COMPARATIVE EVALUATION OF INTRATHECAL DEXMEDETOMIDINE AND MAGNESIUM SULPHATE AS ADJUVANTS TO BUPIVACAINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES

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ABSTRACT

BACKGROUND
Neuraxial anaesthesia is most widely practiced for surgeries of lower abdomen and lower limbs. Hyperbaric bupivacaine along with adjuvants are used with an intention to prolong the duration and quality of sensory and motor block with minimal side effects. The aim of the study was to compare intrathecal dexmedetomidine and magnesium sulphate as adjuvants to bupivacaine in patients undergoing lower abdominal and lower limb surgeries.

METHODS
90 patients of either sex, in the age group of 18-60 years and ASA grade I and II posted for lower abdominal and lower limb surgeries were randomly allocated into three groups of 30 each. Group B: (n= 30) received intrathecal injection of a solution containing 15 mg of 0.5% bupivacaine (hyperbaric) and 0.1 ml of normal saline. Group D: (n= 30) received intrathecal injection of a solution containing 15 mg of 0.5% Bupivacaine (hyperbaric) and 5 mcg of Dexmedetomide. Group M: (n= 30) received intrathecal injection of a solution of 15 mg of 0.5% bupivacaine (hyperbaric) and 50 mg of magnesium sulphate. Each one of the solutions was made to a total volume of 3.1 ml. The time of onset to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes and side-effects were recorded. ANOVA/Kruskal Wallis test, Post Hoc Tukey’s test, Mann Whitney test, Chi-Square test /Fisher’s exact test were applied for interpretation of data.

RESULTS
The mean time to onset of sensory block was significantly faster in group D (5.47 ± 1.81 min) than group B (6.73 ± 1.53 min) and group M (8.8 ± 1.54 min). The mean time to onset of motor block was rapid in Group D (5.92 ± 1.48 min) and delayed in Group M (8.8 ± 1.54 min) in comparison with the control Group B (6.33 ± 1.37 min). The mean duration to S2 segment regression was significantly higher in group D (323.27 ± 21.38 min) and group M (269.53 ± 12.18 min) than group B (203.1 ± 12.13 min). The mean time for total duration of motor block was prolonged in Group D (287.27 ± 19.22 min) and Group M (238.53 ± 11.84 min) when compared with the control Group B (168.77 ± 9.7 min). The patients were haemodynamically stable during the surgery with statistically insignificant adverse events.

CONCLUSIONS
Dexmedetomide has faster onset of sensory and motor blockade with prolonged duration of analgesia than magnesium sulphate. Both can be used as effective adjuvants to intrathecal hyperbaric bupivacaine with insignificant adverse events.

KEYWORDS
Intrathecal, Bupivacaine, Dexmedetomidine, Magnesium Sulphate, Adjuvants

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BACKGROUND
Since the advent of spinal anaesthesia, it has been widely practiced for lower abdominal and lower limb surgeries. As the decades passed various adjuvants came into light with an intention to prolong sensory and motor blocked with minimal side effects. The drugs like alpha-2 agonists, opioids, midazolam, ketamine, magnesium sulphate etc. were used extensively with some of them having their known adverse events. The quality and duration of sensory and motor block and decreased postoperative pain are important aspect of spinal anaesthesia which are very well taken over by use of adjuvants. Following U.S. FDA approval in 1999, dexmedetomide has been widely investigated as an anxiolytic, sympatholytic and analgesic properties related to alpha-2 adrenergic receptor binding. Being highly lipophilic it facilitates rapid absorption into the CSF and binding to the alpha-2 receptors in the spinal cord. Dexmedetomide served as an adjuvant in many of the studies showing its potential to prolong the duration with minimal haemodynamic alterations. Magnesium sulphate, NMDA...
receptor antagonist blocks the voltage dependent channels and improves the quality and duration of spinal blocks. Intrathecal magnesium has shown promising results by prolonging the duration of analgesia in various surgical procedures like lower limb surgeries.

The aim of study was to compare the effects of intrathecal dexmedetomidine and magnesium sulphate as adjuvants to bupivacaine for lower abdominal and lower limb surgeries in relation to characteristics of sensory block, motor block and sedative effect.

METHODS
After obtaining institutional ethical committee approval 90 patients were enrolled for the study from June 2015 to May 2016. The participants were explained about the study and informed written consent was obtained from them. It was double blind, prospective and randomized controlled study. The inclusion criteria for the study were adult patients aged between 18-60 years, of either sex, undergoing lower abdominal and lower limb surgeries, belonging to ASA Class I and II, weighing between 45 Kg to 80 kg, with height between 150 cm and 180 cm. The following patients were excluded from the study: refusal to participate, psychiatric illness, emergency surgeries, history of drug abuse, known hypersensitivity to local anaesthetics or adjuvants, patients with medical complications like raised intracranial tension, anaemia, heart disease, diabetes mellitus, severe hypovolaemia, shock, sepsis, hypertension, coagulopathy disorders, local infection at the proposed site of puncture for spinal anaesthesia, spinal deformities like kyphoscoliosis, lordosis etc. Patients were divided into three groups by computer generated random numbers.

- Group B: (n= 30) received intrathecal injection of a solution containing 15 mg of 0.5% Bupivacaine (hyperbaric) and 0.1 ml of normal saline.
- Group D: (n= 30) received intrathecal injection of a solution containing 15 mg of 0.5% Bupivacaine (hyperbaric) and 5 mcg of Dexmedetomidine.
- Group M: (n= 30) received intrathecal injection of a solution containing 15 mg of 0.5% Bupivacaine (hyperbaric) and 50 mg of Magnesium Sulphate.

Each of the solution was made to a total volume of 3.1 ml.

Following pre-anaesthetic check-up of all patients routine investigations were done. Patients were premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.25 mg on the night before and 2 hour before on the morning of surgery. In the operation theatre, patients were made to lie comfortably on the operation table. After applying the monitors, baseline parameters were noted (pulse rate, blood pressure, oxygen saturation, and ECG). Intravenous access was secured with 18G IV cannula in non-dominant hand and 10 ml/kg of ringer lactate was infused as a pre-loading fluid. Patients were then placed in lateral decubitus position. A second anaesthesiologist, who was blind to study, prepared the study drug solution. L3-L4 intervertebral space was identified by palpation and infiltrated with 2% lignocaine. The study drug was injected using 25G Quincke’s spinal needle following free flow of CSF. Patients were placed supine immediately after the procedure with the table maintained horizontally. Time of completion of injection was noted and labelled as ‘0 min’. Patients were given supplementary oxygen at 2-4 litres/min by nasal prongs. Vital parameters were monitored at 5 minute intervals till the end of surgery. If systolic blood pressure fell below 90 mmHg or 30% below the baseline (hypotension), it was treated by increasing the fluid infusion rate and injection mephentermine 3 mg intravenous, if required. If heart rate falls below 50/min (bradycardia), injection atropine sulphate 0.6 mg intravenous was given. Sensory block was assessed by bilateral pin prick method with a blunt 26 G needle along the mid-clavicular line on both sides every two minutes till two consecutive readings of sensory block remain the same (i.e. when highest cephalad spread of sensory block has occurred), after which it was assessed at ten minute intervals till the end of surgery. In case there was a difference in the height of sensory block achieved on the two sides, the side with the lower level of sensory block was taken as the dermatomal level of the sensory block. The time to reach T6 dermatome (onset time), the maximum sensory level achieved, and time for two segment and S2 segment regression (the total duration of the sensory block) were recorded.

Motor block was assessed by Modified Bromage Scale (Grade 0 - Full flexion of knees and feet, Grade 1 - Just able to flex knees, full flexion of feet, Grade 2 - Unable to flex knees, but some flexion of feet possible. Grade 3- Unable to move legs or feet). Onset of motor blockade was the interval between the end of injecting the drug and complete motor paralysis Bromage 3. As in sensory block, motor block was assessed every two minutes till two consecutive readings remain the same, after which it was assessed every ten minutes till the end of surgery.

Sedation was assessed at 10 minutes interval by Ramsay Sedation Scale (RMS 1-6) with RMS 1 being anxious or restless or both and RMS 6 being no response to stimulus. Patients with maximum sedation score 1 was given injection midazolam 0.02 mg /kg to treat anxiety.

Ramsay Sedation Score
1. Anxious or restless or both
2. Cooperative, orientated and tranquil
3. Responding to commands
4. Brisk response to stimulus
5. Sluggish response to stimulus
6. No response to stimulus

After completion of surgery, level of sensory block and motor block was noted with the patient still on the operation table. The patients were shifted to the Post Anaesthesia Care Unit (PACU) and they were assessed every 30 minutes for motor block by Modified Bromage Scale, till they attain complete motor recovery. Sensory block was also assessed every 30 minutes by the same technique which was used during intra-operative period until complete recovery of sensation (sacral dermatome, S2). Sedation was assessed.
every 30 minutes. Visual analogue scale (0-10) was used to assess the post-operative pain at 0, 30, 60, 90, 120, 150 and 180 minutes after surgery. The postoperative rescue analgesia was provided by diclofenac sodium 75 mg I.M. (VAS>3). Time of the first analgesic was noted. We found that the difference in the mean time for first rescue analgesia was statistically very highly significant among all three groups. (p value <0.0001)

Mean time to requirement of first post-operative analgesic dose was minimum in Group B (190.43 ± 44.14 min) and maximum in Group D (299.27 ± 47.3 min). Mean time to requirement of first post-operative analgesic dose was 243.53 ± 36.94 94 min in Group M. We found that the difference in the mean time for first rescue analgesia was statistically very highly significant among all three groups. (p value <0.0001)

**Statistical Analysis**

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non-parametric test was used. Statistical tests were applied as follows:

1. Quantitative variables were compared using ANOVA/Kruskal Wallis test (when the data sets were not normally distributed) between the three groups and Post hoc comparison was performed by using either Post Hoc Tukey's test after ANOVA or by using Mann Whitney test after Kruskal Wallis test.

2. Qualitative variables were compared using Chi-Square test /Fisher's exact test. A p value of <0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

**RESULTS**

The demographic data such as age, height, weight and sex were comparable among the three groups. ASA physical status, type of surgery and duration of surgery was also comparable among the three groups.

<table>
<thead>
<tr>
<th>6.5</th>
<th>Group B (n=30)</th>
<th>Group D (n=30)</th>
<th>Group M (n=30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.) Mean ± SD</td>
<td>35.93 ± 9.25</td>
<td>39.13 ± 10.71</td>
<td>38.77 ± 8.11</td>
<td>0.3507</td>
</tr>
<tr>
<td>Height (cm) Mean ± SD</td>
<td>157.57 ± 8.82</td>
<td>160.9 ± 6.43</td>
<td>159.87 ± 6.99</td>
<td>0.1276</td>
</tr>
<tr>
<td>Weight (kg) Mean ± SD</td>
<td>55.1 ± 8.1</td>
<td>59.07 ± 7.12</td>
<td>56.57 ± 8.47</td>
<td>0.1520</td>
</tr>
<tr>
<td>Sex (Frequency %) Females/Males</td>
<td>14 (46.67 %)/16 (53.33 %)</td>
<td>14 (46.67 %)/16 (53.33 %)</td>
<td>11 (36.67 %)/19 (63.33 %)</td>
<td>0.665</td>
</tr>
<tr>
<td>ASA (Frequency %) 1/2</td>
<td>26 (86.67 %)/4 (13.33 %)</td>
<td>26 (86.67 %)/4 (13.33 %)</td>
<td>27 (90.00 %)/3 (10.00 %)</td>
<td>0.902</td>
</tr>
<tr>
<td>Duration of Surgery (min) Mean ± SD</td>
<td>89.23 ± 16</td>
<td>90.63 ± 18.58</td>
<td>86.57 ± 16.4</td>
<td>0.6445</td>
</tr>
<tr>
<td>Type of surgery (Frequency %) Lower abdominal/Lower limb</td>
<td>56.7%/43.3%</td>
<td>63.3%/36.7%</td>
<td>56.7%/43.3%</td>
<td>0.378</td>
</tr>
</tbody>
</table>

As shown in table 3, mean time to onset of motor block was rapid in Group D (5.92 ± 1.48 min) and delayed in Group M (8.8 ± 1.54 min) in comparison with the control Group B (6.33 ± 1.37 min). We found that the difference in the onset and total duration of motor block was statistically very highly significant between Group B v/s. Group D (p value <0.001), between Group B v/s. Group M (p value <0.0001) and also between Group D v/s. Group M (p value <0.0001). The difference in the maximum sedation score was statistically not significant amongst all the three groups (p value 0.177). There were no statistically significant difference as regards bradycardia, hypotension shivering, nausea, vomiting and respiratory depression among all the three groups (p value >.05)

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>Onset of motor block B3 (min)</td>
<td>6.87 ± 1.63</td>
<td>5.53 ± 1.72</td>
<td>8.93 ± 1.46</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Total duration of Motor block (min)</td>
<td>168.77 ± 9.7</td>
<td>287.27 ± 19.22</td>
<td>238.53 ± 11.84</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

From table 2 it is evident that mean time of onset of sensory block at T6 was rapid in Group D (5.47 ± 1.81 min) and delayed in Group M (8.8 ± 1.54 min) in comparison with the control Group B (6.73 ± 1.53 min). We found that the difference in the meantime to onset of sensory block at T6 dermatome was statistically very highly significant among all three groups. (p value <0.0001). Mean time taken to S2 segment regression of sensory block was prolonged in Group D (323.27 ± 21.38 min) and Group M (269.53 ± 12.18 min) when compared with the control Group B (203.1 ± 12.13 min). However duration was longest in Group M amongst three groups. We found that the difference in the meantime taken for S2 segment regression of sensory block was statistically very highly significant among all three groups. (p value <0.0001)

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</tr>
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<tbody>
<tr>
<td>Time to onset at T6 (min)</td>
<td>6.73 ± 1.53</td>
<td>5.47 ± 1.81</td>
<td>8.8 ± 1.54</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Time taken for maximum cephalic spread of sensory block</td>
<td>8 ± 2.23</td>
<td>5.8 ± 2.27</td>
<td>7.73 ± 1.8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Time to two segment regression (min)</td>
<td>96.77 ± 1.14</td>
<td>145.27 ± 14.84</td>
<td>120.53 ± 13.85</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Time to S2 segment regression (min)</td>
<td>203.1 ± 12.3</td>
<td>232.27 ± 21.38</td>
<td>269.53 ± 12.18</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Mean time for first rescue analgesia</td>
<td>190.43 ± 44.14</td>
<td>299.27 ± 47.3</td>
<td>243.53 ± 36.94</td>
<td>&lt;.0001</td>
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</tbody>
</table>

Table 2. Sensory Block Characteristics

<table>
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<td>Time to onset</td>
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<td>8.93 ± 1.46</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Total duration</td>
<td>168.77 ± 9.7</td>
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Table 3. Motor Block Characteristics
observed that there was an increase in the total duration of sensory block by 72% when compared to the use of local anaesthetic alone. On the other hand, in the magnesium group, our results are in corroboration with Khalili G et al.9 found that the addition of intrathecal magnesium prolonged the duration of sensory block. Mean time to requirement of first post-operative analgesic was minimum in Group B (190.43 ± 44.14 min) and maximum in Group D (299.27 ± 47.3 min). It was 243.53 ± 36.94 min in Group M. This was consistent with the study results of Rajni Gupta et al.18 and, Malleeswaran et al.21 R.K. Singh et al.22 The study by Hala E A eid et al.16 Rajni Gupta et al.23 also concludes that dexmedetomidine intrathecally prolongs the motor block. They reported a time duration of 280±46 min in 10 μg dexmedetomidine group and 336±58 min in 15 μg dexmedetomidine group in conjunction with a total volume of 3.0 ml heavy bupivacaine. Our results are in corroboration with S. Malleeswaran et al.23 and Mitra Jabalameli et al.8 who showed prolongation of duration of sensory and motor block in magnesium group. Similar result was found by D. Shukla et al.14 who observed prolonged motor block in dexmedetomidine group followed by magnesium and then in control (bupivacaine) group in spinal block. There was no statistically significant difference as regards shivering, nausea vomiting and respiratory depression among all the three groups (p value>0.05). Our results are comparable with the studies conducted by Rajni Gupta et al.18 Al-Ghanem et al.15 Malleeswaran et al.23 Mitra Jabalameli et al.8

CONCLUSIONS

Addition of dexmedetomidine to hyperbaric bupivacaine intrathecally produces an early onset of sensory and motor block, prolongs sensory and motor block and the time to first rescue analgesic requirement significantly with stable hemodynamic parameters and minimal side effects. When added to hyperbaric bupivacaine, intrathecal magnesium causes delayed onset of sensory and motor block but prolongs the duration in comparison to bupivacaine alone, but the prolongation is less than dexmedetomidine.

REFERENCES


