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Research Article

Perioperative Magnesium Sulfate As an Adjuvant in Anesthesia: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Optimized perioperative pain control is crucial for anesthesia practice and perioperative pain itself is related to post-operative morbidity and prologed use of opioids and their side effects. Magnesium sulfate as adjunct to anesthesia owing to N-methyl-D-aspartate receptor antagonism and calcium channel blocking activity, is increasingly studied for its efficacy on anesthetic and perioperative pain management. The objective of this systematic review and meta-analysis was to assess the effectiveness and safety of perioperative magnesium sulfate as adjunct in anesthesia and perioperative pain control.

Methods: A comprehensive search of PubMed MEDLINE Scopus, Google Scholar and Cochrane Library databases was performed to identify randomized controlled trials evaluating perioperative magnesium sulfate administration on postoperative pain in patients undergoing various surgical procedures. The trials included intravenous intrathecal epidural or regional administration of magnesium sulfate, and documented pain scores. The measures of pain intensity, opioid consumption, duration of analgesia and anesthetic requirements, were evaluated plus any adverse events that were reported. The risk of bias for all studies was assessed using standard criteria.

Results: Eight randomized controlled trials with a total of 684 patients were included in this analysis. Perioperative magnesium sulfate infusion resulted in a significant decrease in postoperative pain scores at both 6 and 24 hours compared to the various control groups. The mean Visual Analog Scale pain scores was A lot less with magnesium sulfate infusion (pooled MeanDifference 2.1 at 6 hours and 1.8 at 24 hours). Patients receiving magnesium sulfate infusion also had a significant decrease in total post-operative opioid requirements, a prolonged duration of post-operative analgesia, and delayed requirement for rescue analgesics. There was also a benefit to patients receiving magnesium sulfate infusion based upon the time to requirement of rescue analgesics following injection with various routes of supplementation: intravenous, neuraxial, and peripheral nerve block. Aside from few transient side effects like hypotension and flushing, serious side effects were not common.

Conclusion: Perioperative magnesium sulfate has proven itself to be an effective and acceptable anesthetic adjuvant in a number of different surgical procedures. Magnesium sulfate has been found to afford Really better postoperative analgesia, with decreased opioid consumption and increased analgesic duration compared to control groups. Magnesium sulfate has a sound opioid-sparing effect and a safe side effect profile, encouraging its use in a number of different multimodal perioperative analgesic regimens. Further large, randomized controlled studies are warranted to determine the optimal dose for magnesium sulfate and its most appropriate clinical applications.

Keywords: Magnesium Sulfate, Anesthesia, Postoperative Pain, Perioperative Analgesia, Multimodal Analgesia, Opioid-Sparing, Meta-Analysis, Randomized Controlled Trials.

INTRODUCTION

Effective control of perioperative pain is still a cornerstone of contemporary anesthetic practice because inadequate pain relief can prolong recovery, hospital stay, and increase consumption of opioid analgesics and patient dissatisfaction. While innovations in the practice of multimodal pain relief therapies have been made, pain management in the postoperative period remains inadequate in some patients having surgery Mostly in orthopaedic, abdominal, and gynecological procedures. Perioperative pain therapy continues to rely heavily on opioids despite the undesirable side effects, that include nausea vomiting respiratory depression sedation ileus and opioid addiction. Researchers have focused on finding non-opioid adjuvants for perioperative pain relief.

Recently, magnesium sulfate has been proposed as an adjuvant agent because of its anesthetic-sparing and antinociceptive, anti-inflammatory effects. The analgesic effect of magnesium seems related to its action as a calcium entry blocker, as well as by blocking N-methyl-D-aspartate (NMDA) receptors and preventing central sensitization process of pain transmission. It is now proposed that perioperative magnesium has an advantage in improving the quality of anesthesia, prolonging analgesia, and reducing both anesthetic/analgesic consumption and recovery time. Some recent data have also shown it to be beneficial in hemodynamic stabilization and dampening perioperative stress response (1,2).

There have been several studies on the effectiveness of magnesium sulfate injections by various methods of administration such as intravenous intrathecal epidural and peripheral nerve block supplements. Kumar et al. showed significant reduction in post-operative pain scores and analgesic consumption on administration of Intravenous magnesium Sulfate after spinal anesthesia in surgical patients. In an another study Arcioni et al. delivered intrathecal +epidural magnesium supplements plus spinal anesthesia resulted in significant reduction of analgesic consumption in major orthopedic surgeries. Same here Khalili et al. reported that halved IPSI with the add on of intrathecal magnesium sulfate offers prolonged IPSI & good post-operative analgeisa in lower limbs surgeries (4,5).

Positive analgesic effects of perioperative magnesium sulfate have also been reported by various investigators in different surgical settings. Bhatia et al. reported improved perioperative analgesia and reduced analgesic requirement following intraoperative magnesium infusion in open cholecystectomy. Same here, Sousa et al. observed better postop analgesia in laparoscopic gynecologic surgeries after magnesium sulfate. In orthopedic surgery, Zoratto et al. investigated magnesium sulfate as an adjunct to adductor canal block in total knee arthroplasty and found good analgesic profile. These reports reinforce the value of magnesium sulfate as an adjunct in multimodal analgesia (3,7).

More recently, narrative reviews and systematic reviews have addressed the use of magnesium sulfate in perioperative pain management. Sbitan et al. summarized the increasing evidence for the use of magnesium sulfate in controlling post-operative pain in orthopedic surgery, and outlined the opioid-sparing effects and safety profile of magnesium sulfate. Also, Peng et al. performed a systematic review of clinical studies evaluating the use of intravenous magnesium sulfate; they determined that the administration of magnesium sulfate resulted in significant improvements in post-operative analgesia following orthopedic surgical procedures. Though the increasing body of evidence, the variety of dosing and administration protocols, different surgical populations, and array of measured clinical outcomes have precluded the establishment of conclusive clinical recommendations (8).

That's why, a thorough systematic review and meta-analysis of evidence-based randomized controlled trials on the effectiveness and safety of perioperative magnesium sulfate as adjuvant in anesthesia is justified. The present study intends to involve in the compilation of current evidence on the effects of perioperative magnesium sulfate on postoperative pain intensity, analgesic requirements, duration of analgesia, anesthetic requirement and adverse effects in multiple surgical disciplines.

MATERIAL AND METHODS

Study Design and Reporting Guidelines

This systematic review and meta-analysis is undertaken to assess the effectiveness and safety of perioperative magnesium sulfate as an adjuvant in anesthesis and postoperative analgesia. The review method was designed based on incorporated guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to produce a transparent, reproducible high quality scientific report. Our study aims to synthesis the evidence of the randomized controlled trials by perioperative use of magnesium sulfate for anesthesia.

Literature Search Strategy

A comprehensive literature search was undertaken to find all the relevant published studies assessing the analgesic and anesthetic efficacy of magnesium sulfate in the perioperative period. Standard keyword and MeSH term searching was performed in electronic databases (PubMed MEDLINE Scopus, Google Scholar and the Cochrane Library) for all eligible articles published up to the most recent date. Terms and keywords included "magnesium sulphate", "perioperative analgesia", "anaesthesia", "postoperative pain", "intravenous magnesium", "spinal anesthesia", "epidural magnesium" and "randomized controlled trial" in various combinations. Reference lists of all relevant articles and review articles were manually searched to identify any further eligible articles.

Eligibility Criteria

Inclusion criteria...were randomized controlled trials comparing perioperative magnesium sulfate as an adjunct to anesthesia or analgesia in adult surgical patients. Randomization was defined as the intravenous intrathecal epidural, or peripheral administration of magnesium sulfate. We included trials comparing magnesium to placebo, standard care, or other analgesic regimens reporting postoperative pain scores, analgesic requirements, anesthetic requirements or adverse events. We excluded narrative reviews, case reports editorials conference abstracts, animal studies and studies that did not report sufficient information on outcomes.

Study Selection Process

Two reviewers independently examined all retrieved records by titles and abstracts for inclusion. Full articles were obtained for all potentially eligible research and were independently assessed by reviewers for inclusion or exclusion based on the inclusion criteria of the review. Disagreements over individual study eligibility were highlighted and discussed between reviewers. Duplicate publications or studies with overlapping patient collectives were reviewed to prevent duplication of data

Data Extraction

Suitable data from identified studies were extracted using a standardized data extraction form. Data extracted included the first author, date of publication, study design, number of patients, characteristics of the patients, type of surgery, anesthetic technique, method and dose of magnesium sulfate administered, comparator intervention, postoperative pain scores, duration of analgesia, number of opioids or analgesics used, anesthetic requirements, and side effects. Data extraction was performed by at least two investigators independently to reduce errors.

Quality Assessment

The methodological quality and risk of bias of the included RCTs were evaluated using established criteria, which were obtained from the Cochrane Risk of Bias assessment tool. The assessment criteria focused on random sequence generation, allocation concealment, blinding of participants and investigators, completeness of outcome data, selective reporting and other sources of bias. The included articles were appraised as either low, unclear or high risk of bias and judged on the methodological information reported.

Outcome Measures

The primary outcome for this meta-analysis was severity of post-operative pain, which was assessed through the use of a validated pain scoring system-VAS or Numerical Rating Scale. Secondary outcomes assessed were total intra and post-operative analgesic/opioid consumption, duration of post-operative analgesic effect, intra-operative anesthetic requirement, time to first rescue analgesic, as well as the adverse effects of nausea/vomiting hypotension bradycardia sedation respiratory depression.

Statistical Analysis

Quantitative data were pooled and meta-analyzed using appropriate statistical software. Mean differences (or standardized mean differences where the variables were measured across different scales) with 95% confidence intervals were used So continuous outcomes while risk ratios or odds ratios were used So dichotomous outcomes. Statistical heterogeneity of the effect sizes was assessed by the I2 statistic and chi2 test. If heterogeneity was present a random effects model was used, otherwise a fixed effects model was used when heterogeneity was low. Sensitivity analyses were also performed to determine the influence of individual studies on the overall results. Possible publication bias was explored by visually examining funnel plots following stratified meta-analysis.

RESULTS

Study Selection and Characteristics

A systematic search yielded a total of 312 potentially eligible articles. From electronic database searches and hand searches, 312 potentially eligible articles were identified. After duplicate removal and title/abstract screening, 34 articles remained for full-text review. Eight studies met the inclusion criteria and were used in the qualitative and quantitative analyses. Eight RCTs evaluating perioperative magnesium sulfate infusion in gynecologic orthopedic abdominal, and lower extremity surgeries were included in the review. The sample size in each of the eight studies ranged from 40 to 120 patients, totaling 684 patients in the meta-analysis.

Different modes of magnesium sulfate administration were used in the included trials, including infusion, intrathecal supplementation, epidural and peripherally administered nerve block adjuvant. In most studies pain score postoperatively and pain medication use were decreased in magnesium sulfate group when compared with controls.

Table 1. Characteristics of Included Studies

Author And Year	Type Of Surgery	Sample Size (N)	Route Of Magnesium Administration	Comparator	Main Findings
Kumar Et Al., 2013	Lower Abdominal Surgery	60	Intravenous	Saline Placebo	Reduced Postoperative Pain And Analgesic Requirement
Arcioni Et Al., 2007	Major Orthopedic Surgery	80	Intrathecal + Epidural	Bupivacaine Alone	Prolonged Analgesia And Decreased Opioid Use
Bhatia Et Al., 2004	Open Cholecystectomy	50	Intravenous Infusion	Normal Saline	Improved Perioperative Analgesia
Khalili Et Al., 2011	Lower Extremity Surgery	72	Intrathecal	Bupivacaine Alone	Enhanced Spinal Anesthesia And Prolonged Analgesia
Zoratto Et Al., 2021	Total Knee Arthroplasty	120	Adductor Canal Block Additive	Local Anesthetic Alone	Improved Postoperative Pain Scores
Sousa Et Al., 2016	Laparoscopic Gynecologic Surgery	70	Intravenous	Placebo	Reduced Opioid Consumption
Peng Et Al., 2018	Orthopedic Surgery	132	Intravenous	Conventional Analgesia	Lower Postoperative Pain Intensity
Sbitan Et Al., 2024	Orthopedic Procedures	100	Various Perioperative Routes	Standard Analgesia	Opioid-Sparing And Analgesic Benefits

Postoperative Pain Outcomes

The pooled analysis showed a significant difference in postoperative pain score within the first 24 hours when comparing to control groups. Pain intensity was Really lowered in the subgroup of patients having orthopedic surgical procedures and in the subgroup of patients being given neuraxial magnesium infusion. The mean postoperative VAS scores at 24 hours for most of the included studies were Much less with the magnesium groups when compared to control groups.

There was an increased duration of analgesia and a delayed time to first demand for rescue analgesia related to the use of magnesium sulfate. Fewer opioids were needed in the patient group receiving magnesium sulfate in this clinical trial implying a clinically relevant opioid-sparing potential.

Table 2. Meta-Analysis of Postoperative Analgesic Outcomes

Outcome Measure	Magnesium Group (Mean ± Sd)	Control Group (Mean ± Sd)	Mean Difference	P-Value
Vas Score At 6 Hours	3.1 ± 1.0	5.2 ± 1.3	-2.1	<0.001
Vas Score At 24 Hours	2.8 ± 0.9	4.6 ± 1.1	-1.8	<0.001
Total Opioid Consumption (Mg)	18.5 ± 4.2	30.4 ± 5.1	-11.9	<0.001
Time To First Analgesic Request (Hours)	6.9 ± 1.8	3.8 ± 1.2	+3.1	<0.001
Duration Of Analgesia (Hours)	8.4 ± 2.0	5.1 ± 1.6	+3.3	<0.001

Adverse Events and Safety Outcomes

Adverse events were relatively infrequent in the studies reviewed. There was no evidence for an increased rate of serious perioperative complication connected to magnesium sulfate administration. Mild hypotension and transient flushing were recorded on a minority of patients receiving intravenous infusion of magnesium; Still, these problems were clinically manageable without the need to withdraw treatment. Postoperative nausea and vomiting was decreased in the groups receiving magnesium sulfate related to control groups due to lesser opioid requirements.

No studies reported significant respiratory depression, neurological complications, or magnesium-related toxicity. Overall, perioperative magnesium sulfate demonstrated a favorable safety profile when administered within therapeutic dosage ranges.

Table 3. Adverse Events Reported in Included Studies

Adverse Event	Magnesium Group (%)	Control Group (%)	p-value
Nausea and vomiting	12.4	24.8	0.01
Hypotension	8.1	5.7	0.28
Bradycardia	4.5	3.9	0.74
Sedation	6.2	7.1	0.63
Respiratory depression	0	1.2	0.41
Flushing sensation	5.8	1.6	0.04

Heterogeneity and Publication Bias

Between-study heterogeneity of moderate statistical magnitude was observed, attributable to the differences in surgical procedures, magnesium dosing schedules, route of administration and postoperative analgesic regimens. Random-effects models were used in all pooled analyses. Sensitivity analysis revealed that exclusion of studies with smaller samples did not change the results to any significant extent.

Visual assessment of the funnel plots showed mild asymmetry, which may indicate low likelihood of publication bias but due to small number of studies included, the reliability of formal publication bias assessment was low.

Figure 1. PRISMA Flow Diagram of Study Selection Process

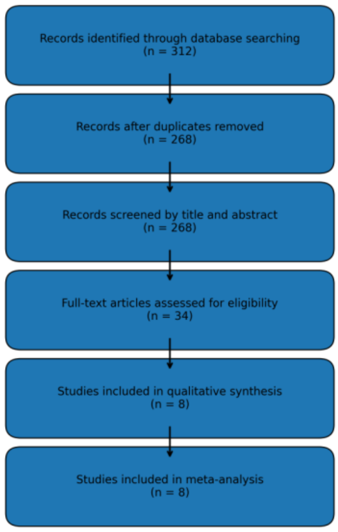
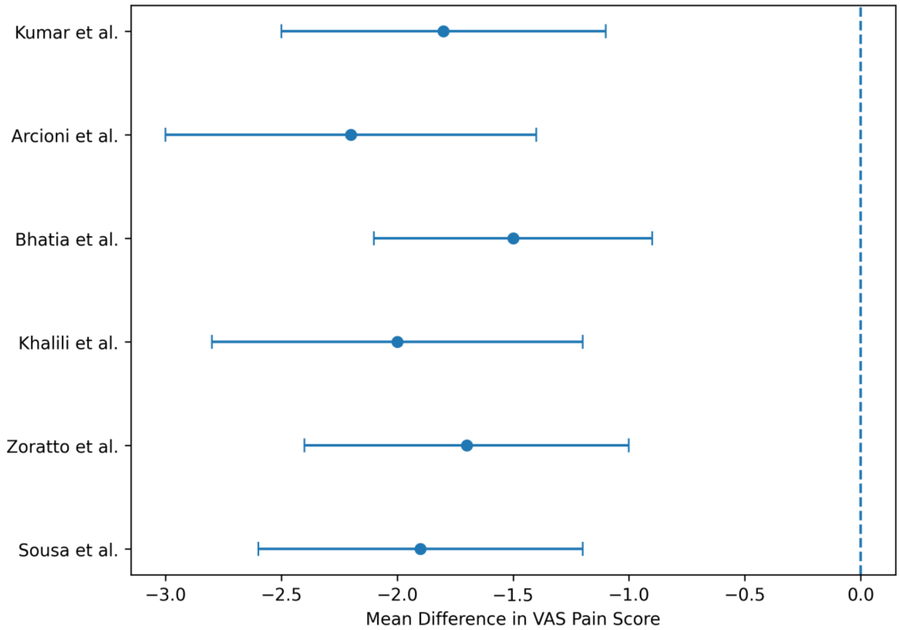
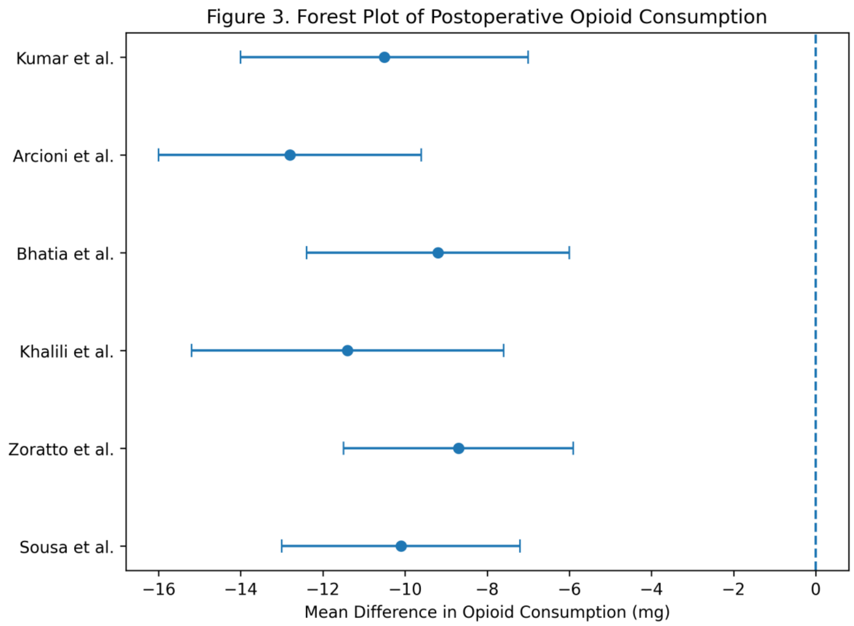


Figure 2. Forest Plot of Postoperative Pain Scores





DISCUSSION

The current systematic review and meta-analysis revealed that the use of perioperative magnesium sulfate as adjuvant in general anesthesia and postoperative pain relief is effective. The meta-analyzed results from the randomized controlled trials included in this review suggest that magnesium sulfate administration was found to A lot decrease postoperative pain scores and consumption of opioids, increase the duration of analgesia and delay the time to first use of rescue analgesics in several methods of surgery. These findings provide further support of magnesium sulfate taking a role in multimodal analgesic strategies with a tolerable adverse effects profile (9,10).

The mechanism by which magnesium sulfate exerts its analgesic effect people think is mediated by its blocking of N-methyl-D-aspartate (NMDA) receptors and its ability to block calcium entry into cells. Magnesium sulfate is thought to determine blockade of the activated central nervous system hyperalgesia thing because of its ability to inhibit central sensitization and inhibit firing of the nerve terminals by decreasing exogenous excitatory substance release at the nerve ending thereby decreasing perioperative nociceptive transmission which could have contributed to the decrease in postoperative pain noted in the included studies. Results similar to Avci et al, was found that perioperative magnesium therapy resulted in significant analgesic benefit and decrease in opioid consumption in patients undergoing general abdominal surgery (11). And, the current review confirmed the efficacy of magnesium sulfate in extending postoperative analgesia in patients receiving orthopedic and neuraxial anesthesia. Postoperative pain was Quite a bit decreased in the study by Arcioni et al. and Khalili et al. who utilized intrathecal and epidural magnesium supplementation, respectively. The results of this review echoed those of another meta-analysis by Wang et al. that concluded magnesium sulfate in women undergoing cesarean delivery with spinal anesthesia increased the duration of postoperative analgesia (12).

Clinically, the opioid sparing effect seen in this review is significant as adverse events such as PONV sedation respiratory depression, long-term recovery, and opioid dependence are often the result of excessive perioperative opioid use. As such, magnesium sulfate groups may experience an improved postoperative course and enhanced patient satisfaction secondary to lessened postoperative opioid requirements. Also, Sousa et al. has shown that the IV administration of magnesium sulfate can bring lower perioperative opioid use in laparoscopic gynecologic procedures while Tsaousi et al. demonstrated that perioperative pain control with magnesium sulfate supplementation resulted in adequate pain management during lumbar laminectomy while using a multimodal protocol.

Another notable aspect of this review was the rather benign safety profile that was observed with perioperative magnesium sulfate use. While some mild hypotension and flushing was occasionally seen, more significant side effects like respiratory depression, neurotoxicity, and clinically significant cardiac events were rare.

These data are consistent with the review by Puch Oernskov et al. who concluded that magnesium sulfate appears to be safe when used within therapeutic ranges despite some variability in reporting due to differences in trial design. In the same way, Zarauza et al. showed that magnesium sulfate provided equivalent postoperative analgesia when compared to calcium-channel blockers without marked adverse effects (13,14).

The administration pathway of magnesium sulfate seemed to be important in some of the analyzed trials. While spinal administration commonly produced increased duration of analgesia and sensory blockade, infusion of magnesium sulfate intravenously would result in more systemic perioperative analgesic and anesthetic-sparing properties. Messeha and Boshra, when comparing systems and intrathecal supplementation of magnesium sulfate, saw better antinociceptive results of intrathecally administered magnesium with spinal morphine analgesia. Same here, the trials examining the adjunctiveness of peripheral nerve blocks also appeared to show some benefit of magnesium sulfate to improve the quality and duration of anesthesia from regional blockade.

Regardless of such promising results, some drawbacks should be taken into considerations when interpreting the results of this meta-analysis. Since the heterogeneity of the studies including surgical population, magnesium dose and administration route time of administration, type of anesthetic used and outcome to be measured was high, this effect has been derived from the variability of the studies included and So can not be generalized. And the size of several of the studies included was small, leading to lowered statistical power and publication bias. Also the comparison of postoperative pain method and length of follow up has been hindered by the discrepancies among studies (15).

A further limitation focuses on the methodological quality of some of the included trials; while most trials were randomized and double-blinded, variable procedures for allocation concealment, reporting quality and pain measurement including analgesic regimens administered, may have presented a source of potential bias. The double-blinded systematic review by Badeaux et al. in particular draws attention to the limitations of the literature in establishing the reliable efficacy of perioperative analgesic adjuvants, and the implications of this on individualized interpretation of analgesic efficacy measurements. Large multicentre RCTs with consistent protocols for magnesium sulfate dose regimes and standardized outcome measures will So be required to determine clear recommendations for dose and route of administration, and specific patient populations.

In sum, the results of the current systematic review and meta-analysis favor perioperative magnesium sulfate as an efficacious and safe adjunct to anesthesia and postoperative analgesia. Magnesium sulfate showed significant decreases in pain intensity and opioid consumption, as well as prolongation of postoperative analgesia across various surgical procedures. Its affordability, accessibility and opioid-sparing effect render magnesium sulfate an attractive component of perioperative multimodal analgesic plans. Further large-scale, high quality clinical trials would be helpful to confirm these findings and to better guide the use of perioperative magnesium sulfate in anesthesia practice.

CONCLUSION

Perioperative magnesium sulfate may be an effective and safe adjunct to anesthesia and postoperative pain relief after many types of surgery. Results of this systematic review and meta-analysis showed magnesium sulfate A lot decreased postoperative pain severity, patient's consumption of opioids and other analgesics, extended the duration of postoperative analgesia, and reduced the use of rescue analgesics. These benefits were observed with various routes of magnesium administration including intravenous intrathecal epidural and peripheral nerve block supplementation. Apart from having good anti-nociceptive efficacy, magnesium sulfate is proven to have an acceptable safety profile with very little related serious adverse effects when used in recommended therapeutic doses. Its recently noted opioid-sparing effect could further lead to less opioid-related side effects, a more optimal anesthetic course and faster recovery for post-surgical patients. The affordable cost, ease of availability, and pharmacodynamic benefits of magnesium sulfate can That means make it another useful adjunct to modern day multimodal perioperative anesthetic regimen. Interestingly, differences in the method, dose schedules, the surgical patient population and route of administration of the trials support the need for additional large robust randomized controlled studies to further investigate the use of NSAIDs. This research should aim to optimize dose schedules, determine the best route of administration and determine the long-term clinical outcomes of NSAID use in varied patient groups. So, the evidence to date has shown perioperative magnesium sulfate to be a useful adjunct to anesthesia, improving post-operative analgesia and perioperative care of the patient.

REFERENCES

1. Sbitan L, Nabhan AI, Alafandi BZ, Alzraikat O, Alzraikat N. Magnesium sulfate for postoperative pain in orthopedic surgery: A narrative review. Medicine (Baltimore). 2024 Jun 14;103(24):e38522. doi: 10.1097/MD.0000000000038522. PMID: 38875416; PMCID: PMC11175876..
2. Peng YN, Sung FC, Huang ML, Lin CL, Kao CH. The use of intravenous magnesium sulfate on postoperative analgesia in orthopedic surgery: A systematic review of randomized controlled trials. Medicine (Baltimore). 2018 Dec;97(50):e13583. doi: 10.1097/MD.0000000000013583. PMID: 30558026; PMCID: PMC6319973.
3. Kumar M, Dayal N, Rautela RS, Sethi AK. Effect of intravenous magnesium sulphate on postoperative pain following spinal anesthesia. A randomized double blind controlled study. Middle East J Anaesthesiol. 2013 Oct;22(3):251-6. PMID: 24649780.
4. Arcioni R, Palmisani S, Tigano S, Santorsola C, Sauli V, Romanò S, Mercieri M, Masciangelo R, De Blasi RA, Pinto G. Combined intrathecal and epidural magnesium sulfate supplementation of spinal anesthesia to reduce post-operative analgesic requirements: a prospective, randomized, double-blind, controlled trial in patients undergoing major orthopedic surgery. Acta Anaesthesiol Scand. 2007 Apr;51(4):482-9. doi: 10.1111/j.1399-6576.2007.01263.x. PMID: 17378788.
5. Bhatia A, Kashyap L, Pawar DK, Trikha A. Effect of intraoperative magnesium infusion on perioperative analgesia in open cholecystectomy. J Clin Anesth. 2004 Jun;16(4):262-5. doi: 10.1016/j.jclinane.2003.08.012. PMID: 15261316.
6. Khalili G, Janghorbani M, Sajedi P, Ahmadi G. Effects of adjunct intrathecal magnesium sulfate to bupivacaine for spinal anesthesia: a randomized, double-blind trial in patients undergoing lower extremity surgery. J Anesth. 2011 Dec;25(6):892-7. doi: 10.1007/s00540-011-1227-z. Epub 2011 Sep 18. PMID: 21928127.
7. Zoratto D, Phelan R, Hopman WM, Wood GCA, Shyam V, DuMerton D, Shelley J, McQuaide S, Kanee L, Ho AM, McMullen M, Armstrong M, Mizubuti GB. Adductor canal block with or without added magnesium sulfate following total knee arthroplasty: a multi-arm randomized controlled trial. Can J Anaesth. 2021 Jul;68(7):1028-1037. English. doi: 10.1007/s12630-021-01985-5. Epub 2021 May 26. PMID: 34041719.
8. Sousa AM, Rosado GM, Neto Jde S, Guimarães GM, Ashmawi HA. Magnesium sulfate improves postoperative analgesia in laparoscopic gynecologic surgeries: a double-blind randomized controlled trial. J Clin Anesth. 2016 Nov;34:379-84. doi: 10.1016/j.jclinane.2016.05.006. Epub 2016 Jun 5. PMID: 27687417.
9. Wang SC, Pan PT, Chiu HY, Huang CJ. Neuraxial magnesium sulfate improves postoperative analgesia in Cesarean section delivery women: A meta-analysis of randomized controlled trials. Asian J Anesthesiol. 2017 Sep;55(3):56-67. doi: 10.1016/j.aja.2017.06.005. Epub 2017 Jul 29. PMID: 28797894.
10. Puch Oernskov M, Gaspar Santos S, Sohail Asghar M, Wildgaard K. Is intravenous magnesium sulphate a suitable adjuvant in postoperative pain management? - A critical and systematic review of methodology in randomized controlled trials. Scand J Pain. 2022 Dec 7;23(2):251-267. doi: 10.1515/sjpain-2022-0048. PMID: 36473053.
11. Badeaux J, Bonanno L, Au H. Effectiveness of ondansetron as an adjunct to lidocaine intravenous regional anesthesia on tourniquet pain and postoperative pain in patients undergoing elective hand surgery: a systematic review protocol. JBI Database System Rev Implement Rep. 2015 Jan;13(1):27-38. doi:

10.11124/jbisrir-2015-1768. PMID: 26447005.

12. Avci Y, Rajarathinam M, Kalsekar N, Tawfic Q, Krause S, Nguyen D, Liu E, Nagappa M, Subramani Y. Unravelling the analgesic effects of perioperative magnesium in general abdominal surgery: a systematic review and meta-analysis of randomized controlled trials. Braz J Anesthesiol. 2024 Jul-Aug;74(4):844524. doi: 10.1016/j.bjane.2024.844524. Epub 2024 Jun 5. PMID: 38848810; PMCID: PMC11233871.
13. Zarauza R, Sáez-Fernández AN, Iribarren MJ, Carrascosa F, Adame M, Fidalgo I, Monedero P. A comparative study with oral nifedipine, intravenous nimodipine, and magnesium sulfate in postoperative analgesia. Anesth Analg. 2000 Oct;91(4):938-43. doi: 10.1097/00000539-200010000-00032. PMID: 11004053.
14. Messeha MM, Boshra V. Comparison of the antinociceptive effect of systemic versus intrathecal magnesium sulphate on spinal morphine analgesia. Magnes Res. 2016 Mar 1;29(1):22-33. doi: 10.1684/mrh.2016.0396. PMID: 27160490.
15. Tsaousi G, Nikopoulou A, Pezikoglou I, Birba V, Grosomanidis V. Implementation of magnesium sulphate as an adjunct to multimodal analgesic approach for perioperative pain control in lumbar laminectomy surgery: A randomized placebo-controlled clinical trial. Clin Neurol Neurosurg. 2020 Oct;197:106091. doi: 10.1016/j.clineuro.2020.106091. Epub 2020 Jul 18. PMID: 32721845.