INTRODUCTION

Spinal anaesthesia is the most common regional anaesthesia technique used for infra-umbilical surgeries.\(^1\)\(^2\) Till recently bupivacaine was the only drug used intrathecally after discontinuation of lignocaine. Levobupivacaine, the S(-) enantiomer of bupivacaine, has emerged as a safer alternative than its racemic sibling, bupivacaine. Levobupivacaine has been found to be equally efficacious as bupivacaine, but with a superior pharmacokinetic profile and less cardiac and neurological toxic adverse effects.\(^3\)\(^4\)

Various intrathecal adjuvants are being used with local anaesthetics for prolongation of the duration and quality of block. However, there is limited benefit either due to the adverse effects or unreliable post-operative analgesia. Opioids are the most common neuraxial adjuvants used. They are associated with a number of undesirable side-effects, including delayed respiratory depression, urinary retention, pruritus, nausea and vomiting.\(^5\)

Addition of magnesium sulphate as an adjuvant to subarachnoid block has been shown to prolong both motor and sensory block in

Original Article:

Comparison of two different doses of magnesium sulphate for spinal anaesthesia: a prospective, randomized double-blind study

P. Hemalatha, Nayyara Banu, M. Hanumantha Rao, Aloka Samantaray, A. Venkatraman, N. Hemanth

Department of Anaesthesiology and Critical Care, Sri Venkateswara Institute and Medical Sciences, Tirupati

ABSTRACT

Background: The present study aim was designed to compare and evaluate the efficacy of adding two different doses of magnesium sulphate to 0.5% hyperbaric levobupivacaine for spinal anaesthesia in terms of block characteristics, haemodynamic and safety profile.

Methods: Ninety American Society of Anaesthesiologist (ASA) grade I–II patients undergoing elective infra-umbilical surgeries under spinal anaesthesia were randomly allocated into three groups. Group C (n=30, control group) received 3 mL (15 mg) of 0.5% hyperbaric levobupivacaine; Group M50 (n=30): received 3 mL (15 mg) of 0.5% hyperbaric levobupivacaine + 50 mg of magnesium sulphate. Group M100 (n=30) received 3 mL (15 mg) of 0.5% hyperbaric levobupivacaine + 100 mg of magnesium sulphate. A standard protocol was followed after which a blinded observer assessed the sensory and motor blocks. The onset and duration of sensory (pin-prick) block, onset, intensity and duration of motor block were recorded.

Results: All the subarachnoid blocks were adequate. The addition of magnesium sulphate to intrathecal levobupivacaine had not only increased the time to onset of sensory block (p=0.007) but also prolonged the duration of sensory (p<0.001) and motor block (p<0.001) to statistically significant level in a dose dependent manner.

Conclusions: Addition of magnesium sulphate does not offer any further advantage in terms of haemodynamic stability. However, it certainly increases the duration of sensory block to a significant level.

Key words: Levobupivacaine, Magnesium sulphate, Spinal Anaesthesia

humans but the ideal effective dose of magnesium sulphate to be added has to be determined. This study was undertaken to study the effect of adding different doses of magnesium sulphate to 0.5% hyperbaric levobupi-vacaine.

MATERIAL AND METHODS

After obtaining the Institutional Ethics and Research Committee approvals, 90 American Society of Anesthesiologists (ASA) physical status I/II patients aged 18 – 60 years who were scheduled for elective lower abdominal, perineal, or lower-limb surgery under spinal anaesthesia were recruited to participate in this prospective, randomized, double-blind study. Patients with contraindications like central neuraxial block, sensitivity to study drugs, obesity (body mass index > 30kg/m$^2$), pregnant and lactating women and patients who were not willing to participate in the study were excluded. Patients were premedicated with tab alprazolam 0.5mg and ranitidine 150 mg on the night and morning before surgery. On arrival in the operation theatre, routine monitoring with electrocardiogram (ECG), non-invasive arterial pressure, and pulse oximetry were commenced, and venous access was secured. The patients were preloaded with 10 mL/kg of Ringer’s lactate over 20 min before surgery. Hyperbaric levobupivacaine (0.5%) was prepared by adding 0.4 mL of 25% dextrose (equal to 16 units in insulin syringe) to 3mL of isobaric levobupivacaine (0.5%). The patients were randomly allocated into one of the 3 groups of 30 patients each using a computer generated randomization code and sealed envelope technique and received their study drugs intrathecally as follows: Group C (n=30) received 3.4 mL (15 mg) of 0.5% hyperbaric levobupivacaine; Group M50 (n=30): received 3 mL (15 mg) of 0.5% hyperbaric levobupivacaine (0.4 mL of 25% dextrose) + 50 mg of magnesium sulphate (0.2 mL of 50% magnesium sulphate equal to 8 units in insulin syringe); and Group M100 (n=30): received 3 mL (15 mg) of 0.5% hyperbaric levobupivacaine (0.4 mL of 25% dextrose) + 100 mg of magnesium sulphate (0.2 mL of 50% magnesium sulphate equal to 16 units in insulin syringe).

Magnesium sulphate used was preservative free. Total volume of study drugs was made uniform up to 3.6 mL by adding normal saline as required. The intrathecal (IT) injections labeled as “study drug” were prepared by an anaesthesia resident who was not involved in the patient care to maintain the double-blind nature of the study. The investigator performing the block and recording the observations of the study parameters was blinded to the intrathecal drug administered. Lumber puncture was performed in left lateral position at L3-L4 intervertebral space using a 25-gauge, Quincke Babcock’s spinal needle. The IT injection was administered over a period of 15 seconds after aspiration of cerebrospinal fluid (CSF) through the spinal needle. All patients received supplemental oxygen at the rate of 5 L/min through a face mask. An infusion of lactated Ringer’s solution at the rate of 4 mL/kg/h was administered during anaesthesia and the rate of infusion was altered depending upon the haemodynamic response. Blood pressure was recorded at every 2 minutes for the first 15 minutes and thereafter every 15 minutes until the end of surgery. Hypotension was defined as a decrease in systolic blood pressure below 90mm Hg or more than 20% of the base line. Bradycardia was defined as decrease in heart rate below 50 beats per minute. Hypotension was treated with intravenous (IV) ephedrine (0.1 mg/kg) and was repeated at the discretion of the attending anaesthesiologist. Bradycardia was treated with IV atropine 0.6 mg, repeated if necessary. The number of incidences of hypotension and bradycardia of each patient was used for statistical analysis. The spinal block characteristics were assessed like sensory
onset time (time between injection of intrathecal anaesthetic to absence of pain at T6 dermatome assessed by pin prick test and duration of sensory block (defined as the time interval from completion of IT drug injection up to regression of sensory block to S1 by pin prick method). The motor level was assessed according to modified Bromage score: (0 = no motor loss; 1 = inability to flex the hip; 2 = inability to flex the knee joint; 3 = inability to flex the ankle). The motor block onset time was defined as the time interval from the completion of IT injection to the onset of Bromage 3 score and duration of motor block to return of Bromage score 3 to 0.

**Statistical analysis**

Data are presented as median (range), mean (SD), or frequencies as appropriate. Normality of the data was tested by Shapiro-Wilk test. Normally distributed continuous variables between the groups were compared using one-way analysis of variance (ANOVA) and, if appropriate followed by the Bonferroni test for post-hoc analysis to see the significance between each pair of groups. Nominal categorical data between study groups were compared using the Chi-square test or Fisher’s exact test as appropriate. A p-value of 0.05 was considered statistically significant.

**RESULTS**

In our study 90 patients in the age-group 18-60 years undergoing elective surgeries below the umbilicus under subarachnoid block were randomized into three groups (Group C, Group M50 and Group M100) of 30 patients each. The groups were comparable with respect to age, weight, ASA status and type of surgery (Table 1).

The mean time to onset of sensory block (absence of pin-prick sensation at T6) in Group C was 5.57 ± 1.98 min, Group M50 was 5.82 ± 1.99 min and in Group M100 was 7.31 ± 2.69 min. Statistically significant differences were observed between the three groups to onset of sensory block (p = 0.007). Post-hoc analysis showed a statistically significant difference between group C and M 100 and group M 50 and M100 (p<0.05) but no difference between group C and M 50 (Table 2). Addition of 50 mg of magnesium sulphate has no effect on onset of sensory block but 100mg of magnesium sulphate resulted in a significant delay in onset of sensory block.

| Table 1: Patient characteristics in levobupivacaine (group C), levobupivacaine + magnesium sulphate 50 (group M50) and levobupivacaine + magnesium sulphate 100 (group M100) |
|-----------------------|---------------------|---------------------|---------------------|---------------------|
| **Variable**          | **Group C** (n = 30) | **Group M50** (n=30) | **Group M100** (n=30) | **p value**          |
| Age (years)*          | 41.3 ± 10.3         | 41.0 ± 11.6         | 42.0 ± 11.00         | 0.937               |
| Female:Male           | 9:21                | 2:28                | 6:24                 | 0.068               |
| Weight (kg)           | 63.2 ±10.3          | 65.5 ± 10.2         | 61.8 ± 8.6           | 0.352               |
| ASA I/II              | 18/12               | 24/6                | 21/9                 | 0.23                |
| Type of surgery       |                     |                     |                      |
| Herniorrhaphy         | 9                   | 8                   | 6                    |
| Lower limb            | 4                   | 6                   | 8                    |
| Urological            | 12                  | 11                  | 13                   |
| Perineal              | 5                   | 5                   | 3                    |

All values corrected to first decimal place
*data are presented as mean ± standard deviation
ASA = American Society of Anesthesiologists
The mean duration of sensory block (regression of sensory block to S1 by pin prick method) in Group C was 165.06 ± 34.3 min, in Group M 50 was 207.5 ± 34.35 min and in Group M 100 it was 245.5 ± 48.8 min. There was statistically significant difference among the three groups with regards to the duration of sensory block (p < 0.001) (Table 2).

The spinal block was adequate. All the patient had reached Bromage 3 within three to seven minutes. The mean time to onset of motor block (to Bromage 3) in group C was 4.71 ± 1.61 min, group M 50 was 5.38 ± 3.82 min and in group M 100 was 6.76 ± 3.91 min. There was no statistical significant difference between the three groups though numerically it appears more in group M 100.

Mean duration of motor block (return of Bromage 3 to 0) in Group C was 155.00 ± 28.97 min, Group M 50 (183.16 ± 24.19 min) and in Group M 100 (219.50 ± 38.37 min) which was statistically significant (p<0.001) (Table 2).

In both M 50 and M 100 groups there was an increase the duration of sensory and motor block but the duration is maximum in M 100 group. (Table 2)

Cardiovascular changes were remarkable with bradycardia (absolute heart rate < 50 beats/min) more common in patients of M 100 group (6/30) which was statistically significant (p=0.02). The incidence of hypotension (decrease in systolic blood pressure below 90 mm Hg or more than 20% of the base line) was similar among the three groups (group C 6/30, group M 50/30 and group M 100/30) (Table 3).

Nausea was noted in three patients in Group C. All the patients in the three groups were alert and had no neurological deficits in the post operative period (Table 3). There was no difference in the incidence of shivering and vomiting. None of the patients had respiratory complications.

**DISCUSSION**

Magnesium sulphate is a well-established IV treatment for many medical conditions like pre-eclampsia, acute asthma and tachyarrhythmias but its use as neuraxial adjuvant is relatively new and may act synergistically with intrathecal 0.5% hyperbaric levobupivacaine to prolong the duration of subarachnoid block. Magnesium is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, and inhibits voltage-gated calcium channels. Adding magnesium to intrathecal lipophilic opioid with or without local anaesthesia or local anaesthesia only was associated with a significant increase in the duration of spinal anaesthesia. Animal studies have shown that intrathecal magnesium suppresses nociceptive impulses in a neuropathic pain setting, and potentiates opioid antinociception. We are not aware of any

### Table 2: Effect of intrathecal magnesium sulphate when used as an adjuvant to hyperbaric levobupivacaine on characteristics (onset, duration and intensity) of spinal blockade

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group C (n = 30)</th>
<th>Group M 50 (n = 30)</th>
<th>Group M 100 (n = 30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Block height</td>
<td>T6 (T6-T8)</td>
<td>T6 (T6-T8)</td>
<td>T6 (T6-T8)</td>
<td></td>
</tr>
<tr>
<td>Onset of sensory block (min)</td>
<td>5.6 ± 1.98</td>
<td>5.8 ± 1.99</td>
<td>7.3 ± 2.7</td>
<td>0.007</td>
</tr>
<tr>
<td>Duration of sensory block (min)</td>
<td>165.1 ± 34.3</td>
<td>207.5 ± 34.4</td>
<td>245.5 ± 48.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Onset of motor block (min)</td>
<td>4.7 ± 1.6</td>
<td>5.4 ± 3.8</td>
<td>6.8 ± 3.9</td>
<td>0.053</td>
</tr>
<tr>
<td>Duration of motor block (min)</td>
<td>155.00 ± 29.0</td>
<td>183.2 ± 24.2</td>
<td>219.5 ± 38.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adequancy of motor block*</td>
<td>Bromage 3</td>
<td>Bromage 3</td>
<td>Bromage 3</td>
<td></td>
</tr>
</tbody>
</table>

All values corrected to first decimal place
data are presented as mean ± standard deviation
*assessed by Bromage score
In our study, the addition of 50 mg and 100 mg magnesium sulphate to intrathecal 0.5% hyperbaric levobupivacaine provided safe and effective anaesthesia similar to other studies.\textsuperscript{15-17} by In these studies\textsuperscript{17,18} the intrathecal local anaesthetics used was 0.5% hyperbaric bupivacaine.

The main findings of our study is, addition of magnesium sulphate to 0.5 % hyperbaric levobupivacaine caused intense prolongation of both sensory and motor block in a dose dependent manner without effecting the onset of motor block to a significant level. All patients in the three groups achieved sensory block upto T6 and motor block of Bromage score three. None of the cases required conversion to general anaesthesia or supplementary sedation because of inadequacy of the spinal block.

The present study findings of delay in onset of sensory block in Group M 100 compared to Group M 50 and C and no difference in onset of motor block among all the three groups was similar to previous studies.\textsuperscript{17-20} In two studies\textsuperscript{17,18} addition of different doses of intrathecal magnesium sulphate to hyperbaric bupivacaine was studied where as in a study\textsuperscript{19} fentanyl was also used as adjuvant. Magnesium sulphate 100 mg as adjuvant to bupivacaine and saline was compared in another study. We found that the mean duration of sensory and motor block was significantly prolonged (Table 2) when magnesium sulphate was added intrathecally. Similar findings were observed in other studies.\textsuperscript{17,21-23} Among these studies, two studies\textsuperscript{17,23} compared magnesium sulphate as adjuvant to intrathecal bupivacaine where as in the other two studies\textsuperscript{21,22} intrathecal fentanyl was also added and concluded the same. The duration of motor block was same in both the groups in another study.\textsuperscript{19} Our study is similar to another study\textsuperscript{24} where the authors compared different doses of magnesium sulphate and fentanyl as adjuvant to intrathecal bupivacaine in infraumbilical surgeries and concluded that the onset of sensory and motor block is prolonged in magnesium groups but the duration of sensory and motor block was similar to fentanyl group. More patients in group M100 in the present study had bradycardia (6/30) which responded to injection atropine 0.6mg (Table 3).

Though the incidence of hypotension was same in all groups (group C6/30, group M50-5/30

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group C (n = 30)</th>
<th>Group M50 (n = 30)</th>
<th>Group M100 (n = 30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>0.92</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0</td>
<td>2</td>
<td>6</td>
<td>0.02</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0.04</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Shivering</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>0.87</td>
</tr>
<tr>
<td>Apnea/hypoventilation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Neurological deficit</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Sedation</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

Group C = levobupivacaine (group C); Group M50 = levobupivacaine + magnesium sulphate 50 mg; and Group M100 = levobupivacaine + magnesium sulphate 100 mg
and group M100-5/30), nausea was present in group C only. There was no nausea in magnesium sulphate group as reported in other studies.\textsuperscript{17,18,23} This finding suggests that magnesium sulphate probably has inhibitory action on nausea which may be advantageous compared to intrathecal opioids.

There are several limitations of the study. The type of surgery was not standardised due to which post-operative pain and the requirement of analgesia could not be assessed. However, further studies using larger sample size are needed to confirm the findings.

We recommend 50 mg of magnesium sulphate intrathecally over 100 mg with 0.5% levobupivacaine as 100 mg of magnesium sulphate increases the duration of sensory block at the cost of increased motor block and more over resulted in a higher incidence of bradycardia a feature which may not be desirable by many anaesthesiologists.

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