Comparison of Effect of Intrathecal Buprenorphine vs Clonidine as an Adjuvant to Hyperbaric Bupivacaine on Subarachnoid Block Characteristics

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ABSTRACT

Background and aims: There are very few reported clinical trials with direct comparison of buprenorphine and clonidine on subarachnoid block characteristics. The aim of the present study was to compare the effect of buprenorphine 75 µg and clonidine 37.5 µg as an adjuvant to 15 mg of 0.5% bupivacaine in lower limb surgeries with respect to the subarachnoid block characteristics, postoperative analgesia and side-effects.

Methods: One hundred patients of 15 to 60 years, either sex and American Society of Anesthesiologist (ASA) I/II undergoing elective lower limb surgeries under planned spinal anesthesia were included and randomly allocated into two equal groups (n = 50 each) to receive 3 ml of intrathecal 0.5% bupivacaine (heavy) with either clonidine 37.5 µg (group C) or buprenorphine 75 µg (group B) to a total volume of 3.25 ml. The patients were evaluated with respect to various sensory and motor block characteristics, duration of postoperative analgesia and adverse effects.

Result: Both the groups were comparable with respect to demographic profile. There was significant prolongation in the duration of sensory block (119.26 ± 24.56 vs 79.40 ± 15.67; p = 0.0), motor block (277.90 ± 37.56 vs 198.80 ± 42.21; p = 0.0) and postoperative analgesia (355.80 ± 63.85 vs 283.20 ± 51.84; p = 0.0) in group C compared with group B. There was clinically significant earlier onset of maximum sensory block (9.20 ± 5.69 vs 11.90 ± 4.78; p = 0.018) and motor block (5.10 ± 3.39 vs 11.90 ± 4.78; p = 0.018) in group C compared with group B however the results were statistically significant only for time to attain maximum sensory block. The incidence of shivering was significantly lower in group C compared with group B.

Conclusion: Intrathecal 37.5 µg clonidine seems to be an attractive alternative to 75 µg buprenorphine as an adjuvant to spinal bupivacaine in terms of duration of sensory and motor blockade, postoperative analgesia and having less side-effects.

Keywords: Analgesia, Anesthesia, Buprenorphine, Clonidine, Subarachnoid.
METHODS

After obtaining approval from institutional ethics committee and written informed consent 100 American Society of Anesthesiologist (ASA) grade I and II adult patients of age group between 15 to 60 years, of either sex undergoing elective orthopedic surgeries under spinal anesthesia were included in the study. The patients with cardiovascular, neurological, respiratory, renal or endocrine diseases, contraindications to spinal anesthesia, allergy to any of the study drugs and pregnant patients were excluded from the study. Patients were kept fasting for 6 hours preoperatively and no premedication was given. The patients were instructed in the use of numerical rating scale (NRS) of pain scale (NRS; 0-No pain, 10-Worst possible pain).

After wheeling the patients in a prepared operation theater on the day of the surgery, monitoring devices like electrocardiography (ECG), pulse oximetry (SpO2), non-invasive blood pressure were attached and baseline vitals recorded. Equipments and drugs necessary for resuscitation and general anesthesia administration were kept ready. An 18 gauge intravenous line was secured on the dorsum of either arm and co-loading done with 10 ml/kg of Ringer lactate solution. The patients were randomly assigned using computer generated random list into two groups to receive intrathecally either: group C: 15 mg hyperbaric bupivacaine 0.5% 3cc + 37.5 µgm clonidine or group B: 15 mg hyperbaric bupivacaine 0.5% 3cc + 75 µgm buprenorphine. The study drugs were made to a total volume of 3.25 ml in identical 5 ml syringes by an independent anesthesiologist not involved in the study. With operation table in neutral position, and under all aseptic precautions, lumbar puncture was done in L3 to L4 interspace in sitting position with 25G Quincke spinal needle. After obtaining free flow of cerebrospinal fluid (CSF), the proposed drug was injected slowly as per group allotment. All the onset and duration times were recorded with respect to completion of intrathecal injection as time 0. The sensory block level (SBL) was assessed by pinprick with sterile 25G hypodermic needle in the mid clavicular line every 30 seconds till the attainment of highest SBL (onset time of highest SBL). Subsequently the SBL was checked every 15 minutes till two segment sensory regression (duration of sensory block). The level of motor block was assessed by modified Bromage scale: 0: Patient able to move hip, knee and ankle, 1: Able to move knee and ankle, cannot move hip, 2: Able to move ankle, can not move hip and knee, 3: Unable to move hip, knee or ankle. The onset and duration of motor block was defined as the time to attain Bromage 3 and return of motor power to Bromage 0 respectively. Pulse rate, blood pressure, respiratory rate, oxygen saturation, sedation and visual analog scale (VAS) were monitored continuously every 2 minutes for first 10 minutes, every 5 minutes for 30 minutes, every 30 minutes for 180 minutes and every 60 minutes till complete recovery from block and till demand for first rescue analgesic by patient. A fall of systolic blood pressure of less than 80 mm Hg or more than 20% of baseline was considered as hypotension and treated with rapid infusion of intravenous fluid Ringer lactate 250 ml and 6 mg intravenous ephedrine if there was no response to intravenous fluid administration. Heart rate of less than 50 beats per minute was considered as bradycardia and treated with injection atropine sulfate 0.6 mg intravenously. In the postoperative period the level of sedation was assessed using Ramsay Sedation Score: I: Patient is anxious, agitated and restless or both, II: Patient is cooperative oriented and tranquil, III: Patients respond to verbal commands only, IV: Patient exhibits brisk response to glabellar tap or loud auditory stimulus, V: Patient exhibits sluggish response to glabellar tap or loud auditory stimulus, VI: Patient exhibits no response. The patients were assessed for postoperative pain and injection diclofenac sodium 1.5 mg/kg was given as the rescue analgesic when numerical rating scale (NRS) ≥ 3. The time to requirement of first rescue analgesia was taken as the duration of analgesia. Intraoperative side-effects like sedation, nausea and vomiting, shivering, bradycardia and dryness of mouth requiring active treatment were also noted.

RESULTS

Both the groups were comparable with respect to demographic characteristics (Table 1). Mean duration of surgery was 118.24 ± 24.41 minutes in clonidine group and 112.52 ± 21.81 minutes buprenorphine group, which was insignificant statistically. The subarachnoid block characteristics have been depicted in Table 2. Forty-one (82%) patients in clonidine group achieved the maximum sensory level within 10 minutes, while only 26 (52%) patients in buprenorphine group could achieve this in 10 minutes (Graph 1). All the patients in both the groups achieved grade III motor blockade, only the difference was time required to achieve this. Almost 82% (41 patients) in clonidine group attained a grade III motor blockade within 6 minutes of commencement of motor blockade, compared to only 11 patients (22%) in Buprenorphine group (Graph 2).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group C (clonidine; n = 50)</th>
<th>Group B (buprenorphine; n = 50)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.24 ± 11.30</td>
<td>44.76 ± 12.24</td>
<td>0.839</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>12:38</td>
<td>13:37</td>
<td>0.823</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163.18 ± 4.71</td>
<td>162.48 ± 5.05</td>
<td>0.476</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.06 ± 8.03</td>
<td>58.70 ± 6.22</td>
<td>0.48</td>
</tr>
</tbody>
</table>

Table 1: Demographic characteristics
Thirty-six (72%) patients in clonidine group had two segment regression time of sensory level in 90 to 120 minutes (Graph 3). It was found that 42 (84%) patients in buprenorphine group depicted a two segment regression time within 90 minutes, and all patients depicted the same within 120 minutes (2 hours). Motor blockade was maintained for 241 to 300 minutes by maximum number of patients, 29 (58%) in clonidine group as compared to only 4 patients (8%) in buprenorphine group, where duration of motor blockade lasted for < 240 minute in 46 (92%) of patients. Twenty-five patients (50%) in buprenorphine group and 16 (32%) in clonidine group had duration of analgesia in between 241 to 300 minutes (Graph 4). Nineteen (38%) of patients in clonidine group had analgesia for 301 to 360 minutes, which was observed in only in 11 (22%) patients in buprenorphine group (Graph 5). A duration of 361 to 480 minutes analgesia was observed in 13 (26%) patients in clonidine group while none in buprenorphine group had analgesia more than 360 minutes.8,9

The mean sedation scores were found to be comparable at all time intervals in both the groups (Graph 6). Thus, the patients remained cooperative, calm and tranquil at all time intervals. Maximum number of patients in both the groups exhibited a score of 2 to 3 at all the time intervals. Mean pulse rate noted at various time intervals were
found to be statistically comparable (p > 0.05) between the groups at all respective time intervals (Graph 7). Mean systolic blood pressure was statistically less in clonidine group than buprenorphine group from 6 to 90 minutes after intrathecal drug administration (Graph 8). The incidence of adverse effects is shown in Table 3.

**DISCUSSION**

Spinal anesthesia is the fastest, predictable and most reliable form of anesthesia for infraumbilical surgeries. Bupivacaine, apart from providing sensory and motor blockade, also provides some pain relief in the initial postoperative period. But the duration of analgesia is
not lengthy enough to relieve pain for extended period in postoperative setting after wearing off of the local anesthetic effect. Relief of intraoperative and postoperative pain is professionally rewarding and is a subject that has gained attention in past few years. Pain during surgery or in the postoperative period increases morbidity by causing (1) Sympathetic stimulation increased heart rate, blood pressure, altered regional blood flow, increased oxygen consumption and (2) stress response due to hormonal surge and depressed immune functions. Benefits of pain prevention and control are moral and ethical, thus postoperative pain treatment must be included in the anesthetic planning even before induction of anesthesia.

Low dose intrathecal buprenorphine increases sensory block, duration of analgesia without affecting motor block and is associated with minimal side-effects. Intrathecal buprenorphine in doses of 75 µg induces rapid onset of analgesia and lacks the side effects that can be attributed to higher doses.10 Dixit et al stated that 60 µg buprenorphine given intrathecally to pregnant patients prolonged the duration of analgesia with negligible side-effects.11 Clonidine prolongs the duration of intrathecally administered local anesthetics and has potent antinociceptive properties. Intrathecal clonidine has been used in a wide range of 15 to 400 µg and has been administered either alone or in combination with local anesthetics or opioids. But, the commonly administered doses of 60 to 75 µg produce hypotension and bradycardia.12,13 Doses of clonidine > 100 µm produces dose dependent hypotension and sedation.14 Until recently only a few studies have focused on small doses of intrathecal clonidine in surgical patients.15 Preliminary studies have shown that small doses of intrathecal clonidine (15–75 µg) significantly increased the duration of postoperative analgesia. Thus, we chose to investigate a low dose (37.5 µg) of intrathecal clonidine with 75 µg intrathecal bupivacaine added to 3 ml 0.5% hyperbaric bupivacaine for our study.

The demographic data, such as age, sex, height, and weight were comparable among the groups thereby not having any influence upon the outcomes. The mean time to achieve maximum SBL in our study was 9.20 ± 5.69 and 11.90 ± 4.78 in group C and B respectively. The faster onset time in our study compared to the earlier studies by other authors might be due to the higher dose of clonidine (37.5 µg) and buprenorphine (75 µg) in our study. The median highest dermatome of T8 in group C in our study is in conjunction with those of De Kock et al and Dobrydnjov et al.16,17

**CONCLUSION**

In conclusion, 37.5 µg clonidine seems to be an attractive alternative to 75 µg buprenorphine as an adjuvant to spinal bupivacaine in lower limb orthopedic surgery especially those of longer duration. In our study, we found that clonidine is better in terms of quality of intraoperative analgesia, sensory and motor blockade, postoperative analgesia and have less side-effects. We found that shivering was significantly less with clonidine in comparison to buprenorphine which could be beneficial for patient during intraoperative and postoperative period. Further due to long motor blocked with clonidine, it is better for long duration orthopedic surgery while buprenorphine may be better in day care orthopedic surgeries like knee arthroscopy.

**REFERENCES**

7. Fonseca NM, TSA, Clarissa Aires de Oliveira C. Effect of combined clonidine and 0.5% hyperbaric bupivacaine on spinal analgesia. Rev Bras Anestesiol 2001;51(6):483-492.


