COMPARISON OF CLONIDINE AND DEXMEDETOMIDINE AS AN ADJUVANT TO 0.5% BUPIVACAINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK: A RANDOMISED PROSPECTIVE DOUBLE-BLIND STUDY

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Abstract

Background and Objectives: Alpha-2 agonists are used as adjuvant with local anaesthetic agents to prolong the duration of spinal, epidural and peripheral nerve blocks as well as to prolong the duration of post operative analgesia. We performed a study to compare clonidine(1μg/kg) and dexmedetomidine (1μg/kg) as an adjuvant to 0.5% bupivacaine in supraclavicular brachial plexus block.

Methods: Eighty ASA I and II patients scheduled for elective upper limb orthopaedic surgeries under supraclavicular brachial plexus block were divided into two groups(n=25 each) in a randomized, double-blinded fashion. Group C received clonidine 1 μg/kg and Group D received dexmedetomidine 1 μg/kg added to bupivacaine 0.5% (30 cc). Onset and recovery time of sensory and motor block, as well as duration of analgesia were studied in both the groups.

Results: Duration of sensory block and motor block was 220.12 ±50.3 and 280.1± 20.12 min respectively in group C, while it was 410.34± 60.12 and 460.4 ± 50.56 min respectively in group D and hence both were significantly prolonged in group D. No statistically significant difference was seen in onset of sensory and motor block between the two groups. The duration of analgesia i.e. time to requirement of rescue analgesia was 270.4± 56.7 mins and 452.7 ±64.23 mins in group C and D respectively and this difference was statistically significant (P=0.001).

Conclusion: Addition of dexmedetomidine to bupivacaine 0.5% in supraclavicular brachial plexus block prolonged the duration of sensory and motor block as well as the duration of analgesia when compared with clonidine.

Keywords: Clonidine, dexmedetomidine, supraclavicular block

Introduction

Brachial plexus block is most commonly used technique for performing upper limb surgeries. In addition to providing intraoperative anaesthesia, peripheral nerve blocks also provide extensive post-operative analgesia without any systemic side-effects.¹

Alpha-2 adrenergic receptor agonists have been shown for providing analgesic, perioperative sympathetic, sedative and cardiovascular stabilizing effects. In addition they cause reduction in other anaesthetic requirements. Various methods of administration such as intrathecal, epidural and peripheral injections are being used to provide and prolong the anaesthesia.²-⁴

Dexmedetomidine is more selective towards the α₂ adrenoceptor than clonidine.⁵ Previous clinical studies have shown a decrease in inhalational anaesthetic requirements and opioid sparing effects, by the use of intravenous alpha-2 adrenergic receptor agonists.⁶ Some previous animal studies have shown dexmedetomidine to cause increase in duration of analgesia in addition to enhancing the sensory and motor blockade.⁷-¹⁰ In humans, alpha-2 adrenergic receptor agonists have been shown to prolong the duration of various regional blocks when used as adjunct to local anaesthetic solutions.¹¹-¹³ The current study was designed to test the hypothesis that when compared to clonidine, addition of dexmedetomidine to local anaesthetics in supraclavicular brachial plexus block, show a greater enhancement of the duration of analgesia as well as duration of sensory and motor block.

Material and Methodology

This double-blind randomized prospective study was carried out on 80 patients of American Society of Anaesthesiologist (ASA) Grade I or II, aged 20–50 years, of either sex, undergoing various upper limb orthopaedic surgeries under supraclavicular brachial plexus block. The patients were randomly assigned to one of the following 2 groups using computer generated random number table:

Group C (n=40): 30 ml of 0.5% Bupivacaine + clonidine 1 μg/kg
10 ml of 2% lignocaine with adrenaline
Group D (n=40): 30 ml of 0.5% Bupivacaine + dexmedetomidine 1 μg/kg
10 ml of 2% lignocaine with adrenaline

Patients excluded from the study were those on adrenoreceptor agonist or antagonist therapy, with bleeding disorders, any known hypersensitivity to local anaesthetic drugs and pre-existing peripheral neuropathy.

On arrival in the operation room, baseline heart rate, blood pressure, ECG and oxygen saturation were recorded. Ringer’s lactate was started by an intravenous line in the unaffected limb. All the patients received supraclavicular brachial plexus block by an experienced anaesthesiologist different from the one who assessed the patient intraoperatively and post-operatively. Both anaesthesiologists were blinded to the two treatment groups. Nerve localization was achieved by using a Plexygon nerve locator connected to a 20 G, 50-mm-long Locoplex nerve stimulating needle. The end motor response was a twitch in the ulnar nerve region with a current of 0.4 to 0.5 mA. Following negative aspiration, 40 mL of total local anaesthetic solution as mentioned above was injected. A little massage was performed to facilitate drug distribution.

Assessment of sensory block was done by pin prick method at each minute after completion of drug injection. Assessment was done till complete sensory blockade occurred in the dermatomal areas corresponding to major nerves of upper limb i.e., ulnar nerve, median nerve, radial nerve and musculocutaneous nerve. Onset of sensory block was considered when there was analgesia and a feeling of a dull sensation to pin prick along the distribution of any of the above-mentioned nerves. Complete loss of sensation to pin prick was considered as a complete sensory block. Sensory block was graded as:

Grade 0: Sharp pin felt
Grade 1: Analgesia, dull sensation felt
Grade 2: Anaesthesia, no sensation felt.

Assessment of motor block was carried out from the time of drug injection till complete motor blockade occurred. Onset of motor blockade was considered when there was Grade 1 motor blockade. Complete motor block was considered when there was Grade 2 motor blockade. Motor block was determined according to a modified Bromage scale for upper extremities on a 3-point scale.[14]

Grade 0: Normal motor function with full flexion and extension of elbow, wrist and fingers
Grade 1: Decreased motor strength with ability to move the fingers only
Grade 2: Complete motor block with inability to move the fingers

The block was considered incomplete when segments supplied by any 1 major nerve did not have analgesia even after 30 min of drug injection. These patients were supplemented with intravenous midazolam (0.02 mg/kg) and fentanyl (1 μg/kg). When more than one nerve remained unaffected, it was considered a failed block and patients were given general anaesthesia intraoperatively. Heart rate, blood pressure and oxygen saturation were recorded at every 30 min interval during the intraoperative period and then at every 60 min post-operatively. Sedation was assessed using the Ramsay Sedation Score.[15] Duration of surgery was also noted. Patients were assessed for duration of analgesia by numeric rating scale (NRS) of 0 to 10. The pain score was recorded post-operatively every 60 min till the score of 5 was reached at which rescue analgesia in the form of inj. diclofenac sodium (1.5 mg/kg) intramuscularly was given and the time of administration of rescue analgesia was noted. Any side-effects like nausea, vomiting, dryness of mouth and complications like pneumothorax, block site haematoma or local anaesthetic toxicity if present were noted.

The sensory block duration was considered from the end of local anaesthetic administration till the complete resolution of anaesthesia on all nerves. The motor block duration was considered between the end of local anaesthetic administration and the complete recovery of motor function of the hand and forearm.

**Statistical Analysis**

The data was analysed by SPSS (Statistical Package for Social Sciences) software version 17.0. Unpaired t-test was applied for demographic data, haemodynamic variables, onset and duration of sensory and motor blockade and for duration of analgesia. *P* value <0.05 was considered significant and *P*-value >0.05 was considered non significant.

**Results**

Out of 100 patients, posted for upper limb surgeries, which were planned to enroll in the study, 20 patients were left out as few of them refused to participate in the study while few were found to be on beta blockers and anticoagulation drugs The remaining 80 patients which fulfilled the inclusion criteria were randomly assigned to one of the two groups..

Both groups were comparable in terms of age, gender and weight [Table 1] (*P*<0.001).

**Table 1: Patient characteristics**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group C (Mean ± SD)</th>
<th>Group D (Mean ± SD)</th>
<th><em>P</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35.25±12.01</td>
<td>36.45 ±11.22</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>56.38± 6.1</td>
<td>57.78 ±5.23</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>27/13</td>
<td>29/11</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>
The baseline pulse rate, systolic and diastolic blood pressures were comparable in both the groups. Lower pulse rate was observed at 60th, 90th and 120th min, in Group D as compared with Group C and the difference was significant [Figure 1] (P<0.01). Systolic and diastolic blood pressure at 30th, 60th, 90th and 120th min were found to be significantly lower in Group D as compared with Group C (Figure 2) (P<0.01). No treatment was required for this fall in blood pressure. The haemodynamic parameters in the two groups were comparable at the end of 3 hrs. [Figure 2].

Onset of sensory blockade was found to be faster in Group D than in Group C, while onset of motor blockade occurred faster in Group C than in Group D, but the difference was not statistically significant [Table 2] (P>0.05). Duration of sensory block was 220.12 ± 50.3 min in Group C as compared with 410.34 ± 60.12 min in Group D. Duration of sensory block was significantly longer in Group D as compared to Group C [Table 2] (P<0.01). The duration of motor block was also significantly longer in Group D as compared to Group C [Table 2] (P<0.01). The duration of analgesia was significantly increased in Group D (452.7 ± 64.23 min) as compared with Group C (270.4 ± 56.7 min). [Table 2] (P<0.01)

Table 2: Onset time, duration of block and duration of analgesia

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group C (Mean ± SD)</th>
<th>Group D (Mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset time to sensory block (mins)</td>
<td>2.1 ± 1.25</td>
<td>1.9 ± 1.34</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Onset time to motor block (mins)</td>
<td>4.0 ± 1.7</td>
<td>4.4 ± 1.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Duration of sensory block (mins)</td>
<td>220.12 ± 50.3</td>
<td>410.34 ± 60.12</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Duration of motor block (mins)</td>
<td>280.1 ± 20.12</td>
<td>460.4 ± 50.56</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Duration of analgesia (mins)</td>
<td>270.4 ± 56.7</td>
<td>452.7 ± 64.23</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

No side-effects (nausea, vomiting, dry mouth) were reported in the post-operative period in both the groups during the first 24 h.

Discussion

In this randomized, double-blind trial, we compared the additive effect of dexmedetomidine and clonidine (α2 receptor agonist), mixed with Bupivacaine, during supraclavicular brachial plexus block. It was found that there was a significantly increased duration of sensory and motor blockade in the dexmedetomidine group than in the clonidine group without any adverse effects.

The central actions of clonidine are mediated through α2 adrenoceptors, which are located at locus coeruleus and in the dorsal horn of spinal cord. The specific peripheral effects of clonidine are less understood because α2 adrenoceptors are absent on the axon of the normal peripheral nerve.4 The direct action of clonidine on the nerve was studied by Dalle et al. They proposed that clonidine, by increasing hyperpolarisation, increases the threshold for initiating the action potential causing blockade or slowing of nerve conduction.16 Kosugi et al. studied the effects of some adrenoceptor agonists including dexmedetomidine, clonidine and tetracaine and also an α2 adrenoceptor antagonist atipamezole, on compound action potential (CAP) recorded from sciatic nerve of frog. They concluded that CAPs were inhibited by α2 adrenoceptor agents and that lead to blockade of nerve conduction.10

Popping et al. in their metaanalysis concluded that the prolongation of duration of analgesia by clonidine was observed with many of local anaesthetics used. They observed that the addition of clonidine to bupivacaine resulted in more prolongation of motor block as compared with ropivacaine.4

Dexmedetomidine and clonidine, both being α2 selective agonists work in a similar manner. In their study, Brumett et al. showed that addition of dexmedetomidine to bupivacaine as an adjunct, prolonged the duration of anaesthesia and analgesia of sciatic nerve block in rats.
without any histopathological report of damage to the nerve.7 In another study, addition of perineural dexmedetomidine to ropivacaine for sciatic nerve block in rats, showed prolongation of duration of analgesia which was proposed to occur due to blocking of the hyperpolarisation-activated cation, which prevented the nerve from returning to resting membrane potential from a hyperpolarized state.9 In an study on sciatic nerve blocks in rats, addition of peripheral perineural dexmedetomidine to local anaesthetics, prolonged the duration of analgesia and it was shown that the effect was peripheral and not centrally mediated.8

Previous studies have demonstrated increased duration of sensory blockade in axillary brachial plexus nerve blocks and greater palatine nerve block by addition of dexmedetomidine to levobupivacaine and bupivacaine, respectively.12,13

In their study, Singelyn et al. added a minimum dose of clonidine (0.5 μg/kg) to mepivacaine and demonstrated the prolongation of the duration of anaesthesia and analgesia in brachial plexus block. No additional benefits were found with doses exceeding 1.5μg/kg.3

The dose compared in our study was dexmedetomidine 1 μg/kg and clonidine 1 μg/kg, as the same dose had already been used previously in a study where they compared dexmedetomidine and clonidine as an adjuvant to lignocaine in Bier’s block.17

The result of our study showed that patients in both the groups, Group C (clonidine) and Group D (dexmedetomidine), were comparable with respect to demographic profile. Haemodynamics were stable in patients except pulse rate in Group D at 60th, 90th and 120th min which was significantly lower as compared to Group C, but was never less than 60 beats/min.

Esmaoğlu et al in their study, mixed dexmedetomidine to levobupivacaine for axillary brachial plexus nerve block and concluded that it shortens the time of onset of both sensory and motor block and prolongs the duration of block.12 However, in our study, we found that onset of sensory block occurred little earlier in Group D as compared with Group C, but it was insignificant statistically. The onset of motor block was a little later in Group D as compared to Group C but again was not statistically significant. In our study we had no control group to comment on time of onset of sensory or motor block with dexmedetomidine or clonidine in comparison to a control group. The duration of analgesia was longer in Group D than in Group C which was statistically significant.

None of the patients in both the groups required sedation intraoperatively and they were comfortable throughout the surgery with little sedative effects but were easily arousable. This might have occurred due to systemic absorption of drug, producing sedation by central action.

The major limitations of our study were that we did not have facility of ultrasound-guided blocks in our institution at the time of our study, which could have helped us to use lower volumes and strength of local anaesthetic. The other limitation was that we had no control group to comment on the different parameters we studied in comparison to the study groups. Also in our study we did not assessed the quality of block achieved.

Conclusion:
To conclude, we would like to state that both dexmedetomidine and clonidine can be used safely in combination with local anaesthetic in peripheral nerve blocks; however, dexmedetomidine in comparison to clonidine provides a longer duration of sensory and motor blockade as well as post operative analgesia when used as an adjuvant to Bupivacaine in peripheral nerve block.

References:
8. Brummett CM, Amodeo FS, Janda AM, Padda AK, Lydic R. Perineural dexmedetomidine provides an increased duration of analgesia to a thermal stimulus when compared with a systemic control in a rat

9. Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. Anesthesiology. 2011;115:836–43.


