Original Article

Intravenous Magnesium Sulphate During Spinal Anaesthesia and its Effect on Postoperative Analgesia in Lower Abdominal Surgery

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Abstract

Background: The implementation of multimodal or "balanced" analgesia strategies, which utilise non-opioid analgesics alongside opioid analgesics, has become standard in modern anaesthesia. Magnesium sulphate ($MgSO_4$) acts as an N-methyl-D-aspartate (NMDA) receptor antagonist and possesses antinociceptive properties. This study evaluated the analgesic efficacy and hemodynamic effects of intravenous $MgSO_4$ infusion in patients undergoing lower abdominal surgery under spinal anaesthesia. **Material and Methods:** In this randomized controlled trial, 96 patients were allocated into two groups: Group M was administered 50 mg/kg of $MgSO_4$ intravenously over 15 minutes, followed by a continuous infusion of 15 mg/kg/hr, while Group N received an equivalent volume of normal saline until the conclusion of the surgical procedure. Time to first rescue analgesic requirement, total analgesic requirement within 24 hours, visual analog scale (VAS) scores, Ramsay sedation scores, block characteristics, and hemodynamics were noted in both the groups. **Results:** Individuals in Group M had a markedly extended duration until the initial rescue analgesia (184.47 ± 12.60 min) in contrast to Group N (145.93 ± 11.18 min; $p < 0.001$). The overall Tramadol intake during a 24-hour period was markedly reduced in Group M (168.32±29.34 mg) in contrast to Group N (253.46±38.21; $p = 0.001$). Haemodynamic metrics were consistent across both cohorts. **Conclusion:** Perioperative intravenous magnesium sulphate infusion significantly enhances postoperative analgesia and reduces rescue analgesic requirements without adverse hemodynamic complications.

Keywords: Magnesium sulfate; Spinal anaesthesia; Postoperative analgesia; Visual analogue scale, Rescue analgesia.

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Introduction

Postoperative pain represents a paramount challenge in the care of patients after surgical procedures. Should it remain unregulated, it will set off a chain of negative physiological and psychological effects that beyond the experience of pain. Poorly regulated postoperative pain is well-established to enhance sympathetic activity, impair recovery, hinder movement, interfere with wound healing, and extend hospital stay.[1] Unmanaged pain has been linked to heightened occurrences of postoperative problems, such as ileus, nausea, vomiting, urine retention, and infections, ultimately resulting in unfavourable clinical outcomes. Effective management of postoperative pain is crucial for facilitating recovery, augmenting patient happiness, and reducing healthcare costs.[2] The prevalent treatment modality is a poly-pharmacological strategy. Neuraxial blockade is the optimal anaesthetic approach for lower abdominal procedures owing to its quick start, superior blockade quality, outstanding pain relief, lower failure rates, and economic viability. Nonetheless, this analgesic effect is generally ephemeral owing to the relatively short action period of currently accessible local anaesthetics (LA), causing patients to encounter a recurrence of pain, at times severe.[3] The primary obstacle in spinal anaesthesia is extending the analgesic effect into the postoperative phase, ensuring patient comfort while minimising reliance on opioids, which are associated with several adverse consequences.[3,4]

Magnesium is an essential divalent cation involved in numerous enzymatic reactions, neuromuscular transmission, vascular tone and neuronal excitability. In anaesthesia, magnesium sulfate has attracted interest because it can modulate calcium-dependent neurotransmitter release, potentiate neuromuscular blockade and antagonize N-methyl-D-aspartate (NMDA) receptors involved in nociceptive transmission and central sensitization. By modulating the Na^+-K^+ ATPase pump, it maintains membrane electrical gradients and influences the activity of electrically excitable tissues.[5-7] Its utility in anaesthesia stems from its ability to potentiate neuromuscular blockade and attenuate catecholamine-induced pressure responses during intubation. Furthermore, as an NMDA receptor antagonist, it prevents

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central sensitization associated with peripheral nociceptive stimulation, making it an attractive adjuvant for acute and chronic pain management.[6] The present study therefore evaluated the effect of intraoperative intravenous magnesium sulfate during spinal anaesthesia on postoperative analgesic requirements and haemodynamic parameters in patients undergoing lower abdominal surgery.

Materials and Methods

Study design and setting: Conducted from August 2017 to February 2018, this randomised controlled study was held in the Department of Anaesthesiology and Critical Care at Veer Surendra Sai Institute of Medical Sciences and Research (VIMSAR), Burla, Odisha, India. Institutional ethical approval was obtained from the VIMSAR Institutional Research Ethics Committee (VIREC No. 2016/I-P-CT-01/002), and written informed consent was obtained from participants.

Sample size: The sample size was calculated from a previous study by Hwang et al,[8] with 80% power and 95% confidence, yielding 44 participants per group. Allowing for 10% attrition, 100 patients were enrolled; after exclusion of four patients because of unwilling to participate, 96 patients were analyzed, 48 in each group.

Participants: Individuals between the ages of 18 and 60, of any gender, classified as ASA physical status I–II, scheduled for non-obstetric lower abdominal surgery with spinal anaesthesia, were deemed eligible.Exclusion criteria encompassed individuals with renal, hepatic, neuromuscular, or cardiovascular impairments, those receiving angiotensin receptor or calcium channel antagonists, a body mass index (BMI) exceeding 30 Kg m-2, any contraindications to spinal anaesthesia, documented hypersensitivity to the investigational drug, a background of opioid or analgesic dependency, pregnant or breastfeeding women, and unsuccessful spinal block.

Randomization and group allocation: The chosen patients were randomly allocated into two groups (Group M and Group N) utilising a computer-generated table [Figure 1].

Group M was administered magnesium sulphate at a dosage of 50 mg/Kg intravenously for 15 minutes, followed by a continuous intravenous infusion of 15 mg/Kg/h until the conclusion of the surgery.

Group N was administered an equivalent volume of isotonic saline via continuous intravenous infusion until the conclusion of the surgical procedure. The experimental medication was created by a neutral anaesthesiologist using a double-blind protocol, without participation in observation or data gathering. Neither the patient nor the anaesthesiologist had knowledge of the patient's group designation, and all recordings were executed by an anaesthesiologist who was kept in the dark regarding the randomisation schedule.

Study Procedure: Each patient received a comprehensive pre-anaesthesia assessment and relevant laboratory evaluations. The complete process of spinal anaesthesia was elucidated to the patient. Patients were instructed on the visual analogue scale (VAS), which is measured in millimetres on a 10-centimeter line marked from 0 to 10, where 0 signifies no pain and 10 indicates the most severe pain, and were educated on how to articulate their pain level using this scale. Administered Alprazolam 0.5 mg and ranitidine 150 mg orally the night prior to surgery and maintained nothing by mouth for 8 hours before the procedure.

In the preoperative room, the patients NPO status was confirmed, and a written informed consent was secured. In the operating theatre, two intravenous lines were implemented, one designated for the bolus and continuous infusion of magnesium sulphate or isotonic saline, and the second for intravenous fluid replenishment and the administration of all other pharmaceuticals. Multiparameter monitor, including pulse oximetry, ECG, and non-invasive blood pressure was attached to the patient and baseline vitals monitored. Following the administration of 10 ml/Kg of Ringer's Lactate solution intravenously for a duration of 15 minutes, an intrathecal injection of 15 mg (3 mL) of 0.5% hyperbaric bupivacaine was delivered in the L3-L4 intervertebral area in sitting position.

Then the patient was positioned supine, and 50 mg/Kg of magnesium sulphate was administered intravenously over 15 minutes, succeeded by an infusion of 15 mg/Kg/h in the magnesium cohort; alternatively, the control group received the equivalent volume of normal saline as both bolus and infusion. Intraoperative sedation ratings (Ramsay Sedation Scale) were documented immediately prior to the commencement of surgery and subsequently every 15 minutes throughout the procedure. During the process, haemodynamic information was meticulously observed. Heart rate and mean arterial pressure (MAP) were assessed every four hours. Bradycardia (heart rate below 50 beats per minute) or hypotension (mean blood pressure less than 70% of baseline) were observed and effectively addressed.

The length of the sensory block was defined as the period from the injection of intrathecal bupivacaine to the reestablishment of sensation at the L1 dermatome level. The length of motor blockade was defined as the period from the injection of intrathecal bupivacaine till the recovery of knee flexion and the ability to raise the knee at least 10 cm above the bed. Subsequent to the surgical procedure, the patients were relocated to the post anaesthesia care unit (PACU), where their pain levels were evaluated utilising the VAS at intervals of 0, ½, 1, 2, 3, 6, 9, 12, 18, and 24 hours. Intravenous injection of tramadol 100 mg was administered if the Visual Analogue Scale (VAS) was equal to or greater than 3, and the duration until the initial rescue analgesia was recorded. Haemodynamic parameters: Mean Arterial Blood Pressure (MAP) and Heart Rate (HR) were documented prior to the infusion of the study medication (baseline), as well as at 10, 20, 30, 45, 60, 90, and 120 minutes post-spinal anaesthesia throughout the surgical procedure, and at 5 minutes and 1 hour following admission to the Post-Anesthesia Care Unit (PACU). Sedation was assessed using the Ramsay Sedation Scale. Patients were observed and suitably managed for additional adverse effects, including a burning or heat sensation at the injection site, or itching. The evaluation of patient satisfaction scores was conducted. At the conclusion of the 24-hour postoperative timeframe, patient contentment was evaluated utilising a 3-point Likert scale to judge their comprehensive experience with postoperative pain treatment. The tiers were delineated as

follows: 1-Not satisfied, 2-Moderately satisfied, 3-Highly satisfied. Patients were instructed to assess their satisfaction about pain alleviation, comfort, and the general recovery process during the 24 hours after the surgical procedure.

Statistical analysis

Data were logged in Microsoft Excel 2010 and evaluated by IBM SPSS Statistics version 22. Typically, data that is normally distributed was articulated as mean and standard deviation, and skewed data was delineated as median and interquartile range. The qualitative data comprised counts and ratios. The unpaired t-test was utilised to compare normally distributed numerical data. The Mann-Whitney test was employed to compare the skewed data. Categorical data were analysed via the Pearson chi-squared test or Fisher's exact test, as deemed suitable. A two-tailed p-value of less than 0.05 was deemed statistically significant.

Results

A total of 100 patients were enrolled. Four were excluded because of unwilling to participate in the study, leaving 96 participants for analysis, with 48 in each group. The CONSORT flow diagram of recruitment, allocation, follow-up, patient analysis, and causes of exclusion is shown [Figure 1].

The two groups exhibited no statistically significant differences (P > 0.05) in terms of ASA classification, gender distribution, age, weight, height, BMI, or length of surgery, so indicating their comparability. [Table 1].

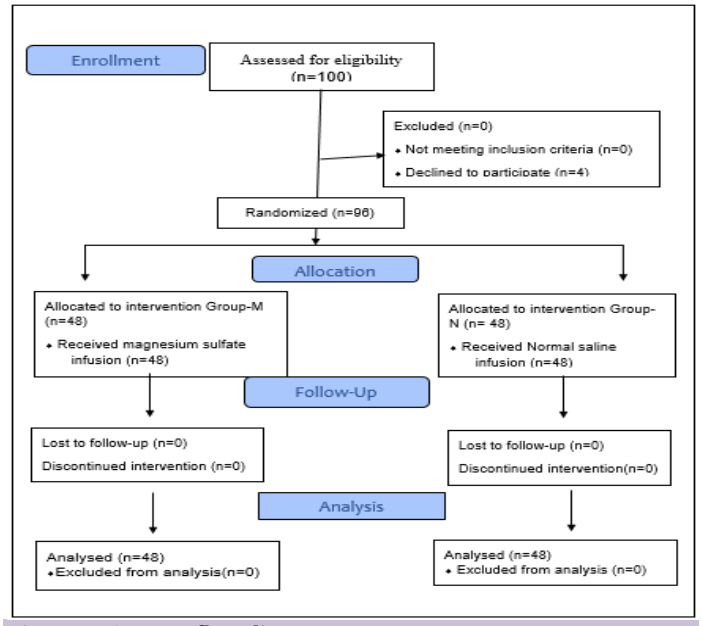

Figure 1: Consort flow diagram.

Table 1: Baseline characteristics between the groups.

Variable	Group M	Group N	Reported p-value
Age (years)	42.29 ± 9.82	44.43 ± 12.39	0.172
Sex, male/female	27/21	29/19	0.057
Height (cm)	159.20 ± 7.14	159.08 ± 6.47	0.929
Weight (kg)	67.37 ± 9.47	68.04 ± 10.00	0.738
BMI (Kg/m2)	21.6 ± 1.3	21.3 ± 1.3	0.37
ASA I/II	33/15	34/14	0.052
Duration Of surgery(mins)	97.3 ± 14.3	97.4 ± 13.7	0.98

The period of sensory blockage (Group M=128.04 ± 14.97 vs Group N= 103.89 ± 12.27, p=0.001) and the period of motor blockade (Group M=154.89 ± 18.73 vs Group N=120.52 ± 11.12, p=0.001) demonstrated a statistically significant difference between the groups [Table 2].

Table 2: Duration of spinal blockade between the groups.

Outcome	Group M	Group N	Reported p-value
Onset of sensory block (min)	4.37±1.35	4.78±1.03	0.78
Onset of motor block (min)	6.38±0.57	6.89±0.53	0.82
Duration of sensory block (min)	128.04 ± 14.97	103.89 ± 12.27	0.001
Duration of motor block(min)	154.89 ± 18.73	120.52 ± 11.12	0.001

Heart rate and mean arterial pressure were generally comparable. Mean arterial pressure differed at the immediate post-spinal measurement (75.75 ± 9.80 mmHg in Group M versus 70.33 ± 10.23 mmHg in Group N; p = 0.010), but subsequent measurements were not statistically different. The incidence of hypotension was similar between the two groups. The incidence of bradycardia was similar between groups: Group M, 4 patients, and Group N, no patients (p = 0.05). No clinically significant haemodynamic instability or magnesium-related complication was reported during the observation period.

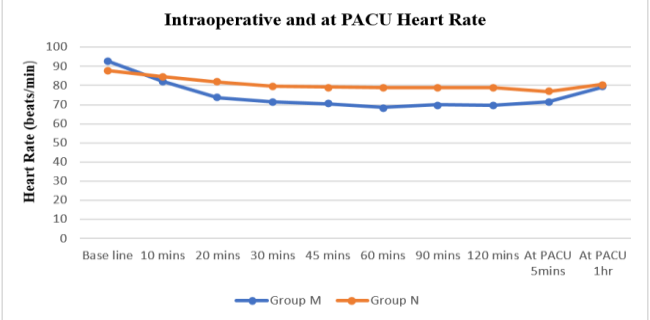

Figure 2: Comparison of heart rate between the groups.

Table 3: Comparison of VAS between the groups

Postoperative period	Group M VAS	Group N VAS	Reported p-value
0 h	0.5 ± 0.61	0.54 ± 0.51	0.84
0.5 h	1.04 ± 0.20	1.12 ± 0.33	0.63
1 h	1.17 ± 0.61	1.81 ± 0.41	0.02
2 h	1.49 ± 1.05	2.71 ± 1.01	0.002
4 h	2.33 ± 0.85	2.81 ± 0.94	0.013
6 h	2.45 ± 1.23	3.0 ± 0.74	0.026
8 h	2.33±0.79	3.2±0.9	0.012
12h	2.73±0.94	3.00±0.45	0.061
16h	2.81±1.01	3.04±0.56	0.067
20h	2.46±0.84	2.78±1.02	0.34
24h	2.34±0.78	2.69±1.13	0.28

Table 4: Primary postoperative analgesic outcomes Level of satisfaction between the groups

Outcome	Group M	Group N	Reported p-value
Time to first rescue analgesia, min	184.47 ± 12.60	145.93 ± 11.18	<0.001
Mean no. of analgesic doses in 24 h	2.43 ± 0.62	3.58 ± 0.99	0.028
Total tramadol doses (mg)	168.32 ± 29.34	253.46 ± 38.29	0.001
Level of satisfaction	2.57±0.48	1.63±0.66	<0.0001

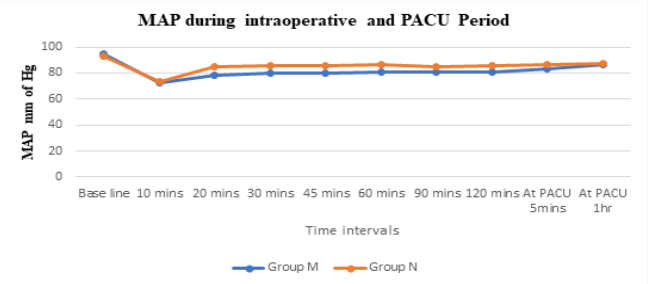

Figure 3: Comparison of mean arterial pressure between the groups

A statistically significant disparity was noted in the VAS scores between the two groups at the 1st, 2nd, 3rd, 6th, 9th, 12th, and 16th hour intervals, with Group M exhibiting lower VAS ratings [Table 2]. The average duration until the initial rescue analgesia was considerably extended in the magnesium cohort: 184.47 ± 12.60 compared to 145.93 ± 11.18 minutes ($p < 0.001$). The average quantity of analgesic dosages needed in the initial 24 hours was significantly reduced with magnesium sulphate (2.43 ± 0.62 compared to 3.58 ± 0.99; $p = 0.028$). The overall Tramadol need was determined to be 168.32 ± 29.34 mg for Group M and 253.46 ± 38.29 mg for Group N after 24 hours. The disparity was statistically significant with a p value of less than 0.05 [Table 3].

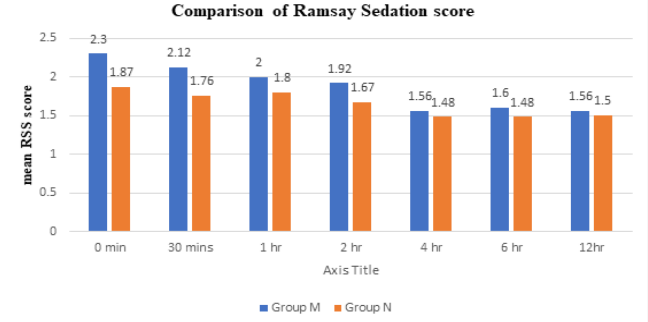

Figure 4: Comparison of Ramsay sedation scores between two groups

No statistically meaningful difference was detected in the Ramsay sedation ratings between the two cohorts (Figure 4), suggesting that magnesium sulphate did not induce any statistically significant drowsiness at the administered doses in the trial. The occurrence of PONV was comparable in both groups: Group M had 3 patients, whereas Group N had 6 patients, ($p = 0.33$). Group M had a markedly elevated degree of patient satisfaction (2.57±0.48 compared to 1.63±0.66). [Table 4].

Discussion

Multimodal or "balanced" analgesia protocols incorporating non-opioid analgesics (such as local anaesthetics, non-steroidal anti-inflammatory medications, acetaminophen, ketamine, and N-methyl-D-Aspartate receptor antagonists) to enhance opioid analgesics have integrated into contemporary anaesthesia practice. The opioid-sparing properties of these substances diminish nausea, vomiting, constipation, urine retention, respiratory depression, and drowsiness, hence enhancing the recovery quality for surgical patients.[9]

The application of intravenous magnesium sulphate in perioperative treatment is on the rise, attributed to its pain-relieving, anti-inflammatory, and muscle relaxation properties. By acting mostly as an NMDA receptor antagonist and inhibiting calcium channels, magnesium sulphate alleviates CNS sensitisation to pain and lowers the demand for anaesthetics and opioids. It has been widely employed to enhance perioperative pain relief, improve the efficacy of regional anaesthesia, and regulate haemodynamic responses after surgery. Magnesium sulphate has demonstrated efficacy in managing postoperative discomfort, averting the development of chronic postsurgical pain, and providing neuroprotection in diverse clinical scenarios.[8]

Group M exhibited a more rapid onset of sensory and motor blockade compared to Group N; nevertheless, the disparity was not markedly significant [Table 2]. Malleswaran et al have suggested that the postponed start of the block may result from alterations in the pH and baricity of the local anaesthetic solution due to the incorporation of intrathecal magnesium sulphate.[11] The same method is ineffective with the intravenous delivery of magnesium sulphate, necessitating further investigation into this matter. In Group M, the length of both sensory and motor blockage was markedly extended. This indicates that magnesium

sulphate enhances the anaesthetic action, facilitating an extended period of analgesia. Yet, the increased time of motor blockade should be judiciously assessed in individuals for whom swift mobilisation is of paramount importance. These insights are consistent with earlier investigations performed by Kumar A et al., Shah PN et al., Hwang JY et al., Farouk S et al., Gupta R et al., and Apan A et al.[8,12-16]

VAS scores throughout the groups were comparable initially, however Group M exhibited significantly lower values starting from one hour postoperatively and maintained this trend for up to twelve hours. The initial demand for rescue analgesia in Group M (Magnesium) was recorded at 184.47 ± 12.60 minutes, whereas Group N (control) exhibited a time of 145.93 ± 11.18 minutes. The total Tramadol demand within the first 24 hours were reduced with magnesium sulphate. This implies a superior and enduring analgesic effect associated with magnesium sulphate, validating the conclusions established in investigations by Kumar A et al., Shah PN et al., Hwang JY et al., Farouk S, Apan A et al., and Shin HJ et al.[8,12-17]

In this investigation, the MAP and HR remained consistent over time between the two cohorts, exhibiting no notable haemodynamic alterations. These findings align with the research conducted by Hwang et al,[8] and Agrawal et al.[18] The authors suggest that the administration of 500 mL of Ringer's lactate for pre-hydration, along with the gradual infusion of the drug, may account for this haemodynamic stability. Conversely, Ryu et al,[19] and Seyhan et al,[20] documented reduced MAP and HR measurements in individuals administered MgSO4. Four instances of bradycardia (with prompt recovery following atropine administration) were documented in Group M, but none occurred in Group N (p = 0.05). Nevertheless, bradycardia was never noted in conjunction with hypotension. Albrecht et al. reported a greater incidence of bradycardia in the magnesium cohort (RR = 1.76; 95% CI 1.01---3.07; p = 0.04), yet no corresponding rise in hypotension was observed (RR = 1.49; 95% CI 0.88---2.52; p = 0.14), and they noted that while bradycardia occurred more frequently post-magnesium administration, there were no instances of sustained haemodynamic instability or bradycardia unresponsive to initial pharmacological intervention.

The satisfaction levels of patients in Group M were considerably superior, demonstrating enhanced comfort and pain control following surgery. These conclusions were reinforced by Kumar A et al., Shah PN et al., and Shin HJ et al.[12,13,17]

Regarding adverse effects, only a small number of Group M participants reported a slight burning sensation at the injection site. Conversely, Group N experienced no adverse effects. Overall, the incidence of adverse events was minimal and self-resolving, as previously reported by Hwang JY et al. and Farouk S et al.

Limitation(s)

The relatively limited patient cohort restricts the generalisability of the findings to a wider demographic. Given that this was a single-centre investigation, the specific practices of the institution and the demographics of the patient population may have impacted the findings, thus introducing bias. The utilisation of subjective pain assessments, like the VAS, resulted in inconsistencies in patients' reports of pain perception. The serum magnesium concentration was not assessed.

Conclusion

The present research indicates that intravenous magnesium sulphate significantly extends the duration of sensory and motor blockade when utilised as an adjunct to spinal anaesthesia in lower abdominal procedures. Furthermore, it enhances patient contentment, offers superior and prolonged postoperative pain relief, and postpones the necessity for supplementary analgesics without inducing considerable haemodynamic or respiratory instability at the dosages employed in this investigation. Due to the rarity and self-resolving nature of adverse effects, the safety of magnesium sulphate in this context was validated. Magnesium sulphate serves as an effective and well-accepted adjunct that enhances the quality of spinal anaesthesia.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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