

Efficacy of magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean sections: A systematic review & meta-analysis

Hubba Ahmed¹, Alina Mahmood², Hanya Javaid³, Tooba Usman⁴, Umama Masnoon⁵, Maryam Younus⁶

Abstract

Objective: To assess the effectiveness and safety of magnesium sulphate as an adjuvant to hyperbaric bupivacaine in spinal anaesthesia for patients undergoing caesarean section, with special focus on the duration of action, postoperative analgesia, maternal and neonatal outcomes.

Method: The systematic review and meta-analysis was conducted from June to August 2025, and comprised literature search on PubMed, Cochrane Library and Google Scholar databases along with manual search for randomised controlled trials comparing the use of magnesium sulphate as an adjuvant to intrathecal hyperbaric bupivacaine, regardless of dose, with intrathecal hyperbaric bupivacaine with or without placebo in cases of caesarean section. Standardized forms were used to extract data from the trials. Risk of bias assessment was done using the Cochrane RoB tool 2.0.

Results: Of the 12 studies short-listed, 4(33.3%) were subjected to meta-analysis. Intrathecal magnesium sulphate significantly prolonged both sensory and motor blockade (pooled mean difference of 2.75 minutes; 95% CI: 0.44-5.06; $p=0.0001$ and 1.14 minutes; 95% CI: 0.6-1.92; $p=0.0001$ respectively, compared with controls. Nausea and vomiting among pregnant women did not show a significant difference between the two groups (odds ratio [OR]=0.79; 95% confidence interval [CI]: 0.30 to 2.10; $p=0.072$). No adverse clinical effects were noted. Inconsistencies across the studies were reported as follows: sensory blockage I²=97.7%, duration of motor block I²=91.6%, time to rescue analgesia I²=97.4%, vomiting or nausea I²=50.5%, postoperative shivering I²=73.8%, and APGAR scores I²=61.4%. All the parameters showed substantial heterogeneity patterns with statistically significant $p<0.05$.

Conclusions: The use of intrathecal magnesium sulphate could enhance the duration of motor block and delay the need for rescue analgesia in caesarean section cases. It appeared to be safe and well-tolerated at dose up to 75mg, while higher doses could be associated with maternal side-effects.

Keywords: Magnesium sulphate, Hyperbaric bupivacaine, Intrathecal, Caesarean section, Spinal anaesthesia, Review.

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Introduction

Caesarean section (CS) is stated to be the most common surgical intervention performed on obstetric patients. Based on the patients' indications, regional anaesthesia (RA) or general anaesthesia (GA) techniques can be applied, with spinal anaesthesia (SA) being the standard method of providing anaesthesia.^{1,2} Hyperbaric bupivacaine (0.5%) is an amide-type local anaesthetic, considered the gold standard to be used intrathecally in these patients, but its associated challenges include hypotension, nausea, limited postoperative analgesia, and a short duration of action. To cope with these problems, various additional drugs are explored to be used as adjuvants, including opioids, ketamine, benzodiazepines, neostigmine and

dexmedetomidine.^{3,4} Magnesium, known to block N-methyl-aspartate, is an ion that blocks calcium's entry into the cells, stopping central pain sensitisation.⁵ It has been administered through various routes, like oral, intramuscular and intravenous (IV) use for RA, with local anaesthetic agents. It was first used in 1906 intrathecally in humans, and since then it has been widely studied as an adjuvant to potentiate SA.⁶

A lot of randomised controlled trials (RCTs)^{5,7-13} have been conducted to assess the effects of magnesium when administered with bupivacaine in the obstetric population, but inconsistent results have been reported regarding maternal side-effects and neonatal safety. Furthermore, no consensus exists regarding the optimal dose or the safety profile of intrathecal magnesium sulphate in CS.

Given the widespread use of SA in the obstetric population and the growing body of literature on magnesium as an adjuvant, a systematic synthesis of current evidence is warranted. The current review was planned to assess the efficacy and safety of intrathecal magnesium sulphate as an adjuvant to bupivacaine in CS, with particular focus on the duration of sensory and motor blockade, time to rescue

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analgesia, and the incidence of maternal and neonatal complications.

Materials and Methods

The systematic review and meta-analysis was conducted from June to August 2025, and comprised literature search on PubMed, Cochrane Library and Google Scholar databases along with manual search for RCTs comparing the use of magnesium sulphate as an adjuvant to intrathecal hyperbaric bupivacaine, regardless of dose, with intrathecal hyperbaric bupivacaine with or without placebo in CS cases. The review was conducted in line with Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA)¹⁴ guidelines, and the protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO)¹⁵ under registration number: CRD420251086377. Since the review comprised published studies, therefore, approval from ethics review board was not required.

All RCTs assessing the efficacy of magnesium sulphate when given intrathecally as an adjuvant to hyperbaric bupivacaine in obstetric patients planned for CS under SA were enrolled. Studies were eligible if they reported on at least one of the following outcomes: duration of sensory or motor blockade, time to first rescue analgesia, maternal side-effects or neonatal outcomes. Studies were excluded if they were not RCTs, if magnesium was not administered intrathecally, or if the surgical population included non-obstetric patients undergoing any other surgeries.

A comprehensive data search was performed across the PubMed and Cochrane databases using a combination of medical subject heading (MeSH) terms and free-text key words including, "magnesium sulphate", "bupivacaine", "intrathecal", "caesarean section", "c-section", "spinal anaesthesia", "intrathecal anaesthesia", "randomized controlled trials", and "RCTs" (Table 1). Google Scholar was also used during the search, but it had its limitations due to a lack of advanced filtering. Moreover, manual search was done to explore references in relevant articles and grey literature. No language restriction was employed.

The RCTs initially identified were uploaded to Rayyan software to check for duplication. Subsequently, independent screening of titles and abstracts was done by two reviewers, followed by full-text screening of probable studies. Any disagreement was settled and decided upon by consulting a third reviewer. Standardised forms were used to extract data from the enrolled studies, including information on study design, sample size, age range, body mass index (BMI), American Society of Anaesthesiologists (ASA) status, inclusion and exclusion criteria, the

Table-1: Search strategy for different databases.

Databases	Search Terms	Results (total = n)
PubMed	("Magnesium Sulphate"[MeSH] OR "magnesium sulfate") AND "bupivacaine" AND "intrathecal" AND "cesarean section" AND "spinal anesthesia"	6
Cochrane Library	Magnesium sulphate AND bupivacaine AND intrathecal AND cesarean section AND spinal anesthesia	38
Google Scholar	Magnesium sulphate + bupivacaine + intrathecal + cesarean section + spinal anesthesia	18, 900

interventions performed, and outcomes, including duration of sensory and motor block, time for rescue analgesia, maternal complications and neonatal outcome. The risk of bias (RoB) assessment was done by two reviewers independently using the Cochrane RoB tool 2.0 across its five domains; the randomisation process, deviation from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The domains were rated as 'low risk', 'some concerns', or 'high risk'.

Results

Of the 18,944 RCTs initially identified, 18,900(99.76%) were from Google Scholar, 38(0.2%) were from Cochrane Library and 06(0.03%) were from PubMed (Table 1). Of them, 12(0.06%) were uploaded to Rayyan software which deleted 4(33.3%) duplicates. The remaining 8(66.6%) were screened after which 4(50%) were subjected to meta-analysis (Figure 1).^{9,10,12,13}

Of the studies analysed, 3(75%) were labelled as having a low risk of bias without any dispute between the reviewers.

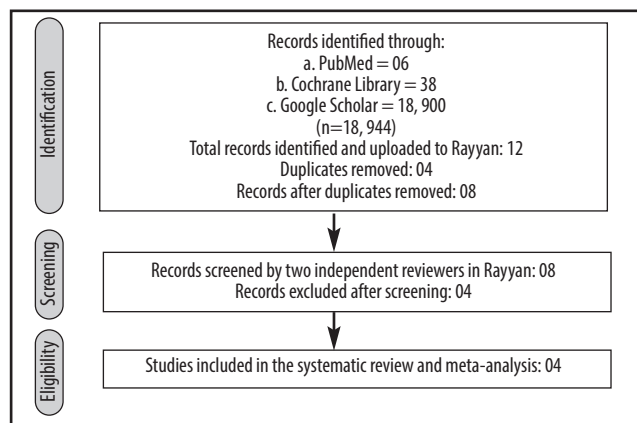


Figure-1: The study flowchart.

Table-2: Characteristics of the studies analysed.

Citations	Study Type	Sample Size	Blinding	Randomization
Jabalamali et al. ⁹	RCT	132	Yes (double blinded)	Yes
Tuteja et al. ¹⁰	RCT	105	Yes (double blinded)	Yes
Banihashem et al. ¹²	RCT	80	Yes (double blinded)	Yes
Hejazi et al. ¹³	RCT	45	Yes (single blinded)	Yes

RCT: Randomised controlled trials.

However, 1(25%) study was labelled as having some concerns due to the presence of performance bias by one reviewer, while the other reviewer considered it to have a low risk. Although the blinding status of the one performing the intervention was not clear, the third reviewer labelled it as having low risk because of the objective nature of the outcomes unlikely to be influenced by the provider behaviour. The sample size of the studies ranged 45-132 (Table 2)

Of the studies, 3(75%) reported a prolongation of the sensory block. Banihashem et al.¹² reported a slight increase in the duration of block (64.28 ± 10.07 minutes) compared to the other group (61.33 ± 10.16 minutes). Tuteja

et al.¹³ also demonstrated an increase in the mean duration of sensory block of 166.86 ± 7.96 minutes and 167.71 ± 7.70 minutes with both 50mg and 75mg magnesium sulphate, respectively, compared to 106.29 ± 11.13 minutes in the control group. Jabalameli et al.⁹ reported a significant dose-dependent increase in the duration of sensory block of 92 ± 10 minutes, 124 ± 12 minutes and 129 ± 21 minutes with 50mg, 75mg and 100mg of magnesium sulphate, respectively, with the maximum increase in the 100 mg magnesium sulphate group (Figure 2).

The forest plot showed a statistically significant impact favouring the magnesium sulphate group ($p=0.0001$), with the pooled mean difference being 2.75 ± 2.20 minutes (95%

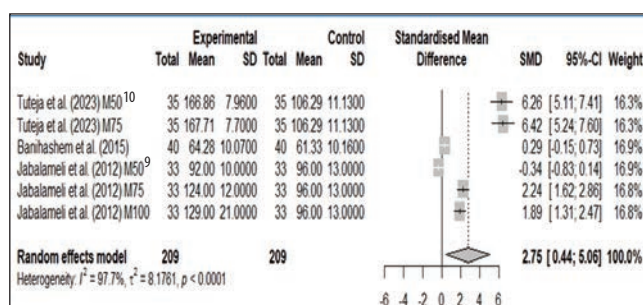


Figure-2: Forest plot comparing magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the duration of sensory blockade.

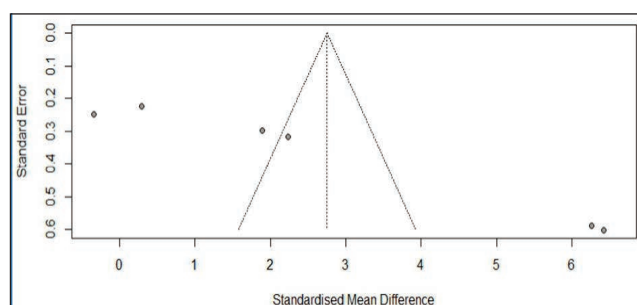


Figure-3: Funnel plot evaluating publication bias for the comparison of magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the duration of sensory blockade.

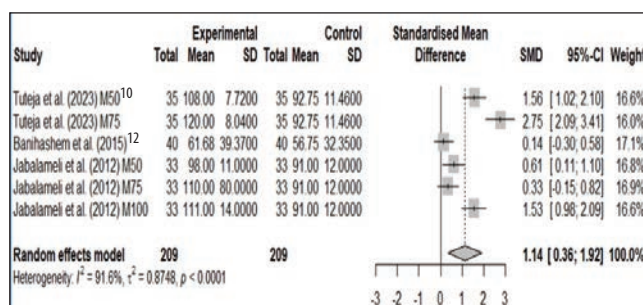


Figure-4: Forest plot comparing magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the duration of motor block.

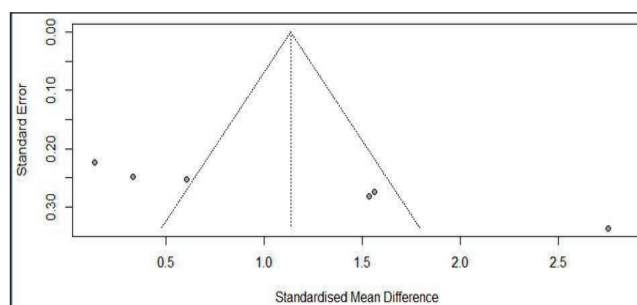


Figure-5: Funnel plot evaluating publication bias for the comparison of magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the duration of motor block.

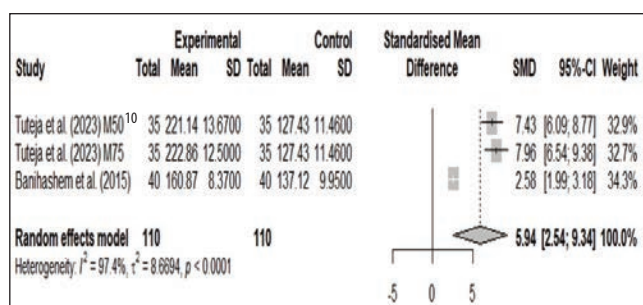


Figure-6: Forest plot comparing magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the time to rescue analgesia.

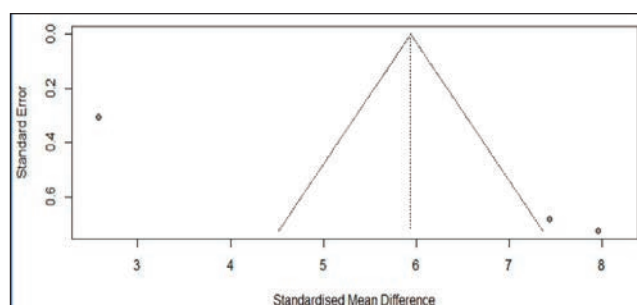


Figure-7: Funnel plot evaluating publication bias for the comparison of magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the time to rescue analgesia.

confidence interval [CI]: 0.44-5.06). On the other hand, there was a significant amount of variability among the studies ($I^2=97.7\%$), which might be due to methodological or clinical variations in the trials. Despite the variability, the steady direction of action points to magnesium sulfate's possible advantage in extending sensory blockage. Asymmetry was visible in the funnel plot. Supported by significant variation among the studies, this distribution raises the possibility of publication bias or small-study effects (Figures 2,3).

Further, 3(75%) of the studies commented on the duration of motor block. Banihashem et al.¹² reported an increased

duration (61.68 ± 39.37 minutes) compared to the control group (56.75 ± 32.35 minutes). Tuteja et al.¹⁰ demonstrated durations of 108 ± 7.72 minutes and 120 ± 8.04 minutes with 50mg and 75mg intrathecal magnesium sulphate, respectively, compared to the other group. A dose-dependent increase in the duration of motor block was observed with increasing doses of intrathecal magnesium; 98 ± 11 minutes, 110 ± 80 minutes and 111 ± 14 minutes with 50mg, 75mg and 100mg of magnesium sulphate, respectively (Figure 3).

With a pooled mean difference of 1.14 ± 0.74 minutes (95% CI: 0.36-1.92; $p=0.0001$), the results showed that patients

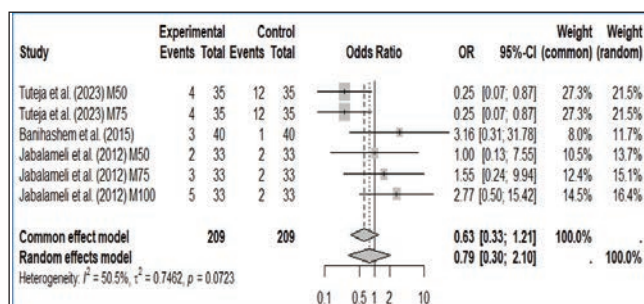


Figure-8: Forest plot comparing magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the incidence of postoperative nausea/vomiting.

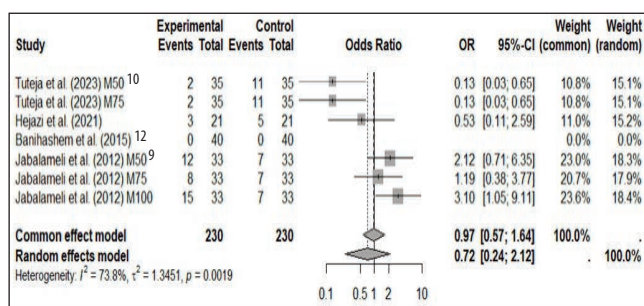


Figure-10: Forest plot comparing magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the incidence of postoperative shivering.

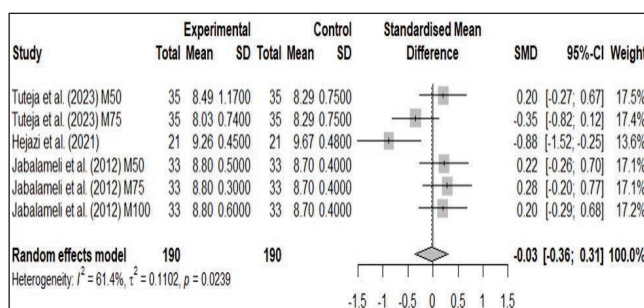


Figure-12: Forest plot comparing magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for Appearance-Pulse-Grin-Activity-Respiration (APGAR) score.

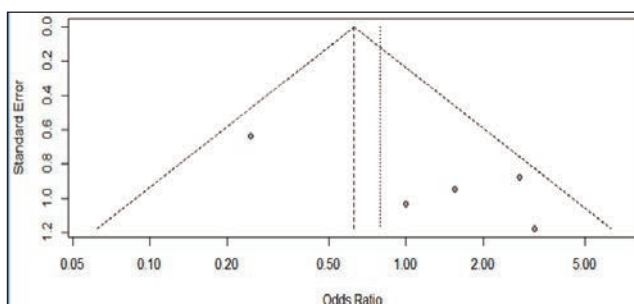


Figure-9: Funnel plot evaluating publication bias for the comparison of magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the incidence of postoperative nausea/vomiting.

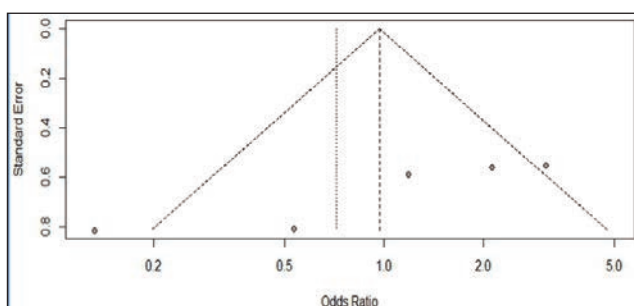


Figure-11: Funnel plot evaluating publication bias for the comparison of magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for the incidence of postoperative shivering.

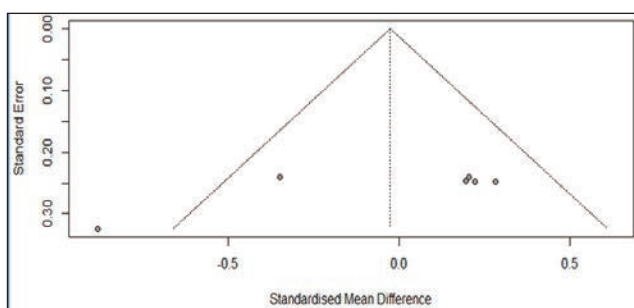


Figure-13: Funnel plot evaluating publication bias for the comparison of magnesium sulphate as an adjuvant for spinal anaesthesia in caesarean section cases versus control groups for Appearance-Pulse-Grin-Activity-Respiration (APGAR) score.

receiving magnesium sulphate as an adjuvant had a statistically significant longer duration of motor block than the control group. However, there was a significant amount of variation in impact estimates among the trials ($I^2=91.6\%$), which might be due to variations in methodology or clinical practice. Asymmetry was visible upon visual inspection of the funnel plot. When evaluating the overall results, the possibility of publication bias or small-study effects existed (Figures 4,5).

Of the enrolled studies, 2(50%) did not mention the time to rescue analgesia,^{9,13} whereas Banihashem et al.¹² reported 160.87 ± 8.37 minutes in those who received magnesium sulphate compared to 137.12 ± 9.95 minutes in the control group. Tuteja et al.¹⁰ reported 221.14 ± 13.67 minutes and 222.86 ± 12.50 in 50mg and 75mg groups, respectively, compared to 127.43 ± 11.46 minutes in the non-intervention group (Figure 6).

A pooled mean difference of 5.94 ± 1.37 minutes (95% CI: 2.54-9.34; $p=0.0001$) indicated a substantial increase in the time to rescue analgesia in individuals receiving magnesium sulphate as an adjuvant. A significant amount of variance in effect sizes was indicated by the heterogeneity among the included studies ($I^2=97.4\%$), which was probably caused by variations in research populations, procedures, or methodological quality. Asymmetry was evident in the funnel plot; notably, no study was found to be inside the funnel's bounds, suggesting that there was no symmetrical distribution around the mean effect size. The possibility of publication bias or small-study effects was raised by the imbalance (Figures 6,7).

Maternal side effects including nausea, vomiting, and hypotension were recorded in 3(75%) of the studies. Banihashem et al.¹² reported minimal side effects in which out of 40 participants, only 3(7.5%) in the intervention group experienced nausea and vomiting compared to the control group in which only 1(2.5%) developed the complications. However, no hypotension was observed in either group. Tuteja et al.¹⁰ reported that 4(11.4%) of the patients developed vomiting in the both 50mg and 75mg magnesium sulphate group, respectively. Nonetheless, the percentage of nausea and vomiting was higher in the control group compared to the intervention group. Jabalameli et al.⁹ demonstrated increasing incidence of hypotension with the increasing doses; 18(55%) (50mg), 13(39%) (75mg) and 21(63%) (100mg), respectively. Nausea and vomiting was reported in 2(6%), 3(9%) and 5(15.2%) patients in the 50mg, 75mg and 100mg magnesium sulphate groups. No study reported the development of pruritus. Overall, the studies showed a dose-dependent increase in complications at higher doses of magnesium

(Figures 8,9).

The meta-analysis comparing the intervention and control groups' probabilities of the outcome (vomiting or nausea) showed a non-significant value ($p=0.072$) with a pooled odds ratio (OR) of 0.79 (95% CI: 0.30-2.10), but the trend pointed to a possible decrease in chances with the intervention. Inconsistency in effect sizes among the included trials was moderate, as evidenced by the moderate heterogeneity across the studies ($I^2=50.5\%$). All five RoB comparisons of the investigations fell inside the funnel's limits, indicating a somewhat symmetrical distribution. A minimal probability of publication bias in this analysis was suggested by the funnel's symmetrical form and clustering (Figures 8,9).

A statistically significant ($p=0.001$) difference was seen in terms of postoperative shivering between the intervention and control groups (pooled OR: 0.72; 95% CI: 0.24-2.12). The large confidence interval that crosses the null value implied ambiguity in the impact estimate, even if the OR pointed to a possible decrease in the chance of shivering with the intervention. The included studies showed significant heterogeneity ($I^2=73.8\%$), indicating significant variation in trial results. The funnel plot showed a little asymmetry, indicating the possibility of publication bias or small-study effects (Figures 10,11).

The neonatal outcome was reported by all 4(100%) studies in terms of Appearance-Pulse-Grimace-Activity-Respiration (APGAR) scores at 1 and 5 minutes, while none among them reported neonatal intensive care unit (NICU) admission. Banihashem et al.¹² and Tuteja et al.¹⁰ noticed no major differences between the groups. According to Tuteja et al.,¹⁰ the magnesium groups had Apgar score about 8.49 ± 1.17 and controls had 98.29 ± 0.75 , with 5-minute scores ranging 8.0-8.5 for all the groups. Hejazi et al.¹³ and Jabalameli et al.⁹ noted comparable APGAR scores as well, citing small differences but nothing clinically significant (Figure 12).

The impact of magnesium sulphate on infant APGAR scores revealed substantial heterogeneity ($I^2=61.4\%$) and a minimal mean difference of -0.03 ± 0.32 (95% CI: -0.36-0.31; $p=0.023$). The impact was clinically modest even though it was statistically significant. Outlier, according to funnel plot analysis, suggested a minimal probability of publication bias with just little asymmetry (Figures 12,13).

Discussion

When given as an adjuvant to hyperbaric bupivacaine during CS, intrathecal magnesium sulphate consistently extended the duration of both sensory and motor blockade across the RCTs analysed by the current

comprehensive review. Additionally, magnesium showed a distinct dose-dependent efficacy trend by delaying the requirement for rescue analgesia, especially at dosages of 75mg and 100mg. Additionally, maternal side-effects were generally mild, and neonatal APGAR scores were not adversely affected, supporting the agent's short-term safety profile.

The current findings align with prior studies evaluating magnesium sulphate as an intrathecal adjuvant. For example, the study demonstrated that 50mg intrathecal magnesium sulphate, when combined with bupivacaine-fentanyl, significantly prolonged sensory and motor block in patients undergoing lower extremity surgery without increasing side effects.^{16,17} Similarly, another study reported prolonged analgesia duration and improved quality of block with magnesium in orthopaedic surgeries.^{11,18}

In the obstetric population, studies discovered that 50mg of intrathecal magnesium delayed rescue analgesia and increased SA duration after CS, which is in line with the dose-response patterns observed in the current review. Likewise, Maleeswaran et al. conducted a study on CS patients and showed that adding 50mg of magnesium sulphate to bupivacaine significantly prolonged analgesia without adverse neonatal effects.^{9,19} By showing improved block quality when magnesium was given to bupivacaine or levobupivacaine in parturients, Deepa and Chandran (2021) corroborated these findings.⁵

In contrast, Lee et al. (2016)²⁰ observed no significant improvement in analgesic duration at 30mg, suggesting that sub-therapeutic dosing may partly explain the variability in efficacy across the studies. The divergence in findings highlights the need for standardised dosing and careful patient selection in subsequent research.

On a clinical level, intrathecal magnesium sulphate exhibits promise as an adjunct in obstetric anaesthetic that spares opioids. Its ability to prolong sensory/motor blockade and to delay postoperative analgesic requirement may reduce reliance on intra- and postoperative opioids particularly relevant in resource-limited or opioid-restricted environments.

It is also suggested that magnesium could enhance intraoperative anaesthesia quality while reducing supplemental analgesic needs. Magnesium could enhance intraoperative anaesthesia quality while reducing supplemental analgesic needs.^{21,22} also suggested that magnesium could enhance intraoperative anaesthesia quality while reducing supplemental analgesic needs. Also suggested that magnesium could enhance intraoperative

anaesthesia quality while reducing supplemental analgesic needs. Additionally, Ozalevli et al. (2005)⁸ in a study involving arthroscopic knee surgery, reported a decrease in total analgesic consumption postoperatively when magnesium was included intrathecally. The evidence suggests that the optimal balance between analgesic efficacy and safety may be achieved around 75-100mg, as shown in several studies.^{9,10}

Although the agent is not yet universally adopted in routine obstetric practice, its non-opioid profile, ease of administration and favourable outcomes suggest it deserves broader clinical consideration especially in opioid-averse or high-risk obstetric patients.

At doses up to 75mg, the intrathecal magnesium safety profile seems to be satisfactory. Both in Ryu et al. (2009)²² and in the current review, no serious maternal complications were observed. In El-Kasaby et al. (2010),²³ APGAR scores were unaltered, and the incidence of nausea and hypotension did not differ significantly from control groups.

However, Jabalameli et al.⁹ reported dose-dependent increases in minor side-effects, such as hypotension and nausea, especially with 100mg doses. Similarly, Shahi et al. (2014)²⁴ found that using 100mg of magnesium intrathecally during lower abdomen operations increased the incidence of bradycardia and hypotension. These findings support a cautious approach to dosing, particularly in haemodynamically unstable or high-risk obstetric patients.

Importantly, none of the included or referenced studies reported neonatal complications requiring NICU admission, and APGAR scores remained within normal limits. However, long-term neurodevelopmental outcomes were not assessed, which remains a significant gap in safety evaluation and warrants attention in future research.

A key strength of the current review is its exclusive inclusion of RCTs, focussing on objective outcome measures, such as block duration and analgesia timing. Moreover, this is one of the few reviews concentrating exclusively on obstetric patients, increasing its clinical applicability. A formal meta-analysis was not feasible due to variations in study designs and outcome reporting.

The current systematic review has its limitations, as the final analysis included only four RCTs, affecting the generalisability and statistical power of the findings. Moreover, exclusion of grey literature, as well as lack of population and regional variety also contributed to this limitation. Further, the RCTs analysed did not provide data on long-term neonatal outcomes. In addition, this review

showed dose-dependent increase in complications and there was no safety threshold identified. For optimal and safe dosage in high-risk obstetric patients, larger studies are needed. Furthermore, there is inconsistency among the studies in terms of dosage variability, patient characteristics and outcomes, which makes it hard to draw reliable conclusions. Due to the limited number of RCTs and variability in design, subgroup analysis on maternal conditions, dose difference and ASA status could not be performed. Larger, multicentre RCTs with consistent magnesium dosage (e.g., 50mg, 75mg, 100mg) and consistent outcome reporting should be the main emphasis of future researchers. Additionally, comparative trials evaluating magnesium against other adjuvants, such as dexmedetomidine, clonidine and fentanyl, are needed. Further investigation into long-term neonatal neurodevelopmental effects, ideally through prospective cohort follow-ups, will also strengthen safety conclusions and support more confident clinical adoption.

Conclusion

Intrathecal magnesium sulphate appeared to be a safe, effective and opioid-sparing adjuvant in CS SA. With appropriate dosing, it can enhance block duration and reduce postoperative analgesic needs. However, before being widely adopted into standard anaesthetic practice, further research is required to improve dose parameters and to evaluate long-term neonatal safety.

Ethical Consideration: This systematic review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 21/07/2025 under registration number CRD420251086377. No substantial amendments to the registered protocol have been made. The full protocol is available at: <https://www.crd.york.ac.uk/PROSPERO/view/CRD420251086377>

Disclaimer: All opinions and interpretations stated in the above article belong to the authors only and do not represent the official views or positions of their respective affiliated organizations. This systematic review and meta-analysis are based on all the information that is currently available in the literature, and thus must be taken in context with all the limitations associated with these studies.

Conflict of Interest: None.

Source of Funding: None.

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Author Contribution:

HA: Concept, methodology, drafting and supervised the project.

AM: Methodology, literature search, selection, data extraction, review and revision.

HJ: Literature search, selection, data extraction and writing.

TU & UM: Critical review, editing and endorsed the final version.

MY: Completed the data analysis.