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Intravenous Magnesium Sulfate for Multimodal Analgesia

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Abstract

Purpose Statement
Magnesium Sulfate has been used as a multimodal approach for analgesia as it may reduce opioid consumption in the first 24 hours after surgery and decrease post-operative pain scores.

Introduction
The use of intraoperative opioids for analgesia is associated with postoperative side effects such as respiratory depression, ileus, nausea, and vomiting. The side effects from opioids can prolong hospital stay and cause patient dissatisfaction. Magnesium acts as a N-methyl-D-aspartate (NMDA) receptor antagonist resulting in an analgesic effect, which can be used as an alternative or adjunct to opioids for pain control.

Literature Review
Magnesium sulfate may be beneficial for multimodal pain management as it reduces opioid requirements and postoperative pain. Targeting various receptors in the pain pathway can optimize analgesia and reduce side effects. Magnesium antagonizes the NMDA receptor and blocks calcium channels to modulate pain and inflammatory responses. Perioperative magnesium administration should be considered as a strategy to reduce postoperative pain in patients undergoing surgical procedures.

Description of the Case
A 67-year-old female presented for a bilateral breast revision, bilateral blepharoplasty of upper lids, neck rhytidectomy, and fat graft injection surgery. The patient had a history of postoperative nausea and vomiting. During the maintenance phase of anesthesia, fentanyl 50 mcg was given as needed for signs of pain, rocuronium was re-dosed to maintain paralysis, and ephedrine and phenylephrine were administered to maintain blood pressure. Intravenous magnesium sulfate 2 g was administered as a multimodal approach to analgesia to decrease post-operative opioid consumption and to prevent post-operative nausea and vomiting. The following day the patient tolerated a regular diet, pain was well controlled, and was hemodynamically stable. The patient was discharged home without complications.

Discussion and Conclusion
Magnesium sulfate may be beneficial for multimodal pain management as it reduces opioid requirements and postoperative pain. Magnesium antagonizes the NMDA receptor and blocks calcium channels to modulate pain and inflammatory responses. It is unclear which mode of magnesium administration provides an advantage to the analgesic effects. The differences in age and gender-related responses to magnesium for analgesia is undetermined. Further research is necessary to examine the use of intravenous magnesium sulfate for postoperative pain in different patient populations, safe and effective dosing ranges, and the effects of analgesia in various surgeries. Intravenous magnesium sulfate should be considered in multimodal analgesic treatment as an adjunct for postoperative analgesia.

Intravenous Magnesium Sulfate for Multimodal Analgesia

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Introduction

- A multimodal analgesic approach with intraoperative magnesium sulfate may reduce opioid consumption in the first 24 hours postoperatively and decrease pain scores.[1-3]
- Opioids can cause a range of side effects such as respiratory depression, postoperative ileus, nausea, vomiting, and hypercarbia.[1,6,12]
- Inadequate pain relief impacts patient satisfaction and contributes to delays in recovery and increased hospital length of stay.[11]
- Magnesium sulfate may be considered as an adjunct for intraoperative analgesia and an alternative to opioid-based therapy.
- Intravenous (IV) magnesium sulfate may minimize postoperative pain and decrease opioid consumption.
- Opioid tolerant patients present a challenge in achieving adequate postoperative pain control.[6]
- Magnesium sulfate may be implemented to reduce opioid reliance and provide time-effective and safe postoperative recovery.
- Magnesium is a noncompetitive antagonist at the N-methyl-D-aspartate (NMDA) glutamate receptor, which exerts a depressant effect (Figure 1).
- Magnesium prevents central sensitization from peripheral nociceptive stimuli at the spinal cord action site by blocking NMDA receptors.
- Magnesium also acts as a calcium channel blocker to inhibit calcium influx, which may contribute to the antinociceptive effects (Figure 1).

Case Description

- A 67-year-old, 88 kg, 172 cm, female presented for a bilateral breast revision, bilateral blepharoplasty of upper lids, neck rhytidectomy, and fat graft injection surgery due to malignant neoplasm of the breasts.
- Past medical history included breast cancer, osteopenia, celiac disease, and basal cell carcinoma of the face.
- Past surgical history included Mohs surgery, breast lumpectomy, mastectomy with sentinel node biopsy, and breast reconstruction with a tissue expander.
- The patient had a history of postoperative nausea and vomiting and was given aprepitant 40 mg PO in pre-op.
- Pre-operative medication: midazolam 2 mg IV
- Pre-oxygenated with 100% oxygen at 10 L/min with a facemask for 5 minutes to reach an expired oxygen concentration of 90%
- Induction medications: fentanyl 50 mcg IV, lidocaine 100 mg IV, propofol 170 mg IV, rocuronium 50 mg IV, ketamine 30 mg IV
- Maintenance medications: fentanyl 50 mcg IV was given as needed for signs of pain, rocuronium IV was re-dosed to maintain train of four less than ¾, ephedrine and phenylephrine IV were administered to maintain blood pressure within 20% of baseline, ***magnesium sulfate 2 g IV***, ketamine 10 mg IV every hour, dexamethasone 8 mg IV, acetaminophen 1,000 mg IV, sevoflurane at 1.5% in a mixture of oxygen 1 L/min and medical air 1 L/min.
- Emergence medications: sugammadex 200 mg IV and ondansetron 4 mg IV
- Fluid totals: Plasmalyte 2,200 mL, urine output 625 mL, and estimated blood loss 25 mL
- Post-operative course: The patient was transported to the post-anesthesia care unit with stable hemodynamics. The patient was admitted to the hospital to be monitored overnight. The patient received acetaminophen 650 mg PO twice for pain control during their hospital stay. The following day the patient tolerated a regular diet, pain was well controlled, and hemodynamics were stable. The patient was discharged home without complications.

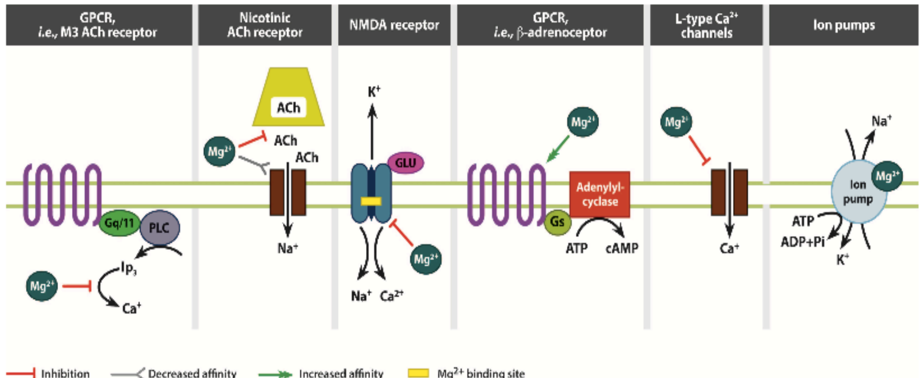
GPCR, i.e., M3 ACh receptor
Nicotinic ACh receptor
NMDA receptor
GPCR, i.e., β-adrenoceptor
L-type Ca2+ channels
Ion pumps
ACh
Mg2+
Gq/11
PLC
IP3
Ca+
Na+
K+
GLU
Na+ Ca2+
Adenylyl-cyclase
Gs
ATP
cAMP
Ion pump
ADP+Pi
Inhibition
Decreased affinity
Increased affinity
Mg2+ binding site

Figure 1. Magnesium Action Sites 10

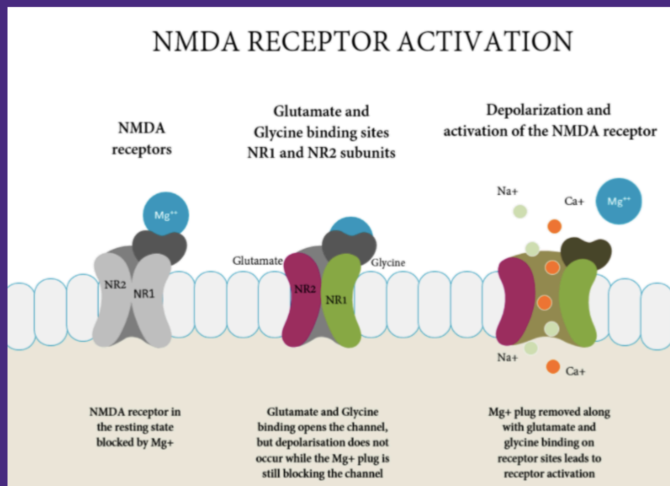
NMDA RECEPTOR ACTIVATION
NMDA receptors
Glutamate and Glycine binding sites NR1 and NR2 subunits
Depolarization and activation of the NMDA receptor
Mg++
Glutamate
Glycine
NR2
NR1
Na+
Ca+
NMDA receptor in the resting state blocked by Mg+
Glutamate and Glycine binding opens the channel, but depolarisation does not occur while the Mg+ plug is still blocking the channel
Mg+ plug removed along with glutamate and glycine binding on receptor sites leads to receptor activation

Figure 2. NMDA Receptor Activation 14

Figure 3. IV Magnesium Sulfate 15

Figure 4. Magnesium Sulfate Vials 15

Safety Considerations for Magnesium Sulfate Administration

- Avoid magnesium sulfate in patients with renal insufficiency because magnesium is excreted by the kidneys.
- Hypermagnesemia and toxicity can occur in renal insufficiency.[6]
- Hypermagnesemia can cause sedation, cardiac arrhythmias, diarrhea, respiratory depression, and potentiation of neuromuscular blockade.[11]
- Magnesium potentiates neuromuscular blockers; therefore, it should be avoided in patients with neuromuscular diseases because it can produce further muscle weakness by inhibiting acetylcholine release.[16]
- Magnesium inhibits calcium channels at the presynaptic nerve terminals that trigger the release of acetylcholine (Figure 1). Also, magnesium ions have an inhibitory effect on post-junctional potentials and decrease the excitability of the muscle fiber membranes.[16]
- The dose of nondepolarizing neuromuscular blockers should be reduced in patients that receive magnesium sulfate and titrated carefully with a nerve stimulator to ensure adequate recovery of neuromuscular function at the end of surgery.[16]
- Loss of deep tendon reflexes and respiratory or cardiac depression can occur at plasma magnesium concentrations above 10-12 mEq/L.[4]
- Magnesium slows sinoatrial node impulses and prolongs conduction time, which can cause heart block and should be avoided in patients with atrioventricular conduction abnormalities.[4]

Discussion

- The presence of a painful stimulus causes the release of glutamate and mediates excitatory neurotransmission, which amplifies nociceptive stimuli.[2] Magnesium is a noncompetitive antagonist at the NMDA glutamate receptor, which exerts depressant effects (Figure 2).[14]
- Magnesium is a noncompetitive calcium channel blocker (Figure 1), which is one of the mechanisms of antinociceptive activity.
- Magnesium decreases the pre-synaptic release of acetylcholine (Figure 1), which reduces the sensitivity of the motor end plate and decreases the amplitude of the action potential.[2]
- The increase of extracellular magnesium with IV magnesium sulfate inhibits the inflammatory response by reducing inflammatory cytokines.[6]

Clinical Rationale:

- Magnesium sulfate was given as a multimodal approach to decrease the amount of opioids required for pain relief and avoid the opioid side effects due to the patient's history of postoperative nausea and vomiting.

Case Critique:

- Magnesium sulfate 2 g IV (Figure 4) was given to the patient during surgery mixed in a 1 L bag of Plasmalyte infused as the maintenance fluid.
- A bolus of 30 mg/kg of magnesium sulfate before induction was not given as mentioned in several of the studies, which may have provided additional analgesia.[5]
- Currently, there is no standard criteria for perioperative use of IV magnesium sulfate.[6]

Conclusion/Recommendations

- Opioids have traditionally been the basis of pain management, although significant risks and side effects are associated with opioids.
- Increased opioid administration is related to a higher incidence of respiratory depression, constipation, emesis, confusion, and prolonged length of hospital stay.[3]
- IV magnesium sulfate bolus of 30 mg/kg before induction followed by an intraoperative infusion at 10 mg/kg/hour resulted in significantly lower pain scores compared to a placebo group and decreased opioid consumption 24 hours following surgery.[5]
- Dabbagh et al. found that the group that received magnesium versus the control group that received normal saline required significantly lower doses of IV morphine in the first 24 hours postoperatively.[8]
- Postoperative administration of magnesium sulfate alone did not demonstrate a significant reduction in morphine consumption.[12]
- Lysakowski et al. discovered in a systemic review of randomized trials for magnesium sulfate as an adjuvant to postoperative analgesia there was no evidence that perioperative magnesium had favorable effects on postoperative pain intensity and analgesic requirements.[13]
- Further research is necessary to examine the use of IV magnesium sulfate for postoperative pain in different patient populations, safe and effective dosing ranges, and effects on analgesia for various surgeries.
- Perioperative magnesium sulfate administration should be considered as a strategy to reduce postoperative pain in patients undergoing surgical procedures.[9]
- IV magnesium sulfate is an alternative analgesic that may be valuable in reducing opioid consumption and beneficial for opioid tolerant patients.

References

1. Egan TD, Newberry C. Opioids. In: Pardo MC, Miller RD. Basics of Anesthesia. 7th ed. Philadelphia, PA: Elsevier; 2018:123-138.
2. Burger K, Warner A. Effect of Intravenous Magnesium on Opioid Consumption Among Total Knee Arthroplasty Patients. [master's thesis]. Saint Louis: Webster University; 2016.
3. Pizzi LT, Toner R, Foley K, et al. Relationship between potential opioid-related adverse effects and hospital length of stay in patients receiving opioids after orthopedic surgery. Pharmacotherapy. 2012;32(6):502-514. doi:10.1002/j.1875-9114.2012.01101.x.
4. Do SH. Magnesium: a versatile drug for anesthesiologists. Korean J Anesthesiol. 2013;65(1):4-8. doi:10.4097/kjae.2013.65.1.4.
5. Kaur S, Baghla N. Evaluation of intravenous magnesium sulphate for postoperative analgesia in upper limb orthopaedic surgery under general anaesthesia: a comparative study. The Internet Journal of Anesthesiology. 2012;30(2):1-6. Retrieved from http://ispub.com/IJA/30/2/13941.
6. Castro J, Cooney MF. Intravenous magnesium in the management of postoperative pain. J Perianesth Nurs. 2017;32(1):72-76. doi:10.1016/j.jopan.2016.11.007.
7. Albrecht E, Kirkham KR, Liu SS, Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia. 2013;68:79-90. doi:10.1111/j.1365-2044.2012.07335.x.
8. Dabbagh A, Elyasi H, Razavi SS, Fathi M, Rajaei S. Intravenous magnesium sulfate for post-operative pain in patients undergoing lower limb orthopedic surgery. Acta Anaesthesiol Scand. 2009;53:1088-1091. doi:10.1111/j.1399-6576.2009.02025.x.
9. De Oliveira GS, Castro-Alves LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology. 2013;119(1):178-190. doi:10.1097/ALN.0b013e318297630d.
10. Herroeder S, Schönherr M, De Hert SG, Hollmann MW. Magnesium: essentials for anesthesiologists. Anesthesiology. 2011;114(4):971-993. doi:10.1097/ALN.0b013e318210483d.
11. Guo BL, Lin Y, Hu W, et al. Effects of systemic magnesium on post-operative analgesia: is the current evidence strong enough? Pain Physician. 2015;18(5):405-418. PMID:26431120.
12. Arumugam S, Lau CSM, Chamberlain RS. Perioperative adjunct magnesium decreases postoperative opioid requirements: a meta-analysis. Int J Clin Med. 2016;7(5):297-308. doi:10.4236/ijcm.2016.75032.
13. Lysakowski C, Dumont L, Czarnetzki C, Tramèr M. Magnesium as an adjuvant to postoperative analgesia: a systematic review of randomized trials. *Anesth Analg.* 2007;104(6):1532-1539. doi:10.1213/01.ane.0000261250.59984.cd.
14. Rege S. Anti-N-methyl-D-aspartate receptor encephalitis: a synopsis. 2018. https://psychscenehub.com/psychinsights/anti-nmda-receptor-encephalitis-a-synopsis. Accessed March 10, 2019.
15. US Food and Drug Administration Website. https://www.fda.gov/default.htm. Updated March 18, 2019. Accessed March 10,2019.
16. Nagelhout JJ, Plaus KL. Autonomic and cardiac pharmacology. In: Nagelhout JJ. *Nurse Anesthesia.* 5th ed. St. Louis, MO: Elsevier; 2014:186-211.