“Comparison Between Bupivacaine And Addition of Clonidine To Bupivacaine in Supraclavicular Brachial Plexus Nerve Block”

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Abstract:
Background: This study compared effect of bupivacaine and addition of clonidine to bupivacaine in supraclavicular brachial plexus nerve block.

Methods: This Randomized, prospective, double blind study was done in 60 patients of ASA grade I and II status undergoing forearm orthopedic surgeries. Group B received 25 ml of 0.5% bupivacaine and Group BC received 25 ml of 0.5% bupivacaine and clonidine 1μg/kg. Onset and duration of both sensory and motor block, duration of analgesia and sedation score and hemodynamic parameters were studied.

Result: Analgesia duration was 224.33 ± 16.30 minutes in group B and 658 ± 95.09 minutes in group BC. There was early onset and prolongation of duration of sensory and motor block. There was decrease in heart rate and systolic blood pressure in group BC compared to Group B without any statistical significant difference in diastolic and mean BP and oxygen saturation. Sedation score was higher and analgesic requirement was lower in group BC.

Conclusion: Addition of clonidine to bupivacaine significantly affects the onset and duration of sensory and motor block and significantly prolongs duration of postoperative analgesia. Effects on vital parameters due to addition of clonidine are inconsistent.

Keywords: bupivacaine, clonidine, supraclavicular brachial plexus block

I. Introduction

Every living being from its very moment of birth seeks pleasure enjoying it as ultimate good while rejecting pain as ultimate adversity. Pain is an unpleasant sensation which the individual feels himself. Therapeutic nerve block act by eliminating pain as well as undesirable reflexes arising from either trauma or disease. Brachial plexus block for upper limb surgery first used by Prof Halsted of John Hopkins hospital in 1884 by directly exposing the nerve roots in neck and blocking them with cocaine solution. The supraclavicular technique was used by Kulenkampff in 1912. In 1964, Winnie described the techniques of the block by single injection. Peripheral nerve blocks for upper extremity offer advantages of minimal discomfort to patient, early ambulation, minimum alteration in human physiology and avoidance of multidrug therapy and its adverse effects. Brachial plexus also offer some other advantages like simple technique, good analgesia and muscle relaxation, can provide longer postoperative analgesia, minimum drugs and equipment, bloodless operative field and early recovery.

The concept of pre-emptive analgesia was given birth to the idea of addition of adjuvant to local anaesthetics for prolongation of postoperative analgesia. First adjuvant to brachial plexus block after cocaine is morphine added by F. W. Braun in 1903. The suggestion that regionally applied opioids might be effective as an analgesics dates back to the mid nineteen’s century when morphine was injected perineurally. Besides morphine a number of different opioids and other adjuvants have been introduced to improve the efficacy of neuraxial/regional analgesia, including NMDA antagonists (ketamine, magnesium), GABA agonists (midazolam) and adrenergic agonists (Clonidine, adrenaline), COX-inhibitors (ketorolac), Acetylcholinesterase inhibitor (neostigmine) etc.

Since 1980 Clonidine has been used as adjuvant in local anaesthesia in various regional techniques to extend the duration of block. In axillary plexus block effect of Clonidine on prolongation of postoperative analgesia shows variable effects. Combination of Clonidine and Bupivacaine only studied by Miligan who applied it epidurally and reported improved postoperative analgesia. Clonidine in brachial plexus block for postoperative analgesia was extensively studied and got the result that Clonidine prolongs postoperative analgesia. Various dose range effect of Clonidine added to lidocaine in supraclavicular brachial plexus block and found dose up to 150 μg effective in producing prolong postoperative analgesia. This study is designed to
compare between bupivacaine and addition of clonidine to bupivacaine in supraclavicular brachial plexus nerve block.

II. Material And Methods

This prospective double blinded study was conducted in Seth Nandlal Dhoot Hospital after institutional ethics committee approval. Written informed consent was obtained from all participants. The study was performed in 60 participants aged 20 years to 60 years undergoing elective orthopaedic upper limb surgeries. Participants were of American Society of Anaesthesiologists (ASA) grade I and ASA grade II physical status. Participants refusing to give consent, those with significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal or hepatic disease, any contraindication to supraclavicular brachial plexus block, and pregnant and lactating females were excluded from study.

In each participant, thorough history was elicited. Patient was clinically examined in detail and investigated. Participants were randomly assigned to 2 groups of 30 each. Group B (Bupivacaine) (n=30) received brachial plexus block with 25 ml of 0.5% of Bupivacaine and group BC (Bupivacaine and Clonidine) (n=30) received brachial plexus block with 25 ml of 0.5% of Bupivacaine with Clonidine 1 μg/kg through supraclavicular approach. Drug preparation was done by an anaesthesiologist not involved in the study. Anaesthesiologist administering block was also blinded. He only received envelopes with name B or BC in it.

When participant brought in operation theater NIBP, Cardiac monitor & pulse oxymeter was applied. Oxygen supplementation was started at rate of 4 l/min. by nasal prongs. Intravenous line was secured with 20 G angiocath in large peripheral vein and intravenous drip was started which was continued throughout the surgery.

Participants were provided anxiolysis and sedation with Inj. Midazolam – 0.02 mg/kg body wt. Anaesthesiologist performing the block was blinded. All observations were carried out by a single investigator who was also blinded to the treatment.

The participant was placed in a supine position with the head turned away from the side to be blocked. The arm to be anaesthetized kept adducted, and the hand extended along the side toward the ipsilateral knee as far as possible. The mid-point of the clavicle was identified and marked. The posterior border of the sternocleidomastoid was palpated when the patient raises the head slightly. The palpating fingers then rolled over the belly of the anterior scalene muscle into the interscalene groove, where a mark was made approximately 1.5 to 2.0 cm posterior to the midpoint of the clavicle. Palpation of the subclavian artery at this site confirms the landmark.

The skin on the side was cleaned with an antiseptic and draped. A skin wheal was made with 1% Lignocaine. After skin disinfection, sterile covering and local anaesthesia at the insertion site the stimulation needle carefully advanced from the puncture site in the direction of anatomical target. The needle was advanced using nerve stimulation. The nerve stimulator was initially set to deliver 1 mA. Drug solution was injected slowly with intermittent aspiration to rule out intravascular injection. During the whole procedure a constant watch was kept for development of any complications like nausea, vomiting, hypotension or bradycardia. Pulse, SpO2 and blood pressure were recorded at 5, 10, 15, 30, 45, 60, 90, 120 minutes, 4, 6, 12, 18 and 24 hours after completion of the injection.

Onset of sensory and motor block were evaluated by each of the author who were unaware of the drug administered. Sensory block was assessed using pinprick sensation and motor block was assessed by using Bromage scale. Block was considered successful when Vester Andersen’s criteria – at least 2 out of 4 nerve territories (Ulnar, Radial, Median and Musculocutaneous effectively blocked – were fulfilled). Injection time was chosen as the beginning of all time intervals for subsequent calculations. Onset of sensory block was defined as the time elapsed between injection of drug and reduction in pinprick sensibility to 30% or less. Onset of motor block was defined as the time interval between injection of drug and Bromage score 2. Assessment of motor blockade was done using the Bromage three point score [0 = Normal motor function with full flexion and extension of elbow, wrist and fingers, 1 = decreased motor strength with ability to move fingers / or wrist only, 2 = complete motor blockade with inability to move fingers]. Recovery from sensory block was noted as the time when patients start responding to the blunt end of needle and recovery from motor block was noted when patient has motor movement Bromage score ≤1.

The duration of analgesia was taken from the time of the onset of block to the first complaint of pain. Rescue analgesic was administered in the form of Inj. Diclofenac sodium intramuscular in the dose of 1.5 mg/kg. Total number of analgesic doses required in first 24 hours was recorded. Vital parameters as heart rate, blood pressure, oxygen saturation were recorded at 0, 5, 10, 15, 30, 45, 60, 90, 120 minutes, 4, 6, 12, 18, 24 hours. Sedation score was assessed by using modified Ramsey sedation scale grade 1 to 6 (1. Anxious, agitated, restless 2. Co-operative, orientated 3. Responds to verbal commands 4. Brisk response to light glabellar tap or loud noise 5. Sluggish response to light glabellar tap or loud noise 6. No response).
The primary outcome measure was duration of analgesia. This was estimated as the time interval from placement of the block till first injection of rescue analgesic. Secondary outcome measures were onset and duration of sensory and motor blockade and any suspected adverse drug reactions.

III. Statistical Analysis

Demographic data are summarized as mean ± standard deviation or as percentages. Patient characteristics were compared by chi square test. The quantitative data obtained in this study was analyzed using student’s unpaired ‘t’ test. All analysis were two tailed and P < 0.05 was considered statistically significant. Table 1 shows demographic data that is age, sex, weight and duration of surgery were found to be comparable. Table 2 shows onset and duration of sensory and motor block. It was found that onset of both sensory and motor block was shorter and duration was greater in participants who received clonidine in addition to bupivacaine. The duration of analgesia was 224.33±16.30 in bupivacaine group and 658.33±95.09 in clonidine group. This difference was statistically and clinically highly significant. The participants who received clonidine were found to be more sedated but the difference in heart rate, blood pressure and oxygen saturation were comparable and not statistically significant at any point of time. The incidence of clinically relevant bradycardia and hypotension were comparable in two groups.

IV. Results

Total 60 participants were included in the study. There were no dropouts. 30 participants in bupivacaine and 30 in bupivacaine and clonidine group. Table 1 shows demographic data and shows age, sex distribution, body weight and duration of surgery were found to be comparable. Table 2 shows onset and duration of sensory and motor blocks. It was found that onset of both sensory and motor block was significantly shorter in group BC. Regarding duration of analgesia in group BC it was 658.33±95.09 min and 224.33±16.30 in group B. This difference is highly significant statistically and clinically as well. Although patients of group BC were found to be more sedated than group B (Table 3), no statistically significant difference was seen in heart rate, blood pressure and oxygen saturation between the two groups. Table 4 shows total analgesics consumption in 24 hours postoperatively in group BC was found to be less compared to group B which was statistically and clinically significant.

Table 1. Comparison of demographic data

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group B (n=30)</th>
<th>Group BC (n=30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37 ± 7.661</td>
<td>36.5 ± 7.908</td>
<td>0.804</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>21/0</td>
<td>22/0</td>
<td>0.77</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58.60 ± 4.760</td>
<td>58.43 ± 5.630</td>
<td>0.90</td>
</tr>
<tr>
<td>Duration of surgery(min)</td>
<td>96.43 ±11.094</td>
<td>94.80 ±8.130</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Here n denotes number of participants and numerical variables have been expressed as mean ± standard deviation.

Table 2. Comparison of sensory and motor blocks and duration of analgesia

<table>
<thead>
<tr>
<th>Characteristics (minutes)</th>
<th>Group B(n=30)</th>
<th>Group BC(n=30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of sensory block</td>
<td>16.77 ± 2.03</td>
<td>8.07 ± 1.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Onset of motor block</td>
<td>21.53 ± 2.06</td>
<td>12.27 ± 1.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of sensory block</td>
<td>203.000±17.757</td>
<td>613.667±90.420</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of motor block</td>
<td>182.967±18.980</td>
<td>538.000±81.002</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of analgesia</td>
<td>224.33±16.30</td>
<td>658.33±95.09</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Here n denotes number of participants and numerical variables have been expressed as mean ± standard deviation.

Table 3. Comparison of Suspected adverse events profile

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Group B (n=30)</th>
<th>Group BC (n=30)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>0</td>
<td>1</td>
<td>0.00</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>1</td>
<td>0.00</td>
</tr>
<tr>
<td>Oxygen saturation&lt;90%</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>0.20% fall in mean BP</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0.20% fall in HR</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Sedation score</td>
<td>1.2 ± 0.407</td>
<td>2.03 ± 0.615</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Here n denotes number of participants.

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Table 4. Consumption of analgesics in 24 hours

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group B (n=30)</th>
<th>Group BC (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesic consumption</td>
<td>3.50 ± 0.30</td>
<td>1.90 ± 0.94</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Here n denotes number of participants and numerical values have been expressed as mean ± standard deviation.

V. Discussion

The study shows addition of small dose of clonidine prolongs the duration of analgesia and shortens the onset of supraclavicular block. Bernard and Macarie\textsuperscript{5} evaluated the effects of adding 30-300 µg of to lignocaine for axillary brachial plexus anesthesia, reported that the addition hastened the onset of block and improved the efficacy of surgical anesthesia. There are reported differences in the effects of administration of low dose clonidine on time of onset and efficacy of nerve block, which may be explained by differences in the type of nerve block, exact mixture injected and technique used to perform the block (single injection verses multiple injections). In fact, multiple injection technique was used, which is known to improve both onset time and quality of nerve block and this could have reduced the differences in onset time between the two groups.

In the dose finding study evaluating minimum effective dose of clonidine required to prolong duration of analgesia after axillary brachial plexus block, Singelyn et al\textsuperscript{4} suggested that 0.5 µg/kg clonidine should be used. At this dose, significant prolongation of analgesia was achieved without undue sedation, hypotension, or bradycardia. Various studies in which Clonidine was used in central neuraxial block found that Clonidine with Bupivacaine improves analgesic characteristic compared to Bupivacaine alone. Dorothée Gaumann et al\textsuperscript{10} found that Bupivacaine and Clonidine combination prolonged postoperative analgesia compared to a Bupivacaine-Epinephrine combination when administered for brachial plexus block. Various studies in which Clonidine was used in central neuraxial block found that Clonidine with Bupivacaine improves analgesic characteristic compared to Bupivacaine alone. Iskandar H et al\textsuperscript{11} added Clonidine to Bupivacaine in a continuous interscalene block and observed improved postoperative analgesia. It has been widely demonstrated in different studies that subcutaneous or intramuscular injection of clonidine is not as effective as perineural administration, suggesting that the local anesthetic-prolonging effect of clonidine is probably mediated locally at the neuron.\textsuperscript{12} This may also explain the variation in response in different types of peripheral nerve blocks, probably related to the rate and extent to which the injectate anesthetic solution penetrate into the nerve.\textsuperscript{13} Many authors favour the hypothesis that clonidine exerts its local anesthetic prolonging effect directly on the nerve fiber, as a result of complex interaction between clonidine and axonal ion channels or receptors\textsuperscript{13,14,12}. Peripheral antinociception induced by clonidine has also been related to 2- adrenoceptor mediated local release of enkephalin-like substances\textsuperscript{16}.

We used 1µg/kg dose of clonidine to avoid inconsistency and keeping in mind the hemodynamic adverse events that might be produced. It was found that it produce satisfactory prolongation of duration of analgesia without producing significant hemodynamic compromise in the patients. However sedation effect was greater in patients during early postoperative period. Therefore this is not the ideal dose of clonidine as adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block. In conclusion, we can suggest that 1µg/kgf clonidine may be used as adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block so as to prolong postoperative analgesia without added problems apart from some sedation in the early postoperative period. The ideal dose of clonidine can be drawn only after a definitive dose finding study.

References


