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Magnesium's efficacy alone and in combinations in reducing perioperative pain and opioid consumption: A comprehensive narrative review

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Abstract

Background: Postoperative pain poses a high risk of psychological and physical trauma to surgical patients. Magnesium sulfate ($MgSO_4$) is inexpensive, safe, and has been used in many anesthesia procedures to evaluate its role in reducing perioperative pain and opioid consumption.

Methods: A comprehensive search was conducted across several databases, including Google Scholar, Cochrane, and PubMed, up to 2024. The study included trials that used magnesium alone or in combination perioperatively.

Results: Our search included clinical trials, totaling 29 articles. Eighteen of them examined magnesium alone compared with various analgesics or placebo in clinical studies, which may help reduce postoperative pain and opioid consumption. The effectiveness of magnesium alone was assessed in various surgical procedures, using different doses of magnesium sulfate and various methods of administration. Eleven articles examined magnesium as an additive to show its effectiveness in combination with conventional anesthetics and analgesics.

Conclusion: Magnesium has been compared with many anesthetics and analgesics, both alone and in combination, showing remarkable efficacy in relieving pain during surgery and reducing opioid consumption. Many studies found that intraperitoneal magnesium sulfate had significantly greater efficacy than intravenous administration. A dose of 30-50 mg/kg of magnesium sulfate, followed by a maintenance dose of 6-12 mg/kg/h, is recommended and was found to be effective and safe in many trials.

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Highlights

What is current knowledge?

Magnesium sulfate ($MgSO_4$) is a safe, cost-effective NMDA receptor antagonist that reduces perioperative pain and opioid consumption when used alone or as an adjunct, with intraperitoneal administration showing longer efficacy than intravenous. While a regimen of 30-50 mg/kg bolus followed by 6-12 mg/kg/h infusion is effective, further research is needed to standardize protocols and confirm long-term benefits.

What is new here?

This review consolidates recent evidence on magnesium's efficacy in perioperative pain management, highlighting its role as both a standalone and adjunct therapy, emphasizing the superiority of intraperitoneal administration, and providing updated dosing recommendations.

Introduction

Postoperative pain is a major problem for patients and a challenge for anesthesiologists and surgeons. The frequency of moderate to severe pain varies worldwide (1). In Western countries, the prevalence ranges from 14% to 55%, peaking on the day of surgery. In low- and middle-income countries, the prevalence may be as high as 95% in Kenya and Ethiopia, based on cohort studies (2). Pain encompasses not only sensory features but also cognitive, affective, behavioral, and social dimensions and is associated with multiple comorbidities such as migraine, anxiety, depression, sleep disturbances, and reduced quality of life (3,4).

Magnesium is a safe, cost-effective substance that has been used for over 20 years in anesthetized surgery as a sedative, analgesic, and muscle relaxant, as well as an organ protectant in a variety of conditions (5-7). In the central nervous system, magnesium exerts its inhibitory effects by acting as an antagonist of N-methyl-D-aspartate (NMDA) glutamate receptors and an inhibitor of catecholamine release (8). The analgesic effect of magnesium is highly beneficial for managing chronic pain and reducing the duration and intensity of postoperative pain (9). The role of magnesium as an adjunct to local anesthetics in minimizing the need for postoperative analgesics has been demonstrated in various clinical studies involving procedures such as hysterectomy, cesarean section, brachial plexus blocks, and laparoscopic surgery (10). Adequate postoperative pain control is essential for reducing discomfort and achieving a rapid recovery after surgery (4).

Although many clinical studies have been conducted in the literature, not all aspects of magnesium have been covered. This review reports on all forms of magnesium, either alone or in combination, as well as the route of administration, different doses, and toxic magnesium levels. The aim of this review is to conduct a comprehensive search of various studies on the role of magnesium in reducing perioperative pain and opioid consumption.

Methods

This review conducted a comprehensive search up to 2024 through various databases, including PubMed, Google Scholar, and the Cochrane Library. We searched for the following keywords: magnesium sulfate, abdominal surgery, analgesia, and postoperative pain. We included clinical trial studies relevant to magnesium's role in analgesia, examining magnesium alone and as an additive in combination with other analgesics for postoperative pain management. In addition, this review included patients of all ages undergoing laparoscopic and open abdominal surgeries. Our search was restricted to the English language.

Results

We obtained approximately 70 articles, 41 of which were excluded due to irrelevance or repetition. The remaining 29 articles met the review's aim and were summarized to provide a clear overview of the findings.

Comparison magnesium with analgesics or placebo

Magnesium sulfate is widely used in medicine (11). This study examined the use of magnesium alone as an analgesic in a short-term study, which may help reduce postoperative pain and opioid consumption. A total of 18 randomized clinical trials were summarized to assess the effectiveness of magnesium alone in various surgical procedures. Some articles examined different doses of magnesium sulfate, while others investigated its administration through various routes (Table 1).

Magnesium as additive to combinations

Magnesium compounds have been used in combination with many conventional analgesics. A total of 11 clinical trials were collected to show the effectiveness of magnesium in combination with various conventional anesthetics and analgesics (Table 2).

Discussion

Comparison magnesium with analgesic or placebo

Postoperative pain poses a significant risk of psychological and physical trauma to surgical patients. Thus, anesthesiologists have tried various drugs and techniques to reduce its frequency (4).

Mechanism of magnesium as analgesic

Numerous studies have demonstrated that magnesium has analgesic properties and reduces postoperative pain by blocking somatic and visceral pain fibers (9). However, its mechanism of pain relief is not unequivocal. It is believed that its mechanism as a non-competitive NMDA receptor antagonist may contribute to this analgesic effect (12,13). Magnesium blocks the NMDA receptor channel complex, which is critical for pain transmission (11). Noxious stimulation leads to excessive release of glutamate from presynaptic nociceptive terminals, which reverses magnesium blockade and activates NMDA receptors, leading to upregulation of NMDA currents. Activation of NMDA receptors results in the entry of Na^+ and Ca^{2+} into the cell, initiating a series of central sensitization processes and leading to long-term enhancement of the responsiveness of spinal cord cells to sustained stimulation (14). Increased intracellular calcium levels seem to play a major role in the initiation of central sensitization, and the build-up of intracellular calcium is associated with various receptors on postsynaptic neurons of the spinal dorsal horn, such as NMDA, α-amino-3-hydroxy-5-methyl-4-isoxazole propionate, kainate, and glutamate receptors (15,16). Central sensitization plays an important role in pain perception and the persistence of postoperative acute and chronic pain, presenting as allodynia (Pain elicited by stimuli that are not normally painful) and hyperalgesia (An amplified response to a painful stimulus) (17,18). Central sensitization leads to pain hypersensitivity, including wind-up or long-term pain potentiation; it causes pain even when peripheral stimuli are not intense and continues to cause pain even after the initiating stimuli have disappeared (14). Magnesium is a physiological inhibitor of calcium channels by controlling calcium influx into cells (9,19). Extracellular magnesium blocks NMDA receptors in a voltage-dependent manner and can thus prevent the establishment of central sensitization and abolish existing hypersensitivity (14). Magnesium boluses and infusions during surgery can prevent central sensitization, reduce allergic reactions, and relieve postoperative pain (14,15,20). NMDA receptor antagonists are best administered before the onset of noxious stimuli to prevent central sensitization (11,12,21). However, regarding shoulder tip pain, it was reported that there was no significant effect on shoulder pain, which especially occurs in laparoscopic surgeries (13). Pain after laparoscopic cholecystectomy is highly variable in intensity and duration and is largely unpredictable (9).

Opioid side effects

Opioids have many side effects; for example, intraoperative infusion of remifentanil may lead to acute opioid tolerance and increase postoperative pain (22). In addition, opioids have adverse side effects, including respiratory depression (Which can worsen postoperative pulmonary complications in more vulnerable obese patients), nausea and vomiting, sedation, confusion, hyperalgesia, chronic postoperative pain, pruritus, and decreased intestinal motility leading to ileus, diarrhea, constipation, and long-term use of opioids can lead to addiction (2,23). Therefore, magnesium can reduce perioperative opioid consumption and help avoid opioid side effects or at least attenuate them.

Multimodal analgesia

Magnesium is among the drugs used in combination with other opioid and non-opioid drugs for the multimodal approach recommended by the American Society of Anesthesiologists Task Force for providing optimal analgesia in acute pain management (24). This approach can provide analgesia while reducing the dose of various medications and their associated side effects. Opioids are often used in combination with other analgesics, such as acetaminophen or nonsteroidal anti-inflammatory drugs (NSAIDs), as well as adjunctive analgesics, such as alpha-2 agonists or anti-NMDA receptor agents (e.g., ketamine or magnesium) (23).

Magnesium doses

Magnesium has been administered in various doses. A dose of 50 mg/kg of magnesium sulfate clearly demonstrated an analgesic effect, which may have caused patients to have higher serum magnesium ion concentrations following surgery (23). In contrast, some studies reported that a reduced magnesium dosage had no analgesic effect (6). Some studies examined a dose of 25 mg/kg of magnesium, demonstrating its efficacy in reducing postoperative pain for 3 hours in major abdominal surgery without side effects (19). Magnesium sulfate at a dose of 50 mg/kg, given intravenously within 30 minutes before induction of anesthesia, was considered safe and showed no side effects (12). However, studies emphasized that an initial dose of 30 to 50 mg/kg of magnesium sulfate, followed by a maintenance dose of 6-12 mg/kg/h, was recommended because continuous intravenous infusion may enhance postoperative analgesia and reduce the need for opioids during the postoperative period (20).

Magnesium toxicity

Magnesium toxicity sets in at serum concentrations of 2.5-5 mmol/l. Some studies have used magnesium sulfate boluses of 50 mg/kg and double infusions of 8 mg/kg/h, and serum magnesium levels have been measured well below toxic levels, suggesting that magnesium sulfate is safe for intraoperative analgesia (23).

Routes of magnesium administration

Many trials have examined magnesium administration by intraperitoneal (IP) or intravenous (IV) methods. Some studies demonstrated that the efficacy of the IP method was greater than that of IV in certain situations, especially in laparoscopic surgeries. A study conducted on patients undergoing laparoscopic cholecystectomy with IP $MgSO_4$ showed that IP was a safer and more effective method for acute postoperative pain compared to IV (15). Another study examined the IP combination of levobupivacaine with $MgSO_4$ and found that the IP combination was effective for postoperative pain in laparoscopic sleeve gastrectomy (25). $MgSO_4$ with bupivacaine via IP instillation contributed to prolonging the duration of analgesia and reducing postoperative pain in laparoscopic cholecystectomy (26,27). Therefore, magnesium through intraperitoneal instillation demonstrated its efficacy. IP local anesthetics block visceral afferent signals, potentially altering visceral nociception and providing analgesia. Absorption of local anesthetics from the large peritoneal surface may also be another mechanism of analgesia (28,29). Since high concentrations of drugs can be delivered intraperitoneally to the target site without exposing other parts of the body to excessive amounts of the drug, this method is particularly important in situations where systemic exposure to the drug could lead to harmful side effects (29).

However, some studies emphasized that the use of intravenous magnesium boluses before and during surgery, followed by infusions, can reduce postoperative pain and provide a longer duration of analgesia and reduced analgesic consumption without significant complications (18,30). Some studies reported that $MgSO_4$ intravenously improved pain after surgery and provided safe, effective, and satisfactory analgesia in major abdominal surgery (20,31). Regarding the use of $MgSO_4$ by IV over 20 minutes followed by infusion, it demonstrated its anesthetic, analgesic, and muscle relaxant features in plastic surgeries (18). In addition, $MgSO_4$ administered over 15 minutes followed by infusion intraoperatively was effective as an adjuvant in general anesthesia for abdominal surgeries (21).

Comparison magnesium with analgesics or placebo

Many trials have examined magnesium with a placebo or with other analgesics. In comparison with remifentanil, it showed remarkable efficacy in controlling pain and autonomic response during surgery and reduced fentanyl consumption intraoperatively (28). Its effectiveness in reducing propofol requirements during induction and maintenance of general anesthesia has been demonstrated when compared with propofol (21). In addition, some studies compared magnesium and ketamine separately to identify the best analgesic drug among two different (NMDA) antagonists in laparoscopic cholecystectomy. Using ketamine (0.5 mg/kg) and magnesium (20 mg/kg) boluses, magnesium was found to be more effective than ketamine in postoperative pain management, cumulative morphine consumption, and reduction of fentanyl consumption without adverse effects (32). At the same time, the analgesic effects of intravenous infusion of magnesium sulfate and ketorolac during anesthesia for laparoscopic surgery were compared, and it was found that postoperative morphine consumption and pain intensity were significantly reduced, similar to ketorolac tromethamine. In addition, ketorolac had fewer side effects, but not magnesium (33).

However, in a study that examined the effects of magnesium sulfate, dexmedetomidine, and lidocaine on hemodynamic response and postoperative analgesia in laparoscopic abdominal surgery, dexmedetomidine was superior in maintaining hemodynamic stability and relieving pain, followed by lidocaine, and magnesium was the least effective. In addition, the need for rescue analgesia was minimal with dexmedetomidine compared to lidocaine and magnesium (34). A comparison of intravenous magnesium and diclofenac for postoperative analgesia in patients undergoing total abdominal hysterectomy showed that patients using magnesium sulfate consumed less narcotic medication, especially pethidine, on the first postoperative day than those using diclofenac (35). Magnesium has been reported to be effective as an alternative to non-opioid analgesics like NSAIDs perioperatively through intravenous infusion for anesthesia, especially when NSAIDs are contraindicated (33). When lidocaine, ketamine, and magnesium sulfate were compared regarding their effect on postoperative analgesia and the need for rescue analgesics intraoperatively in laparoscopic cholecystectomy, they also demonstrated efficacy (36). In most trials, magnesium contributed to reducing opioid consumption for recovery, 6 and 24 hours after surgery (37).

Mechanism of magnesium as additive in combination

Many studies with conventional anesthetic analgesic compounds have been used to relieve pain. A combination of drugs was effective in relieving postoperative pain, and they were well-tolerated with no recorded serious adverse events (38). Magnesium is an important ion involved in the regulation of multiple ion channels and physiological processes. Therefore, it is involved in these combinations (39). It does not have analgesic properties on its own, but its NMDA receptor antagonist properties eliminate central mechanisms of pain transmission and modulation, sensitization, and even modulate pain transmission in peripheral tissues. This unique property of magnesium sulfate promotes its use in combination with local anesthetics (40). The mechanism of magnesium as a combination does not differ from that of magnesium and other analgesics or anesthetic drugs separately. For example, since $MgSO_4$ is a noncompetitive NMDA receptor antagonist and a physiological calcium antagonist, the combination of bupivacaine and magnesium can enhance the analgesic effect of bupivacaine. Therefore, magnesium can be used as an adjunct analgesic both locally and systemically after surgery (41). It increases the number of nerve fibers affected by bupivacaine, thereby increasing its conduction block. Therefore, bupivacaine combined with magnesium is superior to other combinations in relieving postoperative abdominal pain and prolonging the time to first postoperative analgesia. In addition, this combination can effectively reduce postoperative shoulder tip pain during laparoscopic surgery (38,40).

Magnesium plus analgesics or anesthetics as combination

A combination of intravenous magnesium plus ketamine was reported to be effective intraoperatively; morphine consumption was reduced by nearly 50% in the first 12 hours compared with magnesium and ketamine alone in abdominoplasty and liposuction surgeries (7). Furthermore, the addition of a magnesium bolus (50 mg/kg) and continuous infusion (15 mg/kg/h) to ketamine reduced morphine consumption and pain scores at rest, during exercise, and during coughing in obese patients, one of whom underwent open bariatric surgery within 24 hours postoperatively, and reduced perioperative remifentanil requirements (23). Furthermore, the combination of magnesium plus paracetamol plus lidocaine showed a reduction in postoperative pain as indicated by pain scores (20). At 24 and 48 hours after surgery, magnesium plus vitamin C significantly reduced cumulative postoperative fentanyl consumption compared with magnesium and vitamin C alone, suppressed neuropathic pain, enhanced the analgesic effect of opioids, and was safe to use without side effects (39). The addition of dexamethasone or magnesium to bupivacaine during IP instillation: Magnesium was found to have an additive effect over dexamethasone, prolonging the duration of analgesia, reducing postoperative pain scores, and nalbuphine consumption in laparoscopic cholecystectomy (40).

The bupivacaine-magnesium combination was superior to the bupivacaine-tramadol combination in reducing postoperative pain, analgesic consumption, and shoulder pain, particularly during laparoscopic cholecystectomy (9,38). A study on postoperative analgesia in upper abdominal surgery found that regional infiltration of ropivacaine and magnesium sulfate in the first 6 hours provided better postoperative pain control than bupivacaine plus magnesium (40).

In another study, the bupivacaine-magnesium combination had the highest analgesic effect among different combinations, such as bupivacaine plus hydrocortisone and magnesium sulfate plus hydrocortisone, for postoperative abdominal pain in patients undergoing laparoscopic unilateral ovarian cystectomy (38). In a prospective clinical study by Sarenac et al., conducted to evaluate amino acids, lidocaine, and magnesium, it was shown to have both anti-inflammatory and analgesic effects during the first five days after abdominal surgery (41).

Various combinations of intraperitoneal levobupivacaine and/or magnesium sulfate for the relief of postoperative pain in patients undergoing laparoscopic sleeve gastrectomy showed that the addition of magnesium sulfate to levobupivacaine reduced postoperative pain and analgesic consumption within the first 24 hours (25).

This is due to differences in patient populations, types of surgery that may produce varying pain intensities, inconsistent pain ratings, and differences in magnesium doses between surgeries, all of which may affect generalizability. Future studies should aim to address these limitations.

Conclusion

Magnesium has been compared with many anesthetics and analgesics, such as ketamine, propofol, ketorolac, remifentanil, and diclofenac, showing remarkable efficacy in relieving pain during surgery and reducing opioid consumption. Regarding its addition in some combinations, such as magnesium with ketamine, paracetamol, vitamin C, bupivacaine, amino acids, and levobupivacaine, it demonstrated good additive properties in prolonging the duration of anesthesia and reducing perioperative pain and opioid use. Regarding magnesium toxicity, although some studies have used magnesium sulfate boluses of 50 mg/kg and double infusions of 8 mg/kg/h, serum magnesium levels have been measured well below toxic levels. Many studies have found that IP magnesium sulfate was significantly more effective than IV. A dose of 30 to 50 mg/kg of magnesium sulfate, followed by a maintenance dose of 6-12 mg/kg/h, is recommended and has been shown to be effective and safe in many trials.

Table 1. Summary of clinical studies using magnesium sulfate alone

ID	Study	Type of surgery	Magnesium group (MG)	Control or Comparable group (CG)	Conclusion
1	Kiran et al. (2011) (12)	Inguinal Surgery	**MG**: $MgSO_4$ 50 (mg/kg) in 250 ml of isotonic sodium chloride solution IV preoperatively	**CG**: Same volume of isotonic sodium chloride over 30 min preoperatively	$MgSO_4$ IV infusion preoperatively reduced post-op pain and the requirement of rescue analgesia.
2	Ryu et al. (2016) (13)	Laparoscopic Gastrectomy	**MG**: $MgSO_4$ 50 (mg/kg LD) over 10 min and then 15 mg/ kg/h by IV infusion)(n=37)	**CG:** NS (Same volume) (n=37)	$MgSO_4$ improved postoperative pain without any adverse effects.
3	Sousa et al. (2016) (33)	Laparoscopic Gynecologic surgeries	**KG**: IV ketorolac 30 (mg) in bolus followed by saline infusion **MG**: IV $MgSO_4$ 20 (mg/kg) in bolus followed by $MgSO_4$ 2 (mg/ kg /h)	**CG**: IV NS 20 mL in bolus followed by saline infusion	1. Intraoperative improved postoperative pain. 2. Acting as an opioid-sparing adjuvant 3. The same action of ketorolac 30 mg, when administered in the beginning of surgery
4	Elfiky et al. (2018) (15)	Laparoscopic Cholecystectomy	**M(A)G:** $MgSO_4$ 50 (mg/kg) in 250 ml of isotonic 0.9% N. S (IV)over 30 min with the beginning of operation	**M(B)G:** $MgSO_4$ 50 (mg/kg) in 30 ml of isotonic 0.9% N.S (IP) at the end of surgery	IP $MgSO_4$ was a safe and effective method in acute postoperative pain more than IV $MgSO_4$.
5	Tan et al. (2019) (6)	Laparoscopic Gastrointestinal Surgery	**M(A)G:** $MgSO_4$ 30 (mg/kg LD) & 15(mg/kg/h) IV infusion for1h (n=20) **M(B)G**: $MgSO_4$ 50 (mg/kg) IV infusion 30 mg/kg/h (n=20)	**CG**: Same volume and 0.9% saline infusion	Reduced postoperative pain at serum MG > 2 (mmol/L).
6	Wahba et al. (2019) (35)	Abdominal Hysterectomy	**MG**: $MgSO_4$ 50 (mg/kg) in 100ml in NS solution (isotonic saline) just 15-30 min post-operative (n=30)	**CG**: (n=30) 75 mg of diclofenac in 100mL of 0.9% NS (15-30 min) solution post operatively (n=30)	$MgSO_4$ reduced postoperative pain and opioid consumption
7	Mussrat et al. (2019) (4)	Upper abdominal Surgery	**MG**: $MgSO_4$ 50 mg/kg IV in 0.9% N/S at induction & 15 mg/kg $MgSO_4$ per hour, 6 hours postoperatively (n=50)	**CG:** 100 ml of 0.9% N/S at induction & 500 ml of 0.9% N/S 6 hours postoperatively (n=50)	$MgSO_4$ increased the duration of analgesia post-operatively.
8	Thakur et al. (2019) (32)	Laparoscopic Cholecystectomy	**MG:** $MgSO_4$ 20 (mg/kg) IV (n=20) **KG:** Ketamine 0.5 (mg/kg) IV(n=20)	**CG:** Placebo IV NS (n=20)	Magnesium was efficient in post-operative pain, cumulative morphine consumption, and reduced fentanyl consumption. The ketamine effect was superior in comparison with magnesium in terms of reducing analgesic requirements intraoperatively and during the first four hours of the postoperative period.
9	Murumu et al. (2021) (18)	Plastic Surgery	**MG:** $MgSO_4$ 50 (mg/kg) IV in 100 ml of NS over 20 min immediately before induction and then 10 (mg/kg/hr.) by IV infusion until the end of surgery (n=30)	**CG**: NS same volume over same duration (n=30)	1-$MgSO_4$ had anesthetic, analgesic, and muscle relaxant features. 2-$MgSO_4$ reduced vecuronium and isoflurane requirements intraoperatively. 3. Reduced postoperative consumption of ketorolac and VAS score
10	Silva Filho et al. (2021) (28)	Bariatric Abdominoplasty	**MG**: $MgSO_4$ IV an infusion rate 10 (mg/ kg/h) (n=23)	**CG**: Remifentanil IV an infusion rate 0.2 (g/ kg-1min-1) (N=20):	$MgSO_4$ was safe and effective as an intraoperative analgesic and an effective choice to decrease opioid use
11	Toleska et al. (2022) (36)	Laparoscopic Cholecystectomy	**MG**: $MgSO_4$ 1.5 (g/ kg) IV infusion (n=40)	**CG**: Lidocaine 1 (mg/kg) and 2 (mg/kg/h) IV infusion (n=40) **ketamine G**: Ketamine 0.5 (mg/kg) (n=40)	Magnesium sulfate, ketamine, and lidocaine demonstrated their efficacy and safety in the intraoperative part as multimodal analgesia.
12	Yazdi et al. (2022) (19)	Major abdominal Surgery	**MG:** $MgSO_4$ 25 (mg/kg) for 1 h	**CG**: 15 ml/L sterile distilled water was added to isotonic saline as placebo, and infused intravenously	IV $MgSO_4$ improved pain after surgery for 24 h, after six hours, and reduced morphine dosage
13	Sravanthi et al. (2023) (26)	Laparoscopic Cholecystectomy	**MG**: $MgSO_4$ 10%, 50 (mg/kg diluted) in 100 mL over 20 min IP instillation (n=32)	**CG**: Saline (0.9%, 100 mL) was instilled over 20 min (n=32)	Reduced postoperative pain by IP $MgSO_4$
14	Kaur et al. (2023) (21)	Abdominal Surgery	**MG**: $MgSO_4$ 30 (mg/kg) (IV) in 100 ml (NS) over 15 min followed by 10 (mg/kg/h) infusion intraoperatively	**CG**: 100 ml NS over 15 min followed by NS infusion intraoperatively	$MgSO_4$ was effective intraoperatively as an adjuvant in general anesthesia, such as with propofol, and could reduce propofol dosage
15	Singh et al. (2023) (30)	Abdominal Hysterectomy	**M(A)G**: $MgSO_4$ 50 (mg/kg) in 100 ml NS solution IV as bolus followed by infusion of NS (n=20)	**M(B)G**: $MgSO_4$ 50 (mg/kg) in 100 ml NS solution IV as bolus followed by IV infusion of $MgSO_4$ 10 (mg/kg/hr.) (n=20)	$MgSO_4$ as a bolus followed might provide adequate analgesia
16	Akhondi, M. & Sarkoohi, A. (2023) (37)	Laparoscopic Cholecystectomy	**MG**: $MgSO_4$ 50 (mg/kg) and NS (100 ml) within 1 h (n=32)	**CG**: Normal saline (100 ml) (n=32)	$MgSO_4$ was safe and fit to reduce postoperative pain and narcotics
17	Adity et al. (2024) (2)	Abdominal Hysterectomy	**M(A)G**: $MgSO_4$ 30 (mg/kg) 20 min before induction (n=20)	**M(B)G**: $MgSO_4$ 50 mg/kg 20 min before induction (n=20)	A dose of 50 mg/kg of $MgSO_4$ could reduce the need for opioids and increase magnesium levels in the blood
18	Ipsita Roy et al. (2024) (34)	Laparoscopic Abdominal Surgeries	**MG**: $MgSO_4$ 30 (mg/kg LD) over 15 min before induction, followed by 15 (mg/kg/h) throughout surgery (n=35)	**CG**: Lignocaine 1.5 (mg/kg LD) slow IV over 2-4 min before induction, followed by 2 (mg/kg/h) throughout the surgery (n=35) **CG**: Dexmedetomidine 1 (mcg/kg LD) over 10 min before induction, followed by 0.5 (mcg/kg/min) throughout surgery (n=35)	$MgSO_4$ had less analgesic efficacy in comparison to Dexmedetomidine

LD, Loading Dose; IP, Intraperitoneal; IV, Intravenous; VAS, Visual Analogue Scale; NS, Normal Saline

Table 2. Summary of clinical studies using magnesium sulfate in combination

ID	Study	Type of surgery	Magnesium group (MG)	Control/comparative group (CG)	Conclusion
1	Yadava et al. (2016) (9)	Laparoscopic cholecystectomy	**(M+B) G**: $MgSO_4$ (50 mg/kg) + bupivacaine (30 ml of 0.25%) IP (n=93)	**(T+B):** Tramadol 100 mg + (30 ml of 0.25% of bupivacaine IP (n=93)	IP bupivacaine $MgSO_4$ instillation rendered patients relatively pain-free in the first 24 hours after surgery, with a longer duration of the pain-free period and less consumption of rescue analgesics compared to the bupivacaine-tramadol combination.
2	Varas et al. (2020) (7)	Abdominoplasty and/or Liposuction	**MG**: $MgSO_4$ 50 (mg/kg) + ketamine IV bolus of 0.3 (mg/kg) followed by continuous infusion of ketamine (0.15 mg/kg/h) and $MgSO_4$ (10 mg/kg/h) until extubation (n=22)	**CG:** NS (N=21	Intraoperative ketamine plus magnesium reduced morphine consumption by almost 50% during the first 12 hours, while other treatments did not.
3	Moon et al. (2020) (39)	Laparoscopic gynecologic surgery	**MG**: $MgSO_4$ (40 mg/kg) **VG**: Vitamin C (50 mg/kg) **M+VG**: $MgSO_4$ (40 mg/kg) + vitamin C (50 mg/kg) (n=33)	**CG**: NS (40 ml)	A combination of $MgSO_4$ and vitamin C showed less cumulative postoperative fentanyl consumption than either V or M alone.
4	Jabbour et al. (2020) (23)	Open bariatric surgery	**M+KG**: $MgSO_4$ IV bolus (50 mg/kg) + ketamine (0.2 mg/kg) followed by continuous infusion of magnesium (8 mg/kg/h) and ketamine (0.15 mg/kg/h) until extubation (n=20) **KG**: Same bolus and infusion of ketamine, together with a bolus and continuous infusion of normal saline (n=20)	**CG**: NS same volume as placebo	A combination of $MgSO_4$ and a ketamine bolus followed by infusion appears to be safe and decreases morphine requirements in the first 24 hours compared with both ketamine alone and placebo.
5	Khaled et al. (2020) (38)	Laparoscopic unilateral ovarian cystectomy	**(M+B) G**: 20 mL bupivacaine 0.5% + 25 mL $MgSO_4$ 10% + 5 mL saline 0.9%. **(B+H) G**: 20 mL bupivacaine 0.5% + 100 mg hydrocortisone in 30 mL NS 0.9% (n=30) **MG**: 25 mL $MgSO_4$ 10% + 100 mg hydrocortisone in 25 mL saline 0.9%	**CG**: 50 ml NS 0.9% only(n=30)	The IP bupivacaine + $MgSO_4$ combination offered better analgesia and reduced postoperative morphine consumption compared to others.
6	Zakaria A. Mustafa et al. (2021) (25)	Laparoscopic sleeve gastrectomy	**(M+L) G**: IP instillation of 15 ml $MgSO_4$ 10% + 15 ml of 0.25% levobupivacaine to a total volume of 30 ml (n=20)	**MG**: IP instillation of 30 ml $MgSO_4$ 10% alone (n=20) **LG**: Instillation of 30 ml of 0.25% levobupivacaine alone (n=20)	The IP combination of levobupivacaine and $MgSO_4$ was more effective than levobupivacaine or magnesium sulfate alone for postoperative pain.
7	Agrawal et al. (2021) (11)	Upper abdominal surgery	**(M+B) G**: Bupivacaine 50mg (10ml of 0.5% Inj Bupivacaine + $MgSO_4$ 500mg (1ml of Inj 50% $MgSO_4$) diluted with NS 9 ml to make total volume of 20 ml (n=25)	**(M+R) G**: Ropivacaine 50 mg (6.7 ml of 0.75% Inj. Ropivacaine) + Inj $MgSO_4$ 500 mg diluted with NS (12.3 ml) making a total 20 ml (n=25)	$MgSO_4$ + ropivacaine showed better postoperative analgesia without side effects and less rescue analgesia through local infiltration.
8	Zahrra et al. (2021) (27)	Laparoscopic cholecystectomy	**M+BG**: (20 ml) 0.25% bupivacaine +(5 ml) (500 mg) $MgSO_4$ (n=20)	**BG**: Bupivacaine 25 ml (0.25%) bupivacaine (n=20) **D+BG**: (n=20) dexamethasone 20 ml 0.25% bupivacaine + 2 ml (8mg) dexamethasone completed to 25 ml with (3 ml) NS	$MgSO_4$ was a better additive than dexamethasone when combined with bupivacaine in IP instillation, as it prolonged the duration of analgesia and reduced postoperative pain scores and nalbuphine consumption.
9	Samir et al. (2023) (40)	Open abdominal surgeries /(QLB)quadratus lumborum block (on each side)	**BMG**: $MgSO_4$ (5 ml of 10%) + 40 ml (20 ml on each side) of 0.25% bupivacaine (n=22)	**B+DG**: 40 ml (20 ml on each side) of 0.25% bupivacaine +2 ml of 8mg dexamethasone (n=22) **BG**:40 ml (20 ml on each side) of 0.25%bupivacaine(n=22)	Improved postoperative pain both at rest and with movement at 30 postoperative hours, also reduced pethidine consumption, and maintained postoperative analgesia for 36 h.
10	Jain et al. (2023) (21)	Abdominal surgeries	**MG**: (opioid-free G): IV $MgSO_4$ (20 mg/kg) + IV lignocaine (2 mg/kg) + IV paracetamol (15 mg/kg) in 100 ml NS. (n=30)	**CG**: (opioid G) IV tramadol (2 mg/kg) in 100 ml NS (n=30)	Preemptive administration of intravenous paracetamol, lignocaine, and magnesium sulfate provided safe, effective, opioid-free, and satisfactory analgesia.
11	Sarenac et al. (2023) (41)	Abdominal Surgery	**MG**: IV $MgSO_4$ 1% (2 g diluted in 100 ml 0.9% NS infused over 20 min before the incision) + IV10% amino acid solution Aminos + 2% lidocaine 100 mg diluted in 100 ml 0.9% NS over 30 min.	**CG**: 100 ml 0.9% NS administered 30 min before incision.	$MgSO_4$ + amino acid showed reduced inflammation and postoperative pain.

IP, Intraperitoneal; IV, Intravenous; NS, Normal Saline; Inj, Injection.

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Ethical statement

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Conflicts of interest

The authors declare no conflicts of interest.

Author contributions

Conceptualization, HM and TAH; methodology, MM and SGH; software, TAH; validation, HAF; formal analysis, AJ and HM; resources, ON and MM; data curation, HAF and MM; writing-original draft preparation, TAH and HM; writing-review and editing, AJ and HM; visualization, MM; supervision, AJ; funding acquisition, TAH. All authors have read and agreed to the published version of the manuscript.

Data availability statement

Data sharing is not applicable.

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