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RESEARCH ARTICLE
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TO STUDY THE EFFECT OF INTRAVENOUS MAGNESIUM SULPHATE ON ACUTE POST-OPERATIVE PAIN IN PATIENTS UNDERGOING LOWER LIMB ORTHOPEDIC SURGERIES UNDER SUBARACHNOID BLOCK: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

Dr. Patnana Pradeep Kumar[1], Dr. Dasari Preethi[2], Dr. Vuppu Bhavani[3], Dr. Mamidi Ajay Kumar[4*]

[1]Assistant Professor, Department of Anaesthesiology, Government Medical College, Sangareddy, Telangana, India.
[2]Assistant Professor, Department of Anaesthesia & Critical Care, Osmania Medical College, Telangana, India.
[3]Assistant Professor, Department of Anaesthesia, Government Medical College, Sangareddy, Telangana, India.
[4*]Assistant professor, Department of Anaesthesiology, Government Medical College, Sangareddy, Telangana, India.

***Corresponding Author:** Dr. Mamidi Ajay Kumar
*Assistant professor, Department of Anaesthesiology, Government Medical College, Sangareddy, Telangana, India.

ABSTRACT

Background

Acute postoperative pain remains a significant challenge following lower limb orthopedic surgeries. Although intravenous magnesium sulfate has shown promise in reducing postoperative pain in various surgical contexts, its role in orthopedic procedures, particularly under spinal anesthesia, remains underexplored. Magnesium, through NMDA receptor antagonism and calcium channel blockade, is hypothesized to enhance analgesic outcomes.

Methods

A prospective, randomized controlled trial was conducted at Government Medical College Sangareddy, Telangana from December 2023 to December 2024. A total of 116 patients aged 20–60 years undergoing elective lower limb orthopedic surgeries under spinal anesthesia were enrolled and randomized into two groups: Group A (n=58) received 1g intravenous magnesium sulphate preoperatively; Group B (n=58) did not receive magnesium. Standard spinal anesthesia with 0.5% hyperbaric bupivacaine was administered. Postoperative pain scores were assessed using the VAS (Visual Analogue Scale) and the requirement for rescue analgesia (inj. fentanyl 1mcg/kg IV) was recorded for 24 hours.

Results

There were no statistically significant differences in demographic characteristics (age, gender, ASA grade) between the two groups. Patients who received intravenous magnesium sulphate (Group A) demonstrated significantly lower VAS pain scores at 24 hours compared to Group B. Furthermore, the need for rescue analgesia was reduced in Group A, indicating enhanced postoperative analgesia.

Conclusion
Preoperative intravenous administration of magnesium sulphate effectively reduces acute postoperative pain and the requirement for rescue analgesia in patients undergoing lower limb orthopedic surgeries under subarachnoid block. Magnesium sulphate can be considered a useful adjuvant for enhancing postoperative analgesia in this patient population.

Keywords: Magnesium Sulphate, Acute Postoperative Pain, Orthopedic Surgeries, Spinal Anesthesia, Randomized Controlled Trial, Visual Analogue Scale.

INTRODUCTION

Pain is an inevitable part of life, and efforts to alleviate it have existed since ancient times. A major advancement occurred in 1898 when August Bier first used spinal anesthesia for surgery. Since then, spinal anesthesia has become a preferred technique for surgeries involving the lower body due to its rapid onset, efficacy, minimal cognitive effects, and reduced blood loss. It also lowers the risk of vomiting and aspiration, particularly in patients with a full stomach or chronic airway diseases.

Effective postoperative pain management improves recovery by allowing patients to breathe, cough, and mobilize with less discomfort, thereby reducing morbidity. Regional anesthesia, such as spinal anesthesia, offers advantages over general anesthesia by avoiding its associated complications, suppressing the neuroendocrine stress response, and eliminating the need for muscle relaxants.

Magnesium sulphate has gained interest as an analgesic adjuvant for postoperative pain relief.[1] It is thought to work by controlling calcium influx[2] and blocking NMDA (N-Methyl-D-Aspartate) receptors in the central nervous system.[3,4] Additionally, magnesium sulphate has anti-inflammatory properties,[5] which are relevant because inflammation can amplify pain through peripheral and central sensitization.[6]

Evidence suggests that intravenous magnesium sulphate administered during spinal anesthesia enhances postoperative analgesia. Similar improvements in pain control have also been observed when magnesium is used during total intravenous anesthesia.[7]

The premise of this study is that magnesium sulphate can lessen postoperative pain and stop it from getting worse. The primary objective is to assess the effectiveness of magnesium sulphate in reducing postoperative pain in patients undergoing lower limb orthopedic surgeries. The broader aim is to establish a therapeutic approach to manage pain more effectively in such procedures.

AIMS AND OBJECTIVES

The aim of this study was to assess how magnesium sulphate affects immediate postoperative pain in patients having orthopaedic procedures on their lower limbs. Specifically, the objectives are to assess the postoperative analgesic effects of preoperative intravenous magnesium sulphate and to determine its impact on the requirement for additional analgesics during the acute postoperative period within the first 24 hours following surgery.

MATERIALS AND METHODS

This was a prospective, randomized controlled clinical trial study conducted in the Department of Anaesthesia at Government Medical College Sangareddy, Telangana. It included patients of both sexes, aged between 20 and 60 years, who were admitted for lower limb orthopedic surgeries. The study was carried out from December 2023 to December 2024.

Inclusion and Exclusion Criteria

The study included men and women aged 20 to 60 years with ASA physical status class I or II who were admitted for elective orthopedic fixation of long bone fractures in the lower limbs and had provided informed written consent. Patients were excluded if they had any signs or history of existing or previous neuropathy, refused to consent, had a prolonged QTc interval on the preoperative

electrocardiogram, had an underlying coagulation disorder, or had a known allergy to local anesthetics or magnesium sulphate.

Sample Size Calculation

The sample size for the study was calculated to achieve a 95% confidence level with a margin of error of approximately 5%, using the formula:

$$\mathbf{n = (Z^2 \times P \times (1 - P)) / e^2},$$

Where *P* is the estimated proportion, *Z* is the value from the standard normal distribution corresponding to the desired confidence level, and *e* is the desired precision.

By applying the values $P = 0.030$, $Z = 1.96$ (for a 95% confidence interval), and $e = 0.015$, the calculated sample size was 116 participants. These 116 patients were randomly assigned using the block randomization method into two groups: Group A (58 patients), who received preoperative intravenous magnesium sulphate, and Group B (58 patients), who did not receive magnesium sulphate.

Data Collection Procedure

Data collection for the study involved enrolling 116 eligible patients scheduled for elective lower limb orthopedic surgery who met the inclusion criteria and provided informed written consent. Pre-anaesthetic evaluation was conducted one day before surgery, and patients were kept nil per orally for at least six hours. They were randomly assigned to two groups: Group A received 1g of intravenous magnesium sulphate preoperatively, while Group B did not receive magnesium. Upon arrival in the operating room, patients underwent standard monitoring and intravenous access with fluid preloading. Spinal anaesthesia was administered using 0.5% hyperbaric bupivacaine (3.5 mL) without any adjuvant, and sensory and motor blocks were assessed using the pinprick method and modified Bromage scale, respectively. All patients underwent surgery using standard techniques under spinal anesthesia and were monitored postoperatively for 24 hours. Pain intensity was assessed using the VAS, and rescue analgesia in the form of intravenous fentanyl (1 mcg/kg) was administered as needed. Any complications observed during the postoperative period were documented and managed appropriately.

Statistical Analysis

SPSS version 22 software was used to analyze the data after it was entered into a Microsoft Excel datasheet. Continuous variables were presented as mean and standard deviation or as median in cases where the data were skewed. Categorical variables were expressed as frequencies and percentages. The chi-square test or Fisher's exact test, if applicable, was used to compare nominal categorical data between the two groups. Accordingly, relative risk was computed. The Spearman correlation coefficient was used to evaluate the correlation between the variables. P-values below 0.05 were regarded as statistically significant.

RESULTS

Group	N	Mean Age (in years)	Std. Deviation	P-Value
Group A	58	42.65	13.15	0.659
Group B	58	43.72	12.86	

Table 1: Age Distribution between the Study Groups

According to Table 1, Group A's mean age was 42.65 years, whereas Group B's was 43.72 years. Given that the difference was not statistically significant ($p = 0.659$), the age distributions of the two groups were similar.

Gender	Group A (n=58)	Group B (n=58)	Total (n=116)
Male	28 (48.3%)	27 (46.6%)	55 (47.4%)
Female	30 (51.7%)	31 (53.4%)	61 (52.6%)
Chi-Square Value = 0.035	**P Value** = 0.852		
Table 2: Gender Distribution between the Study Groups			

Table 2 shows that gender distribution was nearly equal between both groups and showed no statistically significant difference ($p = 0.852$).

ASA Grade	Group A (n=58)	Group B (n=58)	Total (n=116)
ASA I	28 (48.3%)	25 (43.1%)	53 (45.7%)
ASA II	30 (51.7%)	33 (56.9%)	63 (54.3%)
Chi-Square Value = 0.313	**P Value** = 0.576		
Table 3: ASA Grading between the Study Groups			

According to Table 3, ASA physical status was similarly distributed across the two groups, with no significant difference ($p = 0.576$).

Surgery Type	Group A	Group B	Total
Bipolar Hemiarthro Plasty	8	5	13
PFN	11	8	19
Distal Femur Locking Plate	8	8	16
Femur Nailing	6	9	15
Implant Removal	8	8	16
Tibia Plating	7	9	16
Bimalleolar CC Screws with Semitubular plate fibula	10	11	21
Chi-Square Value = 2.064	**P Value** = 0.914		
Table 4: Type of Surgery Distribution between the Study Groups			

Table 4 shows that the types of surgeries performed were similar in both groups, with no statistically significant difference in distribution ($p = 0.914$).

VAS Score Range	Group A	Group B
0–2	17	12
3–5	27	18
6–8	14	28
Table 5: VAS Score Distribution at 24 Hours Postoperatively		

According to Table 5, Group A had more patients with lower VAS scores (indicating less pain), while Group B had more patients in the higher pain category (6–8). This suggests better analgesia in Group A.

Group	Mean VAS Score	Std. Deviation	P-Value
Group A	3.84	1.83	0.006
Group B	4.97	2.42	
Table 6: Mean VAS Scores between the Study Groups			

Table 6 shows that the mean VAS score was significantly lower in Group A compared to Group B ($p = 0.006$), indicating that preoperative magnesium sulphate administration was effective in reducing postoperative pain.

Rescue Analgesia	Group A	Group B	Total
Yes	14	28	42
No	44	30	74
Chi-Square Value = 7.315	**P Value** = 0.007		
Table 7: Requirement of Rescue Analgesia between the Groups			

According to Table 7, a significantly lower number of patients in Group A required rescue analgesia compared to Group B ($p = 0.007$), supporting the efficacy of magnesium sulphate in postoperative pain control.

DISCUSSION

The use of non-competitive NMDA receptor antagonists, such as ketamine, dextromethorphan, and magnesium ions, as possible anti-hyperalgesic drugs has regained attention since the discovery of the NMDA receptor and its connections to nociceptive pain transmission and central sensitization. Extracellular magnesium ions non-competitively inhibit NMDA receptor channels at resting membrane potential. Magnesium has garnered interest in the fields of anaesthesiology and pain management since the study of magnesium sulphate in clinical anaesthesia started in 1996.

As a non-competitive NMDA receptor antagonist, magnesium sulphate may be able to stop peripheral nociceptive stimulation from causing central sensitization. It has been shown to be useful in reducing perioperative pain and in inhibiting endocrine, autonomic, and somatic reactions triggered by unpleasant stimuli.

In our study, we examined the extent to which magnesium sulphate reduces postoperative pain for patients undergoing lower limb orthopaedic surgeries. We enrolled 116 patients who were assigned to two groups through block randomisation. Group A (n=58) received intravenous magnesium sulphate followed by spinal anaesthesia, while Group B (n=58) received spinal anaesthesia alone without intravenous magnesium sulphate.

Demographic analysis showed no significant difference in gender distribution between the two groups. The mean age in Group A was 42.65 years, and the mean age in Group B was 43.72 years, with no statistically significant difference. There was also no statistically significant difference between both groups with regard to ASA grade.

The majority of surgeries in Group A were PFN (11), followed by Bimalleolar CC Screws with Semitubular plate fibula (10), while in Group B, the majority were Bimalleolar CC Screws with Semitubular plate fibula (10), followed by femur nailing (9) and tibia plating (9). The distribution of operation types did not change significantly between the two groups (p=0.914).

The results of our study demonstrated that in Group A, the mean VAS score was 3.84 with a standard deviation of 1.83, while in Group B, the mean VAS score was 4.96 with a standard deviation of 2.42. The difference between both groups with regard to VAS scores was found to be statistically significant (p=0.006). Additionally, in Group A, only 14 patients required rescue analgesia compared to 28 patients in Group B. This difference in rescue analgesia requirement was also statistically significant (p=0.007).

From these findings, it can be inferred that both groups were well-matched in terms of age, gender, ASA grade distribution, and type of surgery performed. However, the differences in VAS scores and the need for rescue analgesia were statistically significant between the groups, indicating that patients who received intravenous magnesium sulphate preoperatively had lower VAS scores and decreased requirements for rescue analgesia during the first 24 hours of the post-operative period.

Our findings align with several previous studies. Hamid Kayalha et al. in 2017 conducted a randomised double-blind control study with 60 patients undergoing lower limb fracture surgery under spinal anaesthesia. A bolus of 5 mg/kg magnesium sulphate plus 250 cc normal saline was given to the magnesium group (M), and 250 cc normal saline was given to the control group (C). At 12, 24, and 48 hours following surgery, they discovered that Group M experienced lower pain levels and physical dissatisfaction than Group C (p=0.000). Group M had lower total opioid needs than Group C at the end of 48 hours and during the first 24 hours following surgery (p=0.001). Additionally, Group M outperformed Group C in terms of spinal block endurance (p=0.0001). According to their research, a small amount of magnesium sulphate improved spinal block endurance while lowering pain scores, opioid needs, and physical dissatisfaction.[8]

A. Dabbagh et al.. in 2009 conducted a double-blind, randomized, placebo-controlled clinical trial with 60 patients. While the second group received the same volume of a placebo, the first group received 8 mg/kg intravenous magnesium sulphate, which was started before the incision and continued until the end of the surgical procedure. In comparison to the placebo group, they discovered that the magnesium sulphate group's reported pain was noticeably less during the first, third, sixth, and twelfth hours following the procedure. Furthermore, the magnesium group required less intravenous morphine (4.2±1.6 mg) in the first 24 hours following surgery than the control group (9.8±2.1 mg). According to their research, intravenous magnesium sulphate can be used as an additional analgesic treatment to lessen immediate post-operative pain, which will result in a lower need for morphine during the first 24 hours.[9]

A prospective study with 108 patients undergoing spinal anaesthesia surgery was carried out in 2015 by Prerena N. Shah et al. The patients were given either the same volume of normal saline (control group) or 250 mg of intravenous magnesium sulphate followed by an infusion of 500 mg of magnesium sulphate (25 mg/mL) at a rate of 20 mL/hour. They discovered that the control group experienced sensory and motor blockage for 25 and 34 minutes less, respectively. The control group needed rescue analgesia almost three hours before the magnesium group did, and fewer patients in the magnesium group (33% vs. 53.7%) needed it during the postoperative phase. Their research found that intravenous magnesium sulphate, administered as an infusion after a bolus, postponed and reduced the requirement for rescue analgesics following spinal anaesthesia.[10]

In 2014, 80 ASA grade I and II patients between the ages of 20 and 60 who were scheduled for elective orthopaedic treatment of lower limb long bone fractures under spinal anaesthesia participated in a prospective study by Akanksha Agarwal et al. 2.5 ml of strong bupivacaine combined with 10 mcg of fentanyl was used to induce spinal anaesthesia. Group M received a magnesium sulphate infusion of 50 mg/kg/h over 15 minutes, followed by 15 mg/kg/h till the completion of the procedure. Group S received a normal saline infusion of 15 ml over 15 minutes, followed by 100 ml/h until the end of the procedure. They discovered that Group M's motor block lasted an average of 160.63±17.76 minutes, while Group S's was 130.12±20.70 minutes (p=0.000). Group M experienced a regression of sensory block to T12/L1 in 206.88±20.96 minutes, while Group S experienced a regression in 163.88±15.46 minutes (p=0.000). After 262.88±21.11 minutes in Group M and 193.25±17.74 minutes in Group S, the first analgesic necessity was required (p=0.000). Group M required a lower mean dosage of tramadol in the first 24 hours (190±30.38 mg vs. 265±48.30 mg, p=0.000). According to their research, intravenous magnesium combined with spinal anaesthesia lowers the need for analgesics and post-operative pain.[11]

A randomised double-blinded control trial was carried out in 2016 by H.J. Shin et al. to assess the impact of magnesium sulphate on pain in 44 patients having staged bilateral total knee replacement (TKR). Throughout the procedure, the magnesium group (n = 22) and the control group (n = 22) were given magnesium sulphate and isotonic saline, respectively. Both after the first TKR [29(11) vs. 19(9) at 24h and 33(8) vs. 24(10) at 48h; p=0.001] and after the second TKR [44(17) vs. 20(10) at 24h and 43(14) vs. 25(10) at 48h; p<0.001], they discovered that the control group's VAS ratings were considerably higher than those of the magnesium group. According to their research, administering

magnesium sulphate greatly decreased postoperative pain and lessened the variation in pain levels between the first and second procedures.[12]

Based on our findings and the supporting evidence from previous studies, we conclude that preoperative intravenous magnesium sulphate administration significantly reduces postoperative pain scores and subsequently decreases the need for rescue analgesia in patients undergoing lower limb orthopaedic surgeries under spinal anaesthesia.

LIMITATIONS

This study has several limitations. The sample size is relatively small, which may limit the ability to account for all important variables or to draw definitive conclusions regarding the absence of relationships. Although the study is a randomized clinical trial, it is not double-blinded; therefore, the potential for bias cannot be eliminated. Additionally, the investigator was not blinded to the study results, which may have influenced the observations and outcomes reported. Further research involving larger sample sizes is necessary to more accurately assess the comparative advantages of each technique before any guidelines or recommendations can be established.

CONCLUSION

Our study revealed that patients who received preoperative intravenous magnesium sulphate experienced a prolonged duration of postoperative analgesia and consequently required lower doses of rescue analgesia. Based on these findings, we conclude that preoperative administration of intravenous magnesium sulphate effectively reduces postoperative pain and delays the need for additional analgesic intervention. However, given the limitations of this study, these conclusions should be interpreted with caution, and further research is warranted before adopting this approach as a standard medical strategy.

REFERENCES

[1] Albrecht E, Kirkham KR, Liu SS, et al. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. Anaesthesia 2013;68:79-90.
[2] Iseri LT, French JH. Magnesium: nature's physiologic calcium blocker. Am Heart J 1984;108:188–93.
[3] Feria M, Abad F, Sanchez A, et al. Magnesium sulphate injected subcutaneously suppresses autotomy in peripherally deafferented rats. Pain 1993;53:287-93.
[4] Woolf CJ, Thompson SW. The induction and maintenance of central sensitization is dependent on N-methyl-D-aspartic acid receptor activation; implications for the treatment of post-injury pain hypersensitivity states. Pain 1991;44:293-9.
[5] Aryana P, Rajaei S, Bagheri A, et al. Acute effect of intravenous administration of magnesium sulfate on serum levels of interleukin-6 and tumor necrosis factoralpha in patients undergoing elective coronary bypass graft with cardiopulmonary bypass. Anesth Pain Med 2014;4:e16316.
[6] Kidd BL, Urban LA. Mechanisms of inflammatory pain. Br J Anaesth 2001;87:3-11.
[7] Hwang JY, NA HS, Jeon YT et al. IV Infusion of magnesium sulphate during spinal anaesthesia improves postoperative analgesia. Br J Anaesthesiol 2010;104(1):89-93.
[8] Kayalha H, Yaghoubi S, Yazdi Z, et al. Effect of Intervenous Magnesium Sulfate on decreasing opioid requirement after surgery of the Lower Limb fracture by spinal anesthesia. International Journal of Preventive Medicine 2019;10(1):57.
[9] Dabbagh A, Elyasi H, Razavi SS, et al. Intravenous magnesium sulfate for post-operative pain in patients undergoing lower limb orthopedic surgery. Acta Anaesthesiol Scand 2009;53(8):1088-91.
[10] Shah PN, Dhengle Y. Magnesium sulfate for postoperative analgesia after surgery under spinal anesthesia. Acta Anaesthesiol Taiwanica 2016;54(2):62-4.
[11] Agrawal A, Agrawal S, Payal YS. Effect of continuous magnesium sulfate infusion on spinal block characteristics: a prospective study. Saudi J Anaesth 2014;8:78–82.

[12] Shin HJ, Kim EY, Na HS, et al. Magnesium sulphate attenuates acute postoperative pain and increased pain intensity after surgical injury in staged bilateral total knee replacement: a randomized, double-blinded, placebo-controlled trial. Br J Anaesth 2016;117(4):497-503.