

THE EFFECT OF ADDING MAGNESIUM SULPHATE TO BUPIVACAINE FOR SPINAL ANAESTHESIA: A RANDOMISED, DOUBLE- BLIND TRIAL IN PATIENTS UNDERGOING LOWER LIMB ORTHOPAEDIC SURGERY

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ABSTRACT

Objectives: The study evaluated the effect of addition of magnesium sulphate to bupivacaine for spinal anaesthesia

Material and methods: 150 adult patients (ASA I or II) undergoing lower limb orthopaedic surgery were included in the study. Patients were randomly allocated to one of the three groups.

Group I (n=50) received 2.5 ml of 0.5% bupivacaine heavy + 0.2 ml of normal saline.

Group II (n=50) received 2.5 ml of 0.5% bupivacaine heavy + 0.1 ml (50 mg) of 50% magnesium sulphate + 0.1 ml normal saline.

Group III (n=50) received 2.5 ml of 0.5% bupivacaine heavy + 0.2 ml (100 mg) of 50% magnesium sulphate.

Results: The highest dermatomal level of sensory block at 5 min was statistically significant with group I recording higher level as compared to group II and III ($p < 0.05$). The time to achieve the highest level of sensory block was 13.40 ± 2.35 min in group I, 16.33 ± 2.65 in group II and 16.43 ± 2.7 in group III, the difference being statistically very highly significant ($p < 0.001$). Mean duration of sensory analgesia was 273.1 ± 56.7 min in group I, 346.33 ± 56.30 min in group II and 400.10 ± 105.10 min in group III, the difference being statistically very highly significant ($p < 0.001$).

Conclusions: Intrathecal magnesium along with bupivacaine for spinal anaesthesia modifies the quality of sensory block with no increased incidence of side effects.

Keywords: Magnesium sulphate, Intrathecal, Bupivacaine, Adjuvant.

INTRODUCTION

Bupivacaine is the most commonly used local anaesthetic for spinal anaesthesia. One disadvantage with spinal anaesthesia using bupivacaine alone is relatively short duration of action, which means that early analgesic intervention is needed in the postoperative period. [1]

A number of drugs e.g. opioids, benzodiazepenes, α_2 agonists and neostigmine have been used intrathecally as an adjuvant to local anaesthetic with the aim of prolonging the duration of block. These drugs reduce the dose of bupivacaine used in spinal anaesthesia but their use is limited because of their side effects. [2-5] Magnesium sulphate is N- methyl- D- aspartate receptor antagonist when used as an adjuvant inhibits induction and maintenance of central sensitization after nociceptive stimuli. Magnesium sulphate has been used intrathecally as an adjuvant to bupivacaine for postoperative analgesia in differing doses. [6,7,8]

However none of the studies evaluates and compares the effect of addition of two doses of intrathecal magnesium sulphate added to bupivacaine alone on the quality of spinal anaesthesia. So the present study was designed to evaluate the effect of addition of two different doses i.e. either 50 mg or 100 mg of intrathecal magnesium sulphate to bupivacaine on the quality of motor and sensory block in orthopaedic patients requiring lower limb surgery.

MATERIALS AND METHODS

This prospective randomized study was conducted in the Department of Anaesthesiology and Critical Care, Pt. B. D. Sharma PGIMS Rohtak after obtaining approval from the institutional research/ ethical committee. A total of 150 adult patients in the age group of 20-60 years of either sex having physical status I or II according to American Society of Anaesthesiologists (ASA) undergoing lower limb orthopaedic surgery were included in the study. Patients with contraindication to spinal anaesthesia, impaired renal function, central nervous system disorders and peripheral neuropathies were excluded from the study.

All patients were visited a day prior to surgery. The general physical as well as systemic examination was carried out. Basic demographic characters like age, weight and height were recorded. Routine investigations like haemoglobin, bleeding time, clotting time and complete urine examination was carried out in all the patients. Blood urea, blood sugar, chest X ray, ECG and any other specific investigation wherever needed was carried out. A linear visual analogue scale (VAS) on a scale of 0-10 cm (where 0 stands for no pain and 10 for worst possible pain) was explained to each patient and consent to participate in the study was obtained. All patients were premedicated with alprazolam 0.25 mg and ranitidine 150 mg orally on the night before and two hours prior to surgery. Patients were randomly allocated to one of the three groups by using sealed coded envelopes which were opened just before the patient entered the study. The anaesthetic solution to be used during the study was prepared by a fellow anaesthesiologist who was blind to the study hypothesis. The observer anaesthesiologist and the patient were not aware of the drug given. The syringe contained a total of 2.7 ml of solution. The small quantity of study drug was measured with insulin syringe.

Group I (n=50) patients received 2.5 ml of 0.5% bupivacaine heavy + 0.2 ml of normal saline.

Group II (n=50) patients received 2.5 ml of 0.5% bupivacaine heavy + 0.1 ml (50 mg) of 50% magnesium sulphate + 0.1 ml normal saline.

Group III (n=50) patients received 2.5 ml of 0.5% bupivacaine heavy + 0.2 ml (100 mg) of 50% magnesium sulphate.

On arrival of patient in the operating room, intravenous line was secured and usual continuous monitoring of non invasive blood pressure, heart rate, ECG and arterial oxygen saturation was started. Under all aseptic conditions with the patient in sitting position, lumbar puncture was done by 23 G Quincke's spinal needle in L3-L4 or L4-L5 space after infiltrating the space with 2 ml of 2% lignocaine. After ensuring free flow of cerebrospinal fluid, the study drug was injected into the subarachnoid space according to the group of the patients and the time was recorded.

Level of sensory block was assessed by pinprick technique using short beveled 23 G hypodermic needle. At the interval of every 5 minutes for the next 30 minutes the sensory level was evaluated for assessing the highest level of sensory block and the time to achieve the highest level was noted. Thereafter sensory level was assessed every fifteen minutes till the two segment regression was achieved and the time was recorded. Bromage scale was used to assess the degree of motor block at the time of highest sensory block.

Postoperative observations

1. After surgery, the patient was assessed every fifteen minutes till the complete regression of motor block and the time was recorded. The total duration of motor block was assessed from the time of administration of block to the time of complete regression of motor block.

2. The patient was assessed every fifteen minutes till the complete regression of sensory block to S2 dermatome was achieved and the time was recorded. The total duration of spinal anaesthesia was defined as the time period from the time of administration of block to the time of complete regression of sensory block to S2 dermatome.

3. When VAS was equal to 4, all the patients received diclofenac 75 mg IM as analgesia and the time was recorded. The total duration of

Table 1: Showing mean age, weight, height, duration of surgery and sex distribution in group I, II and III

	Group I	Group II	Group III
Age (Years)	37.10 ± 12.09	37.08 ± 13.70	35.50 ± 12.29
Weight (kg)	63.40 ± 12.36	62.32 ± 10.05	64.08 ± 12.94
Height (cm)	166.58 ± 7.02	165.66 ± 6.95	167.46 ± 6.29
Duration of surgery (minutes)	82.80 ± 24.51	80.71 ± 24.72	88.47 ± 29.67
Male/ Female	38/12	40/10	45/5

The mean highest dermatomal level of sensory block at 5 min in group I was T7.8 as compared to T8.7 in group II and T8.6 in group III. At 10 min it was T5.7, T6.4 and T6.3 in group I, II and III respectively. At 15 min it was T4.7, T4.8 and T 5.0 in group I, II and III respectively. At 20, 25 and 30 min it was T4.7, T4.5 and T4.6 respectively in group I, II and III.

Table 2: Showing onset of sensory block

Sensory block at Dermatomal level (Mean ± S. D.)	Group I	Group II	Group III
5 min	7.82 ± 1.57	8.77 ± 1.71	8.61 ± 1.92
10 min	5.78 ± 1.51	6.44 ± 1.64	6.38 ± 1.90
15 min	4.72 ± 1.45	4.89 ± 1.35	5.06 ± 1.58
20 min	4.72 ± 1.45	4.48 ± 1.34	4.65 ± 1.33
25 min	4.72 ± 1.45	4.48 ± 1.34	4.65 ± 1.33
30 min	4.72 ± 1.45	4.48 ± 1.34	4.65 ± 1.33
Highest sensory block	4.72 ± 1.45	4.48 ± 1.34	4.65 ± 1.33

Table 5: Showing characteristics of sensory and motor blocks

Variable	Group I	Group II	Group III
1. Highest level of sensory block	T2-T8	T2-T8	T2-T8
2. Mean time to achieve two segment regression in min (Mean ± S.D.)	83.70 ± 7.47	85.10 ± 7.73	84.00 ± 9.14
3. Mean duration of spinal anaesthesia in min (Mean ± S.D.)	256.20 ± 16.46	260.31 ± 19.88	262.65 ± 20.66
4. Mean Bromage scale values at the time of highest sensory block (Mean ± S.D.)	1.26 ± 0.44	1.37 ± 0.48	1.27 ± 0.44
5. Mean duration of motor block in min (Mean ± S.D.)	151.50 ± 22.32	152.55 ± 21.72	155.61 ± 19.99

sensory analgesia was assessed from the time of administration of block to the time of achieving VAS equal to 4.

4. Return of bladder function (passing urine) or bowel movements (passing flatus/stools) in first 24 hours was recorded as present/absent and the time of their return was recorded.

5. Any other complication like sedation, dizziness, fatigue, tremors, hypotension, bradycardia, shivering, headache, nausea or vomiting was noted.

Statistical Analysis

1. One way ANOVA (analysis of variance) test was used for the comparison of the groups.

2. The independent samples t-test was used for the comparison between the two groups.

3. The Chi square test was used for the analysis of the dichotomous data.

Observations

The patients in the three groups were comparable with regard to demographic data (age, sex, weight and height). Duration of surgery was also comparable between the three groups (Table 1).

These observations reveal that the mean highest dermatomal level of sensory block at 5 min was found to be statistically significant between the three groups with group I recording higher level as compared to group II and III ($p < 0.05$). However, when compared at 10, 15, 20, 25 and 30 min, the groups did not show any statistically significant difference ($p > 0.05$). The mean highest level of sensory block was found comparable in all the three groups.

The time to achieve the highest level of sensory block was 13.40 ± 2.35 min in group I, 16.33 ± 2.65 in group II and 16.43 ± 2.7 in group III.

Table 3: Showing time taken (min) to achieve the highest level of sensory block

Groups	Time taken (Mean ± S. D.)
I	13.40 ± 2.35
II	16.33 ± 2.65
III	16.43 ± 2.70

When analysed statistically using one way ANOVA test, the difference was found to be statistically very highly significant ($p < 0.001$).

Mean duration of sensory analgesia, defined as VAS equal to 4 was 273.1 ± 56.7 min in group I, 346.33 ± 56.30 min in group II and 400.10 ± 105.10 min in group III.

Table: 4 Showing mean duration of sensory analgesia (min)

Group	Mean ± S. D.
I	273.10 ± 56.76
II	346.33 ± 56.30
III	400.10 ± 105.10

When analysed statistically using one way ANOVA test, the difference between the three groups was statistically very highly significant ($p < 0.001$). When the mean duration of sensory analgesia between group II and III was compared using independent samples t- test statistically highly significant difference was found.

The range of highest level of sensory block was T2 to T8 in all the groups. The mean time to achieve two segment regression was 83.70 ± 7.47 min in group I, 85.10 ± 7.73 min in group II and 84.00 ± 9.14 min in group III. The mean time of regression of sensory block to S2 level was $256. \pm 16.46$ min in group I, 260.31 ± 19.88 min in group II and 262.65 ± 20.66 min in group III. The intensity of motor block was assessed using Bromage scale at the time of highest sensory block. The mean duration of motor block was 151.50 ± 22.32 min in group I, 152.55 ± 21.72 min in group II and 155.61 ± 19.99 min in group III. When analysed statistically, all these variables were comparable between the three groups.

When analysed statistically using one way ANOVA test the mean time when patient first passed urine and flatus were found comparable in all the three groups.

Intraoperatively one patient in group I and III each had bradycardia and five patients in group I and III each had hypotension which was treated by atropine and mephentermine intravenously respectively. Postoperatively one patient in group III had bradycardia and two patients in group I and one patient in group II had hypotension which was treated by atropine and mephentermine respectively. Four patients in group I and one patient in group II had postoperative nausea once and one patient in group I had nausea twice. One patient in group I had vomiting once and one patient in group II vomited twice. Both received single dose of 4 mg ondansetron intravenously. Shivering was observed in 22 patients in group I, 9 patients in group II and 6 patients in group III. They got adequate relief with oxygen by face mask and warm blankets. Complications like sedation, dizziness, fatigue, neurological deficit, tremors and headache were not observed in any of the three groups.

DISCUSSION

Postoperative pain is invariably associated with any type of surgery. Although the severity of pain is related to type of surgery yet it has been observed that generally 20-40% patients experience pain of moderate intensity and another 50-70% experience severe pain. Effective treatment of postoperative pain blunts autonomic, somatic and endocrine responses. [9] Magnesium sulphate is N- methyl-D- aspartate (NMDA) receptor antagonist when used as an adjuvant inhibits induction and maintenance of central sensitization after nociceptive stimuli. [10]

The results of present study showed a significant increase in the duration of analgesia when Magnesium sulphate was added to intrathecal bupivacaine. Mean duration of sensory analgesia, defined as VAS equal to 4 was 273.1 ± 56.7 min in group I, 346.33 ± 56.30 min in group II and 400.10 ± 105.10 min in group III. When analysed statistically using one way ANOVA test, the difference between the three groups was statistically very highly significant ($p < 0.001$). When the mean duration of sensory analgesia between group II and group III was compared using independent samples t- test statistically highly significant difference was found [Table 4]. Also, addition of Magnesium sulphate intrathecally significantly delayed the onset of sensory and motor blockade . Other observations regarding highest level of sensory block, time to achieve two segment regression, intensity of motor block and duration of motor block were comparable in all the three groups.

The findings of present study are similar to observations made by Ozalevli et al who conducted a prospective randomized double blind controlled study to investigate the effect of adding intrathecal magnesium sulphate to bupivacaine- fentanyl spinal anaesthesia in 102 adult patients undergoing lower extremity surgery. The patients were randomly allocated to receive either 1.0 ml of preservative free 0.9% sodium chloride (group S) or 50 mg of magnesium sulphate 5% (group M) following 10 mg of bupivacaine 0.5% plus 25 μ g of fentanyl intrathecally. The highest dermatomal level of sensory block was lower in group M than in group S at 5, 10 and 15 min: T12 vs T11 at 5 min ($p < 0.05$), T10 vs T7 at 10 min ($p < 0.001$) and T7 vs T6 at 15 min ($p < 0.005$). However, at 20 min, the sensory block levels were similar in the two groups. The median time to reach the highest level of sensory block was 13 min in bupivacaine + fentanyl group as compared to 17 min in bupivacaine + fentanyl + magnesium sulphate group ($p < 0.05$). [11] It is possible that the

solution to which magnesium sulphate was added had a different pH which might explain these findings. However no satisfactory explanation for this delay can be offered and further studies are needed. Also, increase in metabolism of bupivacaine due to the activation of cytochrome P 450 by magnesium may be responsible for the delayed onset.

The observations of duration of sensory analgesia [Table 4], defined as VAS equal to 4 are consistent with the observations of Ozalevli et al and Buvanendran et al. Buvanendran et al observed significant prolongation in the median duration of analgesia in magnesium + fentanyl group (75 min) as compared to fentanyl alone group (60 min). Similar observations were made by Ozalevli et al who observed significant prolongation of sensory analgesia. This prolongation is consistent with the experimental synergistic interaction between spinal local anaesthetics and NMDA antagonists such as magnesium, which exert anti nociceptive effects via different mechanisms, hence the rationale of combining the two. The NMDA receptor channel complex contains binding sites for non competitive antagonists such as magnesium and ketamine. Activation of c- fibers leads to neuronal excitation, which is diminished by NMDA receptor antagonists; hence the use of magnesium as adjuvant of intrathecal block. It acts as an antagonist at NMDA receptor. NMDA receptor antagonists can prevent central sensitization due to peripheral nociceptive stimulation and can abolish such sensitivity once it is established. [11,12]

The results of our study are in concordance to the study trial of various authors. [6,7,8] However the results of present study are in contrast to the study by Unlugenc et al who reported a decrease in the duration of analgesia with the addition of intrathecal Magnesium. This may be due to lesser dose of intrathecal bupivacaine and different surgical procedure (caesarean section) as compared to the present study. [13]

When analysed statistically, all the groups were found to be comparable regarding intraoperative and postoperative hypotension, bradycardia, nausea and vomiting. The incidence of shivering in the group I is consistent with the observations of Crowley et al who reviewed 21 studies and found that the incidence of shivering was in the range of 40-64% after neuraxial anaesthesia in the control group of these studies. [14] This observation is consistent with the observation made by Wadhwa et al who observed that intravenous magnesium sulphate significantly reduced the shivering threshold in human volunteers. Moreover intravenous magnesium has been shown to suppress postoperative shivering. The drug not only exerts a central effect but is also a mild muscle relaxant. Many postoperative patients have their core temperatures only slightly below the normal shivering threshold. General or neuraxial anaesthesia impairs thermoregulatory control. Consequently, treatments that reduce the shivering threshold by a few tenths of a degree celcius may be sufficient to attenuate postoperative shivering. Thus magnesium can be an effective antishivering agent and yet reduce the shivering threshold by only a few tenths of a degree celcius. [15]

CONCLUSION

Intrathecal magnesium along with bupivacaine for spinal anaesthesia modifies the quality of sensory block with no increased incidence of side effects, rather decreases the incidence of shivering significantly. Moreover, it appears that analgesia seems to have dose related linear relationship with magnesium sulphate. The results of present study suggest that magnesium may be a useful alternative as an adjuvant to local anaesthetics for subarachnoid block. These encouraging findings in a small study sample shows that a low cost, simple change profits the clinical anaesthesiology practice.

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