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Original Research Article

Intrathecal Magnesium Sulphate as an Adjuvant to Bupivacaine for Lower Limb Orthopaedic Surgeries: A Randomized Controlled Trial

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Conflict of interest: Nil

Abstract

Background and Aim: Intrathecal adjuvants have gained popularity for prolonging duration and quality of subarachnoid block. Hence, this study was undertaken to evaluate the effect of addition of magnesium sulphate with bupivacaine (hyperbaric) in spinal anesthesia for prolongation of analgesia.

Material and Methods: This randomized controlled study enrolled 80 patients, comprising both males and females with American Society of Anesthesiologists physical status I or II, who were scheduled for lower limb orthopedic surgeries. Patients were randomly allocated in two groups and were given following drug intrathecally as per group. Group BM – bupivacaine 15 mg(0.5% heavy) with magnesium sulphate (100 mg) Group B – bupivacaine 15 mg (0.5% heavy) with 0.5 ml normal saline. Parameters monitored were onset of sensory and motor block, duration of analgesia, hemodynamic parameters, sedation score and intra and postoperative complication. Data analyzed by student's t test and chi square test.

Results: The time of onset of sensory block was comparable in both the group, the time of onset of motor block was delayed in group BM (77.37 ± 8.69) compared to Group B (72.50 ± 12.40). The mean duration of motor blockade was 322.25 ± 23.91 min in group BM and 272.50 ± 23.01 min in group B. It was statistically significant. The postoperative analgesia was found to be prolonged with addition of intrathecal magnesium sulphate (24 hr VAS score 2.13 ± 1.17 in BM group, and 3.40 ± 1.79 in Group B) and it provided better hemodynamic stability.

Conclusion: The addition of 100 mg of magnesium sulfate to hyperbaric bupivacaine has effectively extended analgesia duration, influenced motor blockade onset, and improved hemodynamic stability without notable adverse effects, making it a valuable adjunct in lower limb orthopedic postoperative pain management. Additional research and trials are warranted to fully understand its therapeutic benefits and optimize its clinical utility.

Keywords: Analgesia, Bupivacaine, Intrathecal Magnesium Sulphate, Lower Limb Orthopedic Surgeries, Spinal Adjuvant.

Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage". Regional anesthesia offers several advantages, including safety, cost-effectiveness, and prolonged postoperative analgesia. Epidural anesthesia can be extended through the use of epidural catheters and the administration of adjuvants along with local anesthetics, which also prolongs intrathecal anesthesia [1-4].

Lower limb surgeries can be performed under regional, general, or local anesthesia, with neuraxial blockade being the preferred method. Intrathecal anesthesia is favored due to its rapid onset, high-quality block, and low risk of catheter-related infections, lower failure rate, and cost-effectiveness. However, its disadvantages include a limited duration of the block and a short duration of postoperative analgesia [5,6].

The use of adjuvants in intrathecal anesthesia is becoming increasingly popular due to the benefits of prolonged blockade duration, improved patient satisfaction, higher success rates, optimal resource utilization compared to general anesthesia, and faster recovery times. Effective pain management accelerates functional recovery, facilitates rehabilitation, and helps patients return to their normal activities more quickly. The duration of

intrathecal anesthesia can be extended using opioids and other drugs such as dexmedetomidine (DXM), clonidine, magnesium sulfate, ketamine, and midazolam. However, each drug has its own adverse effects [7-9].

Magnesium, a non-competitive antagonist to N-Methyl-D-Aspartate (NMDA) receptors, has the ability to prevent central sensitization from peripheral nociceptive stimulation. The antinociceptive properties of magnesium are relevant not only to chronic pain but also in determining the intensity and duration of postoperative pain [10-13]. Hence, in our study we hypothesized that intrathecal magnesium sulphate provides better hemodynamic stability along with potentiating duration of analgesia as spinal adjuvant in lower limb surgeries.

The aim of this study was to assess the effects of intrathecal magnesium sulfate (50% w/v) as an adjunct to hyperbaric bupivacaine 0.5% for spinal anesthesia in 80 patients with ASA physical status I and II, aged between 18 and 60 years, of average height and weight, undergoing lower limb orthopedic (specifically tibia fibula surgery) procedures under spinal anesthesia. The objectives are to evaluate and compare parameters related to subarachnoid block, including sensory block characteristics (highest sensory level achieved, time to achieve highest sensory level, two-segment regression time, and time for sensory regression to L1 level from the highest sensory level), onset and duration of motor block, Ramsay sedation score, absolute and effective analgesia, rescue analgesic requirements within 24 hours, vital parameters (pulse rate, blood pressure, respiratory rate, and oxygen saturation), and intra/postoperative side effects.

Material and Methods

This randomized study was conducted after getting institutional ethical committee approval of the hospital from October 2016 to October 2017, a total of 80 patients scheduled for elective lower limb orthopedic surgeries were selected for the study and randomly allocated in two groups. Patients of either sex of American society of anaesthesiologists physical status grade I or II between the ages of 18-60 years were included in study. Anticipated duration of surgery is 180 min. patient with contraindication to spinal anaesthesia like local infection, bleeding and morbid obesity, who had received magnesium sulphate from any other route have been excluded from study.

Thorough pre anaesthetic checkup and all routine investigation of all patients done. Tablet Ranitidine (150 mg) and Tablet Diazepam (10 mg) given night before surgery. Procedure was explained to patient and written informed consent was taken. After shifting the patient to operation theatre baseline vitals Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Oxygen saturation (SPO2) were recorded. After securing large IV cannula preload of ringer lactate solution given before subarachnoid block. With aseptic and antiseptic precaution, a 23-gaugequinke needle was inserted intrathecally through L3-L4 space in sitting position with midline approach. After successful CSF aspiration, anaesthetic solution was injected. No additional analgesic was administered from any other route.

Blinding was done by envelope method that have been prepared by person not involved in study and were randomly handed over to anaesthetist. Randomization done by computer method (www.randomizer.com). Two group labeled as follows : Group BM – 15 mg bupivacaine (0.5 % heavy) with 100 mg magnesium sulphate (total 3.5 ml volume, magnesium sulphate taken in insulin syringe and diluted up to 0.5 ml with sterile water) and group B – 15 mg bupivacaine (0.5% heavy) with 0.5 ml normal saline. No tilting of table done after giving subarachnoid block and the highest level of block achieved was noted. Sensory level assessed by pin prick method and motor block was assessed using Bromage scale and was assessed at 5 min interval till 20 min. Sedation score assessed using Ramsay sedation scale intra and postoperatively : 1. Awake 2.somnolent 3.Respond to verbal stimuli 4.asleep

Bromagescale

Grade 0 - no blockade or no motor loss
Grade I – Unable to flex hip
Grade II – Unable to flex knee
Grade III – Unable to flex ankle

Baseline systolic and diastolic blood pressure was noted and then recorded every 5 min interval after subarachnoid block until 30 min and after that recorded at every 10 min interval until the end of surgery. Decrease in systolic blood pressure 20% below the baseline or < 90 mm of hg was treated with IV bolus of fluid or inj.ephedrine 5 mg as required.

Visual analogue pain scale (VAS) was explained to patient preoperatively recorded 24-hour post operatively. Rescue analgesia was given when VAS score was ≥ 4. Duration of absolute analgesia recorded from the time of injection to the time of first complaint of pain and duration of effective analgesia recorded from the time of injection to the time of need of first rescue analgesia (VAS ≥ 4). Rescue analgesia consisted of Injection Tramadol (50 mg) Intravenously (IV). The data was analysed using SPSS 2.0 and expressed as mean ± SD. Intra group comparison was done using annova test. Categorical variables and continuous variable

analysis done by chi square andt test respectively. P< 0.05 considered as statistically significant.

Results

Total of 80 patients included in study with 40 in each group. Demographic data was comparable in both the group (Table 1).

Table 1: Demographic data

Demographic data			
	Group BM	**Group B**	**P value**
Age in years	41.52 ±9.90	40.30± 11.64	>0.05
Sex (M:F)	33:7	31:9	>0.05
ASA Grading (I:II)	23:17	27:13	>0.05
Mean duration of surgery	128.52 ±20	135.87 ±18.81	>0.05

The mean duration of motor blockade was 322.25 ± 23.91 min in group BM and 272.50 ± 23.01 min in group B. It was statistically significant (Table 2).

Table 2: Comparison of onset of sensory and motor block, duration and recovery

	Time to onset of sensory at L1 (Seconds)	**Peak level (Minutes)**	**Regression to L1 (Minutes)**	**Onset of motor block (Minutes)**	**Maximum bromage achieved time (Minutes)**	**Duration of blockade (Minutes)**
Group BM	69.62 ±8.72	3.22 ±0.46	167.92± 14.09	77.37 ±8.69	3.43 ±0.49	322.25±23.91
Group B	67.12±11.54	3.10 ±0.41	147.12±16.40	72.50±12.40	3.16 ±0.58	272.50±23.01
P Value	>0.05	>0.05	<0.01	<0.05	<0.05	<0.01

Table 3 shows Comparison of Heart Rate (HR), Systolic Blood Pressure (SBP), and Diastolic Blood Pressure (DBP) in both groups. There was no statistically significant difference between the groups.

Table 3: Comparison of HR SBP DBP in both the group

		HR Mean	**P value**	**SBP mean**	**P value**	**DBP mean**	**P value**
Baseline	Group BM	87.95± 9.50	>0.05	129.20 ±11.40	>0.05	80.55± 6.92	>0.05
	Group B	86.45 ±8.28		129.15± 11.35		98.95± 0.22	
At 5 min	Group BM	83.55 ±9.20	>0.05	124.60± 8.93	<0.05	77.00 ±5.81	>0.05
	Group B	81.10± 9.80		118.35± 9.96		75.55 ±5.86	
At 10 min	Group BM	83.25± 8.34	>0.05	124.55 ±8.72	<0.05	76.30 ±5.73	>0.05
	Group B	80.90± 9.27		115.80± 8.83		74.40 ±5.12	
At 15 min	Group BM	84.40 ±8.60	>0.05	123.25 ±8.03	<0.001	76.00± 5.16	<0.05
	Group B	80.65 ±10.57		113.00± 8.99		72.65± 4.90	
At 20 min	Group BM	84.95 ±8.85	>0.05	121.95 ±7.66	<0.001	75.65± 5.24	<0.001
	Group B	80.80 ±10.19		112.70± 12.28		71.25± 4.74	

The mean duration of absolute analgesia in group BM was 388.67 ± 26.01 min and in group B was 282.55 ± 24.78 min. The mean duration of effective analgesia in group BM was 516.95 ± 48.83 min and in group B was 365.62 ± 35.28 min respectively that was statistically significant in group BM (Table 4). Rescue analgesia was administered when VAS score was ≥ 4.The number of mean rescue analgesic needed were 3.07 ±0.72 in group B as compared to 1.62±0.54 in group BM during 24 hour period, the difference was statistically highly significant (Table 4).

Table 4: Comparison of VAS score and requirement of rescue analgesia

	VAS score				**Duration of absolute analgesia**	**Duration of effective analgesia**	**Total no. of rescue analgesia required in 24 hour**
	4 hour	10 hour	16 hour	24 hour			
Group BM	2.57± 1.57	1.18 ±1.24	2.73± 1.62	2.13± 1.17	388.67± 26.01	516.95+ 48.83	1.62±0.54
Group B	3.07 ±1.80	2.87± 1.72	1.80 ±0.89	3.40 ±1.79	282.55± 24.78	365.62±35.28	3.07±0.72
P Value	<0.001	<0.001	<0.05	<0.05	<0.001	<0.001	<0.001

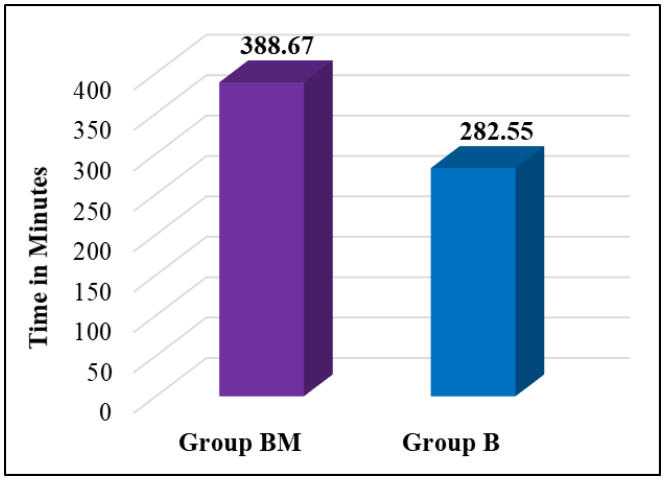

Figure 1: Mean Duration of absolute analgesia (P<0.001)

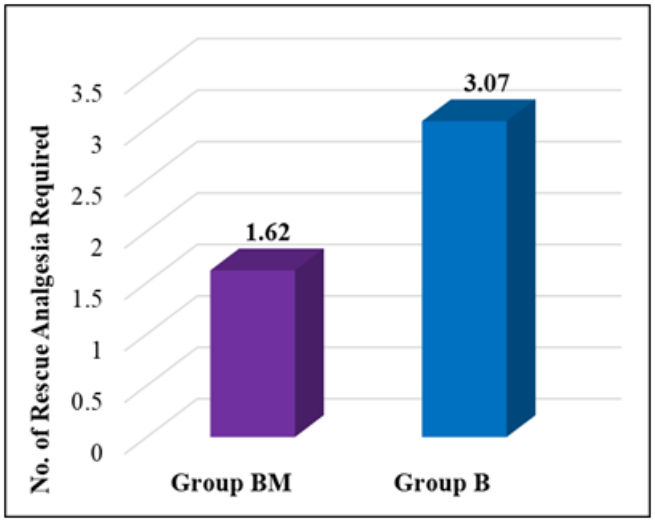

Figure 2: Total no. of rescue analgesiarequired in 24 hour (P<0.001)

Table 5: Intra/postoperative complication

	Group BM (n)	Group B (n)
Bradycardia	1	2
Hypotension	2	7
Nausea/vomiting	0	2
Respiratory depression	0	0
Shivering	1	0
Urine retention	0	0

Discussion

In the present study, it was observed that the onset of motor block was achieved earlier in group B. However, when magnesium was added to group BM, motor blockade was delayed. Sarika et al. [14] reported a similar delay when intrathecal magnesium sulfate was added to hyperbaric bupivacaine, and Ozalevli et al. [15] observed a similar delay with isobaric bupivacaine (hyperbaric bupivacaine 0.5% was used in our study). This delay may be attributed to differences in the pH and baricity of the magnesium sulfate-containing solution, as suggested by Sarika et al. [14] and Arora et al. [16]. Additionally, the increased metabolism of bupivacaine due to the activation of cytochrome P450 by magnesium might be responsible for this delay.

Intrathecal magnesium sulfate did not affect the onset or maximum level of sensory blockade, indicating its effects are primarily at the spinal level. In our study, the majority of patients achieved a block up to the T10 level. It was also noted that the ascent of the drug was slower in comparison to the control group, likely due to changes in the baricity of the drug solution.

The addition of 100 mg of magnesium sulfate to bupivacaine significantly increased the duration of

effective and absolute analgesia without any adverse effects. This prolongation of analgesia is due to the synergistic action between the local anesthetic and NMDA antagonist such as magnesium sulfate. Group BM patients had a reduced total consumption of rescue analgesic (intravenous injection of tramadol) in the first 24 hours postoperatively.

The inclusion of intrathecal magnesium sulfate can potentially replace opioids like fentanyl, thereby avoiding opioid-related side effects such as sedation, pruritus, and respiratory depression. An analysis of intraoperative hemodynamic parameters indicated a lower incidence of hypotension and bradycardia in group BM [17].

Thus, magnesium sulfate can replace various opioids (fentanyl, sufentanil, tramadol) and other adjuvants such as dexmedetomidine, clonidine, and midazolam in spinal anesthesia.

The intrathecal dose of magnesium sulfate used in our study was comparable to that in the studies by Sarika et al. [14] and Khalili et al. [18]. We found that a larger dose (100 mg of magnesium sulfate) provided effective postoperative analgesia and better hemodynamic stability without significant adverse effects. None of the patients in group BM experienced somnolence greater than a score of 2.

However, no long-term follow-up of the patients was conducted. Patients were only monitored during their hospital stay, indicating a need for further studies to establish the long-term safety profile of magnesium sulfate.

Conclusion

The inclusion of a 100 mg dose of magnesium sulfate in the administration of hyperbaric bupivacaine has shown promising results in significantly prolonging the duration of analgesia. This combined regimen has been observed to not only extend the analgesic effect but also to exert a subtle influence on the onset time of motor blockade. Moreover, it has demonstrated an advantageous impact on hemodynamic stability, promoting a more favorable cardiovascular response during and after the procedure.

Importantly, the administration of magnesium sulfate alongside hyperbaric bupivacaine has been well-tolerated, with no significant adverse effects noted in the study population. Based on the observed benefits in analgesia duration, motor blockade onset, and hemodynamic stability, magnesium sulfate emerges as a promising adjunct in the management of postoperative pain in lower limb orthopedic procedures. Further research and clinical trials may elucidate the full extent of its therapeutic potential and optimize its use in perioperative care strategies.

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