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Evaluation of Dexamethasone Versus Dexmedetomidine As Adjuvant to Levobupivacaine in Ultrasound Guided Infraclavicular Brachial Plexus Block for Upper Limb Surgery-A Prospective Randomized Double Blind Clinical Study

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# **ABSTRACT**

**Background:** This study is to compare dexamethasone and dexmedetomidine as adjuvant to levobupivacaine in ultrasound guided (USG) infraclavicular brachial plexus block for distal upper limb surgery.

**Methodology:** Eighty ASA I–II patients posted for elective forearm and hand surgery under infraclavicular brachial plexus block were allocated into 2 equal groups in a random, double blinded fashion. Each group received 30 ml of 0.5% levobupivacaine either with 2 ml of dexamethasone(8mg) (D group, n = 40) or 2 ml of dexamedetomidine (50 microg diluted with normal saline) (DEX group, n = 40). USG guided infraclavicular brachial plexus block was given to all the patients. After performing the block vital parameters were recorded every 5 min until 30 min. The onset time and duration of sensory block, motor block and duration of analgesia were assessed.

**Results:** Demographic data and surgical characteristics were similar in both groups. The onset time of sensory block was similar in both groups. The onset time of motor block was earlier in DEX group. The durations of sensory and motor blockade were longer in group D than in group DEX (p<0.001). Mean arterial blood pressure levels at 5, 10, 15, 20, 25 and 30 minutes were statistically insignificant between the two groups (p>0.05). The mean pulse rate at different time intervals were also statistically insignificant between the groups (p>0.05). There were two failed blocks and excluded from the study and neither of the patients had any side effects.

**Conclusion:** Both dexmedetomidine and dexamethasone are good adjuvants to levobupivacaine in peripheral nerve blocks. The present study suggests that dexamethasone is a better choice as it prolongs the duration of sensory and motor blockade as well as duration of analgesia of infraclavicular brachial plexus block without any adverse side effects.

Key Words: Infraclavicular, ultrasound, levobupivacaine, dexamethasone, dexmedetomidine



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## INTRODUCTION

Brachial plexus block is a popular technique for upper limb surgeries and is alternative to general anesthesia. Infraclavicular approach for brachial plexus block provides anesthesia for surgery of the hand, forearm, elbow and distal arm. Both axillary and musculocutaneous nerves are blocked at the level of the cords before they branch from the brachial plexus sheath. In contrast to interscalene and supraclavicular brachial plexus blockade, an infraclavicular block has the advantage of minimal risk of intravertebral, intrathecal or epidural injection, as well as reduced incidence of phrenic nerve paralysis or stellate ganglion block. <sup>1</sup>

Levobupivacaine, a local anaesthetic with higher toxic threshold produces less cardiac effects, and has similar duration of action as bupivacaine. <sup>2</sup> This favourable clinical profile has made us to switch from bupivacaine to levobupivacaine for peripheral nerve blocks.

Limitations of brachial plexus block are slow onset time, short duration of action and limited duration of postoperative analgesia. To overcome these limitations many adjuvants are tried along with local anesthetics. The search for the ideal adjuvant continues, and led us to try dexmedetomidine and dexamethasone.

Steroids when used for peripheral nerve block have shown to reduce the inflammation and also prolongs the analgesic effects. Dexamethasone which is 40 times more potent than hydrocortisone has been successfully used as an effective analgesic. <sup>3</sup>

Dexmedetomidine, a selective  $\alpha_2$ - adrenoceptor agonist, has been used as an adjuvant to local anesthetics in various regional anesthetic procedures, such as subarachnoid, epidural, and caudal injections,. There is limited knowledge on the analgesic efficacy of adding dexmedetomidine to local anesthetics for peripheral nerve blocks.

Due to paucity of published data on addition of dexamethasone and dexmedetomidine to levobupivacaine for ultrasound guided infraraclavicular brachial plexus block, the study was conducted with respect to onset of sensory and motor blockade, duration of sensory and motor blockade, duration of postoperative analgesia.

#### METHODOLOGY

After institutional ethical committee approval and obtaining informed written consent from the patients, 80 ASA physical status I or II patients of either sex, aged 18-60 yrs scheduled for upper limb surgeries under infraclavicular brachial plexus block were included in the prospective double blinded randomised study. Those excluded from the study were patients having bleeding disorders ,allergy to local anaesthetics, peripheral neuropathy, hepatic or renal insufficiency, infection at the site of block .Patients with systemic use of corticosteroids for 2 weeks or longer within 6 months of surgery were also excluded.

Sample size is calculated based on the duration of motor block. Sample size calculation is done using Open Epi software, version 2.3.1.According to the study done by Naveen et al<sup>5</sup> the mean and SD of duration of motor block in two group were used for calculation of sample size With confidence Interval (2-sided)of 95% and Power of the study 80% sample size was calculated to be 78. To compensate for drop out rate 40 patients were included in each group. The study population was divided in two groups using computer generated random number table.

Ultrasound guided infraclavicular block was given to all the patients. Each patient received 32ml of drug. Group D-Dexamethasone (n=40) received 30 ml of 0.5% levobupivacaine+8mg (2ml) of dexamethasone. Group Dex-Dexmedetomidine (n=40) received 30 ml of 0.5% levobupivacaine +  $50\mu g$  of dexmedetomidine diluted to 2 ml with normal saline.

A routine preanesthetic examination was conducted and all the patients included in the study were kept nil per orally for 6 hours prior to surgery. On arrival to the block room, a 20-gauge intravenous cannula was secured and connected to IV fluid ringer lactate. The patients were connected to multiparameter monitor which recorded heart rate, non invasive blood pressure, and continuous electrocardiography monitoring and oxygen saturation. The baseline blood pressure, and heart rate were recorded after 5 mins of settling in the block room. All patients were given a ultrasound guided posterior parasagittal in plane approach . Patient's arm was abducted to 90° and the elbow flexed during the procedure. The infraclavicular area was cleaned with aqueous iodine solution and draped. The ultrasound probe was covered with sterile sheath and sterile gel applied. The ultrasound probe was placed below the clavicle and medial to the coracoid process in the deltopectoral groove i.e. para-sagittal view. A short-axis view of the axillary artery was obtained. We adopted the technique as described by Hebbard et al <sup>6</sup>. The blocks were performed using a 21G, 100 mm insulated needle(Stimuplex A,BBraun, Melsungen, Germany) without A 32-ml local anaesthetic admixture was administered. The patient and the anesthesiologist performing the block were blinded to the study. The drug admixture was prepared by the third anesthesiologist not involved in the study. We used an ultrasound machine (Sonosite M-Turbo; Sonosite ®, Bothell, WA, USA) with linear transducer probe.

A skinwheal was made with 3 mL lignocaine 2 %. The needle insertion point was over the trapezius muscle sufficiently posterior to allow the needle to pass between the clavicle and the scapula in the direction of the axillary artery. The insertion point was strictly aligned with the long axis of the ultrasound beam i.e. in-plane technique. The needle insertion point was 2 cm posterior to the clavicle to avoid needle tip contact with the inferior surface of the clavicle. The needle was advanced until a fascial click was felt when its tip reaches the posterior aspect of the axillary artery (6 o'clock position) which indicates penetration of the septum posterolateral to the artery, confirming a good needle position with a high chance of block success. At this point, local anaesthetic was deposited incrementally each time after a negative aspiration, ensuring a U-shaped distribution of local anaesthetic with anterior displacement of the axillary artery, known as double bubble sign.

We assessed the adequacy of motor and sensory blockade at predetermined intervals, every 5 min until 30 min; time zero was defined as the time at which the block needle was removed. Success rate was equivalent to surgical anesthesia, defined as the ability to proceed with surgery without the need for intravenous narcotics, general anaesthesia, rescue blocks or local infiltration by the surgeon .

Fig1: Ultrasound scan of infraclavicular region Fig2: Site of drug injection in infraclavicular block

Sensory blockade will be tested using pin prick method along the distribution of the four nerves <sup>7</sup>. Sensory block was graded as-

Grade 0= sharp pin felt

Grade 1= analgesia, dull sensation felt.

Grade 2= anesthesia, no sensation felt.

Assessment of sensory blockade will be done in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve and musculocutaneous nerve.

Onset of sensory blockade is considered when there is dull sensation to pin prick (Grade 1) along the distribution of any of the above mentioned nerves. The duration of sensory block is defined as the time interval between the end of local anesthetic administration and the complete resolution of anesthesia on all nerves that is return to grade 0.

Motor blockade assessment will be done using the modified Bromage scale for upper extremities on a three point scale <sup>7</sup>.

Grade 0 = normal motor function with full extension of elbow, wrist and fingers.

Grade 1=decrease motor strength with ability to move fingers and/or wrist only.

Grade 2= complete motor blockade with inability to move fingers.

Onset of motor blockade is considered when there is Grade 1 motor blockade.

The duration of motor block is defined as the time interval between the end of local anesthetic administration and the recovery of complete motor function of the hand and forearm that is return to grade 0.

Pain was assessed using the Visual Analog Scale (0–10) <sup>8</sup>. Nursing staff administered IM diclofenac 75 mg when the Visual Analog Scale >4. The time between the end of local anesthetic administration and the first analgesic request was recorded as the duration of the analgesia.

After LA injection, measurements of sensory and motor blockade and vital parameters (pulse, blood pressure, spo<sub>2</sub>) will be carried out every 5 min until 30 minutes. Postoperatively motor and sensory blockade and vitals of the patient will be noted half hourly till the block completely wears off. The block will be considered failed when analgesia is absent to pin prick at the site of surgical incision even after 30 min of drug administration. The onset and duration of sensory block, the onset and duration of motor block, duration of analgesia, number of failed blocks and complications will be noted.

Statistical analysis was done using SPSS software 11.0. Data obtained is tabulated in the Excel sheet and analysed. All values are expressed as mean  $\pm$  standard deviation.

Student's unpaired t – test is used for Quantitative data.

P< 0.05 was considered statistically significant.

# **RESULTS**

Table-1 Demographic data

	<b>D</b> group (n = 40)	<b>DEX group (n = 40)</b>	P
AGE	41.5	42.5	0.65
SEX (M:F)	26/14	20/20	-
WEIGHT	68.5±6.4	68.8±7.0	0.85
ASA STATUS 1 / 2	29/11	34/6	0.18

The demographic data was comparable in both the groups.



Fig 1 Sonoanatomy and drug distribution in infraclavicular block



Fig2: Site of drug injection in infraclavicular block

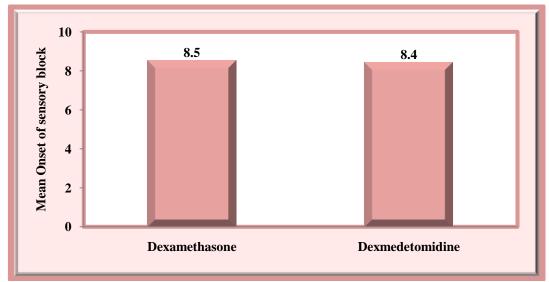


Figure 3: Onset of sensory block

The mean time for onset of sensory block in D group was  $8.5\pm1.0$  min and in DEX group was  $8.4\pm1.0$  min. The statistical analysis by students unpaired' test showed that there is no significant difference in onset time of sensory block between the two groups. (P = 0.73)

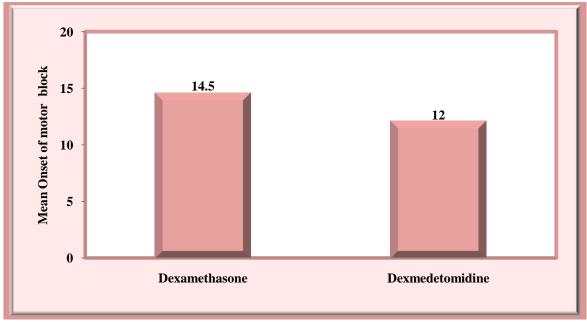


Figure 4: Onset of motor block

The mean time for onset of motor block in D group was  $14.5 \pm 1.9$  min and in DEX group was  $12.0 \pm 1.8$  min. The statistical analysis by student's unpaired t test showed that there is significant difference in onset time of motor block between the two groups. (P = <0.001) and it was earlier in DEX group.

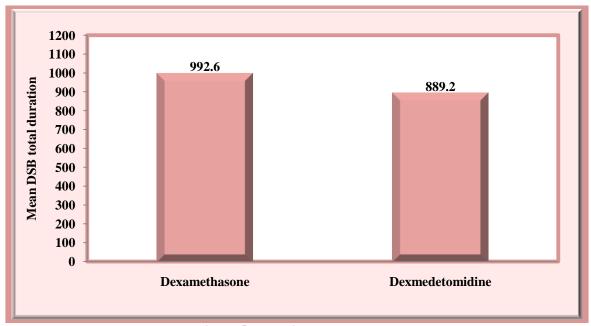


Figure 5: Duration sensory block

The mean duration of sensory block in D group was  $992.6\pm77.0$  min and in DEX group was  $889.2\pm65.7$  min. The statistical analysis by students unpaired t test showed that there is significant difference in the duration of sensory block between the two groups. (P <0.001) and was significantly prolonged in D group.

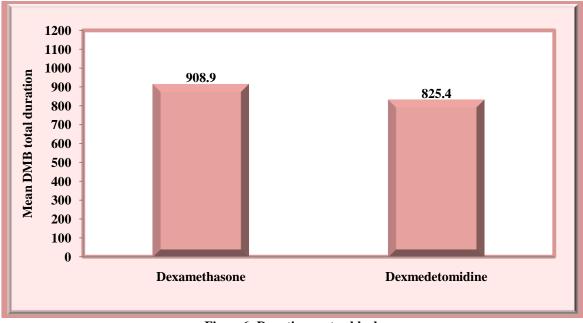


Figure6: Duration motor block

The mean duration of motor block in D group was  $908.9\pm63.3$  min and in DEX group was  $825.4\pm48.6$ min. The statistical analysis by student's unpaired t test showed that there is significant difference in the duration of motor block between the two groups. (P <0.001) and was significantly prolonged in D group.

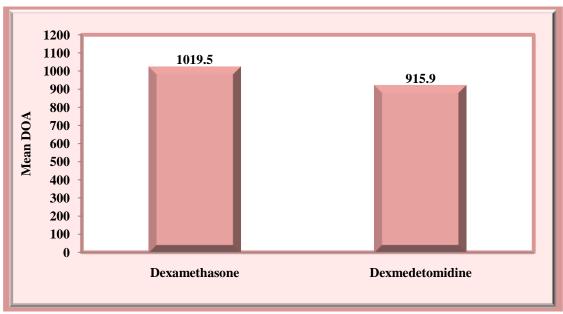


Figure 7: Duration of Analgesia

The total duration analgesia in D group was  $1019.5\pm72.0$  min and in DEX group was  $915.9\pm63.4$  min. There was significant difference in the total duration of analgesia between the two groups. (P <0.001) and was significantly prolonged in group D.

No complications were observed in both groups. Vital parameters like pulse rate, systolic blood pressure, diastolic blood pressure, saturation values were similar in both the groups.

### DISCUSSION

In this prospective, randomized , double blinded study infraclavicular brachial plexus block was performed under USG guidance.80 patients were randomized to receive 30 ml of levobupivacaine with either 8 mg dexamethasone or 50  $\mu$ g dexmedetomidine diluted to 2 ml.

The demographic parameter and surgical characteristics in our study groups were comparable with respect to age, weight, sex and duration of surgery.

The mean time for onset of sensory block in D group(8.5min) and DEX group(8.4min) were comparable. (P = 0.73). These findings correlated with the studies of Esmaoglu A  $^{9}$  in DEX group and yadav et al  $^{10}$  in D group.

The mean time for onset of motor block in D group was 14.5 min and in DEX group was 12.0 min. The statistical analysis showed that there is significant difference in onset time of motor block between the two groups(P <0.001). The mean motor onset time in dex group was similar in the study done by Kenan et al  $^{11}$ , Karthik et al  $^{12}$ . Our study results are similar to the comparative study done by Mandeep kaur et al  $^{13}$  Early motor onset with dexmedetomidine is because of blockade of  $\alpha 2$  adrenoreceptors which resulted in lowering the amplitude and inhibition of complex action potentials resulting in nerve conduction block. Kousugi et al.  $^{14}$ 

The mean duration of sensory block in D group was 992.6 min and in DEX group was 889.2min. There is significant difference in the duration of sensory block between the two groups (P < 0.001).

The mean duration of motor block in D group was 908.9 min and in DEX group was 825.4min. The statistical analysis by student's unpaired' test showed that there is significant difference in the duration of motor block between the two groups. (P = <0.001).

These findings lend support to the observations of various earlier studies by Esmaoglu <sup>9</sup>, Kenan<sup>11</sup>, Karthik et al <sup>12</sup> in DEX group and Mandeep kaur <sup>13</sup> in D group. However total duration of motor block was significantly higher in D group than DEX group (P<0.001).

The mean duration of analgesia in D group was 1019.5 and 915 minutes in group DEX. Significant difference in the total duration of analgesia between the two groups was seen (P < 0.001).In our study total duration of analgesia in DEX group was similar to study done by Saumya Biswas et al <sup>15</sup>,Esmagolu <sup>9</sup> and in D group it was similar to study done by Jasminka Persec <sup>16</sup> and Mandeep kaur <sup>13</sup>. Our study signifies that total duration of analgesia was higher with dexamethasone group than dexmedetomidine group.

Dexamethasone is a potent anti inflammatory agent with potency of 25-30 times of hydrocortisone. The mechanism of action of dexamethasone in prolonging peripheral neural blockade is not clearly understood. The block effect may be due to its local action and not a systemic one. The prolongation of duration of sensory and motor blockade after perineural administration of dexamethasone may be secondary to its local action on nociceptive C fibers mediated via membrane associated glucocorticoid receptors and the up-regulation of the function of potassium channels in excitable cells. Some authors also believe that analgesic properties of corticosteroids are the result of their systemic effect. Preoperative administration of dexamethasone by oral and intravenous routes has been shown to reduce overall pain scores and analgesic requirements in the postoperative period without any adverse effects in various oral and general surgical procedures that the dose range used clinically for postoperative nausea. The 8 mg dose of dexamethasone was chosen because it has been used previously for perineural injection and is within the dose range used clinically for postoperative nausea.

The safety of dexamethasone use in a nerve sheath may raise some concerns. However, the use of dexamethasone at doses between 4 and 12 mg via the intravenous, perineural, and epidural route is described in regional anesthesia and pain medicine text books. Reports of corticosteroid mediated neurotoxicity seem to be related to the vehicle polyethylene glycol and the preservative benzyl alcohol in steroid preparations as well as the presence of insoluble steroid particulate matter in the injectate. Dexamethasone sodium phosphate is a nonparticulate steroid and does not contain either polyethylene glycol or benzyl alcohol.<sup>21</sup> In vivo and in vitro animal studies have demonstrated that locally applied corticosteroid have no long term effect on the structure, electrical properties, or function of the peripheral nerves and that the extrafascicular and intrafascicular injection of dexamethasone in a rat sciatic nerve experimental model caused no or minimal peripheral nerve damage, respectively when compared with other steroids such as hydrocortisone or triamcinolone. Dexmedetomidine is a highly selective a<sub>2</sub> agonist. Highest densities of a2 receptors have been located in the locus coereleus. The hypnotic and sedative effectsof a2 adrenoceptor activation have been attributed to this site in the CNS. It is also the site of origin of the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission.

Proposed mechanism of action of dexmeditomidine in peripheral block is via centrally mediated analgesia,  $\alpha 2$  adrenoreceptor mediated vasoconstriction, attenuation of inflammatory response and direct action on peripheral nerves.on peripheral nerves dexmeditomedine enhances activity dependent hyperpolarisation by repetitive stimulation of Na/k pump causing slowing or blockage of conduction. <sup>14</sup>

Presynaptic activation of a2 adrenoceptor in centralnervous system inhibits the release of norepinephrine, terminating the propagation of pain signals and their postsynaptic activation inhibits sympathetic activity, thereby decreasing the heart rate and blood pressure in higher doses

In the above study total duration of analgesia was higher in dexamethasone group compared to dexmeditomidine. Probably reason could be because of longer duration of action of dexamethasone (36-54 hrs).<sup>22</sup>

Patient in both the groups did not require sedation intraoperatively and they were comfortable throughout the surgery. The mean pulse rate and mean arterial pressurere were comparable in both the groups and statistically insignificant.

Dexmedetomidine can cause side effects such as bradycardia and hypotension with increased dose. However, dexmedetomidine administration should be carefully conducted in patients with a history of cardiac disease, especially clinically significant arrhythmia. Other studies showed dexmedetomidine decreased mean arterial and diastolic blood pressures and heart rate<sup>23</sup>. In our study none of the patient in both the groups suffered marked hypotension or bradycardia because we used only 50 µ g which is relativetly low compared to other studies.

The main limitation of this study was that it was not possible for us to evaluate neurologic complications caused by dexmedetomidine or dexamethasone. It is possible, however, for our patients to self-report any untoward reaction that can mimic late-onset neuropathy, but for future investigation, it will be advisable to establish continuous follow-up using survey questionnaires and periodic checking for a longer period.

Future scope of the study is to find for other multiple combinations like with ropivacaine and dexamethasone, so as to achieve longer duration of analgesia early return of motor function of the upperlimb. By using single shot block with longer duration of analgesia and without significant clinical side effects we can avoid the use of continuous catherterization and compications assosciated with it.

### **CONCLUSION**

Both dexmedetomidine and dexamethasone are good adjuvants for Levobupivacaine in peripheral nerve blocks. Our study of comparison between the two agents, suggests that dexamethasone is a better choice as it extends duration of motor and sensory block as well as duration of analgesia delaying the request for first analgesic.

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