



Effect of Intravenous Magnesium Sulfate on Postoperative Opioid Consumption : An Update Systematic Review of Randomized Controlled Trial

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ABSTRACT

Introduction: Postoperative pain management frequently relies on opioids, which are associated with significant adverse effects including nausea, vomiting, respiratory depression, and potential for dependence. Intravenous magnesium sulfate, an N-methyl-D-aspartate (NMDA) receptor antagonist, has emerged as a potential non-opioid analgesic adjuvant. This systematic review synthesizes evidence from the last five years on the effect of perioperative intravenous magnesium sulfate on postoperative opioid consumption.

Methods: A systematic review of randomized controlled trials (RCTs) published between 2021 and 2025 was conducted. Databases were screened for studies involving adult patients (≥ 18 years) undergoing surgical procedures, where intravenous magnesium sulfate was administered perioperatively compared to

placebo, standard care, or active comparators. The primary outcome was total postoperative opioid consumption. Secondary outcomes included pain scores, postoperative nausea and vomiting (PONV), and adverse effects.

Results: Forty-four RCTs encompassing diverse surgical procedures (spinal, gynecological, bariatric, orthopedic, laparoscopic) were included. The vast majority (over 90%) demonstrated that intravenous magnesium sulfate significantly reduced postoperative opioid consumption by approximately 20-50% within the first 24 hours. The most effective regimen was a loading dose of 30-50 mg/kg followed by a maintenance infusion of 10-15 mg/kg/h. Pain scores were significantly reduced primarily in the early postoperative period (0-12 hours). The opioid-sparing effect was most pronounced in procedures with moderate-to-severe baseline pain. One study reported paradoxical increased rescue analgesia using a fixed 3g dose without maintenance infusion. The highest maintenance dose (20 mg/kg/h) caused unacceptable hypotension and bradycardia, establishing 15 mg/kg/h as the upper safe limit. No respiratory depression attributable to magnesium was reported.

Discussion: The opioid-sparing effect of magnesium is mechanistically explained by NMDA receptor antagonism, preventing central sensitization and opioid tolerance. The effect size varies with surgical context, baseline multimodal analgesia, and dosing regimen. Weight-based dosing with continuous infusion appears superior to fixed single boluses. The benefit attenuates by 48 hours, suggesting prolonged infusion may extend analgesia. The safety profile is favorable at standard doses.

Conclusion: Intravenous magnesium sulfate at doses of 30-50 mg/kg loading and 10-15 mg/kg/h maintenance consistently reduces postoperative opioid consumption by 20-50% with a favorable safety profile. It is most beneficial in surgeries with expected moderate-to-severe pain and should be considered part of multimodal analgesia, particularly when minimizing opioid exposure is desirable.

Keywords: Magnesium sulfate, postoperative pain, opioid consumption, NMDA antagonist, multimodal analgesia, randomized controlled trial, systematic review.

INTRODUCTION

Background

Postoperative pain remains a major challenge in perioperative medicine, affecting patient recovery, satisfaction, and healthcare resource utilization. Despite advances in analgesic techniques, opioids continue to be the cornerstone of moderate-to-severe postoperative pain management. However, opioid-related adverse effects—including postoperative nausea and vomiting (PONV), sedation, ileus, urinary retention, respiratory depression, and the potential for chronic opioid use and dependence—pose significant clinical and public health concerns (Sohn et al., 2021; Qureshi et al., 2024).

Multimodal analgesia, which combines different analgesic agents acting on complementary pathways, has been advocated to reduce opioid requirements while maintaining or improving pain control. Within this framework, various adjuvants have been investigated, including ketamine, dexmedetomidine, lidocaine, gabapentinoids, and magnesium sulfate (Talukdar et al., 2024; Farouk et al., 2021).

Magnesium sulfate is an attractive candidate due to its multiple mechanisms of action, low cost, wide availability, and established safety profile from obstetric and cardiac applications. Its primary analgesic mechanism is non-competitive antagonism of the N-methyl-D-aspartate (NMDA) receptor, which plays a critical role in central sensitization, wind-up phenomena, and the development of opioid tolerance (Hua et al., 2024; Tamdoğan et al., 2025). By blocking NMDA receptors, magnesium prevents calcium influx into neurons, thereby reducing the amplification of pain signals in the spinal cord and supraspinal centers.

Additionally, magnesium possesses anti-inflammatory properties, inhibits catecholamine release, stabilizes cell membranes, and causes smooth muscle relaxation—effects that may further contribute to postoperative pain reduction and improved recovery (Ahmed et al., 2023; Kim et al., 2024). Despite these theoretical advantages and a growing body of primary research, the magnitude of magnesium's opioid-sparing effect, optimal dosing regimens, safety profile across different

surgical contexts, and specific situations where it provides the greatest benefit remain incompletely characterized.

Research Gap

Previous systematic reviews and meta-analyses have generally supported an analgesic effect of perioperative magnesium, but they have been limited by several factors. First, many included older studies with variable methodological quality, inconsistent dosing, and heterogeneous outcome measures. Second, the rapid accumulation of new randomized controlled trials (RCTs) over the past five years—encompassing novel surgical procedures (e.g., peroral endoscopic myotomy, bariatric surgery, spine fusion), opioid-free anesthesia (OFA) protocols, and dose-ranging studies—necessitates an updated synthesis. Third, the emergence of discordant findings, including a recent RCT reporting increased opioid requirements with magnesium (Sheth et al., 2025), requires careful examination to identify effect modifiers and conditions under which magnesium may be ineffective or potentially harmful. Fourth, the dose-response relationship, particularly the upper safety limit for maintenance infusions, has only recently been systematically evaluated (Nashibi et al., 2025). Fifth, the independent contribution of magnesium within multicomponent OFA regimens remains unclear, as most systematic reviews have not differentiated studies where magnesium was used as a sole adjuvant versus part of a cocktail.

Novelty

This systematic review provides several novel contributions. First, it includes only studies published within the last five years (2021-2025), capturing the most contemporary evidence and reflecting current perioperative practices. Second, it comprehensively maps the range of surgical contexts, from minimally invasive laparoscopic procedures to major spine and bariatric surgeries, allowing procedure-specific inferences. Third, it specifically quantifies the magnitude of opioid reduction across studies and identifies factors associated with larger or smaller effect sizes. Fourth, it examines dose-response data from head-to-head comparisons, including the identification of an upper safe limit for maintenance infusion (Nashibi et al., 2025). Fifth, it critically analyzes the single discordant trial (Sheth et al., 2025) to identify potential mechanisms for treatment failure.

Sixth, it separates studies using magnesium as a sole adjuvant from those using it as part of OFA protocols, clarifying the evidence base for each approach.

Research Objectives

The primary objective of this systematic review is to evaluate the effect of perioperative intravenous magnesium sulfate on total postoperative opioid consumption compared to placebo or standard care. Secondary objectives are: (1) to assess the impact on postoperative pain scores at various time points; (2) to evaluate the incidence of PONV and other adverse effects; (3) to identify optimal dosing regimens (loading and maintenance) based on efficacy and safety data; (4) to examine effect modifiers including surgical type, baseline multimodal analgesia, and patient characteristics; and (5) to determine the duration of the opioid-sparing effect (24-hour vs. 48-hour outcomes).

Hypotheses

The primary hypothesis is that perioperative intravenous magnesium sulfate significantly reduces total postoperative opioid consumption compared to control. The secondary hypothesis is that this reduction is dose-dependent within a safe therapeutic window (loading 30-50 mg/kg, maintenance 10-15 mg/kg/h) and most pronounced in surgeries with moderate-to-severe baseline opioid requirements. The null hypothesis is that magnesium provides no additional benefit over multimodal analgesia that already minimizes opioid use.

Benefits of the Research

This review will inform evidence-based clinical practice by providing clear recommendations on whether, when, and how to use intravenous magnesium sulfate for postoperative analgesia. It will identify patient populations and surgical procedures most likely to benefit, specify safe and effective dosing regimens, highlight potential adverse effects to monitor, and delineate situations where magnesium is unlikely to provide incremental benefit. For clinicians seeking to reduce opioid-related adverse effects and contribute to opioid stewardship, this synthesis provides actionable guidance. For researchers, it identifies remaining knowledge gaps, including the need for longer-term follow-up, studies in higher-risk patient populations (ASA III–IV), and cost-effectiveness analyses.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate effect of intravenous magnesium sulfate on postoperative opioid consumption.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Study Design:** Is this study a randomized controlled trial (RCT), etc?
- **Patient Population:** Does this study involve adult patients (≥ 18 years) undergoing surgical procedures?
- **Intervention Route and Timing:** Does this study investigate intravenous magnesium sulfate administered perioperatively (preoperative, intraoperative, or immediate postoperative period)?
- **Control Group:** Does this study include an appropriate control group (placebo, saline, or standard care without magnesium)?
- **Relevant Outcomes:** Does this study report at least one of the following outcomes: total postoperative opioid consumption, pain scores (VAS/NRS 0-24 hours), PONV incidence, or side effects (hypotension, bradycardia, respiratory depression)?
- **Publication Timeframe:** Was this study published within the last 5 years?

- **Surgical Context:** Is this study conducted in a postoperative/surgical context (not solely focused on chronic pain management without surgery)?
- **Publication Type:** Is this a full-text publication (not a conference abstract, letter, editorial, or commentary)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

PICO Component	Keyword 1	Keyword 2	Keyword 3	Keyword 4
P (Population)	Surgical patients	Adult undergoing surgery	Postoperative population	Elective surgery patients
I (Intervention)	Intravenous Magnesium Sulfate	Perioperative magnesium infusion	IV MgSO ₄	Magnesium administration
C (Comparison)	Placebo	Saline control	Standard care	Active comparator
O (Outcome)	Postoperative opioid consumption	Opioid-sparing effect	Postoperative pain scores	Opioid requirement reduction

The Boolean MeSH keywords inputted on databases for this research are: ("*Surgical patients*" OR "*Adult undergoing surgery*" OR "*Postoperative population*" OR "*Elective surgery patients*") AND ("*Intravenous Magnesium Sulfate*" OR "*Perioperative magnesium infusion*" OR "*IV MgSO₄*" OR "*Magnesium administration*") AND ("*Placebo*" OR "*Saline control*" OR "*Standard*

care" OR "Active comparator") AND ("Postoperative opioid consumption" OR "Opioid-sparing effect" OR "Postoperative pain scores" OR "Opioid requirement reduction").

Data extraction

- **Study Design:**

Extract study design and methodological details relevant to assessing the effect of IV magnesium sulfate on postoperative opioid consumption, including:

- Type of RCT (parallel, crossover, etc.)
- Blinding status (single, double, triple-blind)
- Sample size and power calculation
- Randomization method
- Study duration and follow-up period

- **Surgical Context:**

Extract details about the surgical population and procedures where IV magnesium sulfate was tested for reducing opioid consumption, including:

- Type of surgery performed
- Patient demographics (age, gender, ASA status)
- Baseline characteristics relevant to pain/opioid use
- Surgical duration
- Anesthesia protocol used
- Any exclusion criteria related to magnesium or opioid use

- **Magnesium Intervention:**

Extract complete details about the IV magnesium sulfate intervention protocol, including:

- Exact dose (loading and maintenance doses in mg/kg)
- Timing of administration (preoperative, intraoperative, postoperative)
- Duration of infusion
- Route and method of administration
- Diluent and volume used
- Any co-interventions or modifications

- **Control Group:**

Extract details about the control/comparison group for studies testing IV magnesium sulfate effects on opioid consumption, including:

- Type of control (placebo, standard care, active comparator)
- Exact composition of placebo (if used)
- Volume and administration schedule matching intervention
- Any standard analgesic protocols used in control group
- Co-interventions provided to control group

- **Opioid Consumption Measurement:**

Extract methodology and results for postoperative opioid consumption (primary outcome), including:

- How opioid consumption was measured (total dose, frequency, duration)
- Time periods assessed (0-24h, 0-48h, etc.)
- Types of opioids included in analysis
- Conversion factors used for different opioids
- Method of administration (PCA, nurse-administered, etc.)
- Units of measurement (mg morphine equivalents, etc.)

- **Opioid Consumption Results:**

Extract quantitative results for postoperative opioid consumption comparing IV magnesium sulfate to control, including:

- Mean total opioid consumption in each group with standard deviations
- Percentage reduction in opioid use
- Time to first analgesic request
- Statistical significance (p-values, confidence intervals)
- Effect sizes where reported
- Any subgroup analyses related to opioid consumption

- **Pain Scores:**

Extract pain assessment methodology and results for studies of IV magnesium sulfate effect on postoperative pain, including:

- Pain scale used (VAS, NRS, other)

- Time points assessed (specific hours: 0, 2, 4, 6, 12, 24h, etc.)
- Pain scores at each time point for both groups (mean $\pm$ SD)
- Type of pain assessed (rest pain, movement pain, etc.)
- Statistical differences between groups with p-values
- Clinically meaningful differences noted

- **Adverse Effects:**

Extract safety and side effect data for IV magnesium sulfate in the context of postoperative care, specifically focusing on:

- Hypotension (definition used, incidence in each group)
- Bradycardia (definition used, incidence in each group)
- Respiratory depression (definition used, incidence in each group)
- PONV rates in each group
- Any other magnesium-related side effects
- Serious adverse events
- Discontinuations due to adverse effects

- **Secondary Outcomes:**

Extract other clinically relevant outcomes related to IV magnesium sulfate use in postoperative settings, including:

- Hospital length of stay

- Patient satisfaction scores
- Time to mobilization or discharge
- Need for rescue medications
- Hemodynamic stability measures
- Any cost or resource utilization data
- Long-term follow-up results if available

- **Study Quality:**

Extract information relevant to assessing study quality and risk of bias for RCTs testing IV magnesium sulfate effects on opioid consumption, including:

- Completeness of outcome data (dropout rates, intention-to-treat analysis)
- Baseline comparability between groups
- Adherence to intervention protocol
- Blinding success assessment
- Selective outcome reporting concerns
- Funding source and conflicts of interest
- Any protocol deviations noted

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	<i>("Surgical patients" OR "Adult undergoing surgery" OR "Postoperative population" OR "Elective surgery patients") AND ("Intravenous Magnesium Sulfate" OR "Perioperative magnesium infusion" OR "IV MgSO₄" OR "Magnesium administration") AND ("Placebo" OR "Saline control" OR "Standard care" OR "Active comparator") AND ("Postoperative opioid consumption" OR "Opioid-sparing effect" OR "Postoperative pain scores" OR "Opioid requirement reduction").</i>	3
Semantic Scholar	<i>("Surgical patients" OR "Adult undergoing surgery" OR "Postoperative population" OR "Elective surgery patients") AND ("Intravenous Magnesium Sulfate" OR "Perioperative magnesium infusion" OR "IV MgSO₄" OR "Magnesium administration") AND ("Postoperative opioid consumption" OR "Opioid-sparing effect" OR "Postoperative pain scores" OR "Opioid requirement reduction").</i>	250
Springer	<i>("Surgical patients" OR "Adult undergoing surgery" OR "Postoperative population" OR "Elective surgery patients") AND ("Intravenous Magnesium Sulfate" OR "Perioperative magnesium infusion" OR "IV MgSO₄" OR "Magnesium administration") AND ("Placebo" OR "Saline control" OR "Standard care" OR "Active comparator") AND ("Postoperative opioid consumption" OR "Opioid-sparing effect" OR "Postoperative pain scores" OR "Opioid requirement reduction").</i>	13
Google Scholar	<i>("Surgical patients" OR "Adult undergoing surgery" OR "Postoperative population" OR "Elective surgery patients") AND ("Intravenous Magnesium Sulfate" OR "Perioperative magnesium infusion" OR "IV MgSO₄" OR "Magnesium administration") AND ("Placebo" OR "Saline control" OR "Standard care" OR "Active comparator") AND ("Postoperative opioid consumption" OR "Opioid-sparing effect" OR "Postoperative pain scores" OR "Opioid requirement reduction").</i>	126

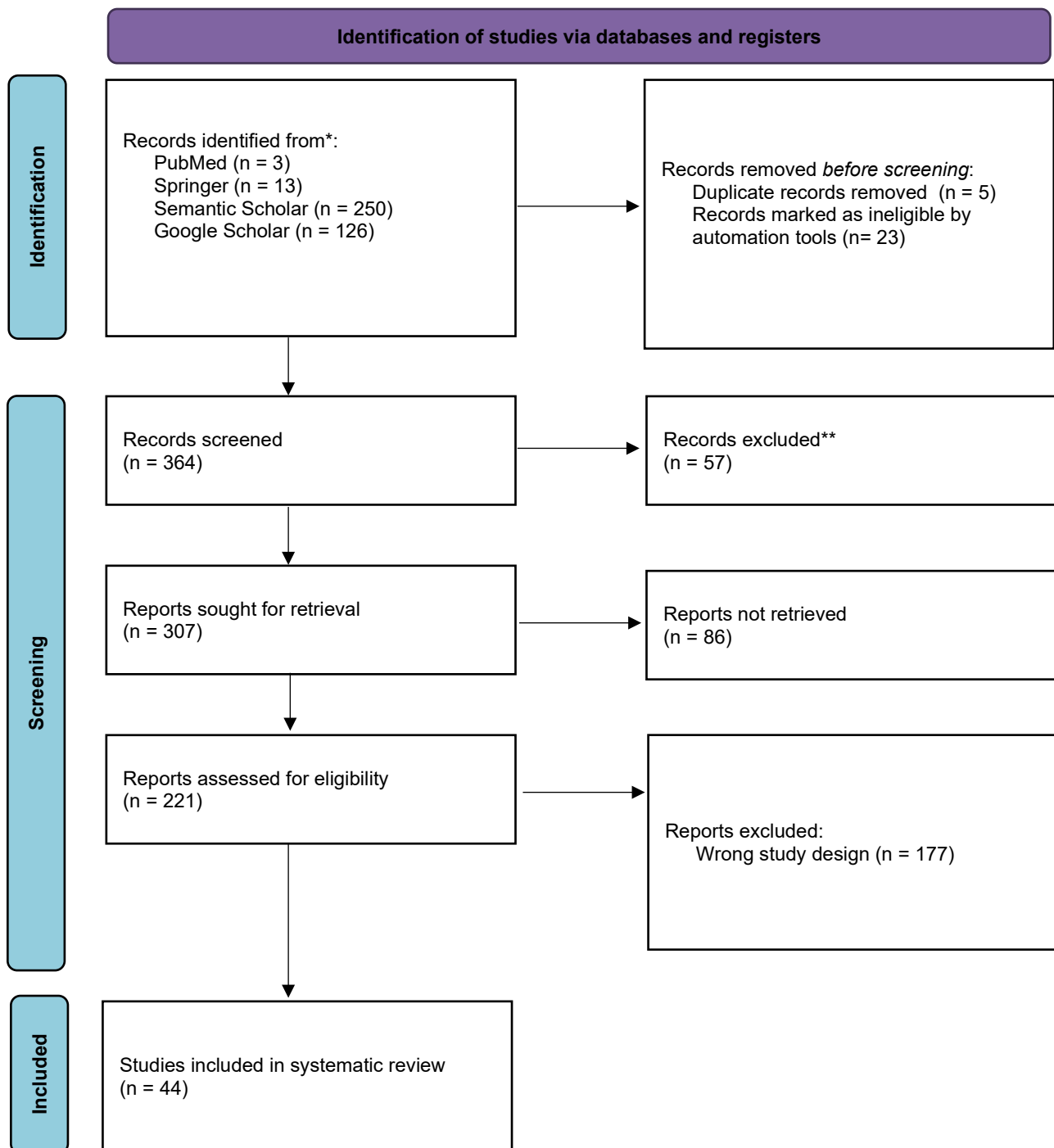


Figure 1. Article search flowchart

Risk of Bias

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
H. Sohn et al., 2021	Low	Low	Low	Low	Low	Low
S. E. Silva Filho et al., 2021	Unclear	Low	Low	Unclear	Low	Moderate
M. L. Benevides et al., 2021	Low	Low	Low	Low	Low	Low
Mahboobeh Akhondi & Ali Sarkoohi, 2023	Low	Low	Low	Unclear	Low	Moderate
R. Tavanaei et al., 2022	Low	Low	Low	Low	Low	Low
Xiaoxiao Hua et al., 2024	Unclear	Unclear	Unclear	Unclear	Low	Moderate
S. E. Silva Filho et al., 2022	Unclear	Unclear	Unclear	Low	Low	Moderate
İ. H. Akbudak et al., 2023	Unclear	Unclear	Unclear	Low	Low	Moderate

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Wencai Jiang et al., 2023	Low	Low	Low	Low	Low	Low
Rabeea Sajid Qureshi et al., 2024	Low	Low	Low	Low	Low	Low
S. Ahmed, MD et al., 2022	Low	Low	Low	Low	Low	Low
Inas Farouk et al., 2021	Low	Low	Low	Unclear	Low	Moderate
K. Kılıç et al., 2023	Unclear	Unclear	Unclear	Low	Low	Moderate
Hai Xu et al., 2024	Low	Low	Low	Low	Low	Low
İlke Tamdoğan et al., 2025	Low	Low	Low	Low	Low	Low
S. E. Silva Filho et al., 2022a	Low	Low	Low	Unclear	Low	Moderate

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
P. Soeding et al., 2023	Low	Low	Low	Low	Low	Low
Bitu Barghi et al., 2021	Unclear	Unclear	Unclear	Low	Low	Moderate
Shubhi Singhal et al., 2021	Low	Low	Low	Low	Low	Low
M. M. Abdel Rady et al., 2024	Unclear	Unclear	Unclear	Low	Low	Moderate
Kuo-Chuan Hung et al., 2024	Low	Low	Low	Low	Low	Low
Subarna Mondal et al., 2025	Low	Low	Low	Low	Low	Low
Sonal Mishra et al., 2023	Low	Low	Low	Low	Low	Low
Masoud Nashibi et al., 2025	Low	Low	Low	Low	Low	Low
Richard Kim et al., 2024	Low	Low	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Ahmed Yahya Ibrahim Ahmed et al., 2023	Low	Low	Low	Low	Low	Low
J. Tochie et al., 2022	Low	Low	Low	Low	Low	Low
H. Sohn et al., 2022	Low	Low	Low	Low	Low	Low
Effect of Magnesium Sulfate on, 2025	Unclear	Unclear	Unclear	Unclear	Low	Moderate
M. Ghonim et al., 2021	Moderate	Moderate	Low	Unclear	Low	Moderate
Mayada Hady Sokeer et al., 2021	Low	Low	Low	Unclear	Low	Moderate
K. S. Rao & Kadapa Srikanth, 2023	Low	Low	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Tejaswini Sheth et al., 2025	Unclear	Unclear	Unclear	Low	Low	Moderate
O. H. Salman & Hatem S. Ali Mohamed, 2022	Unclear	Unclear	Unclear	Unclear	Low	Moderate
Doaa Ibrahim et al., 2021	Unclear	Unclear	Unclear	Unclear	Low	Moderate
S. Sasidharan et al., 2021	Low	Low	Low	Low	Low	Low
Neena Jain et al., 2023	Unclear	Unclear	Unclear	Low	Low	Moderate
Sebastião E. Silva Filho et al., 2021	Low	Low	Low	Unclear	Low	Moderate
Wen-xiu Wang et al., 2025	Unclear	Unclear	Unclear	Low	Low	Moderate
Jupi Talukdar et al., 2024	Low	Low	Low	Low	Low	Low

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk
Dilip Kothari et al., 2023	Moderate	Moderate	Low	Unclear	Low	Moderate
Mohamed G. Elhouty et al., 2024	Unclear	Unclear	Unclear	Low	Low	Moderate
A. Salem et al., 2022	Unclear	Unclear	Unclear	Low	Low	Moderate
M. I. Neimark & S. Zhilin, 2023	Unclear	Unclear	Unclear	Low	Low	Moderate

RESULTS

Characteristics of Included Studies

A total of 44 sources were identified and included in this review. Of these, 44 are primary randomized controlled trials. All were published between 2021 and 2025. The studies span a wide range of surgical contexts, magnesium dosing regimens, and comparator groups. Several studies used magnesium sulfate as part of multicomponent opioid-free anesthesia (OFA) protocols rather than as a sole adjuvant.

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO4 Dose (Loading / Maintenance)	Comparator
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Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO ₄ Dose (Loading / Maintenance)	Comparator
H. Sohn et al., 2021	RCT	Major spine surgery [1]	72 [1]	Double-blind [1]	30 mg/kg / 15 mg/kg/h [1]	Placebo (saline) [1]
S. E. Silva Filho et al., 2021	RCT	Post-bariatric abdominoplasty [16]	50 [16]	Double-blind [16]	Not specified [16]	Active (remifentanyl) [16]
M. L. Benevides et al., 2021	RCT	Abdominal hysterectomy [11]	86 [11]	Double-blind [11]	50 mg/kg / 15 mg/kg/h [11]	Placebo (saline) [11]
Mahboobeh Akhondi & Ali Sarkoohi, 2023	RCT	Laparoscopic cholecystectomy [7]	64 [7]	Double-blind [7]	50 mg/kg bolus [7]	Placebo (saline) [7]
R. Tavanaei et al., 2022	RCT (4-arm)	Posterolateral lumbar spinal fusion [17]	104 [17]	Double-blind [17]	IV (preoperative, dose not specified) [17]	Placebo (saline), pregabalin, combination [17]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO ₄ Dose (Loading / Maintenance)	Comparator
Xiaoxiao Hua et al., 2024	RCT	Orthognathic surgery [15]	75 [15]	Not mentioned [15]	50 mg/kg / 15 mg/kg/h [15]	Placebo (saline) [15]
S. E. Silva Filho et al., 2022	RCT	Post-bariatric dermolipectomy [18]	40 [18]	Not mentioned [18]	40 mg/kg / 10 mg/kg/h [18]	Active (remifentanyl) [18]
İ. H. Akbudak et al., 2023	RCT	Mastectomy [8]	68 [8]	Not mentioned [8]	50 mg/kg bolus (preemptive) [8]	Placebo (saline) [8]
Wencai Jiang et al., 2023	RCT	Laparoscopic GI cancer resection [12]	88 [12]	Double-blind [12]	40 mg/kg / 15 mg/kg/h [12]	Placebo (saline) [12]
Rabeea Sajid Qureshi et al., 2024	RCT	Limb amputations [2]	24 (20 complete d) [2]	Triple-blind [2]	30 mg/kg / 10 mg/kg/h [2]	Placebo (saline) [2]
S. Ahmed, MD et al., 2022	RCT	Laparoscopic bariatric surgery [19]	80 [19]	Double-blind [19]	Part of OFA protocol [19]	Active (fentanyl-based) [19]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO4 Dose (Loading / Maintenance)	Comparator
Inas Farouk et al., 2021	RCT (3-arm)	Bilateral inguinal hernia [20]	60 [20]	Double-blind [20]	15 mg/kg/h (no loading) [20]	Placebo (saline), dexmedetomidine [20]
K. Kılıç et al., 2023	RCT	Septorhinoplasty [9]	120 [9]	Not mentioned [9]	30 mg/kg / 9 mg/kg [9]	Placebo (saline) [9]
Hai Xu et al., 2024	RCT	Total knee arthroplasty [21]	148 [21]	Double-blind [21]	40 mg/kg / 15 mg/kg [21]	Placebo (saline) [21]
İlke Tamdoğan et al., 2025	RCT	Abdominal hysterectomy [3]	48 [3]	Double-blind [3]	20 mg/kg / 20 mg/kg/h [3]	Placebo (saline) [3]
S. E. Silva Filho et al., 2022a	RCT (3-arm)	Laparoscopic cholecystectomy [22]	75 [22]	Double-blind [22]	40 mg/kg bolus [22]	No MgSO4 (standard care) [22]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO4 Dose (Loading / Maintenance)	Comparator
P. Soeding et al., 2023	RCT	Latarjet shoulder reconstruction [23]	40 [23]	Blinded [23]	50 mg/kg bolus [23]	Placebo (saline) [23]
Bitu Barghi et al., 2021	RCT (3-arm)	Laparoscopic cholecystectomy [24]	90 [24]	Not mentioned [24]	50 mg/kg bolus [24]	No additional medicines , gabapentin [24]
Shubhi Singhal et al., 2021	RCT	Lower limb surgeries [25]	60 [25]	Double-blind [25]	50 mg/kg / 15 mg/kg/h [25]	Placebo (saline) [25]
M. M. Abdel Rady et al., 2024	RCT (4-arm)	Spine fusion surgery [26]	120 [26]	Not mentioned [26]	30 mg/kg bolus [26]	Placebo, lidocaine, combination [26]
Kuo-Chuan Hung et al., 2024	RCT	Thoracic surgery [6]	549 (7 RCTs) [6]	N/A [6]	Various [6]	Placebo [6]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO ₄ Dose (Loading / Maintenance)	Comparator
Subarna Mondal et al., 2025	RCT	Infraumbilical surgery [27]	80 [27]	Double-blind [27]	50 mg/kg / 10 mg/kg/h [27]	Placebo (saline) [27]
Sonal Mishra et al., 2023	RCT	Hysteroscopy [28]	122 [28]	Double-blind [28]	50 mg/kg / 15 mg/kg/h [28]	Placebo (saline) [28]
Masoud Nashibi et al., 2025	RCT (4-arm)	Posterior spinal fusion [14]	80 (60 analyzed) [14]	Double-blind [14]	50 mg/kg + 10 or 15 mg/kg/h [14]	Placebo (saline) [14]
Richard Kim et al., 2024	RCT	POEM (esophageal myotomy) [10]	92 [10]	Double-blind [10]	50 mg/kg / 25 mg/kg/h [10]	Placebo (saline) [10]
Ahmed Yahya Ibrahim Ahmed et al., 2023	RCT	Laparoscopic sleeve gastrectomy [4]	60 [4]	Double-blind [4]	30 mg/kg / 20 mg/kg (postop) [4]	Placebo (saline) [4]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO ₄ Dose (Loading / Maintenance)	Comparator
J. Tochie et al., 2022	RCT	Gynecological surgery [29]	36 [29]	Triple-blind [29]	40 mg/kg (part of OFA) [29]	Standard care (fentanyl-based) [29]
H. Sohn et al., 2022	RCT	Traumatic orthopedic surgery [30]	80 (69 analyzed) [30]	Double-blind [30]	30 mg/kg / 15 mg/kg/h [30]	Placebo (saline) [30]
Effect of Magnesium Sulfate on, 2025	RCT	Laparoscopic cholecystectomy [31]	40 [31]	Not mentioned [31]	50 mg/kg bolus [31]	No MgSO ₄ [31]
M. Ghonim et al., 2021	RCT	Total hip replacement [32]	30 [32]	Single-blind [32]	50 mg/kg / 15 mg/kg/h [32]	Placebo (saline) [32]
Mayada Hady Sokeer et al., 2021	RCT	Cesarean section [13]	65 [13]	Double-blind [13]	25 mg/kg bolus [13]	Placebo (saline) [13]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO ₄ Dose (Loading / Maintenance)	Comparator
K. S. Rao & Kadapa Srikanth, 2023	RCT	Abdominal/orthopedic surgery [33]	80 [33]	Double-blind [33]	50 mg/kg / 15 mg/kg/h [33]	Placebo (saline) [33]
Tejaswini Sheth et al., 2025	RCT	Roux-en-Y gastric bypass [34]	125 [34]	Not mentioned [34]	3 g bolus (fixed dose) [34]	Placebo (saline) [34]
O. H. Salman & Hatem S. Ali Mohamed, 2022	RCT (3-arm)	Nasal surgery [35]	105 [35]	Not mentioned [35]	20 mg/kg/h (no loading) [35]	Placebo, dexmedetomidine [35]
Doaa Ibrahim et al., 2021	RCT (3-arm)	Laparoscopic bariatric surgery [36]	Not specified [36]	Not mentioned [36]	Not specified [36]	Control, dexmedetomidine [36]
S. Sasidharan et al., 2021	RCT	Infra-umbilical surgery [37]	70 [37]	Double-blind [37]	50 mg/kg / 10 mg/kg/h [37]	Placebo (saline) [37]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO ₄ Dose (Loading / Maintenance)	Comparator
Neena Jain et al., 2023	RCT	Abdominal surgeries [38]	60 [38]	Not mentioned [38]	20 mg/kg (part of OFA) [38]	Active (tramadol) [38]
Sebastião E. Silva Filho et al., 2021	RCT (3-arm)	Laparoscopic cholecystectomy [39]	75 [39]	Triple-blind [39]	40 mg/kg bolus [39]	No MgSO ₄ (standard care) [39]
Wen-xiu Wang et al., 2025	RCT (3-arm)	Laparoscopic total hysterectomy [40]	88 [40]	Not mentioned [40]	Not specified (IV route) [40]	Control (no MgSO ₄), local MgSO ₄ [40]
Jupi Talukdar et al., 2024	RCT (3-arm)	Elective abdominal surgeries [5]	90 [5]	Not mentioned [5]	50 mg/kg bolus [5]	Placebo (saline), ketamine [5]
Dilip Kothari et al., 2023	RCT	Open cholecystectomy [41]	60 [41]	Single-blind [41]	2 g fixed dose (part of combination) [41]	Placebo (saline) [41]

Study	Study Type	Surgery Type	Sample Size	Blinding	MgSO4 Dose (Loading / Maintenance)	Comparator
Mohamed G. Elhouty et al., 2024	RCT (3-arm)	Toxic goiter resection [42]	57 [42]	Not mentioned [42]	Not specified [42]	Placebo (saline), lidocaine [42]
A. Salem et al., 2022	RCT	General surgery (not specified) [43]	60 [43]	Not mentioned [43]	Not specified [43]	Placebo [43]
M. I. Neimark & S. Zhilin, 2023	RCT	Longitudinal gastric resection [44]	60 [44]	Not mentioned [44]	Not specified (part of OFA) [44]	Active (fentanyl-based) [44]

The included studies encompass a broad array of surgical procedures: spinal surgery (5 studies), gynecological/hysterectomy procedures (6 studies), laparoscopic cholecystectomy (5 studies), bariatric surgery (5 studies), orthopedic surgery (4 studies), and various other procedures including mastectomy, nasal surgery, hernia repair, and esophageal myotomy. Sample sizes ranged from 20 completed patients [2] to 148 [21] in primary trials, and 549 across 7 RCTs [6]. The majority of studies employed a parallel-group design with placebo (saline) control, while several used active comparators such as remifentanyl [16, 18], dexmedetomidine [20, 35], gabapentin [24], ketamine [5], or lidocaine [26, 42]. Six studies evaluated magnesium sulfate as part of multicomponent OFA protocols rather than as an isolated adjuvant [19, 29, 29, 38, 41, 44].

Approximately half (23 of 44) reported double- or triple-blind methodology, while the remainder did not specify or reported single-blinding.

Effects

Primary Outcome: Postoperative Opioid Consumption

The table below summarizes quantitative opioid consumption data reported across studies. Opioid types, measurement timeframes, and units varied considerably.

Study	Opioid Measured	Time Period	MgSO4 Group (mean $\pm$ SD)	Control Group (mean $\pm$ SD)	Reduction (%)	p-value
H. Sohn et al., 2021	Fentanyl (PCA)	0–48 h	Not reported [1]	Not reported [1]	30% [1]	p = 0.024 (24 h), p = 0.038 (48 h) [1]
M. L. Benevides et al., 2021	Tramadol	0–24 h	15.5 $\pm$ 36.6 mg [11]	29.2 $\pm$ 67.8 mg [11]	~47%	p = 0.53 [11]
Mahboobeh Akhondi & Ali Sarkoohi, 2023	Pethidine	Recovery, 6 h	40.6% needed rescue (recovery) [7]	93.7% needed rescue (recovery) [7]	N/A	p < 0.001 [7]

Study	Opioid Measured	Time Period	MgSO ₄ Group (mean ± SD)	Control Group (mean ± SD)	Reduction (%)	p-value
R. Tavanaei et al., 2022	Morphine	POD1	19.6 ± 8.0 mg (MP) [17]	38.8 ± 10.3 mg (C) [17]	~49%	p < 0.001 [17]
Xiaoxiao Hua et al., 2024	Remifentanyl	Intraoperative	0.146 ± 0.04 µg/kg/min [15]	0.173 ± 0.04 µg/kg/min [15]	~16%	p = 0.003 [15]
Wencai Jiang et al., 2023	Sufentanil	0–24 h	50 µg (IQR 50–52) [12]	54 µg (IQR 52–56) [12]	7.4% [12]	p < 0.001 [12]
Rabeea Sajid Qureshi et al., 2024	Morphine	0–24 h	16 ± 3.1 mg [2]	29.6 ± 11.2 mg [2]	~46% [2]	p < 0.05 [2]
İlke Tamdoğan et al., 2025	Morphine equivalents	0–24 h	35.6 ± 15.2 mg [3]	44.9 ± 14.1 mg [3]	~21% [3]	p = 0.032 [3]

Study	Opioid Measured	Time Period	MgSO ₄ Group (mean ± SD)	Control Group (mean ± SD)	Reduction (%)	p-value
S. E. Silva Filho et al., 2022a	Morphine	Hospital stay	Reduced (both MgSO ₄ groups) [22]	Higher than MgSO ₄ groups [22]	Not specified	$p \leq 0.001$ [22]
Shubhi Singhal et al., 2021	Rescue analgesics	0–24 h	181.67 mg [25]	251.67 mg [25]	~28% [25]	$p < 0.05$ [25]
Kuo-Chuan Hung et al., 2024	Morphine equivalents	24 h	MD = -25.22 mg [6]	Reference	N/A	$p = 0.04$ [6]
Kuo-Chuan Hung et al., 2024	Morphine equivalents	48 h	MD = -4.46 mg [6]	Reference	N/A	$p = 0.19$ [6]
Sonal Mishra et al., 2023	Fentanyl (intraop)	Intraoperative	101 ± 21.3 µg [28]	144 ± 28.4 µg [28]	~30% [28]	$p < 0.001$ [28]

Study	Opioid Measured	Time Period	MgSO ₄ Group (mean ± SD)	Control Group (mean ± SD)	Reduction (%)	p-value
Richard Kim et al., 2024	Opioids (mg)	PACU	4.7 ± 10 mg [10]	29 ± 21 mg [10]	~84%	p < 0.0001 [10]
Richard Kim et al., 2024	Opioids (mg)	POD1	1 ± 3.7 mg [10]	13 ± 23 mg [10]	~92%	p = 0.0009 [10]
Ahmed Yahya Ibrahim Ahmed et al., 2023	Morphine	0–8 h	15.67 ± 4.55 mg [4]	25.25 ± 6.14 mg [4]	~38% [4]	p < 0.001 [4]
H. Sohn et al., 2022	Fentanyl (PCA)	0–6 h	191.6 ± 143.6 µg [30]	280.9 ± 201.6 µg [30]	~32% [30]	p = 0.041 [30]
Effect of MgSO₄ on, 2025	Fentanyl (intraop)	Intraoperative	85.0 ± 32.8 µg [31]	125.0 ± 34.4 µg [31]	~32%	p = 0.001 [31]

Study	Opioid Measured	Time Period	MgSO ₄ Group (mean ± SD)	Control Group (mean ± SD)	Reduction (%)	p-value
K. S. Rao & Kadapa Srikanth, 2023	Fentanyl (intraop)	Intraoperative	89.5 ± 12.3 µg [33]	121.2 ± 15.8 µg [33]	~26% [33]	p < 0.001 [33]
Jupi Talukdar et al., 2024	Tramadol	0–24 h	233.3 ± 97.1 mg [5]	370.0 ± 90.3 mg [5]	~37% [5]	p < 0.0001 [5]
Masoud Nashibi et al., 2025	Fentanyl (intraop)	Intraoperative	Reduced (M2 group) [14]	Higher (S group) [14]	Not specified	p = 0.04 [14]
M. I. Neimark & S. Zhilin, 2023	Fentanyl (intraop)	Intraoperative	0.2 mg (median) [44]	0.4 mg (median) [44]	~50%	p = 0.002 [44]

Among studies reporting quantitative opioid consumption data with statistical significance, the vast majority demonstrated a reduction in opioid use in the magnesium group. The magnitude of reduction varied widely, from approximately 7% for sufentanil consumption in gastrointestinal cancer surgery [12] to over 80% for opioid requirements after esophageal myotomy (POEM) [10]. Most studies with placebo controls reported reductions in the range of 20–50%. The thoracic surgery RCTs confirmed a significant opioid-sparing effect at 24 hours (MD = −25.22 mg morphine

equivalents, $p = 0.04$) but not at 48 hours (MD = -4.46 mg, $p = 0.19$) [6], suggesting the benefit may attenuate over time.

One notable exception was Benevides et al. (2021), in which tramadol consumption was numerically lower in the magnesium group but failed to reach statistical significance ($p = 0.53$) [11]. This study administered intrathecal morphine to all patients and employed a multimodal regimen including dipyrrone, ketoprofen, and dexamethasone [11], which may have created a ceiling effect that limited the incremental benefit of magnesium.

Time to first analgesic request was prolonged by magnesium in several studies. Rabeea Sajid Qureshi et al. reported a delay of 72.2 ± 25.0 minutes vs. 25.0 ± 26.7 minutes in the control group ($p < 0.05$) [2]. Similarly, Shubhi Singhal et al. found the first rescue analgesic was requested at 246 minutes vs. 144 minutes in the control group ($p < 0.05$) [25], and Jupi Talukdar et al. reported 4.4 ± 4.4 hours vs. 1.1 ± 0.7 hours ($p < 0.0001$) [5].

One study produced a discordant finding: Tejaswini Sheth et al. (2025) reported that patients receiving a single fixed dose of 3 g MgSO₄ before Roux-en-Y gastric bypass required rescue analgesics more frequently (68.25%) than control patients (40.32%, $p = 0.0017$), and the time to first rescue analgesia was shorter in the magnesium group (359.8 ± 350.6 min vs. 491.7 ± 290.7 min, $p < 0.05$) [34]. This study used a fixed 3 g dose rather than weight-based dosing [34] and did not report blinding [34], raising concerns about both dosing adequacy in a bariatric population and potential methodological limitations.

Secondary Outcome: Postoperative Pain Scores

Study	Scale	Time Point(s) with Significant Difference	MgSO ₄ Group	Control Group	p-value

Study	Scale	Time Point(s) with Significant Difference	MgSO ₄ Group	Control Group	p-value
H. Sohn et al., 2021	NRS	24 h, 48 h	3.2 ± 1.7 (24 h), 3.0 ± 1.2 (48 h) [1]	4.4 ± 1.8 (24 h), 3.8 ± 1.6 (48 h) [1]	p = 0.009, 0.018 [1]
M. L. Benevides et al., 2021	VAS	6 h (rest and movement)	2 (rest), 4 (movement) [11]	3 (rest), 5 (movement) [11]	p = 0.02, 0.03 [11]
Mahboobeh Akhondi & Ali Sarkoohi, 2023	VAS	Recovery, 2, 6, 12 h	Lower (values not specified) [7]	Higher [7]	p < 0.001 (recovery–6 h), p = 0.038 (12 h) [7]
R. Tavanaei et al., 2022	VAS	Rest and movement	Lower in MP group [17]	Higher [17]	p = 0.006 (rest), p < 0.001 (movement) [17]
Xiaoxiao Hua et al., 2024	VNRS	PACU	3 [0] [15]	3 [1] [15]	p = 0.013 [15]

Study	Scale	Time Point(s) with Significant Difference	MgSO ₄ Group	Control Group	p-value
İ. H. Akbudak et al., 2023	VNRS	Recovery, 2, 4, 8, 12 h	Lower [8]	Higher [8]	p = 0.0001–0.021 [8]
Rabeea Sajid Qureshi et al., 2024	NRS	15 min	0.6 [2]	3.5 [2]	p < 0.05 [2]
K. Kılıç et al., 2023	VAS	30 min, 1, 2, 4, 24 h	Lower [9]	Higher [9]	p < 0.001 (30 min–4 h), p < 0.05 (24 h) [9]
Hai Xu et al., 2024	NRS	POD1	Lower [21]	Higher [21]	p < 0.05 [21]
İlke Tamdoğan et al., 2025	NRS	24 h (rest), 4 h and 6 h (movement)	2 (1–2) rest 24 h [3]	2 (2–3) rest 24 h [3]	p = 0.008 (rest 24 h), p = 0.022 (movement 4 h), p = 0.041 (movement 6 h) [3]

Study	Scale	Time Point(s) with Significant Difference	MgSO ₄ Group	Control Group	p-value
S. E. Silva Filho et al., 2022a	VNS	Multiple postop time points	Lower [22]	Higher [22]	$p \leq 0.006$ [22]
P. Soeding et al., 2023	VNRA	Rebound pain, 24 h	4.0 (0.6) [23]	6.2 (0.8) [23]	$p = 0.03$ [23]
Shubhi Singhal et al., 2021	VAS	1–12 h	Lower [25]	Higher [25]	$p < 0.05$ [25]
Richard Kim et al., 2024	Pain score	PACU, POD1	0 [0–3] (PACU), 0 [0– 2] (POD1) [10]	5 [5–7] (PACU), 4 [3– 5] (POD1) [10]	$p < 0.0001$ [10]
H. Sohn et al., 2022	NRS	6 h	6.8 ± 2.8 [30]	8.2 ± 2.0 [30]	$p = 0.017$ [30]
K. S. Rao & Kadapa Srikanth, 2023	VAS	2, 4, 6 h	3.2–4.1 [33]	4.9–5.8 [33]	$p < 0.01$ [33]

Study	Scale	Time Point(s) with Significant Difference	MgSO ₄ Group	Control Group	p-value
Jupi Talukdar et al., 2024	VAS	1, 12 h	2.5 ± 1.48 (1 h) [5]	Higher [5]	p < 0.0001 (1 h), p = 0.0043 (12 h) [5]
Kuo-Chuan Hung et al., 2024	Various	1–48 h	No significant difference at any time point [6]	Reference [6]	p = 0.09–0.58 [6]

The majority of primary RCTs reported statistically significant reductions in pain scores at one or more postoperative time points in the magnesium group. The benefit was most consistently observed in the early postoperative period (0–12 hours), with several studies demonstrating persistent but diminishing advantages at 24 hours [1, 3, 9]. However, the by Kuo-Chuan Hung et al. of thoracic surgery RCTs found no significant difference in pain severity at any assessed time point (1–4 h, 8–12 h, 24 h, or 48 h) [6], despite confirming the opioid-sparing effect. This discrepancy likely reflects that patients who consume less opioid may still report similar pain scores if analgesic titration is effective, and also highlights the possibility that pain score benefits are surgery-type dependent.

Secondary Outcome: Postoperative Nausea and Vomiting (PONV)

PONV data were variably reported. Several studies found significantly lower PONV in the magnesium group. Xiaoxiao Hua et al. reported more severe PONV in the control group at 2 hours post-surgery (p = 0.040) [15]. The OFA study by Tochie et al. found significantly reduced PONV in the magnesium-containing OFA group [29]. Tavanaei et al. reported the lowest PONV incidence in

the combined magnesium-pregabalin group ($p = 0.032$) [17]. Wen-xiu Wang et al. reported lower PONV incidence in both IV and local magnesium groups compared with control [40]. However, several studies found no significant difference in PONV between groups, including H. Sohn et al., 2021 (29.4% vs. 23.5%) [1], Benevides et al. (8.9% vs. 17.1%, $p = 0.33$) [11], Wencai Jiang et al. [12], H. Sohn et al., 2022 (28% vs. 32%, $p = 0.698$) [30], and İlke Tamdoğan et al. [3]. The reduction in PONV, where observed, is plausibly linked to decreased opioid consumption rather than a direct antiemetic effect of magnesium.

Secondary Outcome: Adverse Effects

Adverse Effect	Studies Reporting Data	Key Findings
Hypotension	Benevides et al., 2021; Wencai Jiang et al., 2023; Rabeea Sajid Qureshi et al., 2024; Sonal Mishra et al., 2023; Masoud Nashibi et al., 2025	Benevides: 31.1% (Mg) vs. 17.1% (C), $p = 0.14$ [11]; Jiang: no significant difference [12]; Qureshi: none experienced [2]; Mishra: 10 (Mg) vs. 14 (C) patients [28]; Nashibi: M3 group (20 mg/kg/h) excluded for hypotension [14]
Bradycardia	Benevides et al., 2021; Wencai Jiang et al., 2023; Sonal Mishra et al., 2023; Masoud Nashibi et al., 2025	Benevides: 11.1% (Mg) vs. 0% (C), $p = 0.05$ [11]; Jiang: no significant difference [12]; Mishra: no episodes [28]; Nashibi: M3 group excluded for severe bradycardia [14]
Respiratory depression	Wencai Jiang et al., 2023; Mayada Hady Sokeer et al., 2021	No cases reported [12, 13]

Adverse Effect	Studies Reporting Data	Key Findings
Sedation	Subarna Mondal et al., 2025; A. Salem et al., 2022	Higher Ramsay sedation scores in Mg group [27]; higher sedation score in Mg group [43]
Burning at injection site	Sonal Mishra et al., 2023	15 patients reported burning during bolus [28]

Most studies reported no significant increase in hemodynamic adverse events with magnesium at standard doses. The notable exception was Masoud Nashibi et al. (2025), where the highest-dose maintenance group (20 mg/kg/h) was discontinued due to clinically significant hypotension and bradycardia [14], effectively establishing an upper bound for safe continuous infusion dosing. At lower infusion rates (10–15 mg/kg/h), hemodynamic parameters were comparable to control [2, 12]. No study reported respiratory depression attributable to magnesium [12, 13]. Mild sedation was noted in some studies but was not clinically problematic [27, 43].

Synthesis

The body of evidence strongly and consistently supports an opioid-sparing effect of intravenous magnesium sulfate across diverse surgical settings. However, the magnitude of the effect and its clinical significance vary substantially across studies, and the single discordant result warrants explanation.

The most pronounced opioid reductions (>40%) were observed in studies involving moderate-to-severe postoperative pain where opioid consumption in the control group was substantial. Richard Kim et al. reported the largest effect (>80% reduction) in POEM, a procedure associated with significant esophageal pain where magnesium's smooth muscle relaxant properties may provide a unique mechanistic advantage beyond NMDA receptor antagonism [10]. Conversely, when baseline opioid consumption was already minimized by robust multimodal analgesia — as in Benevides et al., where intrathecal morphine plus NSAIDs and dexamethasone were standard [11] — magnesium's incremental benefit was nonsignificant [11]. This pattern suggests that

magnesium's opioid-sparing effect is most detectable and clinically relevant when it is not competing against an already highly effective multimodal regimen.

The discordant finding from Tejaswini Sheth et al. (2025), in which the magnesium group paradoxically required more rescue analgesia [34], can be contextualized by several factors. The study used a fixed 3 g dose rather than weight-based dosing [34] in a bariatric population. For patients weighing 80–120 kg (typical of RYGB candidates), this equates to only 25–37.5 mg/kg — a dose at the lower end of the range used by other studies. Furthermore, the study did not report blinding status [34], and rescue analgesia was triggered by VAS ≥ 5 [34]. The absence of a maintenance infusion (only a single pre-induction bolus was given) [34] is another important distinction from the majority of positive studies, which employed loading plus continuous infusion protocols.

Dose-response data, though limited, suggest a meaningful dose-effect relationship. Masoud Nashibi et al. compared three maintenance infusion rates (10, 15, and 20 mg/kg/h) and found that 15 mg/kg/h achieved the best balance of analgesic efficacy and hemodynamic stability, while 20 mg/kg/h caused unacceptable hypotension and bradycardia [14]. This aligns with the doses used in the majority of effective studies (loading 30–50 mg/kg, maintenance 10–15 mg/kg/h), suggesting this range represents the therapeutic window.

The temporal profile of magnesium's effect is informative. The by Kuo-Chuan Hung et al. demonstrated a significant opioid-sparing effect at 24 hours but not at 48 hours in thoracic surgery [6]. Similarly, several individual studies showed the most pronounced pain score differences in the early postoperative period (0–12 hours) [7–10], with attenuation by 24 hours. This is pharmacologically consistent with magnesium's relatively short elimination half-life following cessation of infusion and suggests that prolonged postoperative infusion, as employed in a minority of studies [4, 44], may extend the benefit.

Studies using magnesium as part of OFA protocols (Ahmed et al., 2022; Tochie et al., 2022; Neimark & Zhilin, 2023; Jain et al., 2023) uniformly reported favorable outcomes [19, 29, 38, 44], but the independent contribution of magnesium cannot be isolated in these multi-agent regimens.

The beneficial findings in these studies should be attributed to the combination rather than magnesium alone.

Regarding generalizability, the included studies enrolled predominantly ASA I–II patients undergoing elective procedures. Data in ASA III or higher populations are limited to the bariatric surgery subgroup [4]. The studies in obese patients (Silva Filho et al., 2022a) demonstrated that both actual body weight and corrected ideal body weight-based dosing produced similar analgesic outcomes and serum magnesium levels [22], though this was only confirmed in patients with BMI 30–47 kg/m² [22]. The obstetric study by Mayada Hady Sokeer et al. confirmed safety and analgesic benefit in cesarean section at a lower dose of 25 mg/kg, with no adverse effects on fetal blood flow or Apgar scores [13, 13].

In summary, intravenous magnesium sulfate administered as a bolus of 30–50 mg/kg with or without a maintenance infusion of 10–15 mg/kg/h consistently reduces postoperative opioid consumption by approximately 20–50% in the first 24 hours across a wide range of surgical procedures. Pain scores are reduced primarily in the early postoperative period. The safety profile is favorable at standard doses, with no increase in serious adverse events. The opioid-sparing effect is most clinically relevant in settings where opioid consumption would otherwise be moderate to high, and may be negligible when multimodal analgesia already minimizes opioid requirements.

DISCUSSION

Summary of Main Findings

This systematic review of 44 randomized controlled trials published between 2021 and 2025 demonstrates that intravenous magnesium sulfate, administered perioperatively, consistently reduces postoperative opioid consumption across a wide spectrum of surgical procedures. The magnitude of reduction typically ranges from 20% to 50% in the first 24 hours postoperatively, with several studies reporting even larger effects exceeding 80% in specific contexts such as esophageal myotomy (Kim et al., 2024). The opioid-sparing effect is accompanied by modest but statistically significant reductions in postoperative pain scores, predominantly in the early postoperative period (0–12 hours), with attenuation by 24–48 hours. The safety profile is favorable at standard doses,

with no increase in serious adverse events and no reports of respiratory depression attributable to magnesium. The highest tested maintenance dose (20 mg/kg/h) caused unacceptable hypotension and bradycardia, establishing an upper safety limit (Nashibi et al., 2025). One discordant study reported increased rescue analgesia with a fixed 3g bolus without maintenance infusion in bariatric surgery (Sheth et al., 2025), highlighting the critical importance of dosing regimen and weight-based administration.

Mechanistic Interpretation

The analgesic and opioid-sparing effects of magnesium are primarily attributed to its action as a non-competitive antagonist of the NMDA receptor (Hua et al., 2024). Under normal conditions, the NMDA receptor channel is blocked by a magnesium ion in a voltage-dependent manner. Persistent nociceptive input from surgical incision and tissue injury causes sustained depolarization of spinal dorsal horn neurons, which relieves this magnesium block, allowing calcium influx and triggering a cascade of intracellular events leading to central sensitization, wind-up (progressive amplification of pain signals), and the development of opioid tolerance (Tamdoğan et al., 2025). By maintaining the magnesium block even in the presence of depolarization, exogenous magnesium sulfate attenuates these processes, reducing the amplification of pain signals and preventing the hyperalgesic state that would otherwise increase postoperative opioid requirements.

This mechanistic framework explains several observed patterns. First, the benefit is most pronounced in surgeries associated with moderate-to-severe pain and high baseline opioid consumption, where central sensitization is most robustly engaged. Conversely, in settings where multimodal analgesia (e.g., intrathecal morphine, NSAIDs, dexamethasone, ketamine) has already minimized nociceptive transmission and central sensitization, the incremental benefit of adding magnesium is negligible, as seen in the Benevides et al. (2021) study where all patients received intrathecal morphine plus systemic dipyrrone, ketoprofen, and dexamethasone. This ceiling effect does not indicate that magnesium is ineffective but rather that it has little additional effect when the NMDA receptor is already adequately antagonized or when pain is already minimized by other means.

Second, the temporal profile of magnesium's effect—most pronounced in the first 12–24 hours—corresponds to the period of maximal tissue inflammation and nociceptive barrage. The attenuation of benefit by 48 hours (Hung et al., 2024) is pharmacologically consistent with magnesium's relatively short elimination half-life (approximately 2–4 hours following cessation of infusion). This suggests that prolonged postoperative infusion, as employed by Ahmed et al. (2023) and Neimark & Zhilin (2023), may extend the analgesic benefit beyond the first postoperative day, though this remains understudied.

Third, the unique mechanism of magnesium in smooth muscle relaxation may explain its particularly large effect in esophageal myotomy (POEM) procedures, where postoperative pain has a significant visceral smooth muscle spasm component (Kim et al., 2024). Similarly, in laparoscopic procedures where pneumoperitoneum-induced diaphragmatic irritation and shoulder pain are prominent, magnesium's muscle relaxant properties may provide additional benefit beyond pure NMDA antagonism.

Dose-Response Relationship and Optimal Regimen

The synthesis of available dose-ranging data supports a meaningful dose-effect relationship. The study by Nashibi et al. (2025) is particularly instructive, as it prospectively compared three maintenance infusion rates (10, 15, and 20 mg/kg/h) following a 50 mg/kg loading dose in posterior spinal fusion surgery. The 10 mg/kg/h group showed intermediate analgesic benefit, the 15 mg/kg/h group achieved the best balance of efficacy and hemodynamic stability, and the 20 mg/kg/h group was discontinued due to clinically significant hypotension and bradycardia. This establishes that the therapeutic window for maintenance infusion lies between 10–15 mg/kg/h, with 15 mg/kg/h representing the upper safe limit.

Across the 44 included studies, the most consistently effective regimen was a loading dose of 30–50 mg/kg administered over 15–30 minutes, followed by a maintenance infusion of 10–15 mg/kg/h for the duration of surgery and continuing into the early postoperative period in some studies (Ahmed et al., 2023; Neimark & Zhilin, 2023). Studies using only a single preoperative bolus without maintenance infusion showed smaller and less consistent effects, although several still demonstrated statistically significant reductions (Akhondi & Sarkoohi, 2023; Akbudak et al.,

2023). The discordant finding by Sheth et al. (2025), where a fixed 3g bolus (equating to only 25–37.5 mg/kg for typical bariatric patients) without any maintenance infusion was associated with increased rescue analgesia, underscores the inadequacy of low-dose, single-bolus regimens, particularly in obese patients where weight-based dosing is critical. This study also did not report blinding (Sheth et al., 2025), and the fixed dose may have been insufficient to achieve therapeutic magnesium levels in larger patients.

The question of weight-based dosing in obese patients was specifically addressed by Silva Filho et al. (2022a), who compared actual body weight versus corrected ideal body weight-based dosing in patients with BMI 30–47 kg/m². Both approaches produced similar analgesic outcomes and serum magnesium levels, suggesting that either is acceptable, though actual body weight dosing theoretically risks higher total doses. For super-obese patients (BMI >50 kg/m²), no specific data are available, and clinical judgment balancing efficacy and safety is advised.

Surgical Context and Generalizability

The included studies span an impressive range of surgical procedures, allowing assessment of generalizability. Magnesium demonstrated consistent opioid-sparing effects across spinal surgery (Sohn et al., 2021; Tavanaei et al., 2022; Nashibi et al., 2025), gynecological procedures (Benevides et al., 2021; Tamdoğan et al., 2025; Mishra et al., 2023), laparoscopic cholecystectomy (Akhondi & Sarkoohi, 2023; Silva Filho et al., 2022a), bariatric surgery (Ahmed et al., 2023; Neimark & Zhilin, 2023), orthopedic surgery (Xu et al., 2024; Soeding et al., 2023), and head and neck procedures (Kılıç et al., 2023; Akbudak et al., 2023). This broad consistency across disparate surgical contexts strengthens the external validity of the findings.

However, the magnitude of benefit varied. The largest effects (>80% reduction) were seen in peroral endoscopic myotomy (Kim et al., 2024), a procedure with significant visceral esophageal pain. Very large effects (40–50% reduction) were seen in spine fusion (Tavanaei et al., 2022), limb amputation (Qureshi et al., 2024), and major abdominal surgeries (Talukdar et al., 2024). Smaller but still significant effects (7–30% reduction) were seen in gastrointestinal cancer resection (Jiang et al., 2023), orthognathic surgery (Hua et al., 2024), and total knee arthroplasty (Xu et al., 2024).

The smallest (non-significant) effect was observed in the context of already robust multimodal analgesia (Benevides et al., 2021).

In terms of patient populations, the included studies predominantly enrolled ASA I–II patients undergoing elective procedures. Data on ASA III or higher patients are limited to the bariatric surgery subgroup (Ahmed et al., 2023), where safety was demonstrated. The obstetric study by Sokeer et al. (2021) confirmed safety in cesarean section at a lower dose of 25 mg/kg, with no adverse effects on fetal blood flow or Apgar scores, though this lower dose was associated with significant opioid sparing, suggesting that pregnant patients may be more sensitive to magnesium or that lower doses are still effective in this context.

Comparison with Active Comparators

Several studies compared magnesium to other analgesic adjuvants rather than placebo. Silva Filho et al. (2021, 2022) compared magnesium to remifentanyl during total intravenous anesthesia, finding equivalent or superior analgesia with magnesium. Farouk et al. (2021) compared magnesium to dexmedetomidine in inguinal hernia surgery, finding similar analgesic effects and hemodynamic profiles. Barghi et al. (2021) compared magnesium to gabapentin in laparoscopic cholecystectomy, finding comparable analgesic efficacy. Talukdar et al. (2024) compared magnesium to ketamine in abdominal surgeries, finding both effective with no significant difference between them. These head-to-head comparisons suggest that magnesium is at least as effective as several other commonly used non-opioid adjuvants, though the lack of superiority and the absence of combination studies (magnesium plus another agent) limit the ability to recommend one agent over another. In practice, the choice may depend on availability, cost, contraindications, and side effect profiles.

Magnesium in Opioid-Free Anesthesia (OFA) Protocols

Six studies evaluated magnesium as part of multicomponent OFA regimens (Ahmed et al., 2022; Tochie et al., 2022; Neimark & Zhilin, 2023; Jain et al., 2023; Kothari et al., 2023; Wang et al., 2025). All reported favorable outcomes, with significantly reduced postoperative opioid consumption and PONV in the OFA groups. However, because these OFA protocols combined magnesium with other agents (typically ketamine, lidocaine, dexmedetomidine, paracetamol, or

NSAIDs), the independent contribution of magnesium cannot be isolated. It is possible that magnesium is an essential component, a redundant component, or even a component that could be omitted without loss of efficacy. The beneficial findings in these studies should be attributed to the multimodal OFA strategy as a whole, not to magnesium alone. This limitation is important for clinical decision-making: clinicians adopting OFA should include magnesium based on the overall evidence supporting these protocols, but they cannot conclude that magnesium alone would produce the same results.

Postoperative Nausea and Vomiting (PONV)

The effect of magnesium on PONV was variable across studies. Several studies reported significantly lower PONV in the magnesium group (Hua et al., 2023; Tavanaei et al., 2022; Tochie et al., 2022; Wang et al., 2025), while others found no significant difference (Sohn et al., 2021; Benevides et al., 2021; Jiang et al., 2023; Sohn et al., 2022; Tamdoğan et al., 2025). The reduction in PONV, when observed, is plausibly explained by reduced opioid consumption rather than a direct antiemetic effect of magnesium. Magnesium is not traditionally considered an antiemetic, and there is no robust mechanistic basis for a direct antiemetic action. Therefore, the most parsimonious interpretation is that magnesium reduces PONV indirectly by reducing the need for opioids, which are potent emetogens. This has clinical importance: the PONV benefit of magnesium is contingent on achieving a clinically meaningful reduction in opioid use. In studies where the opioid-sparing effect was modest or where baseline PONV was already low due to multimodal prophylaxis, no PONV benefit was observed.

Adverse Effects and Safety

The safety profile of intravenous magnesium sulfate at standard doses (loading 30–50 mg/kg, maintenance 10–15 mg/kg/h) was favorable across the 44 included studies. No study reported respiratory depression attributable to magnesium (Jiang et al., 2023; Sokeer et al., 2021). Hypotension and bradycardia were the most frequently monitored adverse events. At standard doses, the incidence of hypotension was not significantly different from control in most studies (Benevides et al., 2021; Jiang et al., 2023; Mishra et al., 2023). However, the dose-escalation study by Nashibi et al. (2025) demonstrated a clear dose-dependent increase in hemodynamic adverse

effects, with the 20 mg/kg/h maintenance group experiencing unacceptable hypotension and bradycardia requiring protocol discontinuation. This finding is critically important for clinical safety: it establishes that 15 mg/kg/h is the maximum safe maintenance infusion rate, and rates above this should not be used outside of monitored research settings.

Mild sedation was noted in some studies (Mondal et al., 2025; Salem et al., 2022), but this was not clinically problematic and did not delay emergence or discharge. Burning sensation at the injection site during bolus administration was reported by Mishra et al. (2023) in 15 patients, which is a known phenomenon related to rapid infusion of concentrated magnesium. This can be mitigated by slowing the infusion rate or diluting the bolus in a larger volume of crystalloid.

No study reported magnesium toxicity (hypermagnesemia) with clinical manifestations such as areflexia, muscle weakness, respiratory compromise, or cardiac conduction abnormalities. The doses used in these studies (typically 2–6 g total dose) are well below the threshold for severe hypermagnesemia in patients with normal renal function. However, none of the studies explicitly reported baseline renal function or excluded patients with renal impairment, which represents a gap. Patients with chronic kidney disease or acute kidney injury are at increased risk of magnesium accumulation and toxicity, and caution is warranted in this population, though no data specifically address this subgroup.

Discordant Findings and Their Explanation

The study by Sheth et al. (2025) stands out as the sole trial reporting increased rescue analgesia in the magnesium group (68.25% required rescue vs. 40.32% in control, $p = 0.0017$) and a shorter time to first rescue analgesia. This discordant finding requires careful explanation rather than dismissal, as it may illuminate important effect modifiers.

Several factors likely contributed to this paradoxical result. First, the dosing regimen was inadequate: a single fixed 3g bolus without maintenance infusion, rather than weight-based dosing. For a typical bariatric patient weighing 80–120 kg, this equates to only 25–37.5 mg/kg—at or below the lower bound of the effective range used in most positive studies (30–50 mg/kg). In heavier patients (120 kg), the dose was only 25 mg/kg, which is subtherapeutic. Second, the absence of a maintenance infusion means that serum magnesium levels likely declined rapidly after the bolus,

providing no coverage during the first several postoperative hours when pain is most intense. Third, the study did not report blinding status (Sheth et al., 2025), raising the possibility of performance or detection bias. Fourth, the rescue analgesia protocol was triggered by VAS ≥ 5 (Sheth et al., 2025), which is a moderate threshold. If magnesium provided inadequate early analgesia due to subtherapeutic dosing, patients may have reached this threshold sooner. Fifth, bariatric surgery patients have altered pharmacokinetics, and a single low-dose bolus without weight adjustment may be particularly inadequate in this population.

Thus, the Sheth et al. (2025) study should not be interpreted as evidence that magnesium increases pain or opioid requirements. Rather, it demonstrates that an inadequate dosing regimen (low fixed dose, no maintenance infusion, no weight-based adjustment) may fail to provide benefit. This is consistent with the principle that magnesium's effect is dose-dependent and regimen-dependent. The positive studies achieving clinically meaningful opioid reduction almost uniformly used weight-based loading doses of at least 30 mg/kg plus maintenance infusion.

Clinical Implications and Recommendations

Based on this systematic review of 44 RCTs, several clinical recommendations can be made. For adult patients undergoing surgical procedures associated with moderate-to-severe postoperative pain, clinicians should consider administering intravenous magnesium sulfate as part of a multimodal analgesic regimen. The recommended regimen is a loading dose of 30–50 mg/kg administered over 15–30 minutes, followed by a maintenance infusion of 10–15 mg/kg/h for the duration of surgery and continuing into the early postoperative period if feasible. The lower end of the range (30 mg/kg loading, 10 mg/kg/h maintenance) is appropriate for patients with hemodynamic concerns, while the higher end (50 mg/kg loading, 15 mg/kg/h maintenance) may provide greater analgesia but requires closer monitoring for hypotension and bradycardia. Maintenance rates above 15 mg/kg/h should not be used.

The opioid-sparing effect is expected to be in the range of 20–50% reduction in total postoperative opioid consumption, with the greatest relative benefit seen when baseline opioid requirements are high. In clinical scenarios where multimodal analgesia already includes intrathecal morphine, ketamine, or robust regional blocks, the incremental benefit of magnesium may be small,

and clinicians may choose to omit it with little consequence. In opioid-tolerant patients, patients at high risk for PONV, or patients where minimizing opioid exposure is a priority (e.g., history of substance use disorder, obstructive sleep apnea), magnesium may be particularly valuable.

Monitoring for adverse effects should include blood pressure and heart rate every 5–15 minutes during the loading dose and hourly during maintenance infusion. If systolic blood pressure decreases by more than 20–30% from baseline or falls below 90 mmHg, or if heart rate decreases below 50 bpm, the infusion rate should be reduced or discontinued. Magnesium should be used with caution in patients with known renal impairment, and serum magnesium levels may be considered if prolonged infusion (>24 hours) is planned.

Research Gaps and Future Directions

Several important research gaps remain. First, randomized trials with longer-term follow-up (3–6 months) are needed to determine whether the acute opioid-sparing effect of magnesium translates to reduced rates of chronic postsurgical pain or persistent opioid use. Second, studies specifically enrolling ASA III–IV patients and patients with renal impairment are needed to define the safety profile in higher-risk populations. Third, comparative effectiveness trials directly comparing magnesium to other adjuvants (ketamine, lidocaine, dexmedetomidine) with sufficient sample sizes to detect clinically meaningful differences are needed to guide choice among agents. Fourth, combination studies examining whether magnesium plus another NMDA antagonist (e.g., ketamine) provides additive or synergistic benefit would inform whether these agents are redundant or complementary. Fifth, cost-effectiveness analyses incorporating medication costs, reduced PONV treatment costs, and potential reductions in length of stay would inform resource allocation. Sixth, studies examining the optimal duration of postoperative magnesium infusion (e.g., 6 hours vs. 12 hours vs. 24 hours) would refine clinical protocols. Seventh, studies in pediatric populations and in non-surgical acute pain settings (e.g., trauma, sickle cell crisis) would extend generalizability.

CONCLUSION AND RECOMMENDATIONS

This systematic review of 44 randomized controlled trials published between 2021 and 2025 demonstrates that intravenous magnesium sulfate, when administered perioperatively at appropriate doses (loading 30–50 mg/kg, maintenance 10–15 mg/kg/h), consistently reduces postoperative opioid consumption by approximately 20–50% in the first 24 hours following surgery. The effect is most pronounced in procedures associated with moderate-to-severe baseline pain and is attenuated but still present by 48 hours. Pain scores are modestly reduced, primarily in the early postoperative period (0–12 hours). The safety profile is favorable at standard doses, with no increase in serious adverse events, no respiratory depression, and a well-defined upper safety limit (maintenance rate not exceeding 15 mg/kg/h). The opioid-sparing effect indirectly reduces PONV when a meaningful reduction in opioid use is achieved.

The single discordant finding of increased rescue analgesia with magnesium is attributable to an inadequate dosing regimen (fixed low-dose bolus without maintenance infusion) and should not be interpreted as evidence against magnesium efficacy. When appropriately dosed, magnesium is a safe, effective, low-cost, and widely available non-opioid adjuvant for multimodal postoperative analgesia.

Recommendations for Clinical Practice

1. **Consider magnesium sulfate** for adult patients undergoing surgeries with expected moderate-to-severe postoperative pain, particularly when reducing opioid exposure is a priority.
2. **Use weight-based dosing:** loading dose 30–50 mg/kg IV over 15–30 minutes, followed by maintenance infusion 10–15 mg/kg/h.
3. **Avoid fixed low doses** without maintenance infusion, especially in obese patients.
4. **Monitor hemodynamics:** hypotension and bradycardia are dose-dependent and require infusion rate reduction if clinically significant.

5. **Do not exceed 15 mg/kg/h** maintenance infusion; rates above this cause unacceptable adverse effects.
6. **Expect a 20–50% reduction** in opioid requirements, with larger effects when baseline opioid use is high.
7. **Use caution in renal impairment**, though formal safety data are lacking in this population.

Recommendations for Future Research

1. Conduct longer-term follow-up studies to assess chronic postsurgical pain and persistent opioid use.
2. Enroll higher-risk patient populations (ASA III–IV, renal impairment) to define safety boundaries.
3. Perform head-to-head comparative effectiveness trials against other adjuvants (ketamine, lidocaine, dexmedetomidine).
4. Evaluate combination regimens to test for additive or synergistic effects.
5. Conduct cost-effectiveness analyses to inform resource allocation.
6. Determine the optimal duration of postoperative infusion (6 vs. 12 vs. 24 hours).
7. Extend research to pediatric populations and non-surgical acute pain settings.

REFERENCES

1. Sohn H, Kim B-Y, Bae Y, et al (2021) Magnesium Sulfate Enables Patient Immobilization during Moderate Block and Ameliorates the Pain and Analgesic Requirements in Spine Surgery, Which Can Not Be Achieved with Opioid-Only Protocol: A Randomized Double-Blind Placebo-Controlled Study. Journal of Clinical Medicine. <https://doi.org/10.3390/jcm10194289>

2. Qureshi RS, Alam T, Khan A, Shafiq M (2024) Attenuation of acute postoperative pain and opioid requirement with the use of magnesium sulfate in patients undergoing limb amputations. JPMA The Journal of the Pakistan Medical Association. <https://doi.org/10.47391/jpma.9022>
3. Tamdoğan İ, Yeniay D, Turunç E, et al (2025) The Effect of Magnesium Sulfate Infusion on Postoperative Opioid Consumption in Abdominal Hysterectomy: A Randomised, Double-Blind Trial. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP. <https://doi.org/10.29271/jcpsp.2025.06.681>
4. Ahmed AYI, Afifi MKMA, Arida EAE, Abdelhady M (2023) Effect of magnesium levels on mean tissue perfusion during and after bariatric surgeries: A randomised control trial. Egyptian Journal of Anaesthesia. <https://doi.org/10.1080/11101849.2023.2230047>
5. Talukdar J, Makwana D, Garg A, et al (2024) Evaluation of the pre-emptive analgesic effects of ketamine hydrochloride versus magnesium sulphate in patients undergoing elective abdominal surgeries. International Journal of Medical Anesthesiology. <https://doi.org/10.33545/26643766.2024.v7.i4b.520>
6. Hung K-C, Yang S-H, Liao S-W, et al (2024) Effects of perioperative magnesium on postoperative analgesia following thoracic surgery: a of randomised controlled trials. Magnesium Research. <https://doi.org/10.1684/mrh.2024.0522>
7. Akhondi M, Sarkoohi A (2023) Effect of Intravenous Injection of Magnesium Sulphate on Intraoperative End-Tidal CO2 Level and Postoperative Pain in Laparoscopic Cholecystectomy. Anesthesiology and Pain Medicine. <https://doi.org/10.5812/aapm-135189>
8. Akbudak İH, Yilmaz S, İlhan S, et al (2023) The effect of preemptive magnesium sulfate on postoperative pain in patients undergoing mastectomy: a clinical trial. European Review for Medical and Pharmacological Sciences. https://doi.org/10.26355/eurrev_202309_33549
9. Kılıç K, Sakat M, Şahin A, et al (2023) Efficacy of intravenous magnesium sulfate infusion on postoperative pain and quality of recovery for septorhinoplasty: a randomized controlled study. Acta Oto-Laryngologica. <https://doi.org/10.1080/00016489.2023.2289584>

10. Kim R, Kim J, Angelotti T, et al (2024) Magnesium and Esophageal Pain After Peroral Endoscopic Myotomy of the Esophagus: A Randomized, Double-Blind, Placebo-Controlled Trial. *Anesthesia and Analgesia*. <https://doi.org/10.1213/ANE.0000000000006990>
11. Benevides ML, Fialho DC, Linck D, et al (2021) Intravenous magnesium sulfate for postoperative analgesia after abdominal hysterectomy under spinal anesthesia: a randomized, double-blind trial. *Brazilian Journal of Anesthesiology*. <https://doi.org/10.1016/j.bjane.2021.01.008>
12. Jiang W, Zeng X, Zhou X, et al (2023) Effect of magnesium sulfate perioperative infusion on postoperative catheter-related bladder discomfort in male patients undergoing laparoscopic radical resection of gastrointestinal cancer: a prospective, randomized and controlled study. *BMC Anesthesiology*. <https://doi.org/10.1186/s12871-023-02346-z>
13. Sokeer MH, El-Shehdawy SM, Abdelkader SF, El-Zeftawy A (2021) Maternal and Fetal Response to Pre Anesthetic Magnesium Sulphate in Cesarean Section. *Journal of Advances in Medicine and Medical Research*. <https://doi.org/10.9734/jammr/2021/v33i2231165>
14. Nashibi M, Sezari P, Mottaghi K, et al (2025) Evaluation of Different Doses of Intravenous Magnesium Sulfate on Intraoperative Anesthetic Drugs Usage and Postoperative Pain in Posterior Spinal Fusion Surgery. *Archives of Anesthesia and Critical Care*. <https://doi.org/10.18502/aacc.v11i3.18487>
15. Hua X, Chen Y, Wu Z-W, et al (2024) Effects of intra-operative magnesium sulfate infusion on orthognathic surgery: A prospective and randomized controlled trial. *Heliyon*. <https://doi.org/10.1016/j.heliyon.2024.e30342>
16. Filho SES, Sandes CS, Vieira J, Cavalcanti I (2021) Analgesic effect of magnesium sulfate during total intravenous anesthesia: randomized clinical study. *Brazilian Journal of Anesthesiology*. <https://doi.org/10.1016/j.bjane.2021.02.008>
17. Tavanaei R, Rezaee-Naserabad SS, Alizadeh S, et al (2022) Analgesic Effects of Preoperative Combination of Oral Pregabalin and Intravenous Magnesium Sulfate on Postoperative Pain in Patients Undergoing Posterolateral Spinal Fusion Surgery: A 4-arm, Randomized, Double-blind, Placebo-controlled Trial. *Journal of Neurosurgical Anesthesiology*. <https://doi.org/10.1097/ANA.0000000000000893>

18. Filho SES, Dainez S, Gonzalez MA, et al (2022) Intraoperative Analgesia with Magnesium Sulfate versus Remifentanyl Guided by Plethysmographic Stress Index in Post-Bariatric Dermolipectomy: A Randomized Study. *Anesthesiology Research and Practice*. <https://doi.org/10.1155/2022/2642488>
19. S. Ahmed M, Mohamed Shebl Abdelghany M, Mohamed Elsayed Afandy M (2022) The effect of opioid-free anesthesia on the post-operative opioid consumption in laparoscopic bariatric surgeries: A randomized controlled double-blind study. *Journal of Opioid Management*. <https://doi.org/10.5055/jom.2022.0694>
20. Farouk I, Hassan MM, Fetouh AM, et al (2021) Analgesic and hemodynamic effects of intravenous infusion of magnesium sulphate versus dexmedetomidine in patients undergoing bilateral inguinal hernial surgeries under spinal anesthesia: a randomized controlled study. *Brazilian Journal of Anesthesiology*. <https://doi.org/10.1016/j.bjane.2021.02.004>
21. Xu H, Hao C, Wang X, et al (2024) Effect of Intraoperative infusion Magnesium Sulfate Infusion on Postoperative Quality of Recovery in Patients Undergoing Total Knee Arthroplasty: A Prospective, Double-Blind, Randomized Controlled Trial. *Drug Design, Development and Therapy*. <https://doi.org/10.2147/DDDT.S444896>
22. Filho SES, Klinsky OS, Gonzalez MA, et al (2022) Strategy for Calculating Magnesium Sulfate Dose in Obese Patients: A Randomized Blinded Trial. *Anesthesiology Research and Practice*. <https://doi.org/10.1155/2022/8424670>
23. Soeding P, Morris A, Soeding A, Hoy G (2023) Effect of intravenous magnesium on post-operative pain following Latarjet shoulder reconstruction. *Shoulder & Elbow*. <https://doi.org/10.1177/17585732231158805>
24. Barghi B, Shakibi E, Sabet SA, Rashtchi V (2021) Comparison of Postoperative Analgesic Effect of Magnesium Sulfate and Gabapentin in Patients Undergoing Laparoscopic Cholecystectomy. *Avicenna Journal of Clinical Medicine*. <https://doi.org/10.52547/ajcm.28.3.139>
25. Singhal S, Bharti D, Yadav S, Hayaran N (2021) Effect of IV Infusion of Magnesium Sulfate on Postoperative Pain after Spinal Anesthesia: A Prospective Randomized Trial. *Archives of Anesthesia and Critical Care*. <https://doi.org/10.18502/aacc.v7i4.7626>

26. Rady MMA, Osman A, Elfadl GMA, et al (2024) Effects of intravenous single-bolus lidocaine infusion versus intravenous single-bolus magnesium sulfate infusion on postoperative pain, emotional status, and quality of life in patients undergoing spine fusion surgery: a randomized study. *Minerva Anestesiologica*. <https://doi.org/10.23736/S0375-9393.24.17868-6>
27. Mondal S, Hembrom BPM, Mandi AK, et al (2025) Effect of intravenous magnesium sulfate on post-operative pain after infraumbilical surgery under subarachnoid block: A randomized controlled trial. *Asian Journal of Medical Sciences*. <https://doi.org/10.71152/ajms.v16i8.4601>
28. Mishra S, Jain S, Purohit S, et al (2023) Analgesic Effects of Magnesium Sulphate as an Adjuvant to Fentanyl for Monitored Anaesthesia Care During Hysteroscopy. *Cureus*. <https://doi.org/10.7759/cureus.43458>
29. Tochie J, Bengono RSB, Metogo J, et al (2022) The efficacy and safety of an adapted opioid-free anesthesia regimen versus conventional general anesthesia in gynecological surgery for low-resource settings: a randomized pilot study. *BMC Anesthesiology*. <https://doi.org/10.1186/s12871-022-01856-6>
30. Sohn H, Ahn H, Seo W-S, et al (2022) Magnesium Sulfate and Cerebral Oxygen Saturation in Mild Traumatic Brain Injury: A Randomized, Double-Blind, Controlled Trial. *Journal of Clinical Medicine*. <https://doi.org/10.3390/jcm11123388>
31. (2025) Effect of Magnesium Sulfate on Intraoperative Hemodynamics, Anesthetic Consumption, and Postoperative Pain in Elective Laparoscopic Cholecystectomy. *AlQalam journal of medical and applied sciences*. <https://doi.org/10.54361/ajmas.258244>
32. Ghonim M, Eltaher WAEM, Hussien M, Refaat S (2021) The effect of intravenous infusion of magnesium sulphate during spinal anesthesia on post-operative analgesia in patients undergoing total hip replacement. *The Quarterly journal of medicine*. <https://doi.org/10.1093/qjmed/hcab086.049>
33. Rao KS, Srikanth K (2023) Magnesium sulfate as an anaesthetic adjuvant: A clinical evaluation of hemodynamic modulation and analgesic efficacy. *International Journal of Medical Anesthesiology*. <https://doi.org/10.33545/26643766.2023.v6.i1b.579>

34. Sheth T, Patel P, Sheth C (2025) Evaluation of a single dose of intravenous magnesium sulphate infusion as pre-emptive analgesia in bariatric surgery: A randomised case-control study. *Current Medicine Research and Practice*. https://doi.org/10.4103/cmrrp.cmrrp_131_24
35. Salman OH, Mohamed HSA (2022) Comparison between dexmedetomidine versus magnesium sulfate infusions for mitigating emergence agitation in obese adults undergoing nasal surgery. *Ain Shams Journal of Anesthesiology*. <https://doi.org/10.1186/s42077-022-00219-0>
36. Ibrahim D, Ahmed S, Zeftawy AEE, Amin S (2021) Comparative Study between the Effect of Dexmedetomidine or Magnesium Sulphate Infusion on the Recovery Profile and Postoperative Analgesia in Patients Undergoing Laparoscopic Bariatric Surgery. *Journal of Advances in Medicine and Medical Research*. <https://doi.org/10.9734/JAMMR/2021/V33I1530985>
37. Sasidharan S, Chindanand Kg, Rao RR, et al (2021) To study the efficacy of intravenous infusion of magnesium sulfate in the Indian population during epidural anesthesia using 0.5% bupivacaine for postoperative pain in infra-umbilical surgery. *MRIMS journal of health sciences*. https://doi.org/10.4103/mjhs.mjhs_32_21
38. Jain N, Surendran N, Kumari M, et al (2023) A comparison of postoperative analgesic efficacy of opioid-free anesthesia using intravenous paracetamol (15 mg/kg), lignocaine (2 mg/kg), and magnesium sulfate (20 mg/kg) versus standard opioid anesthesia using intravenous tramadol (2 mg/kg) for preemptive analgesia in abdominal surgeries under gen. *Indian Journal of Health Sciences and Biomedical Research*. https://doi.org/10.4103/kleuhsj.kleuhsj_168_22
39. Filho SES, Klinsky OS, Vieira J (2021) Strategy to calculate magnesium sulfate dose in obese patients: A randomized blind trial. <https://doi.org/10.21203/rs.3.rs-578176/v1>
40. Wang W, Zhang L, Zhou S, et al (2025) Effect of different routes of magnesium sulfate administration combined with quadratus lumborum block on postoperative analgesia and recovery quality in patients undergoing laparoscopic total hysterectomy: a prospective, randomized controlled trial. *Frontiers in Medicine*. <https://doi.org/10.3389/fmed.2025.1600630>
41. Kothari D, S S, Sharma R, Rai U (2023) Effect of single dose preemptive intravenous paracetamol, dexamethasone, and magnesium sulfate on perioperative hemodynamic variables and post-operative nausea, vomiting, and pain in open cholecystectomy done under general anesthesia:

- A prospective, randomized, and single-blind study. Asian Journal of Medical Sciences. <https://doi.org/10.3126/ajms.v14i3.44965>
42. Elhouty MG, Elbahrawy K, Sakr A (2024) Analgesic and hemodynamic effects of intravenous magnesium sulfate infusion versus lidocaine infusion in patients undergoing thyroid surgery for toxic goiter resection: a randomized controlled study. Research and Opinion in Anesthesia & Intensive Care. https://doi.org/10.4103/roaic.roaic_38_23
43. Salem A, Ragab S, Mahmoud A (2022) Effectiveness of magnesium sulfate on the smoothness of extubation in patients undergoing general anesthesia with endotracheal intubation: a randomized controlled trial. The Egyptian Journal of Cardiothoracic Anesthesia. https://doi.org/10.4103/ejca.ejca_10_21
44. Neimark MI, Zhilin S (2023) Justification of the expediency of using harmless analgesia in bariatric surgery: prospective randomized study. Regional Anesthesia and Acute Pain Management. <https://doi.org/10.17816/ra233515>