A COMPARATIVE CLINICAL STUDY TO EVALUATE THE EFFICACY OF LEVOBUPIVACAINE WITH CLONIDINE AND LEVOBUPIVACAINE WITH DEXMEDETOMIDINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

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ABSTRACT

OBJECTIVE
The objective of this study is to compare clonidine and dexmedetomidine as an adjuvant to levobupivacaine in supravacular brachial plexus block with respect to onset, duration of sensory and motor block and duration of analgesia.

MATERIALS AND METHODS
A total of 90 ASA grade I and II patients of either sex, aged 18-60 yrs. scheduled for elective upper limb surgeries under supravacular brachial plexus block were divided into 3 equal groups in a randomized fashion. Group L (n=30) received 1 mLNS, group LC (=30) received 1 mL (150 g) clonidine and group LD (n=30) received 1 mL (100 g) dexmedetomidine added to 30 mL of 0.5% levobupivacaine. Onset and recovery time of sensory and motor block, duration of analgesia and quality of block were studied in all three groups.

RESULTS
Onset time of sensory and motor blockade was 12.43±2.56 min and 17.96±3.05 min respectively in group L, 9.03±1.60 min and 15.00±2.40 min respectively in group LC and 8.13±2.51 min and 12.13±2.89 min respectively in group LD. Duration of sensory and motor blockade was 660.16±44.28 min and 535.33±50.66 min respectively in group L, 880.16±55.48 min and 771.83±54.19 min respectively in group LC and 930.66±48.02 min and 811.83±52.08 min respectively in group LD. Time of rescue analgesia was 728.86±45.12 min in group L, 1013.5±59.01 min in group LC and 1159.8±56.8 min in group LD (p<0.05).

CONCLUSION
Dexmedetomidine when added to LA in supravacular brachial plexus block prolongs the duration of sensory and motor blockade and also the time for rescue analgesia as compared to clonidine. Dexmedetomidine also enhances quality of block (LD>LC>C).

KEYWORDS
Supravacular Brachial Plexus Block, Levobupivacaine, Clonidine, Dexmedetomidine.


INTRODUCTION
Peripheral nerve blocks are gaining wide popularity in anaesthesia clinical practice and can be used in variety of surgical procedures, for surgical anaesthesia and postoperative pain. Supravacular approach gives the most effective block for upper extremity and is carried out at the level of trunks of brachial plexus.1 The plexus is blocked where it is most compact.2 I.e. at the middle of brachial plexus, resulting in homogeneous spread of anaesthetic throughout the plexus with a fast onset and complete block.3

The racemic mixture of bupivacaine resulted in cardiac and central nervous system toxic effects in some patients,4,5 which were attributed to the dextrobupivacaine enantiomer.6 Levobupivacaine is the S (-) enantiomer of racemic bupivacaine. It has less cardiotoxicity compared with bupivacaine,7 and its pharmacology and duration of anaesthesia are similar to those of bupivacaine.7

Clonidine, α2 receptor agonist, an imidazoline derivative is highly lipid soluble, acting on both spinal and supraspinal level within central nervous system and has been used as centrally acting antihypertensive agent. It has been used for many years as an additive to local anaesthetic.8,9 Clonidine provides approximately 100 additional minutes of analgesia with long-acting local anaesthetic.8 Most studies used between 100-150μg with higher dose showing side effects including sedation, bradycardia and hypotension.8

Dexmedetomidine is a highly selective α2 adrenoceptor agonist that has been shown to have both sedative and analgesic effects.10,11 compared with clonidine,
dexmedetomidine has an $\alpha_2$-adrenoceptor ratio of approximately 1600:1 (Seven to eight times higher than clonidine).\textsuperscript{12} Dexmedetomidine was first proposed as an adjuvant capable of prolonging duration of sensory and motor block produced by nerve block by Memis and Colleagues.\textsuperscript{13} Dexmedetomidine has shown to prolong the duration of block and postoperative analgesia when added to local anaesthetic in various regional blocks.\textsuperscript{13-16}

In this study, we compare the onset and degree of sensory and motor blockade of levobupivacaine with clonidine and dexmedetomidine in supraclavicular brachial plexus block.

MATERIALS AND METHODS
After ethical committee approval and written informed consent, this double blind randomized, prospective clinical study was carried out in 90 patients of ASA grade I and II of either sex, aged 18-60 yrs. scheduled for upper limb surgeries. Patients with known history of bleeding disorders, peripheral neuropathies allergy or sensitivity or any other reaction to local anaesthetic of amide type, receiving treatment with $\alpha$ adrenergic agonists/antagonists, those with a history of cardiac, respiratory, hepatic or renal failure; and pregnant women were excluded from the study.

Ninety patients who fulfilled the eligibility criteria were chosen, explained about the procedure and written consent was taken. Patients were subsequently randomized into three groups of 30 each.

1. Group L (n=30): 30 mL of 0.5% Levobupivacaine with 1mL normal saline. (Control)
2. Group LC (n=30): 30 mL of 0.5% Levobupivacaine with 150 mcg Clonidine (1 mL).
3. Group LD (n=30): 30 mL of 0.5% Levobupivacaine with 100 mcg Dexmedetomidine (1 mL).

After securing an intravenous access with 18-G cannula, RL solution was started. Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure, respiratory rate (RR) and oxygen saturation (SpO2) were recorded with multiparameter monitor (Beneview T5, Mindray China) Supravascicular brachial plexus block was performed under all aseptic precautions and after local infiltration of 2% Lidocaine 2 mL, neural localization was achieved using a nerve stimulator connected to a 22-gauge, 50mm long stimulating needle. The location end point was a distal motor response, that is the movement of the fingers and the thumb with an output current of 0.5mA.

Onset of sensory block is defined as the time elapsed between injection of drug and complete loss of sensation as analysed by pinprick test using a 3-point scale: 0=normal sensation, 1=loss of sensation of pinprick, 2=loss of sensation of touch. Duration of sensory block was defined as the time elapsed between injection of the drug and the complete resolution of anaesthesia on all nerves.

Onset of motor block was defined as the time elapsed from injection of drug to complete motor block. Motor block was evaluated by thumb abduction (Radial nerve), thumb adduction (Ulnar nerve), thumb opposition (Median nerve), and flexion of the elbow in supination and pronation of the forearm (Musculocutaneous nerve). Measurements were performed using a modification of the Lovett rating scale.\textsuperscript{17}

Grade 6: Normal muscular force.
Grade 5: Slightly reduced muscular force.
Grade 4: Pronounced reduction of muscular force.
Grade 3: Slightly impaired mobility.
Grade 2: Pronounced mobility impairment.
Grade 1: Almost complete paralysis.
Grade 0: Complete paralysis.

Assessment was done at every 1 min interval from the time of injection of test drug until the block was established. Only patient with complete motor block (Grade 0) were included in study and equal number of new cases were added to complete the study. Duration of motor block was defined as time elapsed between injections of the drug to complete return of motor power (Grade 6).

Postoperative pain was assessed using a visual analogue score scale which consisted of a 10cm horizontal scale with gradations marked as '0' means no pain at all and '10' means unbearable pain. VAS score was recorded every 30 min in the postoperative period till the conclusion of study. Sedation was assessed on the basis of Chernik sedation score.\textsuperscript{18}

0 - Completely awake.
1 - Sleeping but responding to verbal command.
2 - Deep sleep but arousable.
3 - Deep sleep not arousable.

Any complications such as nausea, vomiting, bradycardia (HR<50 beats per minute), hypotension (A 20% decrease in relation to the baseline value), haematoma, headache, convulsions, respiratory distress and hypoxemia (SpO2<90%) if occurred were recorded and treated appropriately.

Pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO2), respiratory rate (RR), 3-lead ECG monitoring was done continuously by multi-parameter monitor (Mindray Beneview T5) throughout the operative procedure. Recording of parameters were noted at 0, 5, 10, 15, 20 and at 30min interval up to 90min and then every hour till 750min.

The observations recorded in all groups were tabulated and statistical analysis was carried out using SPSS V.17 software for windows. In the intergroup comparison an independent student "t" test was used. For intragroup comparisons unidirectional repetitive variance analysis was used. Statistical significance was accepted as not significant and significant at P>0.05 and P<0.05 respectively.

RESULTS
All three groups were comparable in terms of age, weight and gender. (Table 1)(p>0.05): There was even distribution of age, weight and sex in all the three groups. The mean (±SD) age of patients in group L, LC and LD were 37.96±14.79 yrs, 40.63±12.94 yrs and 36.63±12.70 yrs respectively. The mean (±SD) weight of group L, LC and LD were 66.30±8.85kg, 63.40±9.01kg and 63.10±4.28kg respectively. Out of 90 patients, 64 patients (71.11%) were male as compared to 26 female patients (28.89%). The randomly selected group were comparable for the weight parameters (Statistically insignificant (p >0.05)).
Sensory Blockade
The onset time of sensory blockade (mean±SD), which was 12.43±2.56 min in Group L, 9.03±1.60 min in Group LC and 8.13±2.51 min in Group LD. The onset of sensory blockade was found to be faster in both group LC and group LD as compared to group L and the difference was statistically significant (p<0.05), whereas onset of sensory blockade was rapid in group LD as compared to group LC, but the difference was statistically insignificant (p>0.05). Mean (±SD) of sensory blockade duration was 660.16±44.28 min in Group L, 880.16±55.48 min in Group LC and 930.66±48.02 min in Group LD. Sensory blockade duration is significantly prolonged in both groups LC and LD as compared to Group L. Duration of sensory blockade in Group LD was also significantly prolonged as compared to Group LC. (Table 2 & 3)

Table 1: Showing Demographic Profile of Patients in Three Groups

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Parameters</th>
<th>Group L</th>
<th>Group LC</th>
<th>Group LD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>±SD</td>
<td>Mean</td>
</tr>
<tr>
<td>1.</td>
<td>Age (yrs.)</td>
<td>37.96</td>
<td>14.79</td>
<td>40.63</td>
</tr>
<tr>
<td>2.</td>
<td>Weight (kgs)</td>
<td>66.30</td>
<td>8.85</td>
<td>63.40</td>
</tr>
<tr>
<td>3.</td>
<td>Sex (M:F)</td>
<td>21.9</td>
<td></td>
<td>22.8</td>
</tr>
</tbody>
</table>

Table 2: Showing Comparison of Sensory Blockade (Min) in the Three Groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group L</th>
<th>Group LC</th>
<th>Group LD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset time of sensory blockade (min)</td>
<td>12.43</td>
<td>2.56</td>
<td>9.03</td>
</tr>
<tr>
<td>Duration of sensory blockade (min)</td>
<td>66.16</td>
<td>44.28</td>
<td>880.16</td>
</tr>
</tbody>
</table>

Table 3: Showing Intergroup Statistical Comparison of Sensory Blockade (Min) Among Three Groups

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Groups</th>
<th>Group L vs. LC</th>
<th>Group L vs. LD</th>
<th>Group LC vs. LD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>t value</td>
<td>p value</td>
<td>t value</td>
</tr>
<tr>
<td>1</td>
<td>Onset time of sensory blockade (min)</td>
<td>6.14</td>
<td>0.00$</td>
<td>6.55</td>
</tr>
<tr>
<td>2</td>
<td>Duration of sensory blockade (min)</td>
<td>16.97</td>
<td>0.00$</td>
<td>22.68</td>
</tr>
</tbody>
</table>

Motor Blockade
Onset time (Mean±SD) of motor blockade was 17.96±3.05 min, 15.00±2.40 min and 12.13±2.89 min in Group L, LC and LD respectively. Onset of motor blockade was found to be rapid in Group LD as compared to Group LC and Group L (LD>LC>L). These changes were statistically significant when compared to each other (p<0.05). (Table 4 & 5).

Table 4: Showing Comparison of Motor Blockade (Min) Among Three Groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group L</th>
<th>Group LC</th>
<th>Group LD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset time of motor blockade (min)</td>
<td>17.96</td>
<td>3.05</td>
<td>15.00</td>
</tr>
<tr>
<td>Duration of blockade (min)</td>
<td>535.33</td>
<td>50.66</td>
<td>771.83</td>
</tr>
</tbody>
</table>

Table 5: Showing Intergroup Statistical Comparison of Motor Blockade Among Three Groups

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Groups</th>
<th>Group L Vs LC</th>
<th>Group L Vs LD</th>
<th>Group LC Vs LD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>t value</td>
<td>p value</td>
<td>t value</td>
</tr>
<tr>
<td>1</td>
<td>Onset of Rescue Analgesia (in min)</td>
<td>20.98</td>
<td>0.00$</td>
<td>32.52</td>
</tr>
</tbody>
</table>

Table 6: Showing Intergroup Statistical Comparison of Time For Rescue Analgesia (Min) Among Three Groups

HEMODYNAMIC CHANGES
Pulse Rate
The mean (±SD) of preoperative PR/min was 83.43±5.70 in Group L, 85.83±5.72 in Group LC and 88.9±7.47 in Group LD. In Group L pulse rate significantly decreased up to 60 min (p<0.00) and thereafter these changes became insignificant (p>0.05), while in Group LC and Group LD significant decrease in pulse rate from baseline was observed (p<0.05). On intergroup analysis, changes in pulse rate between Group L
and Group LC and Group L and Group LD were statistically significant (p<0.05), whereas the difference between Group LC and Group LD were statistically insignificant (p>0.05).

**Systolic Blood Pressure**

SBP fall to basal value till 60min. Thereafter SBP started to rise in group L and remain above basal value till the end of study. In Group LC, these values started to rise but remained below baseline till 390min and reached to basal value at the end of study period. In Group LD, this fall continued till the end of study period and never regains the basal value till the study period.

On statistical analysis, these changes were significant till 60min (p<0.05) in all three groups, whereas in group LC and LD changes were significant (p<0.05) till 330min.

**Diastolic Blood Pressure**

In Group L changes in mean DBP were insignificant from basal value till the end of surgery. In Group LC after an initial fall from basal value up to 150min DBP started to rise, but remain below basal value till the end of study period, whereas in Group LD DBP remained below basal value throughout the study period. On statistical analysis, these changes were statistically insignificant in Group L (P>0.05). In Group LC and LD changes were statistically significant throughout the study period (p<0.05)

**Sedation**

In Group L none of the patient had sedation, in Group LC 43.33% patients had sedation of grade 1, while in group LD 66.66% patients had sedation of grade 2 and 23.33% patients had sedation of grade 1. Thus it was found that Dexmedetomidine added to Levobupivacaine causes more sedation than clonidine when added to Levobupivacaine

**Side Effects**

No complication was found in Group L, while in Group LC 6.66% and in Group LD 30% patients had bradycardia and 43.33% patients in Group LC and 90% patients in Group LD had sedation (Table 7).

<table>
<thead>
<tr>
<th>Complications</th>
<th>Group L</th>
<th>Group LC</th>
<th>Group LD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Nausea</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Vomiting</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Sedation</td>
<td>-</td>
<td>-</td>
<td>13</td>
</tr>
</tbody>
</table>

**DISCUSSION**

We compared dexmedetomidine and clonidine as an adjuvant to levobupivacaine in supravacuicular brachial plexus block and found that there was significantly increased duration of sensory and motor blockade in the dexmedetomidine group than in the clonidine group without any adverse effects.

The onset and duration of sensory blockade was rapid in dexmedetomidine group as compared to clonidine group, but the difference was statistically insignificant (p>0.05). These observations were in accordance with Esmaoglu A, et al.\(^{15}\)

Other researchers also confirmed the same results.\(^{19,20,21,22,23,24,25,26,27,28,29}\)

The time of onset and duration of motor blockade was found to be rapid in dexmedetomidine as compared to clonidine group. These changes were statistically significant when compared to each other (p<0.05). These findings are in accordance with Chakraborty S, et al.\(^{20}\) Duma et al.\(^{19}\), EI Saied AH, et al.\(^{29}\) Other studies also had similar results.\(^{20,21,22,23,24,25,26,27,28,29}\)

The time of rescue analgesia as assessed by VAS score was prolonged in Group LD as compared to other Groups (LD>LC>L). On intergroup comparison, these changes were found to be statistically significant.

These findings are supported by EI Saied AH, et al.\(^{29}\) who evaluated that addition of clonidine to ropivacaine significantly increased duration of analgesia from 587±40min to 829±35 min respectively (p<0.001).

Haemodynamic parameters are better stable in dexmedetomidine group.

It was found that Dexmedetomidine when added to Levobupivacaine causes more sedation than clonidine when added to Levobupivacaine.

Esmaoglu A et al\(^{15}\), Swami SS et al.\(^{25}\) and Ammar and Mahmoud.\(^{30}\) had similar experience.

The analgesic effects of alpha-2 adrenoceptor agonists could be because of vasoconstriction at injection site, direct suppression of impulse propagation through neurons, local release of enkephalin-like substance, a decrease in localized inflammatory mediators and an increase in anti-inflammatory cytokines through an alpha-2 adrenoceptor-mediated mechanism.

**Side Effects**

Bradycardia and sedation is the side effect seen in dexmedetomidine group. Esmaoglu A et al.\(^{15}\) also found bradycardia in 7 patients of dexmedetomidine group.

**CONCLUSION**

When dexmedetomidine added to Levobupivacaine it fastens the onset of motor blockade, prolongs the duration of sensory and motor blockade as compared to Clonidine. Time for rescue analgesia is more prolonged with dexmedetomidine than clonidine. Dexmedetomidine produces higher degree of sedation as compared to clonidine. Haemodynamic parameters are better stable in dexmedetomidine group.

**REFERENCES**

5. Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine [editorial]. Anesthesiology. 1979;51:285-287.

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detomidine, an α2 adrenoceptor agonist, is used as an adjuvant to local anesthetics for peripheral nerve and plexus blocks: a meta-analysis of randomized trials. Anesthesiology. 2020;111:406-415.


