl infusion was adjusted to maintain a heartrate and mean arterial pressure within 20% of the patient's baseline values. 30 minutes prior to the end of the procedure, intravenous patient-controlled analgesia (PCA) was initiated to provide acute postoperative pain relief. Fentanyl was the PCA agent and was set at a basal infusion rate of 1ml/hour with concentrations varying between 9-15mcg/ml. Patients were also allowed a self-administered 1ml bolus every 15 minutes as needed. Pain scores were recorded at 2, 24, and 48 hours after surgery and were assessed using the numerical rating scale (NRS), with 0 being no pain at all and 10 being the worst pain possible. Morphine 5mg was the rescue analgesic administered if needed in the recovery room or on the floor. Results showed that patients in the magnesium group utilized significantly less postoperative Morphine than the control group at postop hours 24 and 48. At the 24-hour mark, the magnesium group had consumed an average of 35.1mg while the control group consumed 44.7mg ($p = 0.042$). Postop hour 48 resulted in the magnesium group having consumed a total of 47.9mg of Morphine and the control group having consumed 68mg ($p = 0.023$). While there was no significant difference in any of the assessed postop pain scores between the two groups, the magnesium group did require significantly less

Morphine after 24 hours postop. This study proved that magnesium is effective in reducing the amount of postoperative opioids needed for patients undergoing VATS procedures.

Ghezel-Ahmadi et al., 2019 published the results of a prospective observational study that demonstrated the efficacy of magnesium sulfate as an analgesic for post-thoracotomy patients. A total of 100 patients participated in the study. The study group received intravenous magnesium sulfate as a 40mg/kg bolus over 10 minutes during induction followed by a 10mg/kg/hour infusion for 24 hours, and the control group received no magnesium sulfate. All participants were given a total intravenous general anesthetic (TIVA) with propofol and remifentanyl infusions. The propofol infusion was maintained at 4-5mg/kg/hour and the remifentanyl was set at 0.2-0.5µg/kg/minute. The numerical rating scale (NRS) was used to measure postoperative pain scores, 0 being no pain and 10 being the worst pain imaginable. Pain was assessed before surgery, on postop days 1-8, postop day 30, and postop day 90. The patients who received magnesium sulfate had significantly lower amounts of opioid consumption in Morphine equivalent on postop day 5 and postop day 30 than those who did not receive perioperative magnesium sulfate, 35.5mg and 5.2mg, compared to 48.1mg and 12.5mg, respectively ($p = 0.036$ and $p = 0.038$). In addition, NRS scores at rest were significantly lower in the magnesium sulfate group than the control group on postop days 1-8 ($p \leq 0.009$). This study provided evidence that magnesium sulfate can be beneficial in reducing and preventing acute postoperative pain at rest while simultaneously reducing opioid consumption in patients undergoing thoracotomy procedures.

Another study by Salah Abdelgalil et al. in 2019 assessed the efficacy of magnesium sulfate as an analgesic adjunct for patients having open thoracotomy procedures. A total of 120 patients were randomized into 4 groups:

Group MP – preoperatively received 300mg pregabalin orally and an intravenous infusion of magnesium sulfate 50mg/kg diluted in 200ml of normal saline

Group P – preoperatively received 300mg pregabalin orally and 200ml of a normal saline intravenous infusion

Group M – preoperatively received a placebo capsule and an intravenous infusion of 50mg/kg magnesium sulfate diluted in 200ml of normal saline

Group C – preoperatively received a placebo capsule and 200ml of a normal saline intravenous infusion

All medications were given one hour prior to surgery and the infusions were administered over 30 minutes. All patients underwent a general anesthetic and were induced with 2-3mg/kg of propofol, 2µg/kg of fentanyl, and 0.6mg/kg of rocuronium. A left double-lumen endotracheal tube was inserted, and sevoflurane 1-2% was utilized to maintain anesthesia throughout the procedure. If the patient had an increase of 20% above baseline in heart rate or mean arterial pressure, 0.5µg/kg of fentanyl was administered. Postoperatively patients received a PCA pump with morphine sulfate as the opioid of choice. Total morphine consumption, pain scores using the VAS scale, and the incidence of nausea and vomiting were assessed for the first 24 hours after surgery. Group MP consumed a total of 28.47mg of morphine, group M consumed 40.87mg, group P consumed 33.97mg, and group C consumed 42.2mg. There was a significantly lower morphine consumption in group MP when compared with group M ($p < 0.001$), group P ($p < 0.008$), and group C ($p < 0.001$). This study showed that as a solo agent, magnesium sulfate does not provide an appropriate level of analgesia, but when used as an adjunctive therapy, it can significantly decrease the administration of opioids given in the first 24 hours postoperatively for open thoracotomy patients.

Magnesium sulfate in ENT surgeries

Elsersy et al., 2017 conducted a randomized, double-blind controlled clinical trial involving 312 patients undergoing functional endoscopic surgery that assessed the efficacy of magnesium sulfate for pain management. The patients were randomly divided into a magnesium sulfate group, who received a magnesium sulfate infusion of 30mg/kg for the first hour of the surgery, and then an infusion of 9mg/kg/hour for the duration of the procedure. The control group received a 0.9% normal saline infusion at the same volume and rate. General anesthesia was induced in all patients using 2.5mg/kg of propofol, 1µg/kg of fentanyl, 0.5mg/kg of atracurium. The Numeric Rating Scale (NRS) was utilized to assess pain postoperatively at 0, 5, 10, 15, and 30 minutes. 0 represented no pain while 10 represented the worst pain. Pethidine 25mg was utilized as a rescue analgesic. were assessed at 30 minutes upon arrival in the PACU. The results showed that the magnesium group had a lower average pain score compared to the control group, 4.5 and 6, respectively ($p < 0.0001$). In addition, total pethidine consumption in the PACU was significantly less in the magnesium group than in the control group, 43mg and 59mg, respectively ($p < 0.0001$). This study showed that magnesium sulfate produced lower pain scores and decreased postoperative opioid consumption in patients undergoing functional endoscopic surgery.

Last but certainly not least, Mostafa, Salem, and Ibrahim (2020) studied patients undergoing thyroid surgery. In this randomized controlled trial, 80 females were randomly divided into two groups: a magnesium group who received 30 mg/kg of magnesium sulfate in 100ml of normal saline over 15 minutes before the induction of general anesthesia followed by a continuous infusion of magnesium sulfate at 10mg/kg/hour for the length of the procedure, and a control group who received normal saline at the same rate and volume as the magnesium. All

patients were induced using 2mg/kg of propofol, 1µg/kg of fentanyl, and 0.5mg/kg of atracurium. Anesthesia was then maintained utilizing Isoflurane at 1-2%, and 25µg of fentanyl was administered for increases in heart rate and/or mean arterial pressure 20% above baseline values. The incidence and severity of a postoperative sore throat (POST) was evaluated at 0, 6, and 24 hours after surgery. POST was scored based on a four-point scale (0 = no pain; 1 = mild sore throat, patient complains only on asking; 2 = moderate sore throat, patient complains of sore throat on own; 3 = severe sore throat, change in voice/hoarseness along with pain). When assessing the overall occurrence of POST in the first 24 hours postop, the magnesium group patients had significantly lower incidence than those in the control group, 15 and 30, respectively ($p < .001$). Not only did the patients who received magnesium experience less incidence of POST, but they also required significantly less fentanyl intraoperatively. During the case, the patients in the magnesium group received an average of 138.8µg of fentanyl while the control group received an average of 195.71µg ($p < 0.0001$). This study concluded that magnesium sulfate can effectively decrease the overall incidence of POST while also reducing the total amount of narcotic administered during thyroid surgery.

Problem Statement

There appears to be a lack of awareness amongst Certified Registered Nurse Anesthetists regarding the efficacy and benefits of magnesium sulfate as an opioid sparing adjunct in the perioperative setting.

Theoretical Framework

Institutional theory offers a notable viewpoint in contemporary organizational scholarly activity. It is known to encompass a large, diverse body of theoretical and experimental work connected by a common emphasis on cultural understandings and shared expectations. It is often

used to explain the adoption and spread of formal organizational structures, including written policies, standard practices, and new forms of organization.

It was identified (informally) that many members of the Michigan Association of Nurse Anesthetists were unaware or uninformed of the efficacy of magnesium sulfate in avoiding overuse of opioid narcotics while managing perioperative pain satisfactorily. Therefore, utilizing an institutional theory framework, this scholarly project permitted the spread of widely accepted clinical anesthesia practices to inform Certified Registered Nurse Anesthetists of the patient benefits and potential outcomes when magnesium sulfate is used as a perioperative analgesia adjunct.

The Praxis Theory of Suffering can be utilized to conceptualize patient pain. It is based on nursing interventions and strategies aimed at relieving patient suffering, which can present itself in the form of emotional or physical pain (Butts & Rich, 2018). Providing adequate pain relief by employing multimodal strategies that include magnesium sulfate can facilitate patient comfort and prevent overwhelming suffering related to pain. In addition, the avoidance of the sole use of opioids for analgesia in the perioperative period can cause catastrophic and long-lasting adverse complications. The theory supporting multimodal perioperative analgesia is described as the use of more than one pharmacological class of analgesic medication targeting different receptors along the pain pathway with the goal of improving analgesia while reducing individual class-related side effects (Schwenk & Mariano, 2018).

Purpose Statement

The purpose of this DNP project was to:

1. Conduct an extensive and comprehensive literature search specific to the efficacy of magnesium sulfate as an anesthesia and analgesia adjunct in the perioperative period.

2. Develop a professional curricular presentation specific to magnesium sulfate as an opioid sparing agent based on the most current scientific evidence
3. Present a one hour continuing education webinar (and offer one Class A credit) to the members of the Michigan Association of Nurse Anesthetists titled: Magnesium Sulfate as an Anesthesia Adjunct: Establishing Opportunities for Enhancing Outcomes of Care
4. Evaluate the CRNA participants feedback following the webinar to identify potential additional methods for disseminating information regarding the efficacy of perioperative magnesium sulfate

Project Methodology

Project Design

This DNP project was part evidence-based change initiative, program development in the form of a CE webinar, and quality improvement initiative. To accomplish the purpose of disseminating evidence-based information of the benefits and uses of magnesium sulfate as an opioid sparing anesthesia and analgesia adjunct, a webinar was comprehensively developed and presented to the members of the Michigan Association of Nurse Anesthetists.

The objectives of the formal webinar included:

1. Describe the role of the magnesium ion in the human body
2. Explain the current therapeutic uses of magnesium in the hospital setting related to anesthesiology
3. Clarify the mechanism of action of externally (intravenously) administered Magnesium Sulfate
4. Outline the pharmacokinetic profile of intravenous magnesium sulfate
5. Illuminate the purposes for administering magnesium sulfate in the perioperative setting

6. Present the published clinical trials and respective patient outcomes when magnesium sulfate when incorporated as a key component of opioid free and/or opioid sparing anesthesia
7. Describe the current dosing regimens of magnesium sulfate when administered intravenously as an anesthesia and analgesia adjunct

There were several steps taken to accomplish the objectives of the project. They are listed in order:

1. Performing an ongoing extensive evidence-based literature review of magnesium sulfate, including but not limited to the information to be included in the planned webinar.
2. Collaborating with Jason McLott, MSN, CRNA, member of the scholarly project team and independent CRNA provider who is an expert in the administration of opioid free anesthesia and analgesia with magnesium sulfate. CRNA McLott is published and well known in the anesthesia community and served dutifully on the project guiding the webinar content.
3. Collaborating with Jennifer Dickie CAE, CMP, Association Manager Specialist and Liv Hagerman CMP Account Manager for the Michigan Association of Nurse Anesthetists (MANA) to plan the webinar. This included describing the purpose of the webinar, obtaining approval to conduct the webinar from the MANA program committee, submitting program objectives and learner outcomes to MANA and validating that attendees of the webinar can obtain a CPC program class A free of charge (explained below), deciding upon a date and time for the on-line webinar, planning the advertisement to MANA members and CRNAs in the state of Michigan, and verifying that evaluation of the webinar by the attendees would be received by the management

firm of MANA who would de-identify the evaluations and comments (see #5) and send to the presenters.

Explanation of the NBCRNA CPC Program Class A Credits

The National Board of Certification and Recertification for CRNAs (NRCRNA) is the national credentialing body for Certified Registered Nurse Anesthetists in the United States. Practicing CRNAs must maintain their credential by engaging in and being compliant with the Continued Professional Certification Program (CPC). Every four years (in an eight-year cycle), CRNAs must accrue 60 Class A Credits. Class A credits are continuing education (CE) credits earned by participating in CE courses or activities that sharpen the skills of the CRNA and grow knowledge (NBCRNA, Class A credits) CRNAs earn class A credits by engaging in CE activities that meet the following three criteria:

1. Be prior approved by an accredited organization authorized to approve continuing education. (e.g., AANA, ANCC, ACGME)
2. Include an assessment, such as self-assessment, polling, case studies, simulations, or post-tests.
3. Be relevant to nurse anesthesia practice or the improvement of the delivery of anesthesia care to patients.

Class A credit examples include online courses, in person CE courses, webinars, workshops, and other. The Michigan Association of Nurse Anesthetists (MANA) is considered (for this entity) a vendor. For example, MANA hosted this webinar (delivered to CRNAs by the authors) and received authorization via prior approval processes to offer one Class A continuing education credit to the CRNAs who participated and completed a post program assessment.

According to the AANA 2019 Continuing Education Program, “Class A credits are those educational activities that have an assessment. AANA has defined assessment in its CE Program in Standard VII (Assessment) where the program provider will be required to have a method, appropriate for the specific learning activity, to assess learner engagement and the effectiveness of learning. The goal of this assessment will be to identify how participation in the activity informed and/or improved the learner’s practice. An assessment can take many forms, such as multiple-choice questions, simulation demonstrations, case studies, or self-assessment”. To meet the requirements for the continuing education requirements, an application was completed by the authors of this scholarly paper in collaboration with the MANA administrative team, and received approval to offer the webinar for one Class A Credit (see Appendix B).

Project Setting/Sample

The online zoom- delivered webinar, a major component of the project, was presented on February 10, 2022, at 7 o’clock pm to pre-registered CRNAs MANA members. There was a total of 89 attendees, 73 of which participated in the post-assessment and evaluation.

Key Personnel/Stakeholders

Key personnel for this project included the CRNA content expert Jason McLott, the management firm administrators for the MANA, and the CRNA webinar attendees who are now better informed of the role of magnesium sulfate as an anesthesia adjunct.

Participants/population

The participants in this project were the CRNAs who attended the live zoom online webinar.

Recruitment strategies

As aforementioned, the online zoom webinar was advertised for MANA members by posting an announcement in the MANA (on-line) Monday Morning Update that is emailed to all members who agree to receive such emails. In addition, the webinar was advertised on the MANA website with detailed registration information and program objectives (See Appendix D).

Project Intervention Plan (Procedures)

The webinar was presented on Thursday February 10, 2022, at 7 pm, as planned. The administrative team at MANA facilitated the admittance of registrants to the webinar and coordinated the zoom technology processes. The presentation took place for 50 minutes and there were 10 minutes of questions from the attendees; answers were fielded by the webinar developers. Attendees were instructed how to complete the evaluation of the webinar (per standard operating procedure) and submit to MANA to receive their Class A credit.

Data Collection Instruments

In accordance with the CPC program of the National Boards of Certification and Recertification (NBCRNA), the self-assessment and evaluation of the program was emailed to the attendees who wanted to submit to the AANA for a Class A credit, per pre-established procedures. See Appendix C.

The administrators of the Michigan Association of Nurse Anesthetists received the self-assessment and evaluation from the registrants who participated in the webinar, and applied to the AANA for each respective CRNA attendee to receive their Class A credit. This is the usual

and customary way educational sessions are processed for Class A credits. In addition, each evaluation completed by the attendees was de-identified and forwarded in an excel spread sheet to the developers of the webinar for data analysis.

Data Analysis

Data was collected from the post-webinar evaluations after the webinar presentation. It was then analyzed utilizing the specific responses from CRNAs that attended the webinar. The data analysis illustrated that the magnesium presentation was successful and that attendees gained new information from the material presented. Additionally, data revealed that most CRNAs did not know typical dosing, benefits of use to patients, and the types of surgical cases to include the drug in the anesthesia plan. The evaluations revealed that the webinar was effective and provided education to CRNAs. It also revealed that CRNAs are going to attempt to incorporate magnesium sulfate into their practice. Some potential barriers to use included disagreements with anesthesiologists or availability of the drug from pharmacy.

Potential Barriers to Implementation and Sustainability

As mentioned above, CRNAs were asked on the post-webinar evaluation to record any potential barriers they thought may hinder using magnesium sulfate in practice. The majority of CRNAs stated that the biggest barriers to using magnesium would be potential conflicts with the anesthesiologist/MDA and the availability of the drug from pharmacy. This is most likely due to some anesthesiologists being resistant because of unfamiliarity, however, the goal of this project was to communicate the benefits of magnesium sulfate as an analgesia adjunct. CRNAs also expressed issues with availability of the drug from pharmacy. Fortunately, magnesium sulfate is a relatively cost-effective drug and hospital-based pharmacies have it on formulary.

Ethical Considerations & Risk

This DNP scholarly project was developed, and the webinar was presented without any disclosure of protected personal information of the CRNAs who participated. For MANA to obtain approval for the program (to offer one Class A Credit), only the administrative team of MANA received CRNAs names and their AANA member identification number.

The project was deemed non-human subjects research by the Oakland University IRB (by verbal communication with the faculty project chair, therefore an application to the IRB was not necessary).

Potential Benefits & Outcomes

There are numerous published clinical trials that support magnesium sulfate as an effective opioid sparing anesthesia and analgesia adjunct in select patient scenarios. Minimizing opioids during the perioperative period while providing analgesia with adjunctive medications enhances quality of care, and therefore patient satisfaction is optimized. Equally as important, minimizing opioid use and their respective adverse effects is a benefit. Other benefits include a reduction in the overall cost of care related to avoiding treatment of the adverse effects of opioids when used as a sole analgesic in an anesthetic plan.

A single injection vial of 1 gram of Magnesium Sulfate costs approximately \$13-14, while a single injection vial of 100 mcg of Fentanyl Citrate (routinely used as a perioperative opioid) costs approximately \$39 (Bound Tree Pharmaceuticals, 2021 & Ascension St. John Pharmacy, 2021). Lastly, perioperative magnesium sulfate can lead to a reduction in the volume of opioid prescriptions given to patients to manage postoperative pain after discharge from the hospital. This means that less opioids are available for use, misuse, overuse, and abuse, all of which contribute to the opioid crisis. (Brown et al., 2018).

Timeline

The idea for this DNP scholarly project began in the summer semester of year I of Oakland University NA BSN to DNP program. The timeline for project development, implementation, and dissemination approximated the timeline as delineated in the DNP handbook. For example, step 1: Identification and approval of the project area and interest, took place in the summer of 2020. The written proposal was approved in the fall of year II of the program, which began a comprehensive literature review. This literature review was expanded until the webinar was fully developed and launched in February of year III. After presentation of the webinar in February 2022, five weeks passed and the self-assessment and evaluation of the webinar by the presenters (de-identified data) were emailed to the project authors. The results of the self-assessment and participant evaluation of the webinar were organized and inserted into this final written report in April and May of 2022. Dissemination of the final project took place on June 30, 2022, to an audience of OUBGPNA nurse anesthesia faculty, Oakland University School of Nursing faculty and leadership, current students enrolled in the OUBGPNA, and other stakeholders vested in the DNP NA program.

Resources, Budget and Funding

There were no anticipated costs nor funding required for this DNP scholarly Project.

Evaluation

The Purpose (and objectives) of this DNP Scholarly project was to:

1. Conduct an extensive and comprehensive literature search specific to the efficacy of magnesium sulfate as an anesthesia and analgesia adjunct in the perioperative period

2. Develop a professional curricular presentation specific to magnesium sulfate as an opioid sparing agent based on the most current scientific evidence
3. Present a one hour continuing education webinar (and offer one Class A Credit) to the members of the Michigan Association of Nurse Anesthetists titled: Magnesium Sulfate as an Anesthesia Adjunct: Establishing Opportunities for Enhancing Outcomes of Care
4. Evaluate the CRNA participants feedback following the webinar to identify potential additional methods for disseminating information regarding the efficacy of perioperative magnesium sulfate

The authors of this DNP Scholarly Project met all the objectives. The comprehensive and ongoing literature review was completed; the professional curricular presentation took place on February 10th, 2022; participants in the one hour continuing education webinar received their Class A Credit by completing the post-webinar assessment and provided extremely positive feedback to the presenters including potential and real barriers to the use of Magnesium Sulfate. This feedback can be used to offer ongoing informational sessions to all anesthesia providers and leaders and decision makers within hospital settings and anesthesiology departments.

The participants evaluated the webinar via a post webinar evaluation distributed by the administrative leadership of MANA. The evaluation 'form' was compromised of 11 questions and respondents answered each question using a Likert scale scoring: satisfied (a score of 4), somewhat satisfied (a score of 3), neutral (a score of 2), somewhat dissatisfied (a score of 1), or dissatisfied (a score of 0). The questions were the established questions in AANA approved formatting for the attendees to receive a Class A Credit. Questions regarding the 'content' of the webinar were also included but analyzed differently because responses were in the form of short answers.

Summarized Results of the Webinar

Most participants found the presentation effective and informative. For example, 97% (n=71) of respondents answered 'satisfied' that the content was related to the objectives; 93% (n = 68) indicated they were satisfied regarding the effectiveness of the teaching method, and 90% (n = 66), felt satisfied that the webinar facilitated learning.

Participants were also asked if the presentation objectives were met -

Objective 1: Acknowledge the current state of the opioid crisis and its relationship to intraoperative opioid use: 95% (n = 69) were satisfied

Objective 2: Acknowledge the multiple uses of magnesium sulfate in the hospital setting: 96% (n = 70) were satisfied

Objective 3: Review the MOA, pharmacokinetic profile, dosing, and patient profiles that benefit from intraoperative magnesium sulfate: 95% (n = 69) were satisfied

Objective 4: Examine numerous case scenarios and the anesthesia plan that includes magnesium sulfate as an analgesia and anesthesia adjunct: 93% (n = 68) were satisfied; four were somewhat satisfied, and one responded as being neutral.

There were two statements on the post-webinar assessment self-evaluations that respondents were asked to address in short answer format:

Statement 1 - State one item you learned from this session that will improve your nurse anesthesia practice.

In summary, most respondents indicated the information they received regarding dosing and detail specific to the efficacy as an effective analgesia adjunct will enhance their nurse anesthesia practice

Statement 2 - State any barriers to implementing magnesium sulfate into practice.

In summary, most respondents indicated there are not any barriers. Interestingly however, others did respond that anesthesiologist involvement and availability of the drug, are potential barriers.

For a complete summary of results of the webinar, please see Appendix E.

Facilitators and Barriers

There were no barriers encountered during the development and implementation of this DNP scholarly project. Communicating evidence based information to CRNAs related to the benefits of magnesium sulfate facilitates quality care. Magnesium Sulfate blocks the NDMA receptors and provides a synergistic effect when used in combination with drugs that have a different MOA. Because of the unique MOA of magnesium sulfate, there is opportunity to decrease the amount of opioids administered during a general anesthetic, as well as reduce the amount of inhalation agent required while producing little or no negative side effects (Altıparmak et al., 2018; Benevides et al., 2021; Dehkordy et al., 2020). Participants in the webinar agreed that magnesium can offer appropriate and effective pain control for patients based on the information they received.

Recommendations & Limitations

The authors of this DNP Scholarly Project recommended that CRNAs consider the use of magnesium sulfate for applicable patients and be incorporated into anesthesia practices. The limitations to incorporating magnesium sulfate into anesthesia management plans are related to local availability of the drug and anesthesiologist standard practice. CRNAs are therefore encouraged to also communicate the potential benefits to members of their respective anesthesiology and hospital leadership.

Recommendation for Sustaining Intervention

Published research and case studies validate magnesium sulfate as an effective analgesia adjunct in select perioperative scenarios. The long-term goal for sustainability is related to including the drug in Enhanced Recovery After Surgery (ERAS) protocols. ERAS protocols are multimodal perioperative care pathways designed to achieve early recovery after surgical procedures by maintaining pre-operative organ function and reducing the profound stress response following surgery. The key elements of ERAS protocols include preoperative counseling, optimization of nutrition, standardized analgesic and anesthetic regimens and early mobilization (Melnik et al., 2011). Based on the research and data, magnesium sulfate should be considered and included in ERAS protocols when appropriate.

Contribution of Project in Achieving DNP Essentials & Personal goals

This project involved extensive data analysis from published cases studies and numerous clinical trials. It allowed us to embrace information system technology for evaluating, integrating, and translating evidence for the purpose of transmitting information that can improve care and promote favorable outcomes of care. We performed a literature review and communicated the findings of numerous research initiatives from varying of levels of evidence and presented this information. Additionally, this project integrated scientific and theoretical knowledge from nursing and other disciplines such as anesthesiology, to develop, identify, evaluate, and disseminate best practices that can enhance quality and safety. It also integrated nursing science with knowledge from the biophysical, psychosocial, analytical, and organizational sciences, all part of the highest level of nursing practice.

A goal of ours is to continue to communicate to our CRNA colleagues' evidence-based information specific to the benefits of magnesium sulfate when used as an analgesic adjunct, and

to acknowledge it as a major component in a multitude of ERAS protocols for select surgical procedures.

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Appendix A: Synthesis Table

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Level I: Systematic Review or Meta-Analysis					X					X											
Level II: Randomized Controlled Trial	X	X	X	X		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
Level III: Controlled Trial without randomization																					
Level IV: Case-control or Cohort Study																					
Level V: Systematic Review of qualitative or descriptive studies																					
Level VI: Qualitative or																					

Descriptive Study																					
Level VII: Expert Opinion or Consensus																					

1 = Sousa et al. (2016); 2 = Taheri et al. (2015); 3 = Mussrat et al. (2019); 4 = Chen and Tao. (2018); 5 = Peng et al. (2018); 6 = Kizilcik and Koner (2018); 7 = Altıparmak et al. (2018); 8 = Elserly et al. (2017); 9 = Tsaousi et al. (2020); 10 = McKeown et al. (2020); 11 = Shah and Dhengle (2016); 12 = Dehkordy et al. (2020); 13 = Benevides et al. (2020); 14 = Mendonca et al. (2020); 15 = Silva Filho et al. (2021); 16 = Shin et al. (2016); 17 = Ghezel-Ahmadi et al. (2019); 18 = Kumar et al. (2016); 19 = Aelgalil et al. (2019); 20 = Sohn et al. (2017); 21 = Mostafa et al. (2020)

Appendix B: Magnesium Sulfate as an Anesthesia Adjunct: Establishing Opportunities for Enhancing Outcomes of Care – Class A Approval

The prior approval application submitted for the program "**Magnesium Sulfate - an Anesthesia Adjunct**" provided by **Michigan Association of Nurse Anesthetists** has been approved. Below please find the AANA prior approval statement for this program. This statement must be included on the certificate of completion that will be issued to participants and on any associated advertising for the program:

This program has been prior approved by the American Association of Nurse Anesthesiology for 1.00 Class A CE credits; Code Number 1041744; Expiration Date 2/10/2022.

The information listed below must be used when reporting the credits earned for this program in the CE Portal.

Course ID: 1041744

Start Date	End Date	Class #
2/10/2022 12:00:00 AM	2/10/2022 12:00:00 AM	- 143608 -

Important:

Please review the critical information regarding CE credit reporting responsibilities and other critical information for you as a provider by accessing the CE Program Provider Responsibilities PDF online: **CE Program Provider Responsibilities** Please use the AANA CE Portal to see this and other course applications and approval information <http://www.aana.com/ceportal>, as well as to report CE credits earned for this program.

Please forward any questions to the Continuing Education department at continuingeducation@aana.com

Appendix C: Post Evaluation Questionnaire

Magnesium Sulfate as an Anesthesia Adjunct: Establishing Opportunities for Enhancing Outcomes of Care

Question 1. *Full Name -*

Question 2. *AANA Number -*

Question 3. *The facilitators were effective in presenting the material*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 4. *The content was related to the objectives*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 5. *Teaching methods were effective*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 6. *Facilitated learning was effective*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 7. *My personal learning objectives were met*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 8. *Objective 1: Acknowledge the current state of the opioid crisis and its relationship to intraoperative opioid use*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 9. *Objective 2: Acknowledge the multiple uses of Magnesium Sulfate in the hospital setting*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 10. *Objective 3: Review the MOA, pharmacokinetic profile, dosing, and patient profiles that benefit from intraoperative magnesium sulfate*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

Question 11. *Objective 4: Examine numerous case scenarios and the anesthesia plan that includes magnesium sulfate as an analgesia and anesthesia adjunct*

Satisfied

Somewhat Satisfied

Neutral

Somewhat Dissatisfied

Dissatisfied

State one item you learned from this session that will improve your nurse anesthesia practice

State any barriers to implement this change

Appendix D: Webinar PowerPoint



Dear MANA Members,

Join us on February 10th at 7:00pm for a FREE webinar for 1 Class A CE!

Magnesium Sulfate - an Anesthesia Adjunct:
Establishing Opportunities for Enhancing
Outcomes of Care

Participants in this webinar will:

- Acknowledge the current state of the opioid crisis and its relationship to intraoperative opioid use
- Acknowledge the multiple uses of **Magnesium Sulfate** in the hospital setting
- Review the MOA, pharmacokinetic profile, dosing, and patient profiles that benefit from intraoperative **magnesium sulfate**
- Examine numerous case scenarios and the anesthesia plan that includes **magnesium sulfate** as an analgesia and anesthesia adjunct



Nurse Anesthesia DNP students, Class of
2022
Oakland University Beaumont Graduate
Program of Nurse Anesthesia

Magnesium Sulfate - an Anesthesia Adjunct:

Establishing Opportunities for Enhancing Outcomes of Care

Magnesium Sulfate

Objectives

- Participants in this session will:
 - Acknowledge the current state of the opioid crisis and its impact on the hospital setting
 - Acknowledge the multiple uses and RDA of Magnesium Sulfate in the hospital setting
 - Review the MDA pharmacokinetics, safety, efficacy and other studies that benefit from Intravenous Magnesium Sulfate
 - Describe numerous case scenarios and the current best practice in our institution regarding MDA for (injured and un-injured) patients

Figure 4. National Drug Overdose Deaths Involving Prescription Opioids* Number Annually All Ages, 1999-2019

Opioid free vs Opioid Sparing

Opioid Sparing

Relies on non-opioid adjuncts that have differing pharmacokinetic profiles and mechanisms of action, yet provide analgesia, and when used together with small quantities of opioids, do maintain the total amount of opioid required

Opioid Free

Opioid free analgesia

Adjuncts

- Corticosteroids
- Anticholinergics
- Anticoagulants
- Antidysrhythmics
- Antidepressants
- Alpha 2 agonists
- Local anesthetics
- Anticoagulants
- Calcium channel blockers
- Beta adrenergic blocking agents
- Central nervous system stimulants
- Neuroleptic anti-inflammatory drugs
- N-methyl-D-aspartate (NMDA) receptor antagonists

The Proposed Solution

- Safely manage acute postoperative pain & reduce contribution to the opioid crisis
- minimize opioid use when applicable
- prevent progression to prolonged post surgical pain

OUR PURPOSE: offer evidence-based information on the efficacy of magnesium sulfate as an analgesic adjunct

The Multiple Uses of Magnesium

CURRENT:

- Management of cardiac arrhythmias
- Management of seizures and preeclampsia
- Management of asthma and COPD
- Management of hypomagnesemia

ACROSS FORWARD:

- Magnesium sulfate has been used for the treatment of various conditions, including:
 - Hypertension
 - Preeclampsia
 - Seizures
 - Asthma
 - COPD
 - Hypomagnesemia

Magnesium - Management of Cardiac Arrhythmias

The management of torsades de pointes and other arrhythmias

- Torsades de pointes
 - 100% to occur as a result of early after-depolarizations
 - Magnesium suppresses the EADs and automatically by decreasing Ca2+ activity and halting the arrhythmia
- Atrial fibrillation
 - Effective for controlling the ventricular response
 - Add in the successful conversion to normal sinus rhythm
 - Both atrial and ventricular refractory periods are prolonged by magnesium sulfate
 - results in greater opportunity for normal sinus rhythm

The Magnesium Ion

Mg²⁺

- Essential physiologic importance
- Essential mineral nutrient for human life
- One of the most abundant cations in the intracellular compartment in the human body
- Serves as a cofactor enzyme from 300 to 400 enzymes from various systems
- Muscle and nerve function
- Blood glucose control
- Blood pressure regulation

Even More on Magnesium

Required for the synthesis of DNA, RNA, and the antioxidant glutathione

Required for energy production, oxidative phosphorylation, and glycolysis

Contributes to the structural development of bone, which is where most is found

Acts in combination of nerve impulses, heart rhythm, and muscle contraction by regulating membrane permeability to sodium, potassium, calcium, and magnesium

The Multiple Uses of Magnesium

CURRENT:

- Management of cardiac arrhythmias
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- Management of hypomagnesemia

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Magnesium - Management of Cardiac Arrhythmias

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 - Effective for controlling the ventricular response
 - Add in the successful conversion to normal sinus rhythm
 - Both atrial and ventricular refractory periods are prolonged by magnesium sulfate
 - results in greater opportunity for normal sinus rhythm

Magnesium & Vasodilation

- Indirectly affects vascular contractility
- Inhibits release of catecholamines from adrenal medulla and peripheral sympathetic ganglia
- decreasing vasoconstriction
- decreases arterial tone through relaxation of arterial blood vessels and arterial smooth muscle
- dilates both the peripheral and resistance coronary arteries

Prevention of Seizures

1st line treatment

- prevention of eclamptic seizures
- creates cerebral vasodilation
- reduces ischemia generated by cerebral vasospasm
- competitively blocks calcium into synaptic ending

Magnesium as an Analgesic Adjunct

- Magnesium as an Analgesic Adjunct
 - Inhibitory effects and indirect blockade of NMDA receptors → analgesia
- NMDA receptors
 - Are ligand-gated cation channels
 - Activated primarily for their role specific to the initiation and maintenance of central sensitization
- Block flow of ions

An Analgesic Adjunct - NMDA Receptor Antagonist

- NMDA receptors
 - Present of excitatory "nerve" synapses
 - participate in excitatory neurotransmission in CNS
- (Block) Glutamate-gated Cation Channels
 - Associated with neuropathic pain, hyperalgesia, and reduced functionality of opioid receptor
- Hyperalgesia = neuropathic pain
 - the result of increased spinal neuron sensitization
 - generalized, diffuse, hyperalgesia, and not always located at the source of injury/ disease

Opioid Induced Hyperalgesia (OIH)

- Receptors can experience decreases in efficiency due to the sensitization of the signaling pathways → opioid-induced hyperalgesia (OIH) and opioid tolerance
- Counter excitation in opioid requirement
- Hyperalgesia to pain
- Combat OIH by preventing its occurrence
- offering a multimodal analgesic approach
- NMDA receptors play a part in the development of OIH
- Magnesium sulfate BLOCKS NMDA receptors

Blocking Calcium Ions

- Although magnesium has no direct anticholinergic effects, it inhibits calcium ions from entering cells by blocking NMDA receptors, resulting in an analgesic effect
- This analgesic effect is related to the prevention of central sensitization caused by peripheral tissue injury

Magnesium as an Analgesic Adjunct

- A competitive and noncompetitive NMDA antagonist
- NMDA antagonist → magnesium can prevent nociceptive central sensitization and produce analgesia
- Block flow of ions
- Although the receptor is the same, its mechanism and site of action are different from other noncompetitive antagonists both at extrinsic
- Reduces the release of catecholamines with sympathetic stimulation
- Leads to decreased peripheral nociception and a decreased stress response to surgery

NO COUNTERPART: Magnesium and ketamine have differing effects on the same receptor

- They can be administered simultaneously to increase the efficacy of analgesia produced

Magnesium & Ketamine

Ca²⁺, Na⁺

Extracellular space

Intracellular space

Epithelial cells

Phospholipid bilayer

Cell membrane

Cell nucleus

Cell organelles

Cell cytoplasm

Cell periphery

Cell surface

Cell interior

Cell exterior

Cell boundary

Cell interface

Cell contact

Cell adhesion

Cell communication

Cell signaling

Cell response

Cell function

Cell survival

Cell death

Cell regeneration

Cell repair

Cell maintenance

Cell homeostasis

Cell balance

Cell equilibrium

Cell stability

Cell resilience

Cell adaptability

Cell flexibility

Cell robustness

Cell durability

Cell longevity

Cell vitality

Cell energy

Cell power

Cell strength

Cell endurance

Cell stamina

Cell vigor

Cell spirit

Cell soul

Cell essence

Cell core

Cell heart

Cell mind

Cell spirit

Cell soul

Cell essence

Cell core

Cell heart

Cell mind

The Pharmacokinetic Profile

- Administration
 - IV, IM, PO
- 30% protein bound
- 1-2% extravascularly distributed → unbound
- Extracellular magnesium ions diffuse rapidly
- cross the placenta
- rapidly reabsorbed by renal tissue
- Onset (IV)
 - Hypotension - 20 minutes
 - DDA - 3-5 hours
 - Normal blood concentration levels = 1.7-2.4mg/dL

Serum Magnesium Levels

Serum magnesium level (mg/dL)

Dose related effects

1.7-2.4

Normal serum levels

5-8

Neuro, headache, light-headedness, cutaneous flushing

9-12

Absent deep tendon reflexes, somnolence, hypotension

12-15

Sinistral and atrioventricular block, muscle paralysis, hyperventilation

20

Cardiac arrest, respiratory arrest, coma

The Pharmacokinetic Profile

- Homeostasis
 - Renal excretion
 - 120 mg - urine/24 hours
 - Renal excretion is regulated
 - ascending limb of the Loop of Henle
- Caution
 - Impaired kidney function
 - decrease dose
 - Avoid hypermagnesemia

Magnesium's Benefits

- Research has demonstrated ability to reduce post-operative pain scores if administered in conjunction with other analgesic adjuncts
- Provides pain relief via an alternative mechanism to opiates and works synergistically with other analgesic medications
- Less opioids needed during general anesthesia
- Reduces inhalation agent requirements
- Produces little to no negative side effects

Magnesium in the Perioperative Setting

- Catecholamines are released during stressful events (like surgery) and elicit a pain response
- Magnesium inhibits catecholamine release from the adrenal medulla decreasing catecholamine release and reducing pain
- It works as a calcium channel blocker to inhibit the release of norepinephrine and blunt the body's response to the stress of surgery

25 [No Title]

Dosing

- Common
 - bolus 30-50 mg/kg over 10-15 minutes
 - followed by continuous infusion 0.5-1.5 mg/kg/hr until surgery and
- OR
- Single bolus of 30-50 mg/kg for shorter cases
- 2 grams diluted in a 50 ml syringe (final concentration = 100 mg/ml)
- 30 min - 1 hour
- 2 gram/100 or 500 ml NS
- 2 gram/1 L NS

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Cost

- A single injection vial of 1 gram of Magnesium Sulfate ~ \$13-14

27

Key Points Review on Magnesium Sulfate

- It acts as a N-methyl-D-aspartate (NMDA) receptor antagonist resulting in an analgesic effect
- It is used as an alternative or adjunct to opioids for pain control
- It has a high therapeutic index and is cost-effective
- It has the potential to improve surgical outcome and enhance satisfaction

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The Proof is in the Pudding

Magnesium sulfate reduces post-operative pain scores when administered in conjunction with lidocaine, ketamine, low-dose opioids such as fentanyl and morphine, etc.

29

Endocrine and Metabolic Targets

- Endocrine target
- Metabolic target
- Cardiovascular target
- Neurological target

30

Review of Literature

GYNECOLOGIC SURGERY

31

Effect of low-dose (single-dose) magnesium sulfate on postoperative analgesia in hysterectomy patients receiving balanced general anesthesia

The comparison of NRS score at different time between two groups and mean postoperative analgesic consumption in two groups over 24 hours.

Variables	Magnesium sulfate (n=25)	Control (n=25)	P-value
Post-operative NRS score at 0-24h	4.84 ± 2.24	5.76 ± 2.79	0.002
Post-operative NRS score at 0-24h	4.84 ± 2.24	5.76 ± 2.79	0.002
Post-operative NRS score at 0-24h	4.84 ± 2.24	5.76 ± 2.79	0.002
Post-operative NRS score at 0-24h	4.84 ± 2.24	5.76 ± 2.79	0.002

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Review of Literature

BARIATRIC SURGERY

33

Magnesium Sulfate Reduced Opioid Consumption in Obese Patients Undergoing Sleeve Gastrectomy: a Prospective, Randomized Clinical Trial

Fig 1. VAS score of group 1 and group 2 patients.

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Review of Literature

ORTHOPEDIC SURGERY

35

Magnesium sulfate attenuates acute postoperative pain and increased pain intensity after surgical injury in staged bilateral total knee arthroplasty: a randomized, double-blind, placebo-controlled trial

Conclusion: Magnesium effectively attenuates not only postoperative pain, but also decreased pain intensity without adverse effects. Magnesium could play an important role in the management of postoperative pain not only after a single operation but also after multiple surgeries of short intervals, in which the risk of enhanced pain sensitivity may be increased.

36

Effects of perioperative magnesium sulfate infusion on intraoperative blood loss and postoperative analgesia in patients undergoing posterior lumbar spinal fusion surgery: A randomized controlled trial

Magnesium group: bolus 50 mg/kg in 100 ml NS + 15 min before induction. Continuous 1 mg/kg/hr infusion intraoperative.

No significant change in hemodynamic variables (heart rate and mean arterial pressure) in the Magnesium group.

Conclusion: Perioperative magnesium sulfate infusion improves postoperative analgesia, decreases the amount of morphine consumption after the operation and does not change the intraoperative bleeding in patients undergoing posterior lumbar spinal fusion surgery.

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Review of Literature

THORACIC SURGERY

38

Perioperative systemic magnesium sulfate to maintain acute and chronic post-thoracotomy pain: a prospective observational study

Conclusion: MgSO₄ administration reduces postoperative pain of chest according to the NRS pain score and is effective in preventing chronic neuropathic post-thoracotomy pain measured by LANSS score.

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Review of Literature

ENT SURGERY

40

Intraoperative magnesium sulphate decreases agitation and pain in patients undergoing functional endoscopic surgery: A randomized double-blind study

Magnesium Group: 30 mg/kg, 10 min before induction, followed by 9 mg/kg/hr continuous infusion until surgery end.

Control Group: 10 ml NS of the same volume and rate.

Hypotension was induced by propofol 3 to 20 mg/kg.

PACU: assessed for agitation and pain using the Richmond Agitation Sedation Scale and numerical rating scale respectively.

Conclusion: Intraoperative infusion of magnesium in patients undergoing endoscopic sinus surgery reduced postoperative agitation, postoperative consumption and pain intensity in the PACU. It also decreased the length of stay in PACU compared with the control group.

41

The prophylactic effect of intravenous magnesium infusion on postoperative sore throat after thyroid surgery: A randomized clinical trial

Magnesium group: 30 mg/kg over 15 min prior to induction, followed by continuous infusion 10 mg/kg/hr for the duration of surgery until the start of skin closure.

Conclusion: Perioperative magnesium sulfate infusion effectively decreased overall PST incidence and severity after thyroidectomy with better hemodynamic stability, at the expense of more post-operative hypotension.

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Other Potential Benefits and Outcomes

The effect of adding intrathecal magnesium sulfate to bupivacaine-fentanyl spinal anesthesia - A meta-analysis of randomized controlled trials.

Conclusion: "Intrathecal magnesium, when added to a combination of intrathecal bupivacaine and fentanyl, prolongs the anesthetic duration of spinal anesthesia without increased incidences of side effects."

• Medicine October 02, 2020; Volume 99; Issue 40; p e23224 doi: 10.1097/JMD.0000000000002524

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Contraindications and Caution

- Contraindications**
 - Heart blocks
 - Neuromuscular disorders
 - Extreme renal impairment
- Caution**
 - Short procedures (<1 hour)

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What About Muscle Relaxation?

A study performed in Brazil in 2019 determined that the duration of intense NMJ as well as the period of no response to nerve stimulation was prolonged with magnesium sulfate administration prior to induction.

Quirica Rangel Micucci et al., July 2019

"Clinical trials have demonstrated the efficacy of Sugammadex in reversing rocuronium-induced neuromuscular block even after prior administration of magnesium sulfate."

Almida et al., July 2021

45

Real Life Uses of Magnesium Sulfate

46

Case Study I

Procedure - 3+ hour colectomy

44 y/o, ASA II

Induction - 100 mcg of Fentanyl

Following induction, magnesium cocktail initiated.

Infusion discontinued with start of closure.

Emergence - timely and comfortable.

Intraoperative VS - stable.

Postoperative - Fentanyl, Acetaminophen & TAP block (EPAS II) (Epidural Analgesia System II) initiated.

Stop to flat analgesia in PACU at 48 minutes after admission.

Pain score - VAS 4/10 no visual signs of pain.

Respiratory status in PACU.

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Case Study II

Surgical Procedure - Exploratory laparoscopy

Magnesium formulation used:

- Magnesium 1 gm
- Lidocaine 10 ml of 2%
- Ketamine 30 mg
- Dexamethasone 40mg

Femoral - 30 ml/hr

Males - 40 ml/hr (at 50% of BW)

Induction - Fentanyl 100 mcg

Pain free for 24+ hours

48

Case Study III

Procedure – Face & Neck Lift with Liposuction

Oploid Nalve patient
ATA – II

Primary Anesthetic – GEDA with Desflurane and Nitrous Oxide

IV Magnesium (5g), Lidocaine (2 mg/kg – induction, followed by 2 mg/kg/hr infusion), Decadron (10mg)

Emergence – reduced risk of respiratory complications and PONV

Minimal Pain



Case Study IV

Procedure –Hyperthermic Intraperitoneal Chemotherapy (HIPEC)
70 year old female, AAA – IV

Primary Anesthetic – GEA with Isoflurane

Induction: Ketamine 10mg; Etomidate 0.3-0.5 mg/kg (can be added intraoperatively for breakthrough)

Ketamine 10-15 mg prior to Incision

IV Magnesium (2-4g): Uloceleste Drip (1 mg/kg/hr); Ketamine 10-15 mg/hr

Epidural bolus at the end of case



Magnesium Cocktail - The McLoft Mix

- Lidocaine 2 mg/kg/hr
- Ketamine 1 mcg/kg/min
- Magnesium 10 mg/kg/hr
- Desflurane 0.6 mg/kg/hr

Normal Saline (100ml)

- 20 ml of 2% Lidocaine
- 20 mg of Ketamine
- 10 mg of Magnesium
- 60 mcg of Desflurane

Syringes (10ml)

- 10 ml of 2% Lidocaine
- 20 mg of Ketamine
- 10 mg of Magnesium
- 60 mcg of Desflurane

Infuse @ 0.5-1.0 mg/kg/hr (20ml or 400µl)
 (Pre-mix in 100ml of NS)

30 ml of syringes with saline up to 100ml

Special Acknowledgement and Thank You To:





Jason McLaff MSN, CRNA

- DNP PROJECT COMMITTEE MEMBER
- Assistant of DCHA, NCANA member
- United States Army Veteran

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Questions? Discussion? Feedback?

A dense, colorful pattern of question marks on various colored squares, including red, yellow, green, blue, and pink. The squares are arranged in a grid-like fashion, creating a vibrant and busy background.[illegible][illegible][illegible]

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55

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[illegible]

Appendix E: Post Evaluation Questionnaire

Question 1. *Full Name -*

Question 2. *AANA Number -*

Question 3. *The facilitators were effective in presenting the material*

<u>Answers</u>	<u>Response</u>
Satisfied	68
Somewhat Satisfied	4
Neutral	1
Somewhat Dissatisfied	0
Dissatisfied	0

Question 4. *The content was related to the objectives*

<u>Answers</u>	<u>Response</u>
Satisfied	70
Somewhat Satisfied	0
Neutral	2
Somewhat Dissatisfied	0
Dissatisfied	0

Question 5. *Teaching methods were effective*

<u>Answers</u>	<u>Response</u>
Satisfied	68
Somewhat Satisfied	3
Neutral	2
Somewhat Dissatisfied	0
Dissatisfied	0

Question 6. *Facilitated learning was effective*

<u>Answers</u>	<u>Response</u>
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Satisfied	66
Somewhat Satisfied	5
Neutral	2
Somewhat Dissatisfied	0
Dissatisfied	0

Question 7. *My personal learning objectives were met*

<u>Answers</u>	<u>Response</u>
Satisfied	66
Somewhat Satisfied	6
Neutral	1
Somewhat Dissatisfied	0
Dissatisfied	0

Question 8. *Objective 1: Acknowledge the current state of the opioid crisis and its relationship to intraoperative opioid use*

<u>Answers</u>	<u>Response</u>
Satisfied	69
Somewhat Satisfied	2
Neutral	2
Somewhat Dissatisfied	0
Dissatisfied	0

Question 9. *Objective 2: Acknowledge the multiple uses of Magnesium Sulfate in the hospital setting*

<u>Answers</u>	<u>Response</u>
Satisfied	70
Somewhat Satisfied	2
Neutral	1
Somewhat Dissatisfied	0
Dissatisfied	0

Question 10. Objective 3: Review the MOA, pharmacokinetic profile, dosing, and patient profiles that benefit from intraoperative magnesium sulfate

<u>Answers</u>	<u>Response</u>
Satisfied	69
Somewhat Satisfied	3
Neutral	1
Somewhat Dissatisfied	0
Dissatisfied	0

Question 11. Objective 4: Examine numerous case scenarios and the anesthesia plan that includes magnesium sulfate as an analgesia and anesthesia adjunct

<u>Answers</u>	<u>Response</u>
Satisfied	68
Somewhat Satisfied	4
Neutral	1
Somewhat Dissatisfied	0
Dissatisfied	0

State one item you learned from this session that will improve your nurse anesthesia practice

Answers

Use of mag for pain control

Use of mag sulfate for pain

Using Magnesium can decrease your usage for narcotics

Using the McLott mix for long cases so I can decrease opioid use.

Utilization of Magnesium in multimodal pain management

Was not familiar with doses related to increase in Mg. Also review of relative contraindications was helpful. Will continue to use magnesium but be braver with somewhat larger doses

Will dose higher than we have been (30-50 mg/kg).

Will implement this more in my practice

Would like to rewatch webinar. Surprised at the comfort level of patients without opioid.

More astute practitioner

More confidence discussing the use of Magnesium in my clinical setting

Need to give a larger induction dose of magnesium before starting maintenance drip.

Potential use in outpatient surgery center

Revise student lecture presentation to reflect the current data presented

Thank you for including all the different ways to integrate Magnesium into an anesthetic!

That 2g of Mg only raises serum Mg by 0.2

The many good uses of Magnesium in Anesthesia for pain control;

The mechanism of action of magnesium at the NMDA receptor

The mechanism of action of magnesium sulfate, dosing, administration methods, and its efficacy is providing analgesia.

The need to find non opioid meds

The use of magnesium sulfate as an analgesic adjunct

to consider Magnesium as part of my multimodal Post-op pain regimen

To incorporate in practice safely regarding magnesium levels not being largely affected. Understanding the analgesic effects of mag sulfate.

Use for pain management

I want to try mag on teens to see if it helps with emergence agitation

I was impressed with the multitude of clinical situations/procedures where Magnesium Sulfate as an anesthesia adjunct could be utilized.

I was unable to view the webinar due to OR conflict

I will start utilizing magnesium for post op pain control

Indications for administering intra op Magnesium

Infusions vs bolus magnesium. Will try the infusions!

Infusions vs bolus magnesium. Will try the infusions!

It was great to learn about multiple minimal/opioid free “recipes”. Also how well mag helps with pain management.

I'm going to try to start implementing the use of magnesium during cases to decrease narcotic requirements

I've given 2 gms Mg which is actually under dosed for the average adult. I'm going to adjust my Dosing. Excellent and well-prepared talk. Great job!!!

Mag can work on NMDA receptors Mag intraop pain

Mag sulfate hits nmda receptors Magnesium dosing.

Magnesium is a good adjunct to opioid free anesthesia

Magnesium use in clinical practice is very beneficial!

Magnesium works on nmda receptors and can be used intrathecally.

Many different areas/types of use

2gm of magnesium IV is generally very safe to administer to the majority of patients even without checking a pre operative magnesium level.

A useful modality (mag sulfate) with potential to decrease/replace opioid use during anesthesia.

Appropriate dosing between patient populations. Concerns in musculoskeletal disease and renal patients

As an adjunct therapy in pain control when other options are limited.

Better timing of the drug and safe limits.

Bolus dose for renal impairment

Bolus dosing prior to incision

Careful with renal patients. Great job ladies, OU should be very proud.

Contraindications/caution to the using MgSo4 in certain patients

Decrease opioids by using magnesium

Different ways of administering magnesium for cases.

Dosage and implementation

Dosage of magnesium for analgesia

Dosing of Mag for perioperative situations.

Dosing of magnesium

Fantastic application to real world practice. Thank you for providing renal inefficient doses and standard dosing

Give more mag

Giving 50mg/kg of magnesium- previously just giving 2gm.

How mag works on the NMDA receptor

I can safely give larger doses of Magnesium. So far, I've limited to 2gms

I didn't realize that the toxicity threshold was so high. I think I will use it more frequently as an adjunct to my anesthesia plan to even further the use of opioids.

I had questions about the kinetics on set duration safety dose and time that over which one should infuse the dose. These questions were all answered it was very helpful and scholarly presentation thank you both

I learned how much 1 g of magnesium raises a Sierra magnesium level which was very helpful.

I learned how to use magnesium sulfate as an adjunct for postoperative analgesia.

I learned that Magnesium is a great adjunct to decrease the use of opioids unless contraindicated. I learned the proper dosing to utilize magnesium in a way proven to help with pain management. I liked the Mclott formula and might use it in my practice to decrease narcotic use.

I should start using MgSo4 as an anesthetic adjunct!

State any barriers to implement this change

Answers

Anesthesiologists.

Availability

availability

Availability in our OR Omni cell

Comfort level of other members of the healthcare team

Convincing coworkers and pharmacy to use off label

Cost? \$13/vial seems like it could be expensive for our uninsured patients

Culture at our facility and availability of magnesium with ease.

Drug shortages these days

Getting other peers on board with this change.

Hospital pharmacy

I am supervised by MDAs

I provide anesthetic IV sedation at a Gastroenterology outpatient clinic, which limits the use of any additional adjunct therapies.

I work mostly outpatient cosmetic cases. Might be too much to give magnesium to these patients. If there is a possibility to view a recorded version I would appreciate that

Like in person better

Magnesium not a typical intra op medication at my institution.

Magnesium not stocked in Pyxis at this time. MDA disinterest

my hospital pharmacy

N/a

N/a

Na

Need copy of presentation

No barriers. Although I would suggest that it would have been easier to follow along had the pdf been available before the seminar. That way I could have printed the pages earlier and would have gotten more out of the seminar.

None x 29

None. I practice at a facility where we already use multimodal on all our patients.

Not common use where I work.. I will have to bring up an interest to using it to my educator to help implement.

Patient population and narcotic use prior to surgery Pharmacy control

Resistance from MDAs

Shortages of magnesium on occasion.

supply in OR

Supply, and possible resistance from supervising physician

Systemic changes - having MDAs, surgeons and pharmacy agree to implementing this may require teaching.

The pharmacy purchases IVPB bags without the ability to change dosing. It's either 2 or 4 grams.....

There are no barriers to implement this in my practice. I really appreciated learning the various cases that have used Magnesium with success.

Time constraints, I will be in an outpatient setting.

Time, mixing the drip seems complicated

Unknown.

Willingness of facility to add to formulary

Willingness of other anesthesia care team members to also be on board with magnesium usage.

Wondering if I could get some of the slides?? I ended up getting out of work late and missed the first 15 minutes..... Would appreciate it. Thanks