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Original Research Article

Evaluation of Intrathecal Magnesium Sulphate as Adjuvant in Bupivacaine Spinal Anesthesia - A Study

N Ratan Singh[1], Alem O Wapang[2], S Sarat Singh[3]

[1]Associate Professor, [2]PGT, [3]Professor,
Department of Anesthesiology, Regional Institute of Medical Sciences, Imphal - 795004

Corresponding Author: N Ratan Singh

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ABSTRACT

Background: Magnesium because of its antinociceptive action without increased adverse effects is used in anaesthetic practice recently. The effect of magnesium sulphate as intrathecal adjuvant in bupivacaine spinal anesthesia as regards of the onset and duration of sensory and motor blockade as well the side effects is studied.

Methods: In this prospective, randomized, double-blinded study, 60 (sixty) patients undergoing elective lower abdominal and lower limb surgeries under spinal anaesthesia were randomly allocated into two groups to receive: Group M (n=30): 2.5ml (12.5mg) hyperbaric bupivacaine 0.5% plus 0.1ml (50mg) magnesium sulphate 50% intrathecal and Group C (n= 30): 2.5ml (12.5 mg) hyperbaric bupivacaine 0.5% plus 0.1ml preservative free normal saline intrathecal as control. Then, the onset and duration of sensory and motor blockade as well the side effects were studied and statistically analysed.

Results: The mean sensory onset time to reach T10 in Group M vs. Group C was 8.00±1.29 vs. 4.10±0.55 min respectively (p=0.002). The time to first analgesic request (TFAR) in Group M was 193.00±18.78min and 158.00 ±12.42 min in group C, which is significant statistically (p=0.031). Haemodynamic stability was observed intraoperatively in both the groups.

Conclusion: Intrathecal magnesium prolonged the duration of spinal analgesia but with a delayed onset. However, more studies are required to establish the adequate dose of intrathecal magnesium to potentiate the analgesia of the local anaesthetic and reduce opioid dose requirements.

Key words: Spinal anesthesia, adjuvant, intrathecal, magnesium, analgesia.

INTRODUCTION

Spinal anesthesia is widely used for lower limb and lower abdominal surgeries; however, shorter duration of block and inadequate postoperative analgesia are some of its drawbacks. Various adjuvants like opioids, α2 agonists, etc. are widely used to improve the quality of anaesthesia.

Magnesium sulfate ($MgSO_4$) has been used as a pharmacological agent in a

variety of clinical conditions viz. tachyarrythmia, myocardial and neuronal ischemia, asthma, and seizures in preeclampsia. [1] It has also been shown to potentiate the analgesic effect of bupivacaine when co-administered intrathecally in rats. [2] The use of magnesium has recently been highlighted in anaesthetic practice because of its antinociceptive action without increased adverse effects. [3] There are considerable evidences that intrathecally administered magnesium potentiates opioid nociception and prolongs duration of anaesthesia. [4]

The analgesic properties of magnesium are primarily related to the regulation of calcium influx into cells [5] and antagonism of N-methyl-D-aspartate (NMDA) receptors [6,7] The addition of low dose $MgSO_4$ without opioid supplements to spinal bupivacaine have been found to be potentiating the analgesic effect of opioids to be used postoperatively without prolonging the sensory and motor blocks. [8]

Based on the earlier studies, [9] it was hypothesized that intrathecal 50 mg magnesium sulphate would provide the effective characteristics of bupivacaine spinal anaesthesia with minimal side-effects. In orthopaedic surgery, $MgSO_4$ when used as an adjunct in spinal anesthesia improved postoperative analgesia. [3,10] This study was conducted to evaluate the effect of magnesium sulphate as intrathecal adjuvant in bupivacaine spinal anesthesia as regards the onset and duration of sensory and motor blockade as well the side effects in patients undergoing lower abdomen and lower extremity surgeries.

MATERIALS AND METHODS

After institutional ethical committee approval and written informed consent, 60 (sixty) ASA [11] physical status I and II patients aged 18-60 years of both sexes, scheduled for elective lower abdominal and lower limb surgeries under spinal anaesthesia were included in this prospective, randomized, double-blinded study. Based on previous studies, [9] it was calculated that a sample size of 30 patients would be required per group to demonstrate a clinically significant difference among the groups, at $\alpha = 0.05$ with a power $(1-\beta)$ of 80%.

Patients were randomly allocated into two groups by a computer generated randomization chart to receive the drugs during the study as follows: Group M (n=30): received 2.5ml (12.5mg) hyperbaric bupivacaine 0.5% plus 0.1ml (50mg) magnesium sulphate 50% intrathecal and Group C (n= 30): received 2.5ml (12.5 mg) hyperbaric bupivacaine 0.5% plus 0.1ml preservative free normal saline intrathecal as control.

Exclusion criteria included: refusal by the patient, hypertension, infection at the site of injection, post spinal surgeries, spinal deformity, neurological disorder, coagulopathy, hypovolemia or bradycardia, patients on calcium channel blockers or adrenergic receptor blockers, history of hypersensitivity to the study drugs.

Upon arrival in the operating room, the patients were preloaded with lactated Ringer's solution at 15mL/kg after pre-anesthetic evaluations. The patients were monitored with electrocardiogram (ECG), pulse oximetry (SpO2) and non-invasive blood pressure (NIBP). Under full aseptic conditions in the sitting position, lumbar puncture was performed at the level of L3-L4 through a midline approach using a 25-gauge Quincke spinal needle (Spinocan, B Braun Medical, Melsungen, Germany). The investigator performing the block and collecting the data was blinded to the study drug. After performing the spinal block, patients were positioned in the supine position and received 4L/min of oxygen via a face mask. The heart rate, mean arterial

blood pressure and oxygen saturation were monitored in the baseline and every 15 minutes until the end of surgery.

The time of intrathecal injection was taken as time "0" (zero) ; the sensory block levels were assessed bilaterally by pin-prick sensation using a blunt 25-guage needle along the mid-clavicular line every 2 minutes until the highest level has stabilized for four consecutive tests, and then every 10 minutes until the point of two segment regression of the block. Then, further assessment was done at 30 minutes interval until the recovery of S1 dermatome. The time to reach the T10 dermatome sensory block, the peak sensory block level, a two-dermatome regression and sensory regression to the S1 dermatome were recorded.

Motor blockade were assessed by using the Modified Bromage Scale: [12] (Bromage 0 - able to move hip, knee and ankle; Bromage 1 - unable to move the hip, but is able to move the knee and ankle; Bromage 2 - unable to move the hip and knee but is able to move the ankle; Bromage 3 - unable to move the hip, knee and ankle). Motor blockade were assessed every 2 min. before the onset of the surgery and then every 15 minutes thereafter. The times to reach modified Bromage 3 motor blockade and regression to modified Bromage Scale 0 were noted.

Intraoperative side-effects like nausea/vomiting, hypotension, bradycardia or respiratory depression, shivering, etc. were recorded. Hypotension, defined as a decrease in systolic blood pressure >30% from baseline values, was corrected with fluids or injection mephentermine intravenously.

Then, the findings were statistically analysed using statistical package for social sciences (SPSS) version 16.0 for windows and compared between the groups using chi square test for categorical variables, independent 't' test for continuous variables wherever appropriate; $p < 0.05$ was considered as statistically significant.

RESULTS

The demographic profile of the patients in the two groups viz. age, sex, weight, height and ASA physical classification were similar, and no significant difference ($p>0.05$) was observed between the two groups (Table 1).

Table 1: Demographic profile

Parameters	Group M (n=30) (Mean ± SD)	Group C (n=30) (Mean ± SD)	*p-value*
Age (years)	36.27±11.26	34.80±10.82	0.373
Sex(M: F)	13:17	12:18	0.721
Weight (kg)	55.13±7.82	54.30±8.60	0.980
Height (cm)	161.77±6.16	159.40±6.34	0.923
ASA (I:II)	27:3	27:3	0.894

As shown in Table 2, The mean sensory onset time to reach T10 in Group M vs. Group C was 8.00±1.29 vs. 4.10±0.55 min respectively ($p=0.002$). Peak sensory block level (PSBL) and time to reach peak sensory block (TPSBL) was similar in the two groups ($p= 0.125$ and 0.441 respectively). The time taken for two segment regression (TTSR) in Group M was 91.83±9.69 min. compared to 97.67±10.06 min. in Group C, and it was statistically insignificant ($p=0.403$). The time to first analgesic request (TFAR) in Group M was 193.00±18.78 min and 158.00 ±12.42 min in group C, which is significant statistically ($p=0.031$).

There was only one incidence of hypotension (1/30; $p=2.069$) and shivering (1/30; $p=2.069$) in the control group as shown in Table 3. Haemodynamic stability was observed intraoperatively in both the groups, and there was no significant difference in the mean heart rate and mean arterial pressures at different time intervals as shown in Fig 1.

Table 2: Showing the characteristics of the spinal block in the two groups

Parameters	Group M (n=30) (mean ± SD)	Group C (n=30) (mean ± SD)	*p value*
Sensory onset to reach T_{10}(min.)	8.00±1.29	4.10±0.55	0.002
Motor onset to modified Bromage 3(min.)	9.80±1.63	5.37±0.56	0.008
Peak sensory block level(PSBL*)	T4-1;T512; T6-9;T7-6; T8-2	T4-0;T5-5; T6-18;T7-6; T8-1	0.125
Time to peak sensory block(TPSBL-min)**	17.53±1.72	13.07±1.36	0.441
Time to two segment regression(TTSR-min)***	91.83±9.69	97.67±10.06	0.403
Sensory regression to S_1(min)	184.50±11.92	175.50±11.25	0.855
Motor regression to Modified Bromage 0	156.50±12.26	148.50±12.05	0.436
Time to first analgesic request(TFAR-min)****	193.00±18.78	158.00±12.42	0.031

(p <0.05, considered significant)
* PSBL- peak sensory block level;
** TPSBL- time to peak sensory block level;
***TTSR-Time to Two Segment Regression;
****TFAR -Time to First Analgesic Request

There was only one incidence of hypotension (1/30; p=2.069) and shivering (1/30; p=2.069) in the control group as shown in Table 3. Haemodynamic stability was observed intraoperatively in both the groups, and there was no significant difference in the mean heart rate and mean arterial pressures at different time intervals as shown in Fig 1.

Table 3: Side effects

Side effects	Group M (n= 30)	Group C (n= 30)	*p value*
Bradycardia	0	0	NA
Hypotension	0	1(3.3%)	2.02
Nausea	0	0	NA
Vomiting	0	0	NA
Respiratory depression	0	0	NA
Shivering	0	1(3.3%)	2.02

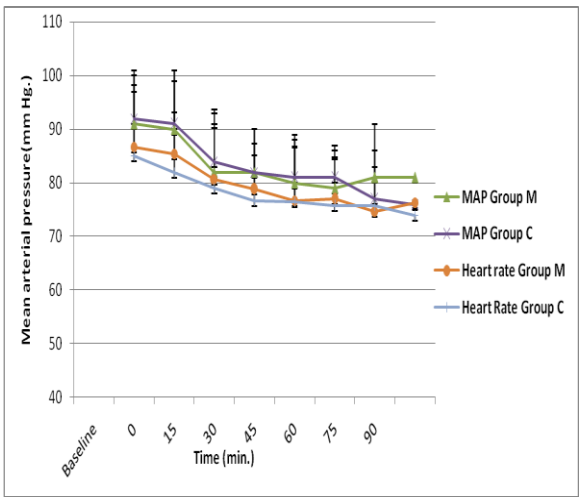

Fig 1. Showing the MAP±SD and mean heart rate ± SD in the two groups

DISCUSSION

Magnesium is the fourth most abundant cation in our body and it is also known as 'nature's physiological calcium channel blocker'. [13] It exerts its analgesic action as a non-competitive NMDA receptor antagonist, blocking ion channels in a voltage dependent manner. [6] The addition of magnesium reduces the activation of C-fibres by inhibiting the slow excitatory postsynaptic currents produced by NMDA receptor activation. [14] There are no selective NMDA receptor antagonists available for pain management; hence, drugs with other clinical uses such as magnesium and ketamine have been used effectively as analgesics. [15] Several studies have investigated the effect of intrathecal and intravenous magnesium as an adjuvant to bupivacaine and fentanyl spinal anesthesia on postoperative pain and analgesic consumption, and have shown that both intrathecal and intravenous magnesium are safe and prolong the time to first analgesic requirement. [16,17]

In a study by Mitra and Seyed, [17] addition of 50, 75, or 100 mg magnesium sulphate 50% led to a significant delay in the onset of both sensory and motor blockade, and prolonged the duration of sensory and motor blockade without increasing major side effects. In the present study, the onset

and resolution of motor blockade and the time to attain maximum sensory level were longer in the magnesium group compared to the control group. Ozalevli et al. observed a delay in onset of spinal anesthesia when intrathecal magnesium was added to fentanyl and isobaric bupivacaine. They suggested that the difference in pH and baricity of the solution containing magnesium contributed to the delayed onset. [3] Similar findings were observed by Malleswaran et al. [18] It is also possible that analgesic effect of magnesium occurred at the supra-spinal level and might be related to its systemic absorption. [19]

In our study, the time to motor regression to modified Bromage 0 was 156.50±12.26 min in the intrathecal magnesium group which is in agreement with the study of Jaiswal et al. [20] where it was 152.55 ± 21.72 min. The prolongation of motor and sensory block in our study is also in agreement with the study of Arcioni et al where intrathecal and epidural magnesium were studied, [10] Similar findings were observed by Buvanendran et al. [21] where the addition of magnesium to intrathecal fentanyl improved labour analgesia.

Several randomized control trials comparing 50mg to 100 mg dose of intrathecal magnesium sulphate vs. placebo in addition to an intrathecal local anaesthetic and/or opiate showed that the 'time to first analgesic request' was at least 35 min longer where intrathecal magnesium was included in the intervention. [22] This may be favourably compared with the findings of our study where the time to first analgesic request (TFAR) in the magnesium group was 193.00±18.78min compared to 158.00 ±12.42 min in the control group.

There was no significant difference in the mean values of heart rate and mean arterial pressures during the perioperative period between the two groups. Similar findings were observed by Shukla et al. [9] Magnesium causes peripheral vasodilatation which improves the cutaneous circulation thereby decreasing the incidence of shivering, [23] and this may explain the absence of shivering as side effect in the magnesium group of the present study.

CONCLUSION

Intrathecal magnesium prolonged the duration of spinal analgesia but with a delayed onset. However, more studies are required to establish the adequate dose of intrathecal magnesium to potentiate the analgesia of the local anaesthetic and reduce opioid dose requirements.

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