The Effects of Dexmedetomidine Added to Spinal bupivacaine for lower limb surgery

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Abstract:

**Background:** Intrathecal \(\alpha_2\) agonists prolong the duration of action of local anesthetics and reduce the required dose. Dexmedetomidine is a \(\alpha_2\) receptor agonist and its \(\alpha_2/\alpha_1\) selectivity is 8 times higher than that of clonidine.

**Aims:** In this study, we aimed to investigate the effect of adding dexmedetomidine to intrathecal bupivacaine on the onset time and duration of motor and sensory blocks.

**Methods:** Patients were randomly assigned into two groups. Group B \((n=30)\) patients received 3ml \((15mg)\) of 0.5% bupivacaine +0.5ml normal saline and Group BD \((n=30)\) patients received 3ml \((15 mg)\) of 0.5% bupivacaine + 0.5ml \((5\mu g)\) dexmedetomidine. The parameters studied were - onset and total duration of sensory block, onset and total duration of motor block, the most elevated dermatome level, hemodynamic alterations, and any intraoperative and postoperative complications.

**Results:** The two groups were matched for demographic data. Sensory and motor block onset times were similar in both groups. The regression of the sensory block to S1 dermatome and regression of complete motor block were longer in Group BD than Group B \((p<0.001)\). No significant difference were seen between the groups relative to the maximum level of sensory block \((p=0.340)\). Statistically there were no significant differences in hemodynamic alterations and other adverse effects between the groups.

**Conclusion:** We conclude that intrathecal dexmedetomidine addition to bupivacaine for spinal anaesthesia prolongs sensory and motor block durations without any significant adverse effects.

**Key Words:** Dexmedetomidine, bupivacaine, spinal block

I. **Introduction**

While spinal anaesthesia has many advantages, the limited duration of action appears to be one of its downsides. Intrathecal \(\alpha_2\) agonists prolong the duration of action of local anaesthetics and reduce the required dose. The intrathecal use of clonidine, a partial \(\alpha_2\) adrenoceptor agonist, has been shown as an effective and safe procedure \((1,2)\). Dexmedetomidine is a \(\alpha_2\) receptor agonist and its \(\alpha_2/\alpha_1\) selectivity is eight times higher than that of clonidine. In animal models, intrathecal dexmedetomidine has been demonstrated to have an analgesic effect \((3,4)\). In this study, we aimed to investigate the influences of dexmedetomidine added to bupivacaine on the time of onset of spinal block and durations of sensory and motor blocks in patients undergoing lower limb surgery under spinal anaesthesia.

II. **Materials and Methods**

With the approval of ethics committee of the institution, 60 patients of ASA grade I- II of either sex in the age range of 20 to 50 years, undergoing lower limb surgery (below knee including arthroscopy of knee) under spinal anaesthesia were selected for the study and these were divided into two groups of 30 patients each. Using the sealed envelope method, the patients were randomly allocated into two groups: Group B \((n=30)\) or Group BD \((n=30)\). Patients who were taking \(\alpha\)-adrenergic agonist or antagonist therapy, as well as patients who had labile hypertension, autoimmune disorders, known allergy to study drugs, heart block or any contraindication to spinal anaesthesia were excluded from the study. After arrival at the operating theatre, baseline systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR) measurements, peripheral oxygen saturation (SpO2) and electrocardiography monitoring were measured by an anaesthesiologist who was blind to group allocation. After prehydration with 10ml/kg of normal saline, we performed dural puncture between L3-4 or L4-5 interspace, under sterile conditions and with the patients in the sitting position, through a 25-gauge Quincke needle. Group B received 3 ml of bupivacaine 0.5% hyperbaric (Anawin Heavy; Neon Laboratory Ltd. India) with 0.5ml of normal saline in spinal anaesthesia and group BD received 3ml of hyperbaric bupivacaine 0.5% with 0.5ml \((5\mu g)\) of dexmedetomidine (Dextomid; Neon Labs, India) in spinal anaesthesia. Standard monitoring was continued throughout the operation. Sensory blockade was
assessed by using pinprick test on each side of the midclavicular line; motor blockade was assessed based on a modified Bromage scale (5) (0= free movement of legs and feet, 1= just able to flex knees with free movement of feet, 2= unable to flex knees, but with free movement of feet, 3= unable to move legs or feet). The sensory level and Bromage scale were recorded intra-operatively every 2 min for a period of 20 min, at the end of the surgery and in the Post-Anaesthesia Care Unit (PACU) every 15 min until the patient was discharged from PACU by an anaesthesiologist who was blinded to group allocation. Further testing was recorded at 15 minute intervals until the recovery of S1 dermatome. Sensory block onset time to T10 dermatome, the highest dermatomal level, sensory block complete regression time, motor block onset time, reaching Bromage 3 and regression to Bromage 0 times were recorded. The haemodynamic variables were recorded before spinal anaesthesia and thereafter every 2 min for 10 min, every 5 min until the end of the procedure in the operating room and every 15 min in the PACU until the patient was discharged to the ward. Follow-up was carried out 5 days postoperatively by the blinded anaesthetist who asked about any neurological deficits secondary to spinal anaesthesia. A decrease >20% from baseline, or to <90 mmHg in systolic blood pressure, was defined as hypotension and was treated with incremental doses of 5 mg intravenous ephedrine. Bradycardia was defined as heart rate <50 beats/min and was treated with atropine. Intraoperative analgesic requirement, intraoperative and postoperative nausea and vomiting and other side effects were recorded.

Intergroup comparison of demographic data, durations of sensory and motor blocks, mean arterial pressure, and mean heart rate values were carried out by Student’s t test, whereas intragroup comparisons were performed with Repeated Measure ANOVA test. Chi-square or Fisher’s Exact Test, as appropriate, were applied for intergroup analysis of side effects. Values of p<0.05 were accepted as statistically significant. Determination of patient number was made according to the study of Kanazi et al. (2). A minimum of 13 patients in each group was recruited according to the power analysis (α=0.05 and, β=0.05, power 95%).

III. Results

The two groups were matched for demographic data and duration of operation (Table 1).

<table>
<thead>
<tr>
<th>Table 1. Characteristics of patients :-</th>
<th>Group B (n=30)</th>
<th>Group B (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(years)</td>
<td>30.2±5.1</td>
<td>29.3±6.7</td>
<td>0.561</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172±8.1</td>
<td>169±6.3</td>
<td>0.099</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>62±5.1</td>
<td>66±3.2</td>
<td>0.439</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>90±30.2</td>
<td>98±28.3</td>
<td>0.089</td>
</tr>
</tbody>
</table>

p values calculated using Student’s t-test

Time for sensory block to reach T10 level was similar in both the groups (p=0.296). There was no difference between the groups relative to the maximum level of sensory block (p=0.340). In both groups, all patients demonstrated complete motor block (Bromage 3). Time to reach complete motor block was similar in both of the groups (p=0.856). Time to regression of the sensory block to S1 dermatome and time to complete recovery of motor block was more prolonged in Group BL than in Group B and the intergroup difference was statistically significant (p<0.001) (Table 2).

<table>
<thead>
<tr>
<th>Table 2. Sensory and motor block characteristics:-</th>
<th>Group B (n=30)</th>
<th>Group BD (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to sensory block to reach T10 dermatome (min)</td>
<td>7.5±2.7</td>
<td>8.3±3.3</td>
<td>0.296</td>
</tr>
<tr>
<td>Highest level of sensory block (T)</td>
<td>8.6±1.0</td>
<td>8.2±2.0</td>
<td>0.340</td>
</tr>
<tr>
<td>Time to onset of complete motor block (Bromage=3) (min)</td>
<td>14.3±7.1</td>
<td>13.9±6.9</td>
<td>0.856</td>
</tr>
<tr>
<td>Time to sensory regression to S1 segment (min)</td>
<td>226.6±26.4</td>
<td>356.3±35.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to motor block regression to Bromage 0</td>
<td>201.0±26.9</td>
<td>332.0±36.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

p values calculated using Student’s t-test

<table>
<thead>
<tr>
<th>Table 3: Adverse effects:-</th>
<th>Group B (n=30)</th>
<th>Group BD (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>2</td>
<td>0.492</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>2</td>
<td>1.00</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>3</td>
<td>2</td>
<td>1.00</td>
</tr>
</tbody>
</table>

p values calculated using χ²-test (Fisher’s exact test)
The Effects of Dexmedetomidine Added to Spinal bupivacaine for lower limb surgery

There was no difference between the groups with regard to mean arterial pressure values at baseline and during all time points (p>0.05) (figure 1). There was no statistically significant difference between the groups relative to baseline HR values (p>0.05) (figure 2). The comparison of HR values at baseline and at other time points both in Group B and Group BD did not show any statistically significant difference (p>0.05). Adequate nerve block was established in both groups and none of the patient’s required additional analgesia. None of the patients had an observed neurological deficit or any transient neurological symptoms at the postoperative follow-up. The side effects that were observed in the groups are summarised in Table 3. No statistically significant difference was determined between the groups with regard to the frequency of side effects.

IV. Discussion

In this study, we observed that adding dexmedetomidine to bupivacaine prolonged the sensory and motor block duration in patients subjected to lower limb surgery under spinal anaesthesia. Although the mechanism is unclear, α2 adrenoceptor agonists have been observed to extend the sensory and motor block durations of local anaesthetics. Ossipov et al. (6) conducted a study where they delivered intrathecal clonidine to rodents and reported that adrenergic receptor agonists induced analgesia by a mechanism other than that of opioids. Clonidine increases acetylcholine concentration in cerebrospinal fluid and activates α2 adrenergic receptors in the dorsal horn of the spinal cord (7). The α2 adrenoceptors are localised over the primary afferent terminals of neurons in the superficial lamina of the spinal cord and in the nuclei of the brainstem associated with pain. This localisation supports that α2 agonists show their analgesic effects through both peripheral and central pathways (8). Clonidine, an intrathecal α2 adrenoceptor agonist, has been used intrathecally in many studies which provided adequate clinical experience about the agent; studies focusing on intrathecal use of dexmedetomidine and its combined use with local anaesthetics are not sufficient (1, 9, 10). Although dexmedetomidine has been approved by the Food and Drug Administration as a sedative for mechanically-ventilated adult intensive care unit patients, it has not been approved for intrathecal use. However, dexmedetomidine used in neuraxial blocks in experimental and clinical studies without neurological deficits has encouraged the use of dexmedetomidine by the intrathecal route with bupivacaine (2, 11-20). The intrathecal application of dexmedetomidine in the 2.5-100μg dose range has been investigated in rats, rabbits, dogs, and sheep (11-16). A 100μg dose of intrathecal dexmedetomidine was employed in sheep but no neurological deficit was observed during a follow-up period of 7 days (11). In the study of Strebel et al. (1) on orthopaedic cases, using clonidine at a dose below 150 μg in combination with isobaric bupivacaine in a dose-dependent fashion was shown to provide significantly prolonged duration of spinal anaesthesia and analgesia without disrupting the haemodynamic stability and inducing sedation. Santiveri et al. (21) used 75μg clonidine to prilocaine in patients undergoing transurethral resection of bladder tumours under spinal anaesthesia and reported prolonged sensory and motor blocks along with reduced postoperative analgesic requirement. De Kock et al. (9) used spinal anaesthesia by adding varying doses of clonidine (0, 15, 45 or 75μg) to ropivacaine in arthroscopy patients. The quality of anaesthesia was lower in the ropivacaine-only group, the quality of intraoperative analgesia was elevated while motor and sensory block durations were unchanged in the 15μg clonidine group, and sensory block duration was prolonged in the 75μg clonidine group. Kanazi et al. (2) reported that the addition of dexmedetomidine (3μg) or clonidine (30μg) to bupivacaine in spinal block shortens the time to onset of motor block and extends the sensory and motor block durations. Al-Mustafa et al. (17) added 5μg and 10μg dexmedetomidine to spinal bupivacaine and noted shorter times to onset of sensory and motor blocks along with longer block durations. Gupta et al. (20)
added 5μg dexmedetomidine or 25μg fentanyl to 12.5mg bupivacaine in spinal blocks and noted a longer duration of both sensory and motor blockade, and good patient satisfaction. Niemi et al. (22) reported that the addition of clonidine to bupivacaine in spinal anaesthesia prolonged block duration, but decreased the mean blood pressure and heart rate significantly compared with the control group. Kanazi et al. (2) noted that dexmedetomidine or clonidine added to intrathecal bupivacaine did not cause a significant reduction in blood pressure. In the study of Gupta et al. (20), hypotension was more severe in the dexmedetomidine group than in the fentanyl group, but no statistically significant difference was determined between the groups. In this study, we observed hypotension and bradycardia in only 2 patients.

In conclusion, the combined use of 5μg dexmedetomidine and bupivacaine in spinal anaesthesia prolongs sensory and motor block durations without causing any significant side effects.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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**References**


