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Research Article
General Adult Cardiac

Magnesium as an adjuvant in perioperative analgesia: data from randomised trials and meta-analyses

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Abstract

Introduction: The role of magnesium in perioperative analgesia has been investigated by an increasing number of authors in recent years. The implementation of ERAS (Enhanced Recovery After Surgery) protocols in clinical practice necessitates the search for new co-analgesics (adjuvants) to include in a multimodal analgesic regimen that would reduce or eliminate the use of opioids. Their side effects, combined with the current opioid epidemic, have catalysed efforts to find new models of balanced anaesthesia and analgesia.

Methodology: This literature review includes and analyses 38 clinical studies examining the analgesic properties of magnesium sulphate ($MgSO_4$) over the past three decades. It covers 32 randomised controlled trials (RCTs), 5 systematic reviews and meta-analyses of RCTs, and one retrospective cohort study. The search was conducted in databases (PubMed, DeepDyve) using the following keywords: anesthesia, analgesic request, consumption, $MgSO_4$, multimodal, opioids, postoperative, pain, recovery, requirements, scores

Results: Approximately 90% of the analysed studies demonstrate a positive effect of perioperative magnesium administration on intraoperative anaesthetic and postoperative analgesic requirements, pain scores, quality of recovery, haemodynamic profile, and other measures, without leading to adverse effects or complications at the dosing regimens used.

Conclusion: Analysis of the data indicates that intravenous magnesium is a potential analgesic with a favourable safety and cost-effectiveness profile and can play an important role as an adjuvant in perioperative analgesia. However, additional large-scale studies with standardised protocols are needed to determine its optimal dosages, as well as the indications and contraindications for its use in clinical anaesthesia practice.

Keywords

Anesthesia, analgesic request, consumption, $MgSO_4$, multimodal, opioids, postoperative, pain, recovery, requirements, scores

Introduction

The role of magnesium in perioperative analgesia has been the subject of increasing investigation in recent years. The introduction of ERAS protocols in clinical practice necessitates searching for new co-analgesics (adjuvants) to be included in a multimodal analgesic regimen that would reduce or eliminate the use of opioid agents. Their side effects, combined with the current opioid overuse epidemic, have catalysed efforts to develop new models of balanced anaesthesia and analgesia. Magnesium sulphate ($MgSO_4$) attenuates pain signals by blocking NMDA (N-methyl-D-aspartate) receptors and calcium channels, which leads to improved perioperative pain management. Additionally, it possesses anti-inflammatory properties that further reduce pain, especially in conditions with an inflammatory component. Multimodal general anaesthesia (also known as balanced anaesthesia) is based on the idea that combining several drugs with different mechanisms of action allows optimal results while minimising side effects. The goal is to achieve an additive or synergistic effect using various drug combinations, which can reduce doses or eliminate opioids and the undesirable effects associated with them, such as hyperalgesia, postoperative nausea and vomiting (PONV), etc.

Methodology

This review includes and analyses 38 clinical studies investigating the analgesic properties of $MgSO_4$ over the last three decades (from 1996 to 2024). The included studies involved adult patients who received intravenous $MgSO_4$ as an adjuvant during anaesthesia, with primary outcomes including postoperative pain, opioid and anaesthetic consumption, time to first analgesic request, quality of recovery, safety, etc. The search was conducted in databases (PubMed, DeepDyve) using the keywords: anesthesia, analgesic request, consumption, $MgSO_4$, multimodal, opioids, postoperative, pain, recovery, requirements, scores.

The potential benefits of $MgSO_4$ as an adjuvant in a multimodal analgesic regimen were evaluated under general inhalational anaesthesia, total intravenous anaesthesia (TIVA), MAC (Monitored Anaesthesia Care), and spinal anaesthesia. These studies were performed in patients undergoing surgical interventions of various types, extents, and complexities across diverse fields, including abdominal surgery (7 studies), gynaecology (10), orthopaedics (6), urology (2), neurosurgery (3), otorhinolaryngology (1), ophthalmic surgery (1), and breast surgery (1), as well as in special patient groups such as obstetrics and transplant surgery (Fig. 1).

In total, 32 RCTs, 5 systematic reviews and meta-analyses of RCTs, and one retrospective cohort study were analysed (Fig. 2).

Results

The most frequently measured outcomes were: intraoperative anaesthetic and opioid consumption, postoperative analgesic requirements and pain scores, time to first analgesic request, quality of recovery (QoR), comfort and quality of sleep, incidence of PONV, recovery time from anaesthesia, shivering, changes in haemodynamic parameters, and potential complications. A few studies additionally assessed the sensory level of the spinal block, time to regression of the sensory block, bispectral index (BIS), and duration of mechanical ventilation (MV).

The first randomised double-blind trial investigating the role of magnesium sulphate in postoperative analgesia was conducted by Tramer M.R. et al. in Geneva University Hospital, including 42 patients undergoing elective hysterectomy under general anaesthesia. They found that total morphine consumption over 48 hours was 30% lower in the magnesium group compared to the control group, while postoperative pain scores were similar in both groups. This was the first clinical study to demonstrate that perioperative $MgSO_4$ administration is associated with lower analgesic requirements, less discomfort, and better sleep quality in the postoperative period, without unwanted effects. This investigation spurred dozens of subsequent studies examining the potential of magnesium as an adjuvant in perioperative analgesia [1].

For clarity, the results below are organised by the type of outcome measured:

- **Intraoperative opioid and anaesthetic requirements:** Almost half of the studies reported a reduction in intraoperative opioid and anaesthetic requirements with magnesium [2–13].

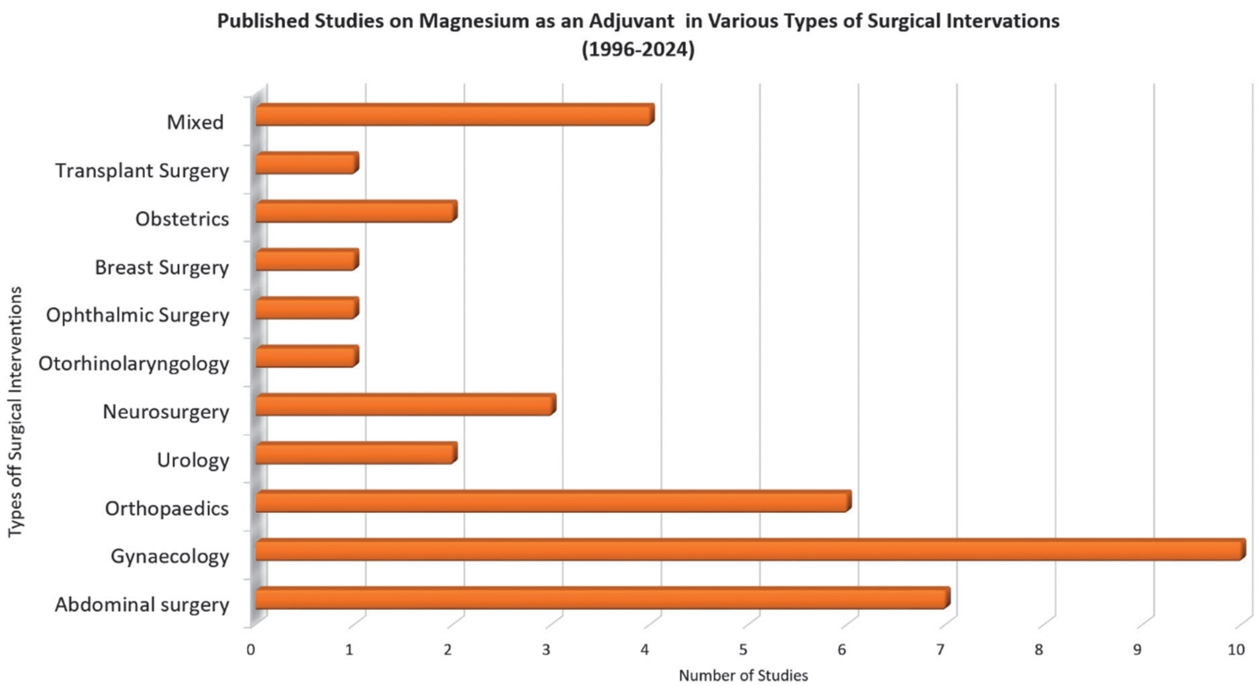

Figure 1.

- **Postoperative opioid consumption and pain scores:** The majority of studies demonstrated a reduction in postoperative opioid consumption [1–3, 5, 7–8, 10–25] and lower pain scores [2–3, 8, 10–14, 16–20, 22, 24–29] in magnesium-treated patients.
- **Timing of analgesia and rescue analgesics:** Some studies recorded a longer time to first analgesic request [12–13, 18, 21, 23, 27] and a reduced frequency of "rescue" analgesia in the magnesium group [26].
- **Postoperative nausea and vomiting (PONV):** In terms of PONV incidence, some studies found similar outcomes between magnesium and control groups [20, 22, 30], while others reported fewer PONV cases in the magnesium groups [3, 13].
- **Sleep quality and psychological outcomes:** Several RCTs noted that preoperative $MgSO_4$ administration led to better quality of sleep and higher comfort levels postoperatively [1, 10, 14, 31]. One study observed that combining lidocaine with magnesium resulted in lower anxiety and depression, greater patient satisfaction, and improved quality of life [27].
- **Quality of recovery:** Xu H. et al. found higher QoR (Quality of Recovery) scores on the first postoperative day in the magnesium group compared to controls, primarily due to improvements in pain, emotional state, and comfort [13].
- **β-endorphin levels:** Haryalchi K. et al. observed lower serum levels of β-endorphins (natural ‚opioids') at the end of surgery in the magnesium group compared to baseline ($p = 0.04$), an effect not seen in the control group [24].
- **Haemodynamic effects:** Regarding haemodynamics, magnesium improved haemodynamic control [16], reduced mean arterial pressure (MAP) after intubation and in the early postoperative period [17], and suppressed the pressor response to surgical stimuli [9], during skin incision and anaesthesia [12]. In other studies, haemodynamic parameters were similar between magnesium and control groups [8, 19, 20, 26].
- **Recovery from anaesthesia:** The effect of magnesium on recovery from anaesthesia varied. Some reported no effect [16]; one noted prolonged awakening with a higher dose of magnesium [5]; others found no difference in time to awakening and extubation [11, 32]; and one observed a longer stay in the PACU (Post-Anaesthesia Care Unit) for the magnesium group [32].
- **Postoperative shivering:** Patients who received magnesium preoperatively experienced a lower incidence of postoperative shivering in some studies [17, 33, 34], while other studies found no difference between groups [20].
- **Other findings:** Gucyetmez B. et al. found a shorter duration of mechanical ventilation after liver transplantation in the magnesium group compared to controls [23]. Toker M.K. et al. reported that BIS values were significantly higher in control groups than in magnesium groups ($p < 0.001$), indicating deeper anaesthesia in magnesium-treated patients [28]. Kahraman F. et al. observed a longer regression time of the sensory block in spinal anaesthesia for abdominal hysterectomy with magnesium use [29].

In terms of safety and complications, most studies did not find significant differences between magnesium and control groups. Haemodynamic side effects were comparable, for instance showing similar rates of hypotension (with no bradycardia) [25]. Some differences noted include a slightly longer PACU stay [32] and lower Aldrete scores

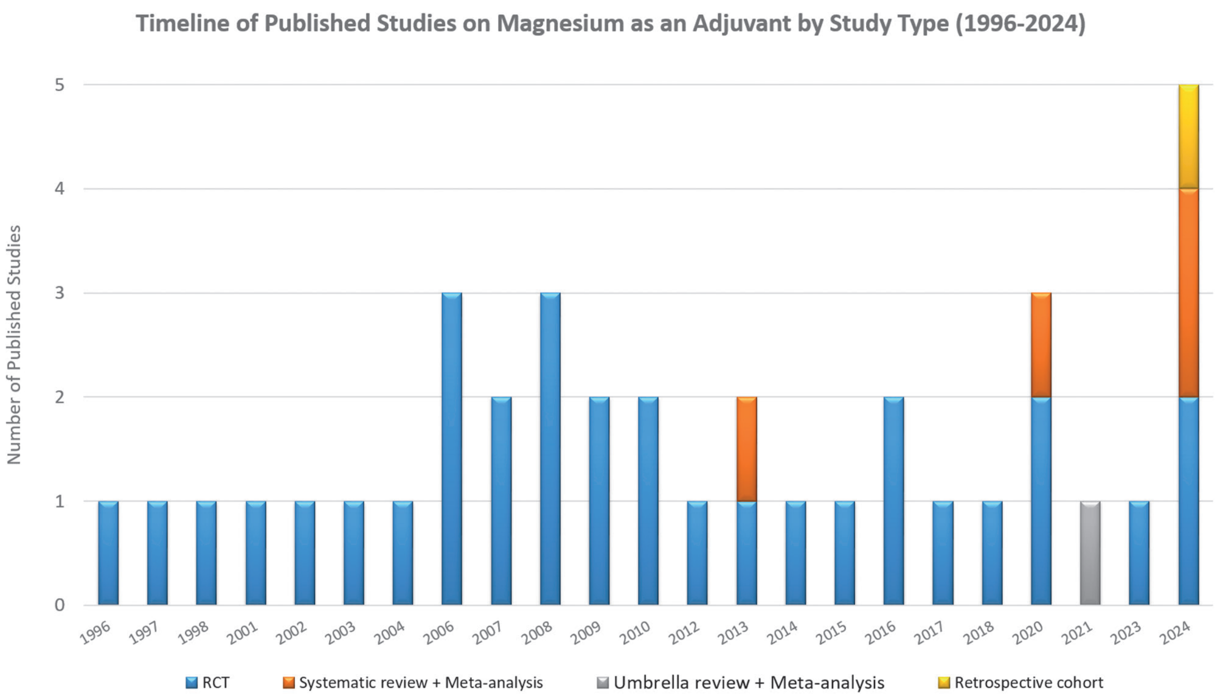

Figure 2.

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with a higher incidence of postoperative intubation in the magnesium groups [11], but there were no reports of serious adverse events. Notably, the incidence of intraoperative awareness in patients under general anaesthesia for Caesarean section was similar between groups [28] (Fig. 3).

It should be mentioned that a subset of RCTs failed to confirm the hypothesised analgesia-enhancing effect of magnesium. Only one year after the first positive RCT by Tramer et al., Wilder-Smith C.H. et al. concluded that a perioperative magnesium infusion did not improve postoperative analgesia at the doses tested – in fact, a transient reduction in the efficacy of postoperative pain relief was observed in the magnesium group. That study, conducted in 20 patients undergoing hysterectomy under general anaesthesia, found no analgesic benefit from magnesium [35]. Bhatia A. et al. reported in their RCT of 50 patients that the role of $MgSO_4$ as an adjunct analgesic in open cholecystectomy remains unclear and warrants further research. Magnesium did not produce a significant analgesic effect, though it did improve patient comfort without causing additional side effects [31]. Similarly, Frassanito L. et al. concluded that intravenous perioperative $MgSO_4$ administration did not influence postoperative pain control or analgesic consumption after total knee arthroplasty under spinal anaesthesia [30]. In a contemporary retrospective cohort study of 182 patients who underwent robot-assisted radical prostatectomy (RARP) with intraoperative $MgSO_4$, Salevitz D. et al. found that magnesium was not associated with demonstrably improved pain control in urological surgery, and they noted that prospective studies are needed to confirm these findings [36].

Some studies have compared different dosing regimens of $MgSO_4$. Seyhan T.O. et al. evaluated three dosing protocols in 80 patients undergoing gynaecological surgery under general anaesthesia. All patients received an initial 40 mg/kg of $MgSO_4$ before induction. Subsequently, one subgroup was infused with placebo, another with $MgSO_4$ at 10 mg/kg/h, and a third with $MgSO_4$ at 20 mg/kg/h for 4 hours. The authors concluded that in their study the lower infusion dose (10 mg/kg/h) struck the optimal balance, significantly reducing propofol and atracurium requirements without prolonging anaesthesia recovery time [5]. Khafagy H.F. et al. similarly examined two $MgSO_4$ dosing regimens in an RCT with 60 patients undergoing hernioplasty. Magnesium groups received a 50 mg/kg $MgSO_4$ bolus followed by an infusion of either 8 mg/kg/h (Mg_1) or 16 mg/kg/h (Mg_2), while the control group - an equal volume of saline. They found that a regimen of 50 mg/kg bolus + 8 mg/kg/h infusion of $MgSO_4$ significantly reduced intraoperative propofol and vecuronium requirements as well as postoperative fentanyl consumption. Doubling the infusion rate to 16 mg/kg/h provided minimal additional benefit, at the expense of haemodynamic side effects and prolonged recovery time [7].

Other trials have directly compared the analgesic effect of magnesium to that of established adjuvant analgesics. Saadawy I.M. et al. conducted the first study directly comparing magnesium with another well-established analgesic adjuvant, lidocaine, and found their efficacy to be similar. They demonstrated that intravenous lidocaine or magnesium administration improved postoperative analgesia and reduced intra- and postoperative opioid requirements in patients undergoing laparoscopic cholecystectomy [10]. Abdel Rady

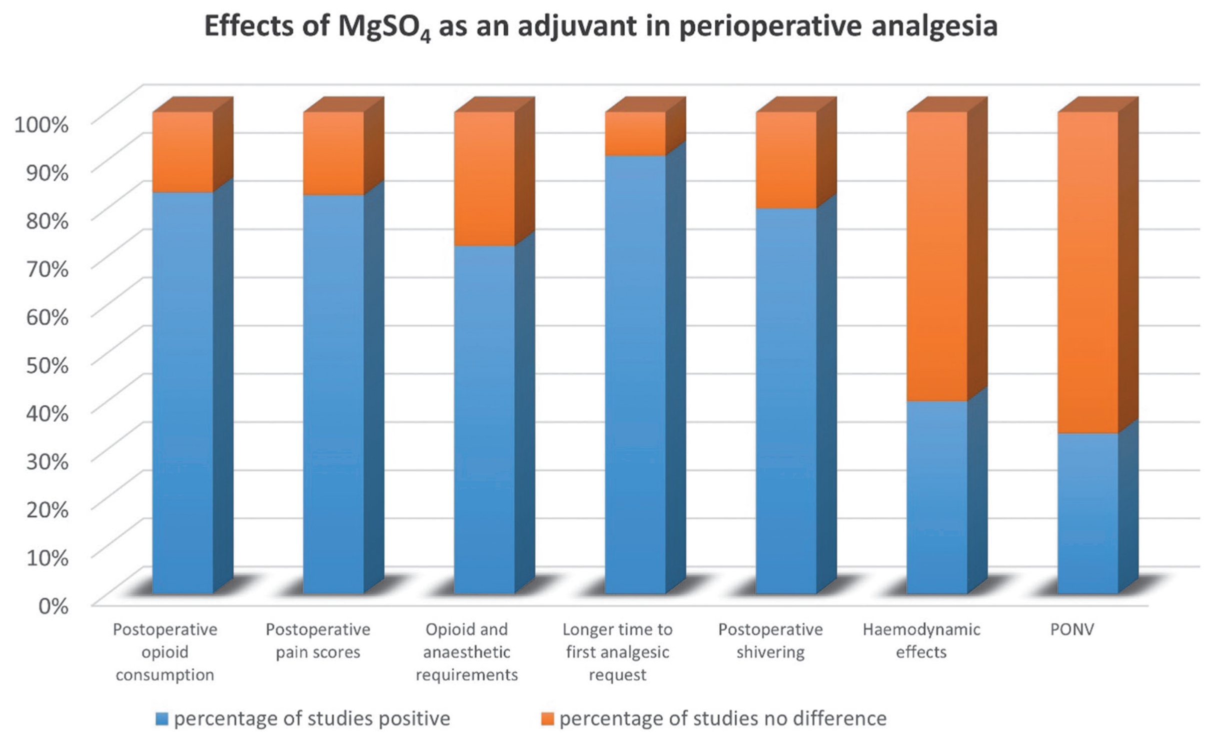

Figure 3.

M.M. et al. compared a single-bolus dose of $MgSO_4$ versus a single-bolus dose of lidocaine on postoperative pain, emotional state, and quality of life in patients undergoing spinal stabilisation surgery. In this RCT, 120 patients were randomised into four groups: group L (4 mg/kg lidocaine), group M (30 mg/kg $MgSO_4$), group L+M (both lidocaine and $MgSO_4$ at those doses), and group C (saline placebo). The study showed a synergistic effect from the combination of lidocaine and $MgSO_4$, leading to reduced analgesic consumption, lower depression and anxiety scores, and improved quality of life for up to 3 months after surgery [27]. Sousa A.M. et al. performed an RCT comparing the analgesic effect of IV $MgSO_4$ infusion to that of ketorolac during laparoscopic gynaecologic surgery. They found that $MgSO_4$ improved postoperative pain control with an effect similar to 30 mg of ketorolac given at the start of the operation. The implication is that magnesium may substitute for or complement NSAIDs (non-steroidal anti-inflammatory drugs) in postoperative pain management protocols [22].

In summary of the recent evidence, attention should be drawn to the systematic reviews and meta-analyses of RCTs published from 2013 onward. Murphy J.D. et al. published a systematic review and meta-analysis on "the analgesic efficacy of continuous intravenous magnesium infusion as an adjuvant to morphine in postoperative analgesia." They analysed 22 clinical trials comprising a total of 1,177 patients (599 magnesium, 578 control). The results showed a significant reduction in morphine use among patients receiving magnesium, with no differences in side effects such as PONV. Pain scores on the visual analogue scale (VAS) at 4–6 hours postoperatively were substantially lower in the magnesium groups, although by 20–24 hours post-op this difference was no longer observed. The authors concluded that perioperative magnesium can be a useful adjuvant for postoperative pain control, providing analgesia via a mechanism distinct from opioids, and could be a valuable addition to multimodal analgesic regimens [37].

Ng K.T. et al. conducted a systematic review and meta-analysis to investigate the effect of intravenous magnesium on postoperative morphine consumption in the first 24 hours after non-cardiac surgery. They included 51 studies (n = 3311 patients) in a quantitative meta-analysis. The meta-analysis found that, compared to placebo: (1) postoperative morphine consumption was significantly reduced in magnesium-treated groups ($p < 0.001$); (2) time to first analgesic request was substantially prolonged ($p < 0.001$); and (3) the incidence of shivering was markedly lower ($p < 0.001$). There were no significant differences in postoperative pain scores within the first 24 hours ($p = 0.13$), incidence of bradycardia ($p = 0.80$), or incidence of PONV ($p = 0.49$). The cumulative evidence from trials on magnesium's effect in reducing postoperative morphine consumption was deemed convincing. However, the authors noted that many included studies were of low methodological quality and exhibited substantial heterogeneity. They concluded that magnesium is likely an effective component of multimodal analgesia (by reducing opioid requirements), but further large, high-quality studies are needed to confirm this effect and to determine the optimal dosing regimen [33].

Choi G.J. et al. carried out an umbrella review of systematic reviews and meta-analyses (17) of RCTs (258), along with an updated meta-analysis incorporating trial sequential analysis (TSA). For this updated analysis, data from 109 adult RCTs and 13 paediatric RCTs were included. TSA was used to assess whether the existing evidence is sufficient. The results showed that magnesium significantly lowered pain scores (both at rest and during movement) within the first 24 hours post-surgery, and markedly reduced postoperative analgesic consumption. The TSA indicated that the existing evidence was sufficiently convincing. Magnesium also extended the time to first analgesic request, indicating a longer-lasting analgesic effect. According to the GRADE system (Grading of Recommendations, Assessment, Development and Evaluation), the quality of evidence ranged from low to moderate. The updated meta-analysis confirmed the positive effect of magnesium on postoperative analgesia. The TSA suggested that current evidence is adequate, but additional research is needed for confirmation. Notably, this was the first umbrella review to systematically analyze the efficacy of magnesium as an adjuvant in postoperative analgesia [38].

Avci Y. et al. published a systematic review and meta-analysis of RCTs entitled "Unravelling the analgesic effects of perioperative magnesium in general abdominal surgery." They included 31 RCTs with a total of 1,762 patients (800 magnesium, 802 control). The results demonstrated: (1) significantly lower pain scores in the magnesium group in both the early postoperative period (up to 6 hours, $p < 0.0001$) and the late postoperative period (up to 24 hours, $p = 0.006$); (2) a substantial reduction in opioid consumption (in morphine milligram equivalents, MME) in the magnesium group in both the early ($p = 0.0002$) and late ($p = 0.0005$) postoperative periods; (3) a markedly prolonged time to first analgesic request in the magnesium group compared to controls ($p = 0.005$); and (4) no significant differences between magnesium and control groups in intra- or postoperative complications such as hypotension, bradycardia, or PONV [34].

In the same year, Hung K.C. et al. presented a meta-analysis of RCTs on the impact of IV $MgSO_4$ infusion on postoperative quality of recovery, assessed via a QoR questionnaire encompassing various recovery domains. Seven RCTs with a total of 622 surgical patients were included. The meta-analysis found that $MgSO_4$, compared to placebo: (1) significantly improved the global QoR score on the first postoperative day ($p < 0.00001$); (2) improved specific QoR domains, with a strong effect on pain ($p < 0.00001$) and physical comfort ($p < 0.0001$), a moderate effect on emotional state ($p = 0.002$), and a mild effect on physical independence ($p < 0.00001$) and psychological support ($p < 0.0001$); (3) reduced intraoperative opioid consumption ($p < 0.0001$); (4) reduced postoperative pain intensity; and (5) lowered the incidence of PONV ($p = 0.008$). There were (6) no differences in extubation times, and (7) only a slightly prolonged PACU stay in the magnesium group. These findings highlight the potential of $MgSO_4$ as a valuable adjuvant for multimodal analgesia and enhanced recovery after surgery [32]. Table 1 summarizes the evidence from the clinical studies.

Discussion

The RCTs in this review were conducted under general inhalational anaesthesia, TIVA, MAC, and spinal anaesthesia in patients undergoing a wide range of surgical procedures (spanning abdominal surgery, gynaecology, orthopaedics, urology, neurosurgery, otorhinolaryngology, ophthalmic and breast surgery), including special populations such as obstetric and transplant patients. Most of the RCTs clearly demonstrate that $MgSO_4$ reduces intraoperative opioid and anaesthetic requirements [2–13], decreases postoperative opioid consumption [1–3, 5, 7–8, 10–25], lowers pain scores [2–3, 8, 10–14, 16–20, 22, 24–29], and extends the time until the first request for analgesia [12–13, 18, 21, 23, 27]. Some trials also report a lower incidence of shivering [17, 33, 34] and PONV [3, 13], better postoperative sleep quality and comfort [1, 10, 14, 27, 31], improved recovery profiles [13], a more favourable haemodynamic profile [9, 12, 16, 17], shorter duration of mechanical ventilation [23], prolonged regression of sensory block in spinal anaesthesia [29], lower postoperative β-endorphin levels [24], and lower BIS values indicating adequate anaesthetic depth [28]. Importantly, with the $MgSO_4$ analgesic regimens used, no serious complications or prolonged recoveries from anaesthesia were observed [11, 16, 32].

Several studies investigated different $MgSO_4$ dosing regimens [5, 7], and others compared magnesium's analgesic effect with that of other adjuvants such as lidocaine and ketorolac [10, 22, 27]. The findings from five me-

Table 1. Summary of clinical studies on magnesium sulfate ($MgSO_4$) as an adjuvant in anesthesia and analgesia.

Author / Year	Study type	Surgery / Anaesthesia / Population	Main finding	Effect of $MgSO_4$	Quality / Level of Evidence (GRADE / OCEBM)	Strength of Recommendation (GRADE)	Strength of Recommendation (SORT)
Tramer 1996	RCT	Elective hysterectomia GA (n=42)	~30% less morphine over 48h; better sleep; no major AEs	Positive	Moderate / 1	Weak/Conditional	B
Wilder-Smith 1997	RCT	Hysterectomy GA (n=24)	No improvement; transient reduction in analgesia efficacy	Negative	Low/ 2	Weak	B
Koinig 1998	RCT	Arthroscopy TIVA (n=46)	Reduced intra- and postoperative analgesic requirements	Positive	Moderate / 1	Weak/Conditional	B
Schulz-Stübner 2001	RCT	Vitrectomy TIVA (n=50)	Magnesium reduced anaesthetic requirements	Positive	Moderate / 1	Weak/Conditional	B
Choi 2002	RCT	Elective hysterectomia Propofol–N2O anesthesia (n=74)	Reduced propofol infusion; BIS supported adequate depth	Positive	Moderate / 1	Weak/Conditional	B
Levaux 2003	RCT	Lumbar orthopedic surgery GA (n=24)	Improved pain relief and patient comfort	Positive	Moderate / 1	Weak/Conditional	B
Bhatia 2004	RCT	Open cholecystectomy GA (n=50)	No significant analgesic effect; improved comfort	Neutral	Moderate / 1	Weak/Conditional	B
Gupta 2006	RCT	Spinal surgery TIVA (n=50)	Reduced anesthetic requirements	Positive	Moderate / 1	Weak/Conditional	B
Tauzin-Fin 2006	RCT	Radical prostatectomy GA (n=30)	↓ tramadol requirements	Positive	Moderate / 1	Weak/Conditional	B
Seyhan 2006	RCT	Gynecologic Surgery TIVA (n=80)	10 mg/kg/h optimal; higher dose prolonged awakening	Positive	Moderate / 1	Weak/Conditional	B
Khafagy 2007	RCT	Hernioplasty TIVA (n=60)	50 mg/kg + 8 mg/kg/h reduced requirements; 16 mg/kg/h added side-effects	Positive	Moderate / 1	Weak/Conditional	B
Cizmeci 2007	RCT	Septorhinoplasty TIVA (n=60)	Improved analgesia with Mg	Positive	Moderate / 1	Weak/Conditional	B
Oguzhan 2008	RCT	Lumbar disc surgery GA (n=50)	↓ sevoflurane and perioperative opioids	Positive	Moderate / 1	Weak/Conditional	B
Ryu 2008	RCT	Gynecology TIVA (n=50)	↓ anesthetic and analgesic requirements	Positive	Moderate / 1	Weak/Conditional	B
Benhaj Amor 2008	RCT	Abdominal surgery GA (n=48)	Improved postoperative pain control	Positive	Moderate / 1	Weak/Conditional	B
Kaya 2009	RCT	Remifentanil-based anesthesia (n=40)	↓ postoperative morphine requirement	Positive	Moderate / 1	Weak/Conditional	B
Lee 2009	RCT	Cesarean section GA (n=72)	Beneficial adjuvant effects	Positive	Moderate / 1	Weak/Conditional	B
Saadawy 2010	RCT (head-to-head)	Laparoscopic cholecystectomy GA (n=120)	Mg ≈ Lidocaine efficacy	Positive	Moderate / 1	Weak/Conditional	B

Author / Year	Study type	Surgery / Anaesthesia / Population	Main finding	Effect of $MgSO_4$	Quality / Level of Evidence (GRADE / OCEBM)	Strength of Recommendation (GRADE)	Strength of Recommendation (SORT)
Hwang 2010	RCT	Hip replacement SA (n=40)	Improved analgesia	Positive	Moderate / 1	Weak/Conditional	B
Olgun 2012	RCT	Laparoscopic cholecystectomy GA (n=60)	↓ desflurane requirement; better recovery	Positive	Moderate / 1	Weak/Conditional	B
Kumar 2013	RCT	Abdominal surgery SA (n=60)	↓ postoperative pain	Positive	Moderate / 1	Weak/Conditional	B
Murphy 2013	Systematic review + Meta-analysis	Various 22 RCTs, n=1177	↓ morphine, ↓ pain at 4–6h; no AEs	Positive	High / 1	Strong	A
Kahraman 2014	RCT	Abdominal hysterectomy SA (n=40)	Longer sensory block regression; ↓ pain	Positive	Moderate / 1	Weak/Conditional	B
Frassanito 2015	RCT	Total knee arthroplasty SA (n=40)	No difference vs control	Neutral	Moderate / 1	Weak/Conditional	B
Sousa 2016	RCT	Laparoscopic gynecologic surgery GA (n=60)	Analgesic effect similar to 30 mg ketorolac	Positive	Moderate / 1	Weak/Conditional	B
Gucyetmez 2016	RCT	Liver transplantation GA (n=70)	↓ tramadol need; shorter ventilation	Positive	Moderate / 1	Weak/Conditional	B
Haryalchi 2017	RCT	Abdominal hysterectomy GA (n=40)	↓ serum β-endorphin; improved pain perception	Positive	Moderate / 1	Weak/Conditional	B
Toker 2018	RCT	C-section GA (n=100)	Lower BIS vs control; Lower VAS score	Positive	Moderate / 1	Weak/Conditional	B
Tsaousi 2020	RCT	Lumbar laminectomy GA (n=74)	Reduced pain/opioids needs vs placebo	Positive	Moderate / 1	Weak/Conditional	B
Gao 2020	RCT	Hysteroscopy MAC (n=70)	Antinociceptive effect; improved comfort	Positive	Moderate / 1	Weak/Conditional	B
Ng 2020	Systematic review + Meta-analysis	Non-cardiac surgery 51 RCTs, n=3311	↓ 24h morphine, ↑ time to first analgesic, ↓ shivering	Positive	High / 1	Strong	A
Choi 2021	Umbrella review + Meta-analysis	Various 258 RCTs TSA-109 RCTs	↓ pain; ↓ analgesic use; TSA-sufficient evidence	Positive	High / 1	Strong	A
Hatice Akbudak 2023	RCT	Mastectomy GA (n=68)	↓ postoperative pain	Positive	Moderate / 1	Weak/Conditional	B
Avci 2024	Systematic review + Meta-analysis	Abdominal surgery 31 RCTs, n=1762	↓ pain, ↓ opioids; ↑ time to first analgesic; no ↑ AEs	Positive	High / 1	Strong	A
Hung 2024	Meta-analysis	Various surgeries 7 RCTs, n=622	Improved global QoR; ↓ intraop. opioids; ↓ PONV	Positive	High / 1	Strong	A
Xu 2024	RCT	Total knee arthroplasty TIVA (n=148)	Higher QoR; ↓ pain; ↓ intraop. opioids	Positive	Moderate / 1	Weak/Conditional	B
Abdel Rady 2024	RCT	Spinal surgery GA (n=120)	Mg+Lidocaine synergy; ↓ analgesics] ↓ anxiety; better QoL up to 3 months	Positive	Moderate / 1	Weak/Conditional	B
Salevitz 2024	Retrospective cohort	Urologic surgery(RARP) GA (n=182)	No association with improved pain control	Neutral	Low / 2	Weak	B

Notes: RCT - Randomized Controlled Trial; **GA** - General Anaesthesia; **SA** - Spinal Anaesthesia; **TIVA** - Total Intravenous Anaesthesia; **MAC** - Monitored Anaesthesia Care; **QoR** - Quality of Recovery; **QoL** - Quality of Life; **AEs** - Adverse Events; **BIS** - Bispectral Index; **VAS** - Visual Analogue Scale; **PONV** - Postoperative Nausea and Vomiting; **TSA** - Trial Sequential Analysis; **GRADE** - Grading of Recommendations Assessment, Development and Evaluation; **OCEBM** - Oxford Centre for Evidence-Based Medicine Levels of Evidence; **SORT** - Strength of Recommendation Taxonomy; **RARP** - Robot-Assisted Radical Prostatectomy.

ta-analyses underscore the value of $MgSO_4$ as a useful adjuvant in multimodal analgesia and in improving recovery outcomes [32–34, 37–38]. However, it must be acknowledged that not all studies demonstrated significant analgesic or opioid-sparing effects from magnesium [30–31, 35–36] (Fig. 4). These discrepancies highlight the need for further research to clarify magnesium's role and efficacy in various clinical contexts.

Various dosing protocols (~30–50 mg/kg bolus and 8–20 mg/kg/h infusion) have been employed across the studies. Some evidence suggests that increasing the dose of magnesium beyond a certain point yields minimal additional benefit but introduces haemodynamic side effects and delays recovery from anaesthesia [5, 7]. When incorporating magnesium into a multimodal analgesic regimen, its potentiating effect on neuromuscular blockade must be

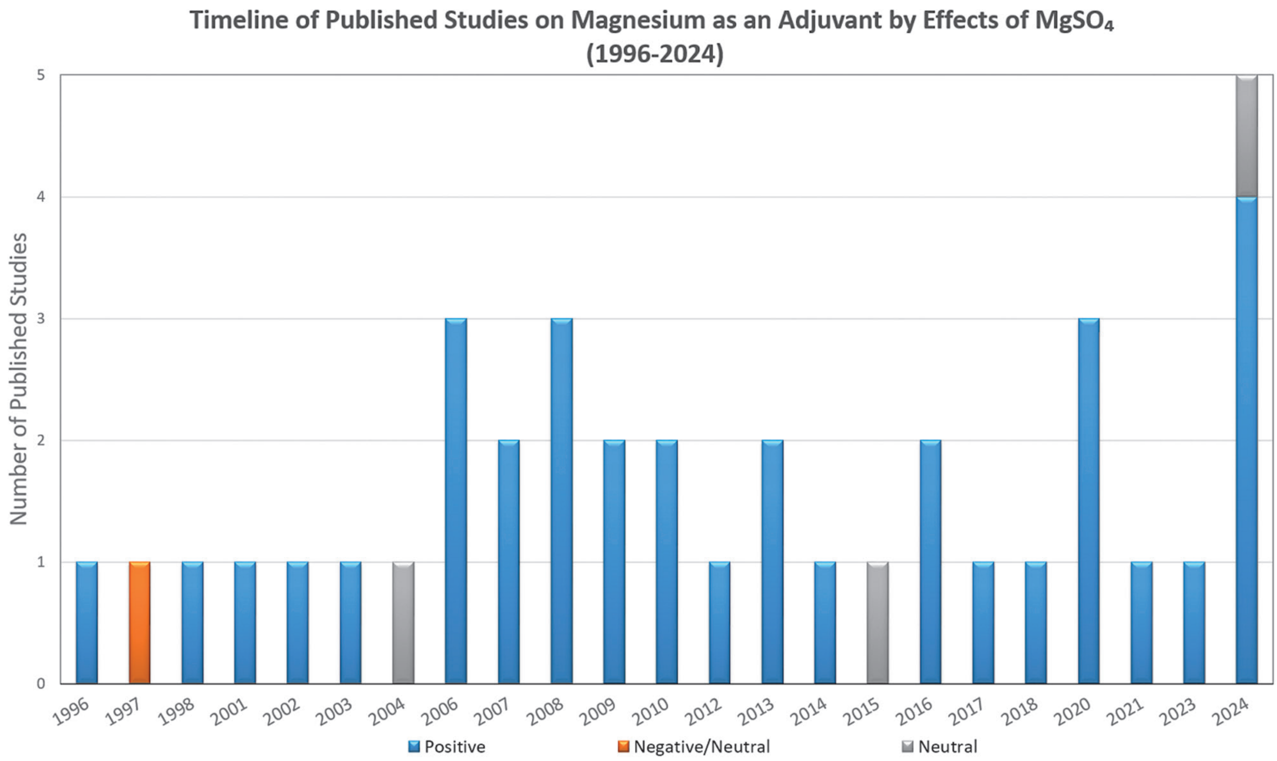

Figure 4.

taken into account. Therefore, dose adjustments and monitoring of neuromuscular transmission are imperative to avoid potential complications and ensure timely recovery.

Conclusion

Analysis of the data indicates that intravenous magnesium is a promising analgesic with a favourable safety profile and cost-effectiveness, and it can play an important role as an adjuvant in perioperative pain management. Included in multimodal analgesic regimens, magnesium has the potential to reduce opioid and anaesthetic consumption, lower pain scores and analgesic requirements, and improve postoperative comfort and patient satisfaction. The existing evidence base is quite convincing.

However, further large-scale studies with standardised protocols are needed to determine the optimal dosing, administration methods, and timing, as well as to define the indications and contraindications for magnesium use in clinical anaesthesia practice. It is essential to conduct more in-depth evaluations of safety and to investigate various dosing regimens across different types of surgical procedures. To ensure the optimal utilisation of $MgSO_4$'s advantages as an anaesthetic adjuvant and to minimise the risk of potential complications, its administration should be accompanied by strict monitoring of anaesthesia depth (e.g. BIS) and neuromuscular transmission (NMT).

Additional information

Conflict of interest

The author have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

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Author contributions

The author solely contributed to this work.

Data availability

All of the data that support the findings of this study are available in the main text or Supplementary Information.

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