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Comparison of Intrathecal Bupivacaine 0.5% (H) With or Without Addition of Magnesium Sulfate in Adult Patients Undergoing Lower Limb Orthopaedic Surgery

Dr Abhishek Dhanjal, Dr Rama Wason
VMMC & Safdarjung Hospital, New Delhi

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ABSTRACT
BACKGROUND: Spinal anaesthesia is widely used for orthopedics lower limb surgeries. As opioid can cause side effects like respiratory depression, hemodynamic instability, urinary retention, pruritis, nausea and vomiting and so that may limit their use. Magnesium has been shown to provide analgesia without complication when administered into the epidural space in combination with bupivacaine.
AIM: To compare intrathecal bupivacaine 0.5% (H) with or without addition magnesium sulfate in adult patients undergoing lower limb orthopedics surgery.
METHODS: Ninety were divided into Group B: 2.8 ml of 0.5% (H) bupivacaine + 0.2ml of 0.9% normal saline and Group B+M: 2.8 ml of 0.5% (H) bupivacaine + (100mg) of preservative free 50% magnesium sulfate. Primary objective is to assess the onset of sensory and motor block. Secondary objective is to assess the duration of analgesia by the time to first postoperative analgesic requirement.
RESULTS: The addition of magnesium sulfate to bupivacaine significantly prolong the duration of sensory blockade and motor blockade. There was no difference as regard the time for onset of sensory blockade and motor blockade with addition of magnesium sulfate when compared with control group. The time of first rescue analgesia was better in group B+M than group B with less incidence of PONV.
CONCLUSION: Magnesium sulfate can be considered as an alternative adjuvant with 0.5% (H) bupivacaine for patients undergoing lower limb orthopedics surgery.

I. INTRODUCTION

Spinal anaesthesia is widely used for orthopaedic lower limb surgeries.It reduces intraoperative and post operative morbidities in elderly patients with age related impairments and also therisk of airway complications and prevents hemodynamic instability associated with laryngoscopy and intubation. Among all the local anaesthetics 0.5% hyperbaric bupivacaine is the most common drug for neuraxial block however the disadvantage of the single injection is its limited duration.[1]Intrathecal adjuvants have become popular for prolonging the duration of block, few clinical trials have examined the effect of adding intrathecal magnesium sulfate to anaesthetic agents such as bupivacaine, yet the mechanism is not clear. These spinal adjuvants allow the use of lower dose of local anesthetics to prolong the duration and intensify theeffects of subarachnoid block.Opioids can cause side effects like respiratory depression, hemodynamic instability, urinary retention, pruritis, nausea and vomiting and so that may limit their use. Newer methods to replace the opioids for prolonging duration of subarachnoid block and reducing the requirement of post operative analgesics are of great interests in surgical procedures.[2-5]

Several agents have been employed such as opioids and N-methyl D-aspartic acid (NMDA) receptor antagonist to improve the quality of anaesthesia increase post-operative analgesia and health early recovery and rehabilitation.[6]

Magnesium is the fourth most common cation in the body, and the second most common intracellular cation after potassium. It has a fundamental role as a co-factor in more than 300 enzymatic reactions involving energy metabolism and nucleic acid synthesis. It is also involved in several processes including: hormone receptor binding; gating of calcium channels; transmembrane ion flux and regulation of adenylate cyclase; muscle contraction; neuronal activity; control of vasomotor tone; cardiac excitability; and neurotransmitter release. In many of its actions it has been likened to a physiological calcium antagonist.[7,8]

Magnesium is an ion that inhibits calcium entry into the cells by non-competitive blockage of the dorsal horn and NMDA receptor, which modulates or prevent central pain sensitisation.

Therefore, exogenously administered magnesium sulphate may act as analgesic

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adjuvant.[9] Magnesium has been shown to provide analgesia without complication when administered into the epidural space in combination with bupivacaine.[10] Studies also showed that addition of magnesium sulfate is associated with less analgesic requirement and less discomfort during post operative period.

Literature shows that the use of magnesium intrathecally prolongs the action of subarachnoid anaesthesia. However, most of these studies used an opioid along with magnesium, which could have contributed to the prolongation of blockade after subarachnoid block, magnesium alone with local anesthesia in a dose of 50 mg and maximum upto 100 mg has been used in a few studies. Although the results of adding magnesium sulphate 50 mg to bupivacaine are conflicting, the effect of increasing the dose of additional magnesium sulphate has not been fully investigated. So this study was planned to study the addition of magnesium sulfate with intrathecal bupivacaine in patients undergoing lower limb orthopaedic surgery.

II. MATERIALS AND METHODS

VENUE OF STUDY

The proposed study was carried out in the department of anaesthesiology and intensive care at V.M.MC and Safdarjung Hospital, New Delhi, after obtaining clearance from the college ethical committee.

TYPE OF STUDY

Randomized,interventional study.

SAMPLE SIZE

At 95% confidence level and 80% power, taking mean onset of sensory block time as 5.65±0.92 minutes Bupivacaine Group and 6.60±1.12 minutes in bupivacaine with magnesium sulphate group (Banihashem N et al)[10], sample size was calculated as 36 per group

$$N=\frac{(0.92+1.12)^2(1.96+0.84)^2}{(6.60-5.65)^2}$$

$$n=(\sigma_1+\sigma_2)^2\frac{\left(z_{1-\alpha/2}+z_{1-\beta}\right)^2}{(m_1-m_2)^2}$$

- Where m1=mean on set of sensory block time in Bupivacaine Group
- m2=mean on set of sensory blocktime in Bupivacaine with MgSO4 Group
- σ1=SD of the outcome variable in group 1
- σ2=SD of the outcome variable in group2

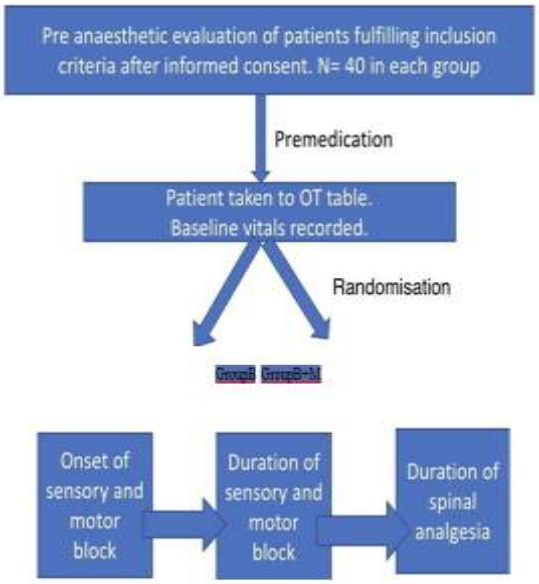
Zα = The standard normal deviate for α

Zβ=The standard normal deviate for β (80% power)

PATIENT SELECTION

INCLUSION CRITERIA: Ninety patients of age18-60 years of either sex, belonging to ASA (American Society of Anesthesiologists) physical status I and II scheduled for orthopaedic lower limb surgery under subarachnoid block.

EXCLUSION CRITERIA: Patients with history of significant co-existing diseases, like cardiovascular diseases, severe respiratory disease, coagulopathies, morbidobesity, allergy to local anaesthetic drugs were excluded from the study.



A thorough pre-anesthetic check up was conducted a day prior to surgery. The pre- operative anesthesia checkup, included in structions about visual an alogue scale(VAS) (mark0
=no pain, 10=worst pain imaginable).

All the patients were kept nil per oral for at least six hours prior to surgery and were given premedication with Tab Alprazolam0.25 mg and Tab Ranitidine 150 mg a night prior to and on the morning of surgery. After shifting the patient to the operation theatre, baseline parameters like Electrocardiography (ECG), Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure(DBP), Respiratory rate(RR), Peripheral Oxygen Saturation (SpO2) was recorded. The patients were allocated with block randomization in which 8 envelopes of 10 drugs each was prepared with each having either bupivacaine 0.5% (H) or bupivacaine 0.5% (H) plus magnesium sulfate. The various treatment groups were as under:

GroupB: Received heavy bupivacaine (0.5%), 14mg (2.8ml) + 0.2ml of preservative free 0.9% normal saline.
GroupB+M: Received heavy bupi vacaine (0.5%), 14mg + 0.2ml (100mg) of preservative free 50% magnesium sulphate.

After achieving an intravenous access and preloading with 10ml/kg of lactated ringer's solution, all patients were administered subarachnoid block under all aseptic precautions in the sitting position using a 25-gauge Quincke's spinal needle at the L2-3 or L3-4 vertebral level. With the needle orifice cephalad and after confirmation of free flow of CSF, the drugs were injected through the spinal needle.

Theonset, duration, highest dermatomal level and recovery of sensory block. Onset, duration and recovery of motor block was recorded. Also duration of first post operative analgesic requirement.

The onset of sensory block was defined as time between injection of the anesthetic and the absence of pain at (T10) dermatome, assessed by pinprick. The highest level of sensory block was evaluated by pinprick at midclavicular line anteriorly every minute (mins) for 6 mins then every 2 mins for 20 mins after injection, thereafter every 15 mins. The duration of sensory block was defined as time of regression of two segments from the maximum block height, evaluated by pinprick. Motor block onset was assessed by modified bromage score.[28] Time for motor block onset was assumed when modified bromage score became three. Complete motor block was assumed when modified bromage score was one and onset of motor block regression was assumed when modified bromage score became two(able to move feet only) and was recorded every 2 mins for 20mins and every 15 mins till the complete regression of motor block. The duration of spinal analgesia was defined as the period from spinal injection to the first occasion when the patient complained of pain requiring analgesic (VAS more than 4) in thepost-operative period. SBP, DBP, HR,RR and SpO2 were recorded every 2mins for the first 20 mins and thereafter every 5mins. VAS was assessed in the postoperative period immediately after patient was shifted to postoperative anesthesia recovery room and every 15mins for three hours.

SBP20% below baseline or less than 90 mm Hg was noted and treated by, intravenous (i.v.) Mephentermine 3mg/6mg along with intravenous fluid supplementation. HR< 50 beats/min associated with fall in blood pressure was noted and treated by 0.6mg of atropine sulphate.

The incidence of hypotension (mean arterial pressure, <20% of baseline), bradycardia (HR<50 beats/min), hypoxemia and excessive sedation, pruritus, dizziness, nausea and vomiting was recorded. Immediately after shifting the patient to post-operative recovery room HR, SBP, DBP, RR and SpO2 was recorded every 15 mins for first 1 hour and every 30 mins for next 2 hours. Motor block recovery (modified bromage score of 5) and sensory block regression was assessed by recording the time of first post operative requirement of analgesia by the patient after completion of surgery.

III. RESULTS:

The analysis was performed on observations recorded from 90 patients. There were no missing values considered in the study. They were randomly put equally in two groups, namely, Bupivacaine (Group B) and Bupivacaine with $MgSO_4$ (Group BM). Thus, there were 45 patients in each group.

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Table1:Distribution and comparison of age of participants in study groups

Age in years	Group B (n=45)	Group BM (n=45)	p-value
Mean ± SD	28.8 ± 8.2	27.7 ± 7.8	0.983
Range	17-60	15-60	
15-30 years	20 (44%)	20 (44%)	1.000
31-45 years	15 (33%)	15 (33%)	
46-60 years	10 (23%)	10 (23%)	

Figure 1:Distribution of age in study groups

As shown in Table 1, in group B, the mean age of patients was 28.8 (± 8.2) years, while ingroup BM, the mean age was 27.7 (± 7.8) years. There were 20 (44%) participants in age group of 15-30 years,15 (33%) in31-46 years of age group and 10 (23%) in 46-60 years in both groups. There was no statistical difference observed between two groups.

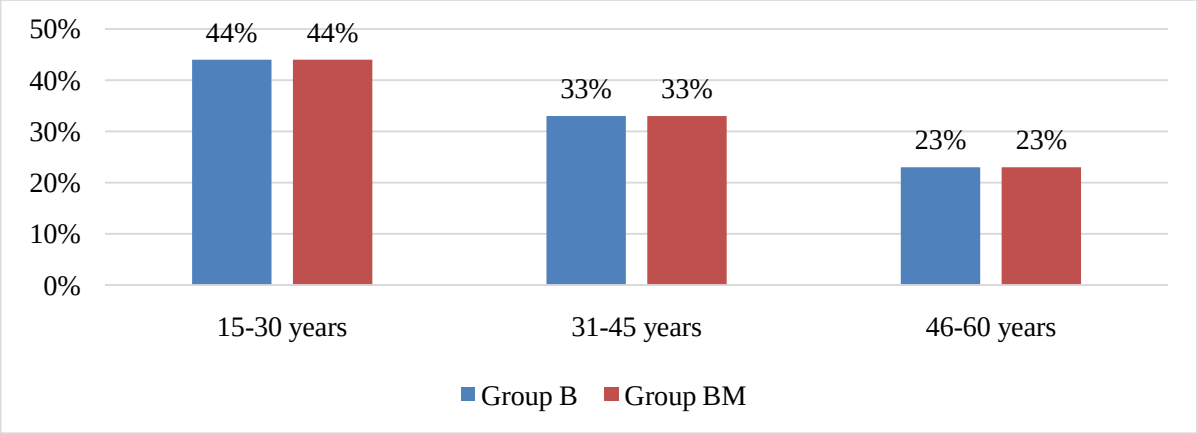

Table 2:Distribution and comparison of gender in study groups

Gender	Group B (n=45)	Group BM (n=45)	p-value
Male	38 (84%)	39 (87%)	0.922
Female	7 (17%)	6 (13%)	

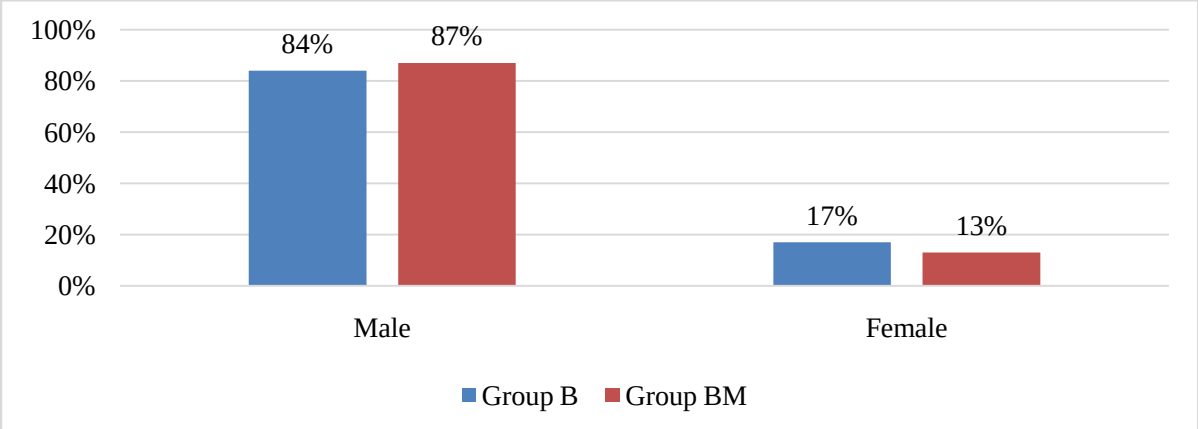

Figure 2: Distribution of gender in study groups

As shown in Table 2, there were 38 (84%) male and 7 (17%) females in Group B, while 39 (87%) male and 6 (13%) females in group BM. There was no statistical difference observed between both groups.

Table3:Distribution and comparison of ASA grade in study groups

Parameters	Group B (n=45)	Group BM (n=45)	p-value
ASA Grade 1	45 (100%)	45 (100%)	1.000

Figure3: Distribution of ASA grade in study groups

As shown in Table 3, the ASA grade 1 was in all patients in both the groups. There was no statistical difference observedin the groups.

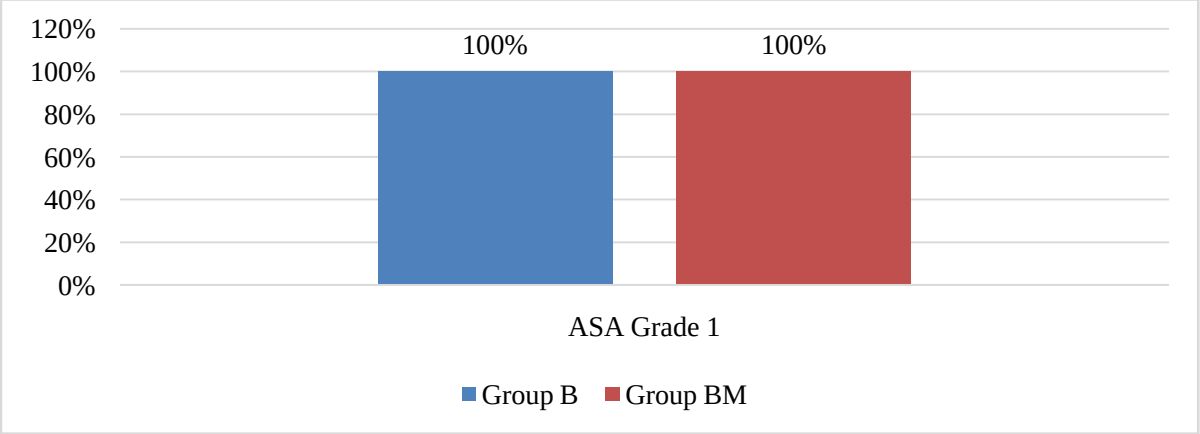

Table 4:Comparison of durationsurgical procedurein study groups

Duration of surgery in minutes	Group B (n=45)	Group BM (n=45)	p-value
Mean ± SD	65.4 ± 24.4	64.1 ± 23.1	0.862
Range	30-120	30-90	

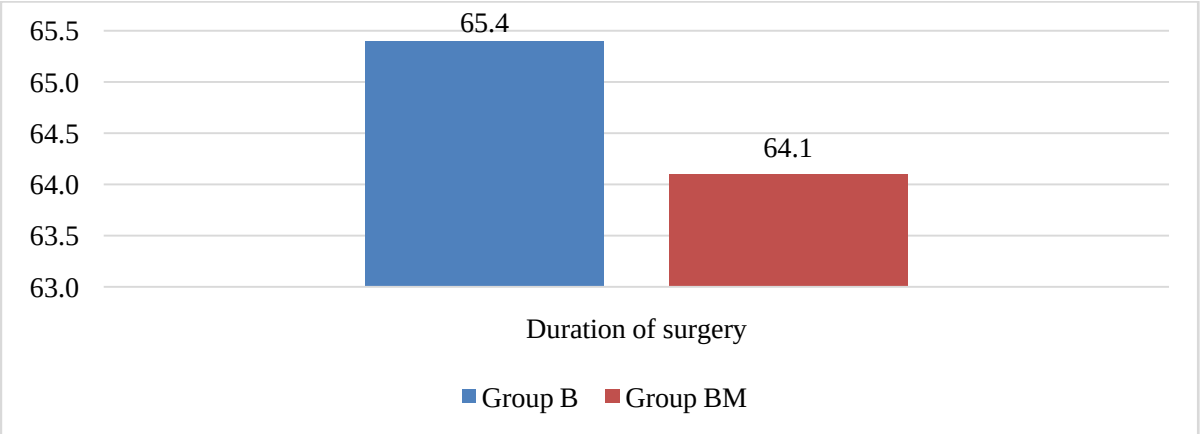

Figure 4: Comparison of duration surgical procedure in study groups

As shown in Table 4, in group B, the mean duration of surgery was 65.4 (± 24.4) minutes, while in group BM, the mean was 64.1 (± 23.1) minutes. There was no statistical difference observed in the groups.

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Table5:Comparison of onset and duration of sensory and motor block in study groups

Onset of sensory block in minutes	Group B (n=45)	Group BM (n=45)	p-value
Mean ± SD	3.1 ± 0.7	2.8 ± 0.7	0.862
Range	2-5	2-5	
Total duration of sensory block in minutes			
Mean ± SD	99.5 ± 8.1	128 ± 9.4	<0.001
Range	85-120	110-140	
Onset of motor block in minutes			
Mean ± SD	4.7 ± 0.7	5.1 ± 0.8	0.237
Range	4-6	4-7	
Total duration of motor block in minutes			
Mean ± SD	128.4 ± 12.2	149.5 ± 9.6	<0.001
Range	100-160	130-170	

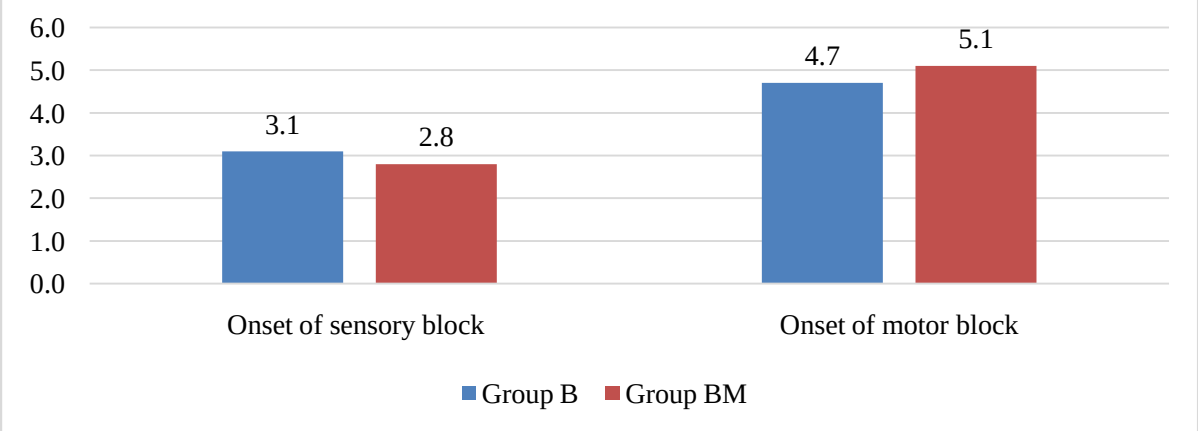

Figure 5: Comparison of onset of sensory and motor block in minutesin study groups

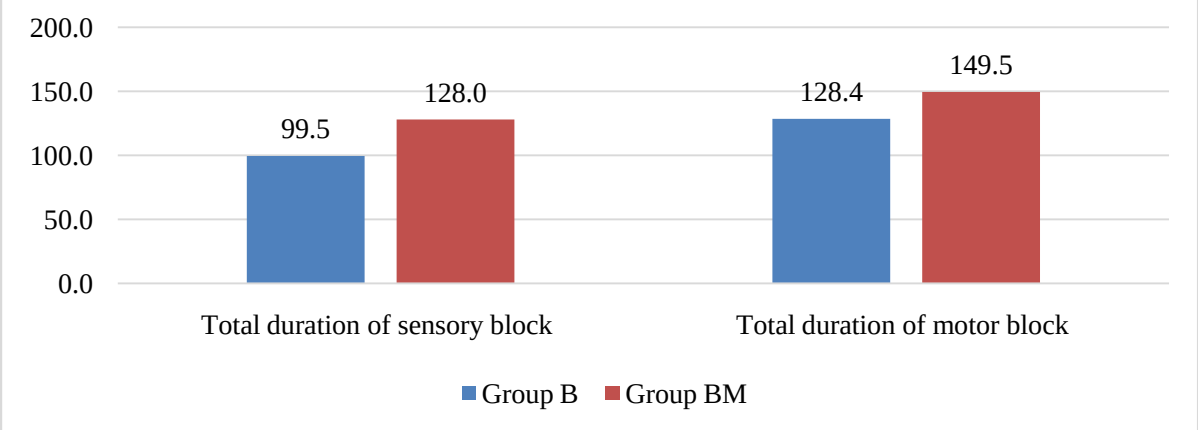

Figure 6: Comparison of total duration of sensory and motor block in minutes in study groups

As shown in Table 5, in group B, the mean onset time of sensory block was 3.1 (± 0.7) minutes, while in group BM, the mean was 2.8 (± 0.7) minutes. Similarly, in group B, the mean onset time of motor block was 4.7 (± 0.7) minutes, while in group BM, the mean was 5.1 (± 0.8) minutes. In group B, the mean total duration of sensory block was 99.5 (± 8.1) minutes, while in group BM, the mean was 128 (± 9.4) minutes. In group B, the mean total duration of motor block was 128.4 (± 12.2) minutes, while in group BM, the mean was 149.5 (± 9.6) minutes. There was statistically significant difference observed in the groups with total duration of sensory and motor block.

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Table 6:Comparison of time of first rescue analgesia in study groups

Time of first rescue analgesia in minutes	Group B (n=45)	Group BM (n=45)	p-value
Mean ± SD	123.4 ± 11.3	149.5 ± 9.7	<0.001
Range	100-140	130-170	

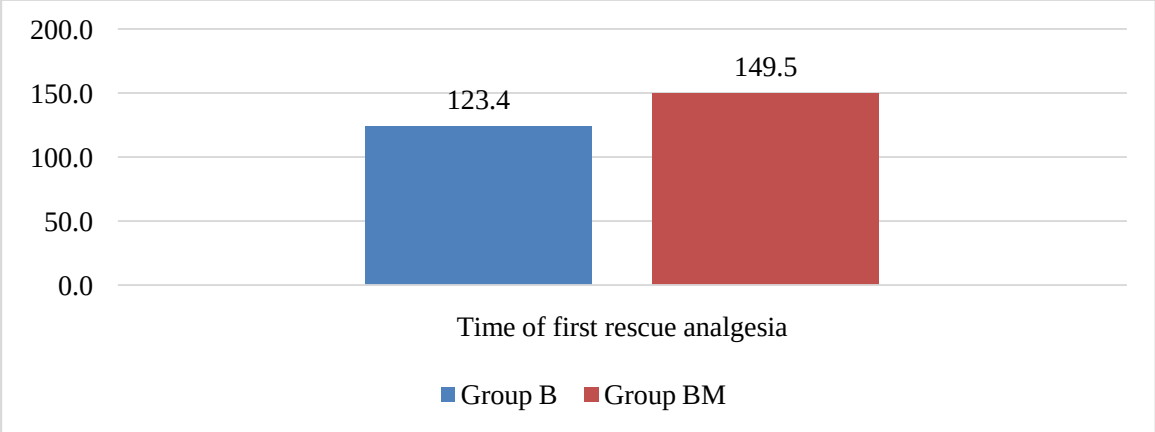

Figure 7: Comparison of time of first rescue analgesia in minutes in study groups

As shown in Table 6, in group B, the mean time of first rescue analgesia was 123.4 (± 11.3) minutes, while in group BM, the mean was 149.5 (± 9.7) minutes. There was statistically significant difference observed in the groups.

Table7: Comparison of heart rate at different intervals in study group

Heart rate in beats/minutes	Group B (n=45)	Group BM (n=45)	p-value*
At Baseline Mean ± SD	75.2 ± 4.8	77.4 ± 4.9	0.648
At 2 mins Mean ± SD	82.0 ± 4.1	80.3 ± 5.6	0.296
At 4 mins Mean ± SD	76.4 ± 4.2	80.4 ± 6.6	<0.001
At 6 mins Mean ± SD	75.0 ± 5.9	80.7 ± 6.3	<0.001
At 8 mins Mean ± SD	76.2 ± 4.2	79.6 ± 5.2	<0.001
At 10 mins Mean ± SD	74.6 ± 4.3	79.6 ± 5.4	<0.001
At 12 mins Mean ± SD	73.8 ± 4.1	79.4 ± 5.5	<0.001
At 14 mins Mean ± SD	73.4 ± 4.9	78.7 ± 5.2	<0.001
At 16 mins Mean ± SD	73.6 ± 4.7	78.1 ± 4.9	<0.001
At 18 mins Mean ± SD	73.2 ± 4.8	77.6 ± 5.8	<0.001
At 20 mins Mean ± SD	73.5 ± 4.8	77.5 ± 5.1	<0.001
At 35 mins Mean ± SD	71.2 ± 4.3	76.4 ± 5.3	<0.001
At 50 mins Mean ± SD	70.6 ± 3.7	75.6 ± 5.7	<0.001
At 65 mins Mean ± SD	72.4 ± 6.3	76.4 ± 6.1	<0.001
At 80 mins Mean ± SD	75.5 ± 7.9	77.7 ± 6.6	<0.001
At 95 mins Mean ± SD	78.9 ± 7.2	78.4 ± 6.2	0.963
At 110 mins Mean ± SD	81.1 ± 7.2	80.1 ± 6.6	0.920
At 125 mins Mean ± SD	80.6 ± 6.9	78.6 ± 4.3	0.134
Post-operative			
At 15 mins Mean ± SD p-value^{+}	82.7 ± 4.9 <0.001	82.6 ± 4.5 <0.001	0.885

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At 30 mins Mean ± SD p-value+	78.5 ± 3.1 <0.001	80.2 ± 3.9 <0.001	0.824
At 45 mins Mean ± SD p-value+	82.1 ± 5.1 <0.001	82.2 ± 3.5 <0.001	0.992
At 60 mins Mean ± SD p-value+	92.3 ± 6.4 <0.001	87.5 ± 3.6 <0.001	<0.001
At 90 mins Mean ± SD p-value+	85.1 ± 3.8 <0.001	84.2 ± 4.5 <0.001	0.945
At 120 mins Mean ± SD p-value+	99.2 ± 7.7 <0.001	101.7 ± 7.5 <0.001	0.742
At 150 mins Mean ± SD p-value+	84.8 ± 4.9 <0.001	84.8 ± 3.5 <0.001	0.992
At 180 mins Mean ± SD p-value+	84.8 ± 2.4 <0.001	85.6 ± 3.4 <0.001	0.992

*Comparison between study groups +Comparison with baseline in same group

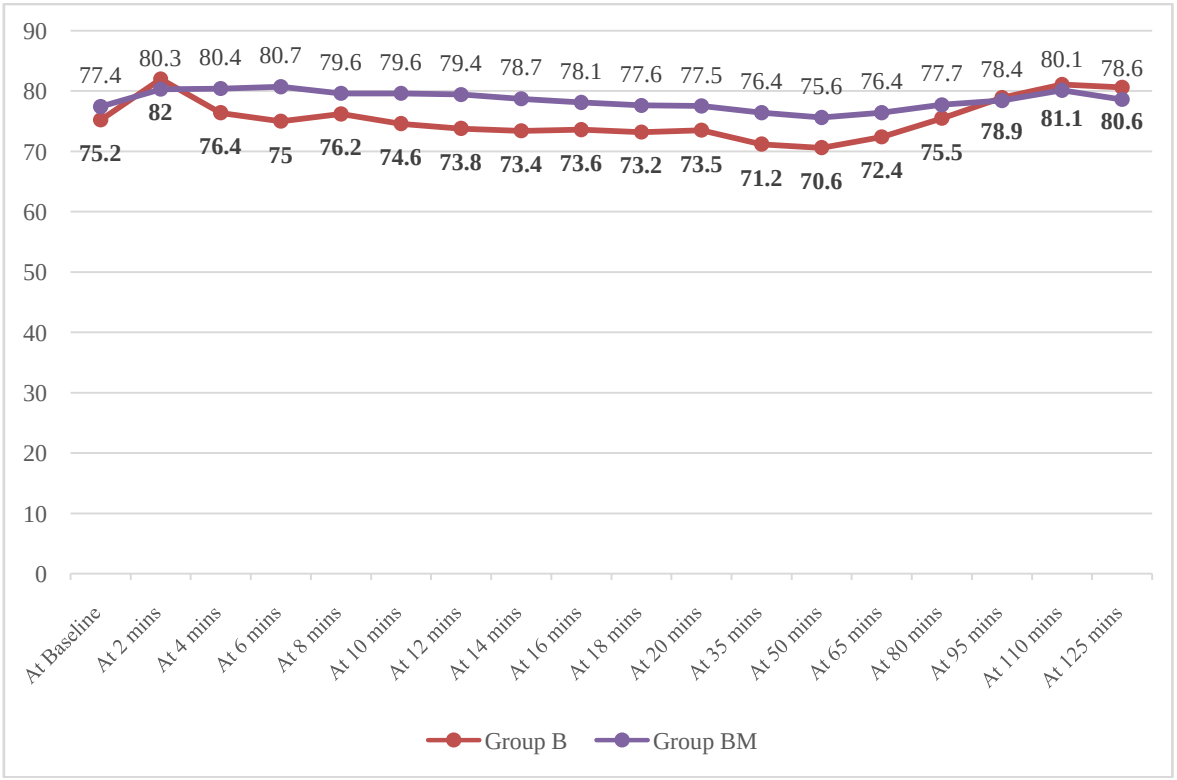

Figure 8: Mean values of heart rate at baseline and pre-operativein beats/minutes in study groups

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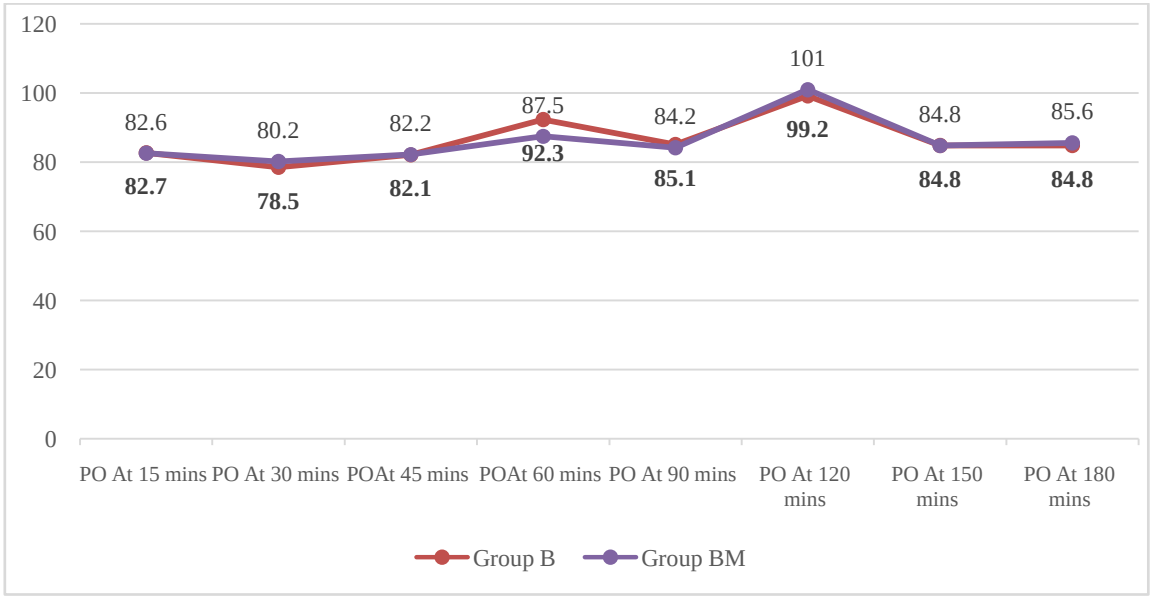

Figure 9: Mean values of heart rate at post-operative in beats/minutes in study groups

As shown in Table 7, the heart rate is compared at various intervals. There was statistically significant difference observed in groups at 4-80 mins, post operative at 60 mins and between baseline and post-operative values.

Table8: Comparison of systolic blood pressure at different intervals in study groups

Mean Systolic blood pressure in mmHg	**Group B (n=45)**	**Group BM (n=45)**	**p-value**
At Baseline Mean ± SD	121.1 ± 3.9	120.1 ± 5.1	0.648
At 2 mins Mean ± SD	127.4 ± 5.5	127.9 ± 4.9	0.296
At 4 mins Mean ± SD	108.8 ± 5.9	110.3 ± 4.7	0.785
At 6 mins Mean ± SD	107.1 ± 4.5	102.6 ± 4.4	0.775
At 8 mins Mean ± SD	98.3 ± 3.4	106.8 ± 3.8	0.689
At 10 mins Mean ± SD	98.3 ± 5.5	98.8 ± 6.1	0.843
At 12 mins Mean ± SD	105.9 ± 5.6	105.1 ± 4.5	0.882
At 14 mins Mean ± SD	106.1 ± 5.4	105 ± 6.5	0.765
At 16 mins Mean ± SD	106.3 ± 5.1	104.7 ± 4.4	0.752
At 18 mins Mean ± SD	106.2 ± 6.1	106.9 ± 6.4	0.993
At 20 mins Mean ± SD	106.5 ± 5.8	107.9 ± 5.6	0.910
At 35 mins Mean ± SD	106.7 ± 5.8	10.7.4 ± 6.1	0.863
At 50 mins Mean ± SD	119.1 ± 4.5	119.3 ± 5.9	0.991
At 65 mins Mean ± SD	126.6 ± 4.5	126.5 ± 4.8	0.941
At 80 mins Mean ± SD	126.1 ± 3.8	125.9 ± 3.8	0.953
At 95 mins Mean ± SD	119.4 ± 4.5	117.5 ± 4.6	0.913
At 110 mins Mean ± SD	120.7 ± 4.1	118.9 ± 4.4	0.740
At 125 mins Mean ± SD	120.5 ± 5.2	118.3 ± 9.5	0.324
Post-operative			
At 15 mins Mean ± SD	119.5 ± 4.3	117.6 ± 4.4	0.885
At 30 mins Mean ± SD	118.1 ± 4.1	117.3 ± 3.4	0.824
At 45 mins Mean ± SD	119.6 ± 5.5	117.3 ± 3.6	0.992

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At 60 mins Mean ± SD	119.6 ± 4.5	117.1 ± 3.5	0.886
At 90 mins Mean ± SD	120.5 ± 4.5	118.6 ± 3.6	0.945
At 120 mins Mean ± SD	128.1 ± 3.9	128.4 ± 4.2	0.742
At 150 mins Mean ± SD	126.6 ± 3.5	126.3 ± 3.8	0.992
At 180 mins Mean ± SD	124.3 ± 4.5	122.1 ± 4.6	0.492

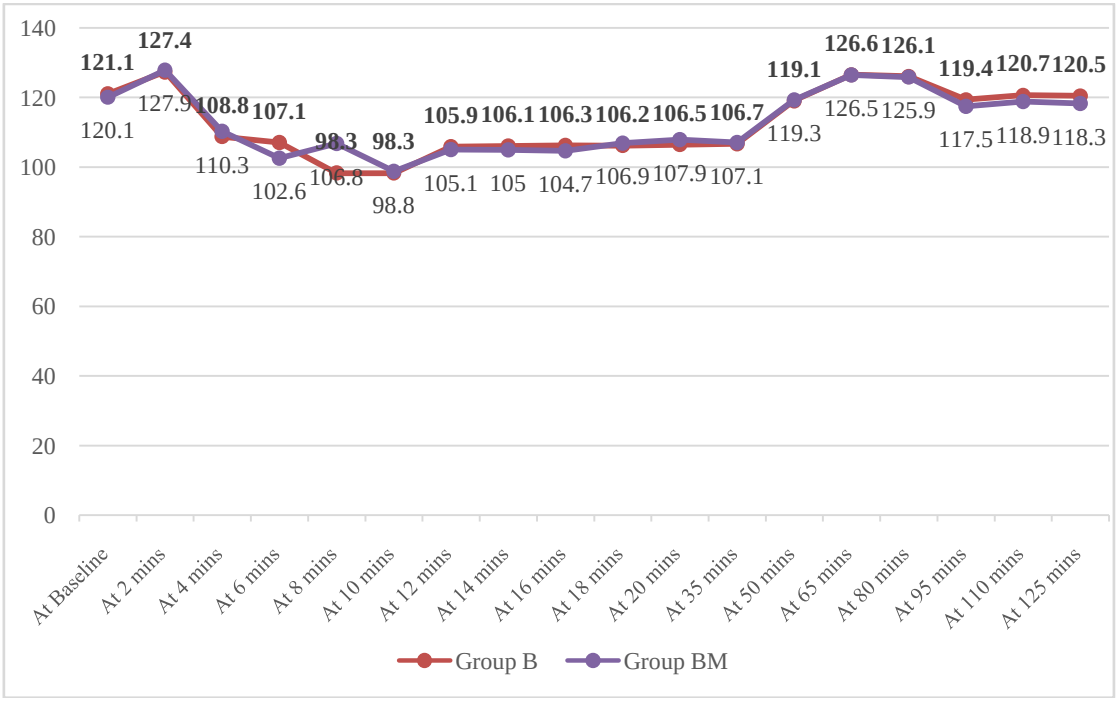

Figure 10: Mean values of Systolic Blood pressureat baseline and pre-operative in mmHg in study groups

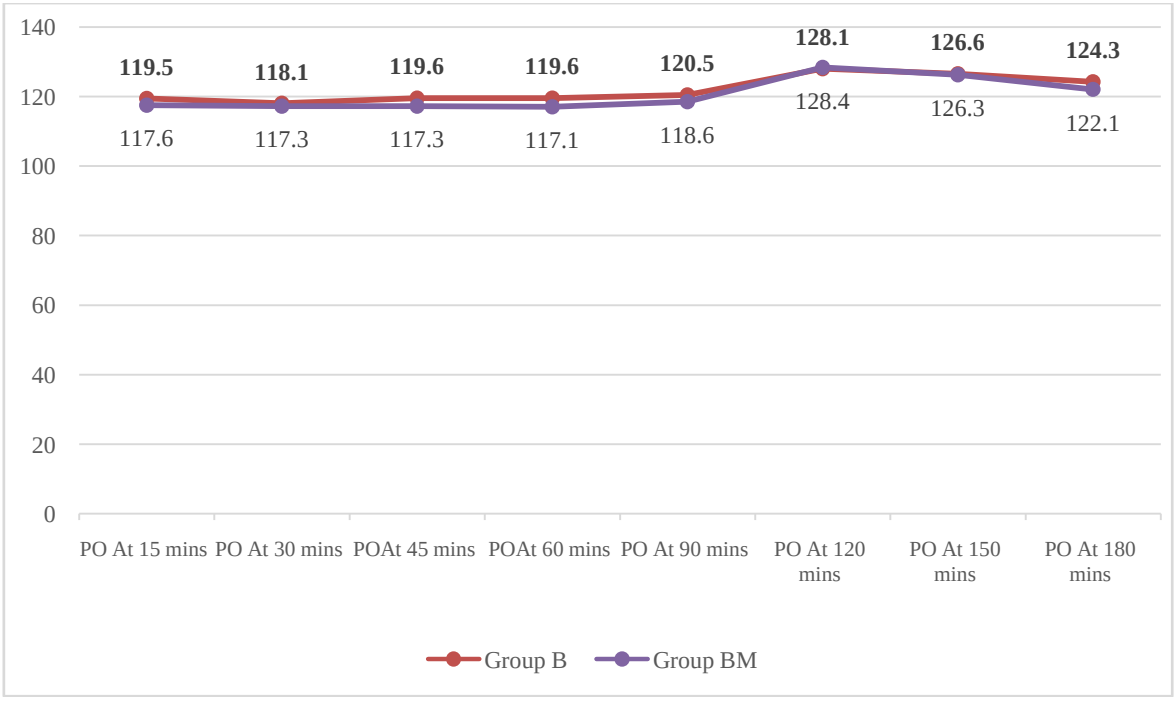

Figure 11: Mean values of Systolic Blood pressureat post- operative in mmHg in study groups

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As shown in Table 8, the systolic blood pressure is compared at various intervals. There was no statistically significant difference observed in groups at all intervals.

Table9: Comparison of Diastolic blood pressure at different intervals in study groups

Mean Diastolic blood pressure in mmHg	**Group B (n=45)**	**Group BM (n=45)**	**p-value**
At Baseline Mean ± SD	71.2 ± 4.8	69.5 ± 2.9	0.238
At 2 mins Mean ± SD	78.4 ± 4.1	78.8 ± 3.6	0.266
At 4 mins Mean ± SD	65.5 ± 3.9	66.1 ± 2.6	0.735
At 6 mins Mean ± SD	64.4 ± 3.2	63.8 ± 3.3	0.683
At 8 mins Mean ± SD	64.5 ± 3.8	64.7 ± 4.2	0.541
At 10 mins Mean ± SD	63.4 ± 4.3	63.3 ± 3.9	0.991
At 12 mins Mean ± SD	65.4 ± 3.1	65.4 ± 4.5	0.992
At 14 mins Mean ± SD	65.8 ± 4.9	66.2 ± 3.2	0.773
At 16 mins Mean ± SD	60.6 ± 4.5	62.1 ± 4.9	0.529
At 18 mins Mean ± SD	59.9 ± 4.1	60.6 ± 4.8	0.833
At 20 mins Mean ± SD	58.4 ± 3.8	59.3 ± 4.1	0.814
At 35 mins Mean ± SD	60.8 ± 4.7	61.7 ± 3.3	0.823
At 50 mins Mean ± SD	65.1± 3.7	66.3 ± 5.7	0.891
At 65 mins Mean ± SD	71.7 ± 2.8	72.8 ± 5.1	0.844
At 80 mins Mean ± SD	72.5 ± 2.9	71.7 ± 5.6	0.753
At 95 mins Mean ± SD	71.7 ± 3.2	74.4 ± 5.2	0.129
At 110 mins Mean ± SD	72.3 ± 3.7	74.5 ± 5.6	0.140
At 125 mins Mean ± SD	72.3 ± 2.9	75.1 ± 4.9	0.324
Post-operative			
At 15 mins Mean ± SD	73.7 ± 2.5	77.8 ± 4.5	<0.001
At 30 mins Mean ± SD	74.6 ± 2.4	75.2 ± 3.9	0.224
At 45 mins Mean ± SD	74.4 ± 2.1	73.8 ± 3.5	0.892
At 60 mins Mean ± SD	74.2 ± 3.4	74.4 ± 3.6	0.910
At 90 mins Mean ± SD	74.4 ± 3.8	75.4 ± 2.5	0.862
At 120 mins Mean ± SD	75.0 ± 2.7	74.7 ± 3.5	0.842
At 150 mins Mean ± SD	73.9 ± 3.9	74.3 ± 3.5	0.972
At 180 mins Mean ± SD	75.2 ± 2.4	74.6 ± 2.4	0.780

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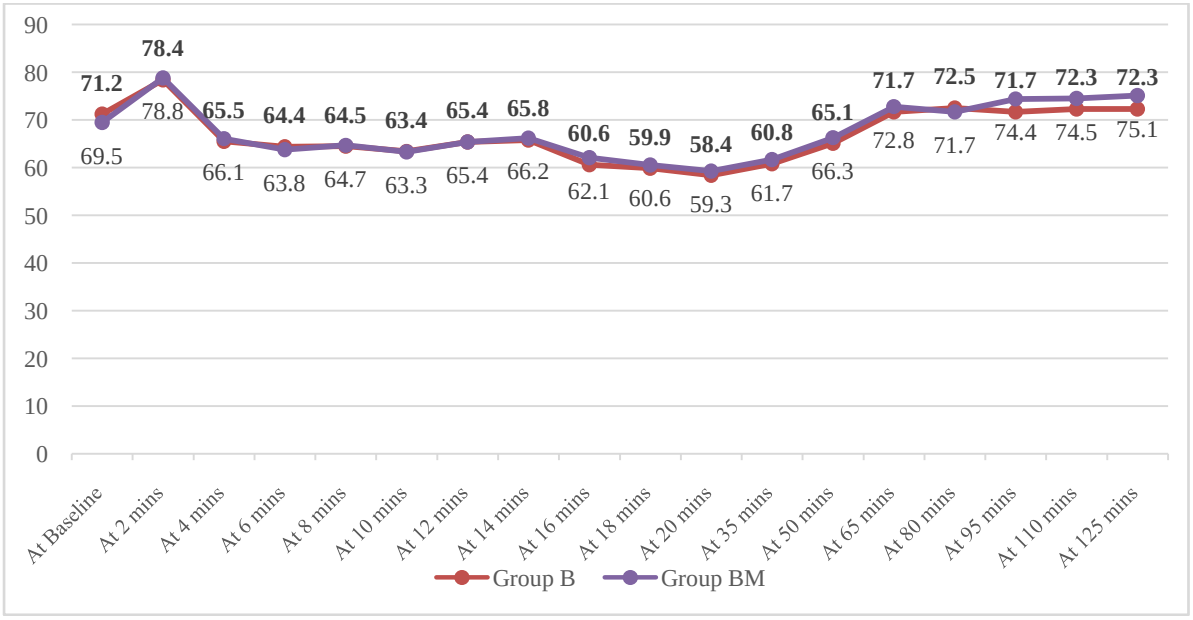

Figure 12: Mean values of Diastolic blood pressure at baseline and pre-operative in mmHg in study groups

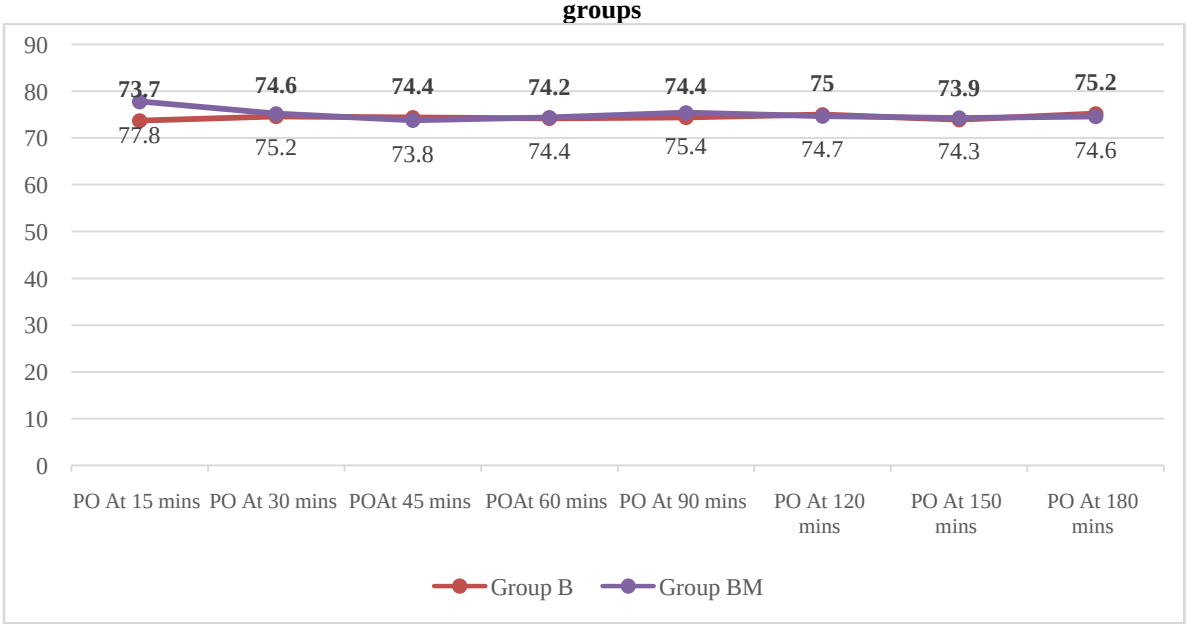

Figure 13: Mean values of Diastolic blood pressure at post-operative in mmHg in study groups

As shown in Table 9, the diastolic blood pressure is compared at various interval.There was no statistically significant difference observed in groups at all intervals, except post-operative follow-up at 15 mins.

Table10: Comparison of mean arterial pressure at different intervals

Mean arterial pressure in mmHg	**Group B (n=45)**	**Group BM (n=45)**	**p-value**
At Baseline Mean ± SD	87.2 ± 2.8	86.4 ± 2.9	0.848
At 2 mins Mean ± SD	94.7 ± 3.1	94.3 ± 3.6	0.996
At 4 mins Mean ± SD	79.7 ± 2.2	80.5 ± 3.1	0.785
At 6 mins Mean ± SD	76.8 ± 2.9	76.4 ± 3.3	0.775

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At 8 mins Mean ± SD	76.2 ± 2.2	78.6 ± 3.2	0.689
At 10 mins Mean ± SD	78.4 ± 3.3	74.8 ± 3.4	0.843
At 12 mins Mean ± SD	74.8 ± 2.1	78.4 ± 3.5	0.882
At 14 mins Mean ± SD	78.4 ± 3.9	78.7 ± 3.2	0.765
At 16 mins Mean ± SD	75.6 ± 3.7	76.0 ± 2.9	0.752
At 18 mins Mean ± SD	74.2 ± 3.8	75.9 ± 3.8	0.993
At 20 mins Mean ± SD	74.5 ± 2.8	75.2 ± 3.5	0.910
At 35 mins Mean ± SD	75.7 ± 3.3	76.6 ± 4.3	0.863
At 50 mins Mean ± SD	82.8 ± 3.7	83.6 ± 5.7	0.991
At 65 mins Mean ± SD	92.3 ± 3.5	93.3 ± 4.2	0.941
At 80 mins Mean ± SD	89.7 ± 2.9	89.5 ± 4.1	0.953
At 95 mins Mean ± SD	87.2 ± 2.5	78.4 ± 4.2	0.913
At 110 mins Mean ± SD	88.0 ± 2.2	89.0 ± 4.1	0.740
At 125 mins Mean ± SD	87.9 ± 2.5	89.1 ± 4.3	0.324
Post-operative			
At 15 mins Mean ± SD	88.7 ± 2.9	90.6 ± 3.5	0.124
At 30 mins Mean ± SD	88.5 ± 1.7	88.2 ± 2.9	0.926
At 45 mins Mean ± SD	89.1 ± 2.1	88.1 ± 2.5	0.973
At 60 mins Mean ± SD	89.2 ± 2.4	88.5 ± 2.6	0.785
At 90 mins Mean ± SD	89.7 ± 2.8	89.7 ± 2.5	0.945
At 120 mins Mean ± SD	92.2 ± 2.3	92.5 ± 2.5	0.942
At 150 mins Mean ± SD	91.3 ± 2.2	91.7 ± 2.5	0.992
At 180 mins Mean ± SD	91.5 ± 2.4	90.3 ± 3.4	0.713

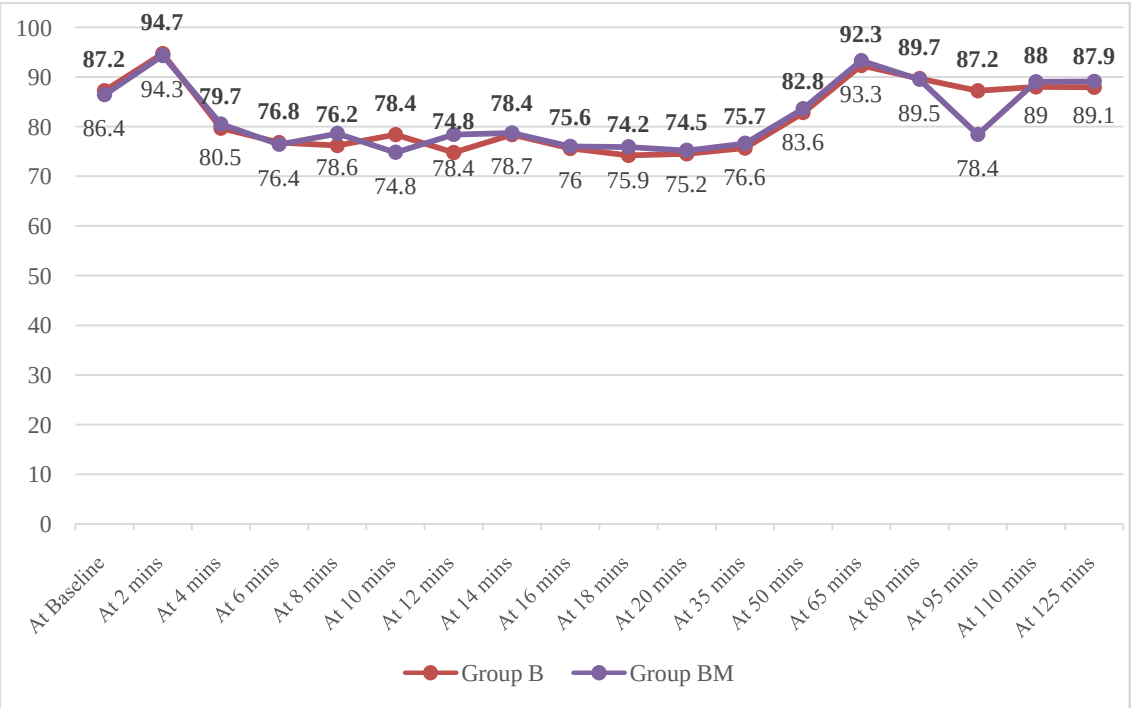

Figure 14: Mean values of mean arterial blood pressure at baseline and pre-operative in mmHg in study groups

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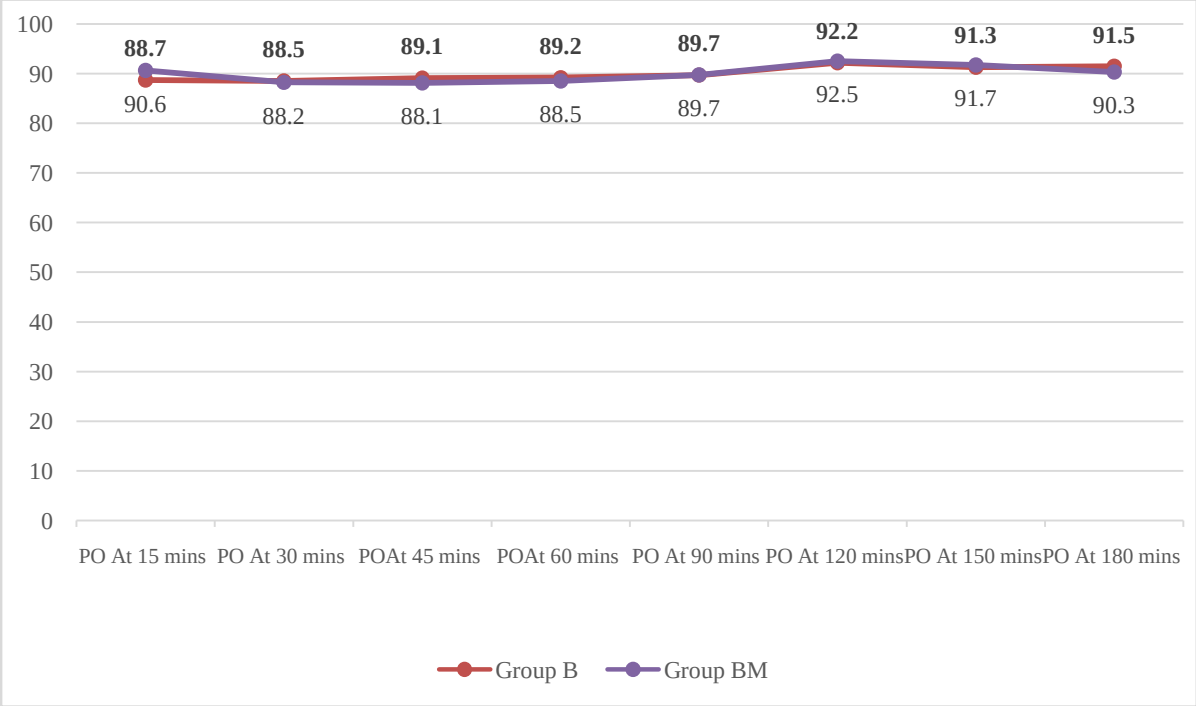

Figure 15: Mean values of mean arterial blood pressure at post-operative in mmHg in study groups

As shown in Table 10, the mean arterial blood pressure is compared at various intervals. There was no statistically significant difference observed in groups at all interval

Table11: Dermatome level at different intervals in study groups

Dermatome level	**Group B (n=45)**	**Group BM (n=45)**	**p-value**
At 1 min Mean ± SD	T12- 45 (100%)	T12- 45 (100%)	1.000
At 2 mins Mean ± SD	T12- 34 (76%) T10- 11 (24%)	T12- 29 (64%) T10- 16 (36%)	0.126
At 3 mins Mean ± SD	T12- 3 (7%) T10- 42 (93%)	T12- 1 (2%) T10- 44 (98%)	0.535
At 4 mins Mean ± SD	T12- 2 (4%) T10- 32 (71%) T9- 11 (24%)	T12- 1 (2%) T10- 28 (62%) T9- 16 (36%)	0.675
At 5 mins Mean ± SD	T10- 2 (4%) T9- 26 (58%) T8- 17 (38%)	T10- 1 (2%) T9- 21 (47%) T8- 23 (51%)	0.889
At 6 mins Mean ± SD	T10- 2 (4%) T8- 43 (96%)	T10- 1 (2%) T8- 44 (98%)	0.989
At 8 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 10 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 12 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 14 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 16 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 18 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 20 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 35 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 50 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000

At 65 mins Mean ± SD	T6- 45 (100%)	T6- 45 (100%)	1.000
At 80 mins Mean ± SD	T7- 45 (100%)	T7- 45 (100%)	1.000
At 95 mins Mean ± SD	T7- 24 (53%) T8- 21 (47%)	T7- 45 (100%)	<0.001
At 110 mins Mean ± SD	T12-3 (7%) T8- 41 (91%) T7- 1 (2%)	T8- 4 (9%) T7- 41 (92%)	<0.001
At 125 mins Mean ± SD	T12- 21 (47%) T8- 24 (53%)	T8- 18 (40%) T7- 27 (60%)	<0.001
At 140 mins Mean ± SD	T12- 23 (51%) T8- 1 (2%) L1- 21 (47%)	T12- 4 (9%) T8- 91 (91%)	<0.001

Table12: Bromage score at different intervals in study groups

Bromage score	**Group B (n=45)**	**Group BM (n=45)**	**p-value**
At 1 min Mean ± SD	5 ± 0	5 ± 0	1.000
At 2 mins Mean ± SD	5 ± 0	5 ± 0	1.000
At 3 mins Mean ± SD	5 ± 0	5 ± 0	1.000
At 4 mins Mean ± SD	3.6 ± 0.5	3.7 ± 0.4	0.675
At 5 mins Mean ± SD	3 ± 0	3.2 ± 0.4	0.889
At 6 mins Mean ± SD	3 ± 0	3.1 ± 0.2	0.989
At 8 mins Mean ± SD	3 ± 0	3 ± 0	1.000
At 10 mins Mean ± SD	2 ± 0	3 ± 0	1.000
At 12 mins Mean ± SD	1 ± 0	2 ± 0	1.000
At 14 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 16 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 18 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 20 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 35 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 50 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 65 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 80 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 95 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 110 mins Mean ± SD	1.2 ± 0.3	1 ± 0	0.986
At 125 mins Mean ± SD	1.4 ± 0.5	1.1 ± 0.2	0.864
At 140 mins Mean ± SD	2.3 ± 0.6	1.37 ± 0.4	0.765
At 160 mins Mean ± SD	2.9 ± 0.2	2.4 ± 0.5	0.886
At 180 mins Mean ± SD	4 ± 0	3.4 ± 0.5	0.986

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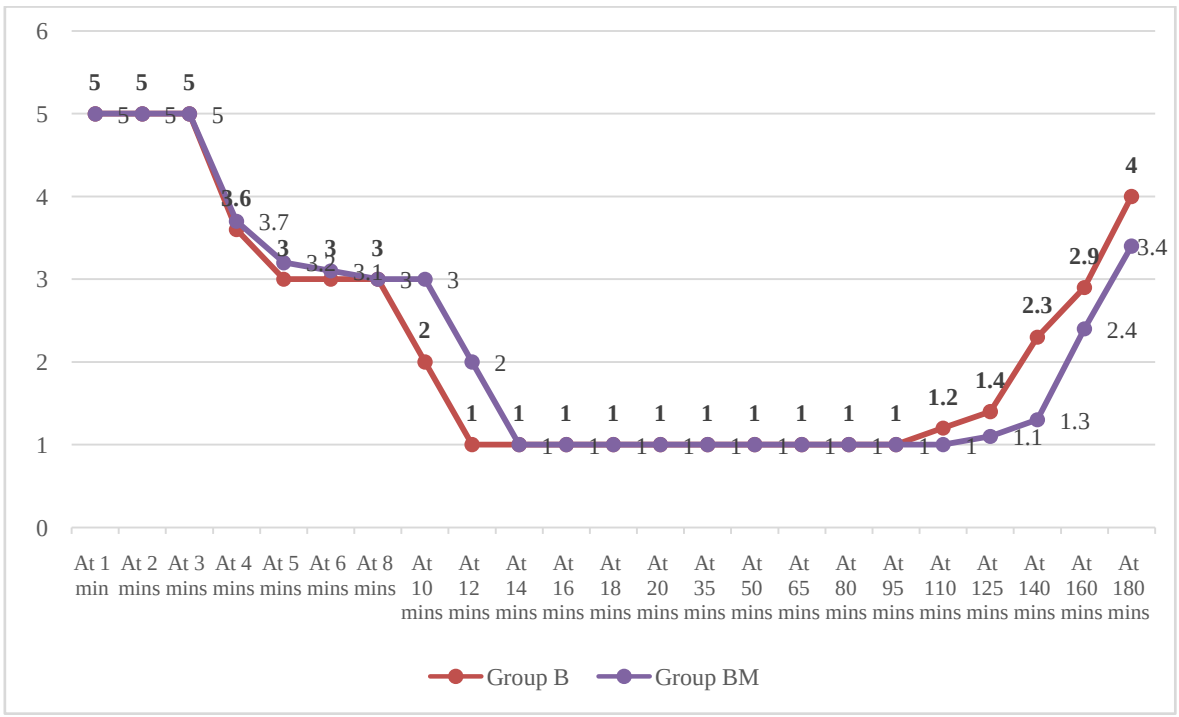

Figure 16: Mean values of Bromage score at different interval in study group

As shown in Table 12, the mean Bromage score is compared at various intervals. There was no statistically significant difference observed in groups at all intervals.

Table13: VAS score post-operativelyat different intervals in study groups

VAS score	Group B (n=45)	Group BM (n=45)	p-value
At 15 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 30 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 45 mins Mean ± SD	1 ± 0	1 ± 0	1.000
At 60 mins Mean ± SD	2.6 ± 0.5	2.3 ± 0.5	0.675
At 90 mins Mean ± SD	3.1 ± 0.3	3 ± 0	0.889
At 120 mins Mean ± SD	3.6 ± 0.6	3.1 ± 0.3	0.989
At 150 mins Mean ± SD	2.8 ± 0.9	3.7 ± 0.6	<0.001
At 180 mins Mean ± SD	2 ± 0	2 ± 0	1.000

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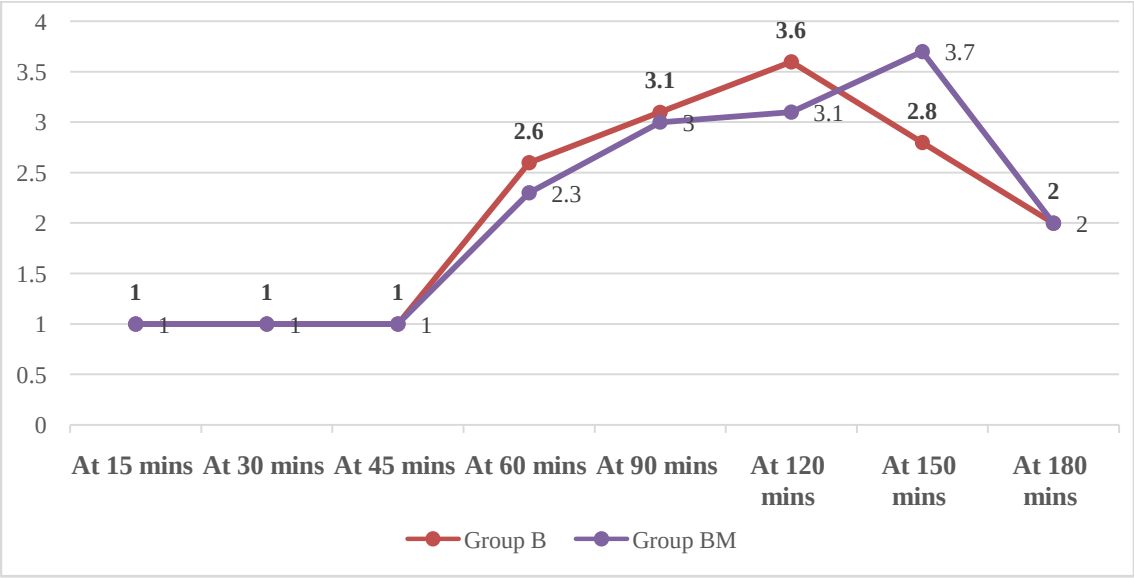

Figure 17: Mean values of VAS post-operatively in study groups

As shown in Table 13, the mean VAS score is compared at various intervals, post-operatively. There was no statistically significant difference observed in groups at all intervals, except at 150 mins.

Table14:Comparison of side effects in study groups

Parameters	Group B (n=45)	Group BM (n=45)	p-value
PONV	4 (9%)	3 (7%)	0.173

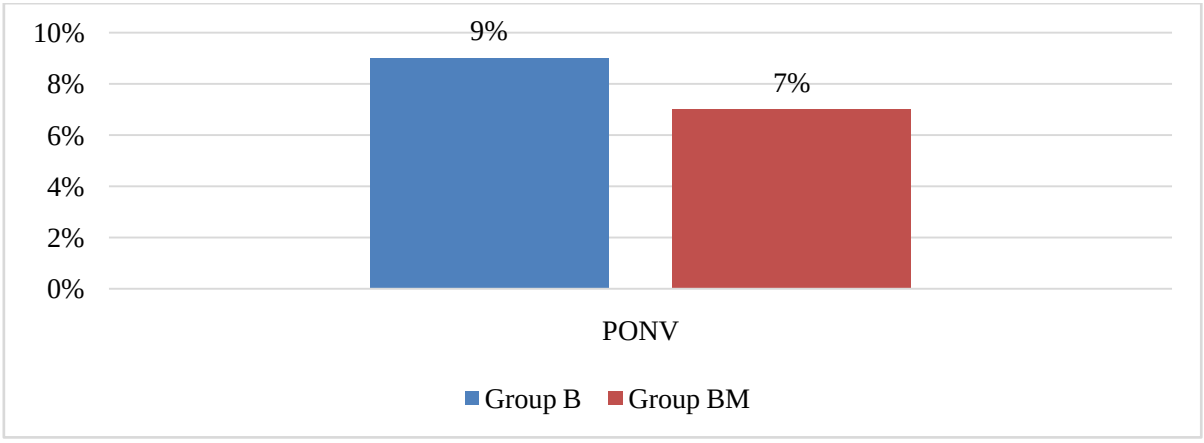

Figure 14: Comparison of side-effects in study groups

As shown in Table 14, post-operative shivering, nausea and vomiting was observed in 4 (9%) patients in group B and 3 (7%) in group BM. There was no statistical difference observed between the groups.

IV. DISCUSSION

Many adjuvants have been added intrathecally to maximise analgesia post operatively. Midazolam, dexmeditomidine, ketamine have been used intrathecally but magnesium sulfate is not well studied for intrathecal administration and studies which have been done show equivocal results. Most of the studies are done with 50mg magnesium sulfate 5% or 10% or 25% or 50% but our study is done with 100mg magnesium 50% (0.2ml)

The present clinical study is a randomised prospective study in 90 patients belonging to age group 18-60 yrs of both sexes and ASA grade I and

II who were scheduled to undergo various elective lower limb orthopaedic surgeries under subarachnoid block. The group B received 2.8 ml of 0.5% (H) bupivacaine + 0.2 ml NS and group BM received 2.8ml of 0.5% (H) bupivacaine + 0.2 ml (100mg) 50% magnesium sulfate intrathecally.
The results of present clinical study were discussed under the following headings:

Time of onset of sensory blockade:
In present study ,there was no difference as regard the time for onset of sensory blockade with addition of magnesium sulfate when compared with control group (p=0.862).

Attari et al.[52] have also reported that there was no signicant differences between groups in regard to time of onset of sensory block where p value was (p=0.82). In our study, 100mg magnesium sulfate was used but Attari used 50mg magnesium sulfate and 25µg fentanyl.

Josef Attia et al.[51] found delay in the onset of sensory blockade with 50mg magnesium sulfate (6.6 ± 2.7 min) as compared to control group (5 ± 1.1 min).

Nadia Banihashem et al.[48] showed that on addition of 50mg magnesium sulfate showed delayed in onset of sensory blockade when compared with control group (6.60 ± 1.12 mins and 5.65 ± 0.92 respectively) where p value was (p<0.01). Ozalevliet al. also showed that addition of 50mg magnesium sulfate and 25µg of fentanyl showed delayed onset of sensory blockade where p value was (p<0.01).

M Jabalameli et al.[46] observed the comparison of 50, 75, or 100 mg magnesium sulphate with hyperbaric bupivacaine in patients undergoing the caesarean section. Onset time of sensory block was shorter in control group than group M50, M75 and M100 (p<0.01)**.** The authors suggested that the difference in pH and baricity of the solution by addition of magnesium contributed to the delayed onset.

Binesh Kathuria et al.[47] and **Bharat Arora et al.**[49] too observed delay in onset time of sensory block in their studies.
Most of the studies are done with 50mg magnesium sulfate 5% or 10% or 25% or 50% but our study is done with 100mg magnesium 50% (0.2ml)
The results at present study are consistent with Attari et al.[52] with regards to onset of sensory blockade.

Time of onset of motor blockade:
In present study, the time for onset of motor blockade for the two group was not statistically significant between groups when compared (p=0.237).

Similarly, **Nadia Banihashem et al.**[48] found the onset of motor blockade was not different between 50mg magnesium sulfate (7.83 ± 5.67 mins) and control group (8.57 ± 5.83 mins) p<0.56. As well as **Attari et al.**[52] also found no significant differences between groups in regard to onset of motor block (p=0.58).

In contrast, **M Jabalameli et al.**[46], **Binesh Kathuria et al.**[47] and **Bharat Arora et al.**[49] have found delayed onset of motor blockade with addition of 50mg, 75mg or 100mg magnesium sulfate intrathecally when compared with control group (p<0.01).

Duration of sensory blockade:
In the present study, in group B, the mean total duration of sensory block was 99.5 ± 8.1 minutes, while in group BM, the mean was 128 ± 9.4 minutes (p<0.001). So the addition of magnesium sulfate to bupivacaine has made significant difference with regard to duration of sensory blockade.

Josef Attia et al.[51] reported significant increase in duration of sensory blockade in group B with 50mg magnesium sulphate 10% (0.5ml) intrathecally (157 ± 36 min), as compared to the control group C (112 ± 15 min);(p<0.05).

Jabalameli et al.[46], **Binesh Kathuria et al.**[47],**Bharat Arora et al.**[49], **Attari et al.**[52] and **Khandelwal et al.**[54] also reported that addition of magnesium sulfate intrathecally prolonged duration of sensory blockade (p<0.01).

The results at present study are consistent with Josef Attia et al.[51], Jabalameli et al.[46], Binesh Kathuria et al.[47], Bharat Arora et al.[49], Attari et al.[52] and Khandelwal et al.[54] with regards to duration of sensory blockade.

Duration motor blockade:
In the present study, in group B, the mean total duration of motor block was 128.4 (± 12.2) minutes, while in group BM, the mean was 149.5 (± 9.6) minutes. There was statistically significant difference observed in the groups with total duration of motor block where the p value was

p<0.001. So the addition of magnesium sulfate to bupivacaine has made significant difference with regard to duration of motor blockade in our study.

Similar to our results, **Attari et al.**[52] reported that the time to complete recovery of motor function was significantly longer with magnesium sulfate when compared with control group(130.2±15.7 min & 116.4±18.4 respectively, p=0.016).

Bharat Arora et al.[49] reported prolonged duration of motor block after addition of 12.5 mcg fentanyl and 50mg (0.1ml) 50% magnesium sulfate when compared with control group (210 ± 10 min & 186.3 ± 12 min; p< 0.001).

Jabalameli et al.[46] reported that resolution of sensory and motor block significantly longer in 75mg and 100mg magnesium sulfate than 50mg magnesium sulfate and control group. Recovery time was longer in M100 group (65 min) compare with C group (49 min) (p<0.001) and it was observed that 75 mg of this drug was enough to produce desired effects.

Binesh Kathuria et al.[47], **Sarika Katiyar et al.**[50] and **Khandelwal et al.**[54] have also reported in their studies that duration of motor block was prolonged in patients given magnesium in the dose of 50mg, 75mg or 100mg along with local anaesthetic intrathecally (p<0.001).

On the other hand, **Nadia Banihashem et al.**[48] reported that the duration of motor blockade was not significantly different between 50mg magnesium sulfate (61.68 ± 39.37 mins) and control group (56.75 ± 32.35) where p value was (p=0.54).

The results at present study are consistent with Sarika Katiyar et al.[50], Josef Attia et al.[51], Jabalameli et al.[46], Binesh Kathuria et al.[47],Bharat Arora et al.[49], Attari et al.[52] and Khandelwal et al.[54] with regards to duration of motor blockade.

Time of first post operative rescue analgesia requirement:

In the present study, in group B, the mean time of first post op rescue analgesia was 123.4 (± 11.3) minutes, while in group BM, the mean was 149.5 (± 9.7) minutes where p value was (p<0.001). There was statistically significant difference observed in the groups. So the addition of magnesium sulfate to bupivacaine has made significant difference with regard to time of first rescue analgesia requirement in our study.

Attari et al.[52] also reported time to first analgesic requirement was longer with 50mg magnesium (group B) in patients undergoing lumbar disk herniation surgery when compared with 25mcg fentanyl (group A) and control (group C). Group A, group B & group C (3.26±1.12, 5.57±0.92, 6.91±1.27 hrs, respectively p<0.001).

Khandelwal et al.[54] also found that the time to first rescue analgesia in 50mg magnesium sulfate Group M (246.3 ± 55.9 mins) was significantly prolonged than control Group B (134.4 ± 17.9 mins) where the p value was (p<0.01).

Bharat Arora et al.[49] and **Sarika Katiyar et al.**[50] have also reported that magnesium sulfate asadjuvant to intrathecal bupivacaine significantly prolongs the duration of analgesia (p<0.001).

Nadia Banihashem et al.[48] reported that duration of analgesia was longer in the magnesium sulfate group yet this difference was not significant (p=0.07).

Hemodynamic variability

In present study, the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was stable at all points of observation and did not show variation of more than 10-15% during the intra operative and post operative period.

Rana et al.[53] reported that the addition of 50mg magnesium sulfate provides better haemodynamic stability in parturients undergoing elective cesarean section.

Kavita Jain et al.[57] reported that patients remained hemodynamically stable in both groups after addition of 75mg magnesium sulfate intrathecally in patients undergoing infraumbilical surgery (p>0.05).

Whereas, **Nadia Banihashem et al.**[48] has found no significant difference between group M50, M75, M100 and control group as regards hemodynamic variability.

Post-Op VAS Score:

The mean VAS score is compared at various intervals, post-operatively. There was no statistically significant difference observed in groups at all intervals, except at 150 mins.

Lee et al.[44] reported that after addition of 50mg magnesium sulfate 50% (0.1ml) there were no differences in the VAS scores at the postoperative period in patients undergoing total knee replacement.

Rana et al.[53] reported that the addition of 50mg magnesium sulfate 50% (0.1ml) prolong the duration of post operative analgesia with lesser VAS scores and lesser dose of rescue analgesia in parturients undergoing elective cesarean section.

Side Effects:

Post-operative nausea and vomiting was observed in 4 (9%) patients in group B and 3 (7%) in group BM. There was no statistical difference observed between the groups. **Bharat Arora et al.**[49] has found minimal side effects in their study. **Sarika Katiyar et al.**[50] also reported that 100 mg magnesium provides better hemodynamic stability than 25 mcg fentanyl and control group, with fewer side effects.

Kavita Jain et al.[57] reported that patients remained hemodynamically stable in both groups without undue sedation and minimal side effects ($p>0.05$) after addition of 75mg magnesium sulfate intrathecally in patients undergoing infra umbilical surgery.

Lee et al.[44] reported in patients undergoing total knee replacement after addition of 50mg magnesium sulfate that the incidence of PONV, pruritus and urinary retention was significantly lower in group M than in group C at 12 and 36 hours after surgery.

Heba Omar et al.[55] reported that intrathecal injections of both 5mcg dexmedetomidine and 25mg magnesium sulfate were effective in reducing the incidence of post-spinal anesthesia shivering. Whereas, in present study there was no significant difference between 2 groups with regards to incidence of post-spinal anesthesia shivering.

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