

# Comparison of Two Different Doses of Dexmedetomidine as an adjuvant to Bupivacaine in Ultrasound Guided Infraclavicular Brachial Plexus Block: A Prospective Randomized Study.

Vrishali Yashvant Apte, Sumedha Mehta, Jyoti Deshpande<sup>1</sup>, Vishal Dhondiram Jadhav

## Abstract

**Introduction:** Dexmedetomidine, an  $\alpha_2$  adrenergic receptor agonist has been used as a safe adjuvant in diverse clinical applications. It is increasingly being used nowadays for regional anaesthesia. Different doses of dexmedetomidine have been added perineurally. The present study has been undertaken to investigate the optimal dose of perineural dexmedetomidine with bupivacaine in ultrasound guided infraclavicular brachial plexus block in patients undergoing below elbow surgeries. **Methods:** Sixty patients of ASA grade I or II were divided into two groups of 30 each. Patients in group I received dexmedetomidine 0.25mcg/kg + bupivacaine 0.5% (20ml) and patients in group II received dexmedetomidine 0.5mcg/kg + bupivacaine 0.5% (20ml) in ultrasound guided infraclavicular block. The following parameters were assessed: the duration of sensory and motor block, onset of block and postoperative duration of analgesia. Also patients were evaluated for haemodynamic effects and side effects if any. **Results:** In both the groups all parameters were comparable i.e. statistically insignificant. Onset of sensory block ( $12.6 \pm 2.32$  vs  $11.69 \pm 2.108$  mins,  $p=0.112$ ), onset of motor block ( $14.96 \pm 1.266$  vs  $14.5 \pm 1.52$  mins,  $p=0.164$ ), duration of sensory block ( $6.01 \pm 0.969$  vs  $6.44 \pm 1.685$  hrs,  $p=0.194$ ), duration of motor block ( $5.933 \pm 1.406$  vs  $6.423 \pm 1.568$  hrs,  $p=0.186$ ) and duration of analgesia ( $7.533 \pm 1.217$  vs  $8.017 \pm 1.429$  hrs,  $p=0.129$ ). There were no significant haemodynamic effects or side effects. **Conclusion:** 0.25 $\mu$ g/kg dose of dexmedetomidine is optimal, safe and effective dose as an adjuvant to 0.5% bupivacaine for ultrasound guided infraclavicular block in terms of sensory and motor onset of nerve block and duration of analgesia with minimal incidence of side effects.

**Keywords:** Dexmedetomidine, Ultrasound guided Infraclavicular Block, Bupivacaine.

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## Introduction

Brachial plexus block is superior to general anaesthesia for upper extremity surgeries as it is associated with lesser complications and good postoperative analgesia. Also it is cost effective for patients as well as hospital and reduces economic burden. Infraclavicular block (ICB) is gaining popularity nowadays as ultrasound (US) allows the ICB to be performed with high success rate, low complication rate and excellent analgesia. It is easy to perform, avoids neurovascular structures in the neck, provides dense anaesthesia for procedures below elbow with minimal risk of pneumothorax and phrenic nerve block when compared to supraclavicular approach making it excellent choice in patients with respiratory disorders [1]. The use of ultrasound provides good visualization of the needle position, the local anaesthetic spread around the cords, increases the success rate and minimizes complications [2]. This technique can be useful especially in obese and patients with anatomical variations where performing block

using other technique can be difficult. Traditional local anaesthetics used for blocks lead to short lived analgesia usually lasting less than 6 hours. So various adjuvants have been used in an attempt to prolong analgesia like epinephrine, fentanyl, clonidine, dexamethasone etc. [3]. Dexmedetomidine is one of them. Dexmedetomidine, an  $\alpha_2$  adrenergic receptor agonist with  $\alpha_2/\alpha_1$  selectivity ratio of 1600:1, has been used as a safe adjuvant in diverse clinical applications. This increased selectivity results in more predictable and effective analgesia with fewer side effects than its precursor clonidine [4]. It is increasingly being used nowadays for regional anaesthesia. Different doses of dexmedetomidine have been added perineurally [5,6]. Higher doses of dexmedetomidine like 1-2mcg/kg provide prolonged analgesia but at the cost of side effects like bradycardia and hypotension [7]. Hence, the present study has been undertaken to compare the effects of different doses of perineural dexmedetomidine with bupivacaine on the perioperative pharmacodynamic parameters of ultrasound guided infraclavicular brachial plexus block and to

investigate the optimal dose in patients undergoing below elbow surgeries.

The primary aim of this study is to compare two different doses of dexmedetomidine in combination with bupivacaine (0.5%) in terms of the duration of sensory and motor block, onset of block and postoperative duration of analgesia and the secondary aim was to evaluate haemodynamic effects and side effects if any.

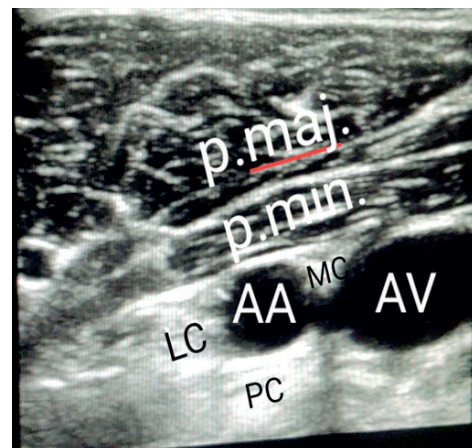
## Materials and Methods

The present study was a hospital-based, prospective, double-blinded, randomized study. After ethical committee approval and written informed consent in local vernacular language, 60 patients of ASA grade I or II in the age group of 18–60 years posted for below elbow surgeries were included in the study and divided into two groups of 30 each by using computer generated randomization charts. Each patient was given all information and details about the procedure and drugs used. Patients in group I received dexmedetomidine 0.25 mcg/kg + bupivacaine 0.5% (20ml) and patients in group II received dexmedetomidine 0.5mcg/kg + bupivacaine 0.5% (20ml). Study drugs were prepared by the anaesthesiologist under aseptic precautions who was not participating in the study. Prepared syringes were masked and drugs were given by another anaesthesiologist for blinding. Patients having sinus bradycardia, hypotension, hypersensitivity to local anaesthetics or study drug dexmedetomidine, local site infection, deranged coagulation profile, uncontrolled diabetes mellitus, pregnancy, pre-existing peripheral neuropathy and adrenergic receptor agonist or antagonist therapy and patients refusing consent for regional anaesthesia were excluded from the study. All patients underwent thorough pre-anaesthetic evaluation and were kept nil by mouth for eight hours.

Basic routine laboratory investigations were conducted. The anaesthetic procedure to be carried out was explained and patients were reassured to alleviate their anxiety. After confirming NBM status and checking informed written consent, a 20 G intravenous access was taken in non-operative limb and Ringer Lactate was started intravenously at a rate of 4 ml/kg/hour for maintenance. Inside OT standard monitors like ECG, SpO<sub>2</sub> and NIBP were attached and baseline values of pulse, BP, SpO<sub>2</sub> were noted.

Infraclavicular block was given using USG guided parasagittal approach using single shot injection technique. The patient was made to lie in supine position with ipsilateral arm in any position with the anaesthesiologist performing the procedure standing at the head of the table behind the shoulder. The part of anterior chest wall below clavicle on the operative side was aseptically cleaned and draped. A subcutaneous local anaesthetic infiltration was done at the site of injection with 1ml of Lignocaine 1%. The high frequency linear ultrasound probe (Sonosite HFL38x/13-6 MHz; Fujifilm SonoSite, Bothell, WA) was placed in the parasagittal plane medial to the coracoid process angled to best visualize the axillary artery in cross section and the three cords. A 8cm, 22g short bevel needle was introduced by in line technique, confirmed with hydrodissection by one ml of normal saline and then drug was slowly injected first in lateral and posterior cord regions and then in the medial cord area with frequent aspirations to avoid inadvertent intravascular injection. Performance time for block was measured as the time taken to prepare and drape the field, scan the area, insert the needle and inject the drug.

Sensory block was assessed by the pin prick method using hypodermic needle every 3 minute after completion of drug injection in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve and musculocutaneous nerve till complete sensory



**Ultrasound image of Infraclavicular Block (p.maj= pectoralis major muscle, p.min.= pectoralis minor muscle, AA=Axillary artery, AV= Axillary vein, LC= lateral cord, PC= posterior cord, MC= medial cord )**

blockade. Sensory block was graded as- Grade 0: Sharp pin felt . Grade 1: Analgesia, dull sensation felt. Grade 2: Anaesthesia, no sensation felt .

The time between drug injection and the attainment of complete sensory block in dermatomal area of all the three nerves is considered as the onset time for sensory blockade. Sensory onset was considered when grade 2 block was achieved.

Assessment of motor block was carried out by the same observer at every 3 minute till complete motor blockade after drug injection Motor block was determined according to a modified Bromage scale for upper extremities on a 3-point scale. 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. Onset of motor blockade was considered when grade 2 motor blockade was achieved.

Block was considered inadequate if the onset of sensory and motor block was not achieved in 20 minutes or any supplemental analgesics were required for completion of surgery. Such patients were excluded from the study.

Patients were monitored for pulse rate, mean arterial pressure (MAP), respiratory rate, SpO<sub>2</sub> and ECG after performance of block every 5minutes for first half an hour, then every 15 minutes intraoperatively. Possible side effects like hypotension (>30% fall in MAP from baseline MAP), bradycardia (>20% fall in heart rate from baseline heart rate), respiratory depression (defined as respiratory rate <8/min or fall in Oxygen saturation of less than or equal to 90%) were recorded and managed accordingly. Patients were monitored for duration of sensory and motor block, duration of analgesia and side effects like bradycardia, hypotension and sedation postoperatively 1 hourly for 24 hours. Sensory and motor block was assessed as mentioned earlier. The visual analogue scale score >4 (moderate pain) was regarded as the endpoint for duration of analgesia and rescue analgesia was given in the form of IV paracetamol (15-20 mg/kg) and thereafter 1gm IV paracetamol was given twice a day(BD) according to institutional protocol, further if pain was not relieved by paracetamol Inj. Tramadol (1mg/kg) was given IV.

Patients were assessed for sedation by Ramsay sedation score.

With power of study 80% and type 1 error of 5% (level of significance  $[\alpha]=0.05$ ), the sample size required was calculated as 25 in each group and to compensate for any possible dropouts and for better validation of results, a sample size of 30 subjects per group was chosen. The data were expressed as mean  $\pm$  SD (standard deviation). Two sample t-test is used to investigate and model impact of various parameters like age, weight, sex, onset of sensory blockade, onset of motor blockade, duration of sensory and motor block, duration of surgery and duration of analgesia in groups I and II. A p-value  $<0.05$  was considered statistically significant. Statistical analysis was performed using SPSS software 20.0.

## Results

Both the groups were comparable in terms of demographic variables and duration of surgery (p-value $>0.05$ ) as shown in table 1.

The baseline hemodynamic parameters of the study population including heart rate, mean arterial pressure, oxygen saturation and respiratory rates were comparable in both the groups.

Performance time for block was comparable in both the groups (11.23 $\pm$ 2.87 Vs 10.23 $\pm$ 2.47 mins) (p-value = 0.174).

The details of onset of sensory and motor block, duration of sensory and motor block and the duration of analgesia are mentioned in Table 2. The duration of sensory block, duration of motor block and duration of analgesia were comparable in both the groups. (P value $>0.05$ ).

Bradycardia was seen in one patient of group II and was treated with Inj. Glycopyrrolate (0.2 mg). All of the patients in both groups were calm and comfortable with Ramsay sedation score of II/III. No other complications were noted in any patient enrolled in this study.

## Discussion

In our study, we found that the onset and duration of sensory and motor block as well as the duration of analgesia were comparable in

both the groups.

Dexmedetomidine has been used as an adjuvant to different local anaesthetics in various types of peripheral nerve blocks. Most of the studies have used dexmedetomidine in dose ranging between 0.5-2 $\mu$ g/kg or 50-100  $\mu$ g. Higher doses have been associated with side effects like bradycardia, hypotension, sedation. Hence, this study was conducted to find the minimum dose of dexmedetomidine required to prolong analgesia with less side effects. So, we chose comparison between 0.25 $\mu$ g/kg and 0.5 $\mu$ g/kg of dexmedetomidine as it is not studied before.

Dexmedetomidine in low dose as an adjuvant to bupivacaine has been studied in spinal anaesthesia where Kanazi GE et al. found that it provides shorter onset to motor blockade and prolongation of sensory and motor blockade along with the preservation of haemodynamics and absence of sedation [8].

Dexmedetomidine (1 $\mu$ g/kg) was also studied in paediatric caudal anaesthesia along with bupivacaine where Saadway et al. found that it prolongs analgesia leading to less rescue analgesic consumption and also improved sleep quality with no clinically relevant adverse effects [9]. In another study, El-Hennawy and coworkers compared dexmedetomidine with clonidine as an adjuvant to bupivacaine in paediatric caudal anaesthesia for lower abdominal surgeries where they found that both dexmedetomidine(16hrs) and clonidine(12hrs) significantly prolonged analgesia as compared to bupivacaine alone (5hrs) but the difference was not statistically significant (p value 0.796) [10].

In metaanalysis, Vorobeichik et al. have stated that dexmedetomidine prolonged the duration of analgesia by at least 39% in ICB and can effectively decrease the total opioid consumption [11]. Esmaoglu et al. added dexmedetomidine to levobupivacaine in axillary brachial plexus block where they found that it shortened the onset time to block and prolonged duration of block and postoperative analgesia [12]. Our findings coincide with the findings of these studies. Many mechanisms for analgesic effect have been suggested: synergistic action of alpha 2 agonists with local anaesthetics, induction of vasoconstriction at injection site [13], release of anti-inflammatory

**Table 1: Comparison of demographic variables and duration of surgery in two groups**

Variable	Group I (n=30) (Dexmed 0.25mcg/kg+ Bupivacaine0.5%)	Group II (n=30) (Dexmed 0.5mcg/kg+ Bupivacaine0.5%)	p-value
Age(years)	36.96 $\pm$ 11.90	37.63 $\pm$ 12.59	0.94
Weight(Kgs)	55.5 $\pm$ 5.25	55.36 $\pm$ 7.07	0.93
Duration of Surgery(Mins)	111.67 $\pm$ 22.79	111.3 $\pm$ 22.53	0.95

(p-value  $<0.05$  is significant)

**Table 2: Comparison of onset and duration of sensory and motor block, duration of postoperative analgesia in two groups**

Variable	Group I (n=30)	Group II (n=30)	p-value
Onset of sensory Block(mins)	12.6 $\pm$ 2.32	11.69 $\pm$ 2.108	0.112
Onset of motor Block(mins)	14.96 $\pm$ 1.266	14.5 $\pm$ 1.52	0.164
Duration of sensory block(hrs)	6.01 $\pm$ 0.969	6.44 $\pm$ 1.685	0.194
Duration of motor block(hrs)	5.933 $\pm$ 1.406	6.423 $\pm$ 1.568	0.186
Duration of analgesia(hrs)	7.533 $\pm$ 1.217	8.017 $\pm$ 1.429	0.129

(p-value  $<0.05$  is significant)

cytokines and local release of enkephalin like substances<sup>(14)</sup>. Dexmedetomidine activates presynaptic alpha 2 receptors in CNS causing inhibition of norepinephrine release. This leads to termination of pain signal propagation. Dexmedetomidine may act on supraspinal (locus coeruleus) or spinal level or peripheral  $\alpha_2$ -adrenoreceptor to reduce nociceptive transmission, leading to analgesia. Another mechanism of analgesia suggested is by inhibition of neuronal conduction by blocking hyperpolarization activated cation currents [11]. Andersen et al. suggest that Dexmedetomidine prolongs duration of block by peripheral mechanism also [15].

Nallam et al. compared two doses of dexmedetomidine 50 $\mu$ g and 100 $\mu$ g with 0.5% levobupivacaine in supraclavicular brachial plexus block. They found that 100 $\mu$ g dose of dexmedetomidine in brachial plexus block hastens the onset and prolongs the duration of sensory motor blockade and analgesia, but with higher incidence of bradycardia and sedation [16].

Keplinger et al. assessed the dose dependency of dexmedetomidine when added to ropivacaine for peripheral nerve blockade. In their study, an ulnar nerve block was given with ropivacaine alone, or mixed with 50 $\mu$ g, 100 $\mu$ g or 150 $\mu$ g dexmedetomidine. There was a significant dose-dependent increase in the mean duration of analgesia with dexmedetomidine. Sedation was also enhanced in a dose-dependent manner [17].

Zhang et al. reported prolonged duration of analgesia in patients who received a higher dose of dexmedetomidine (100 $\mu$ g) in 40 ml of 0.33% ropivacaine when compared to 50 $\mu$ g of dexmedetomidine in axillary brachial plexus block. They found prolonged duration of sensory and motor block after addition of 100  $\mu$ g of dexmedetomidine to ropivacaine compared to the ropivacaine alone but the incidence of hypotension and bradycardia was more [18].

We did not encounter any drug related side effects like bradycardia, hypotension and sedation in our study. The use of low dose of dexmedetomidine may be the cause for this. The maximum dose of dexmedetomidine used in our study was 40 $\mu$ g. Hussain et al. also reported that the incidence of bradycardia is dose dependent and is seen more frequently when dose more than 50 $\mu$ g is used [19]. Additional advantage of using dexmedetomidine in nerve blocks is its neuroprotective effect. Rojas et al. have reported significantly less perineural inflammation at 24 hrs when combination of dexmedetomidine and bupivacaine was used as compared to bupivacaine alone [20]. In various animal studies also, dexmedetomidine has been reported to be neuroprotective [21,22].

## Limitation

We did not measure serum dexmedetomidine levels, as with higher doses systemic absorption can be the cause of dose related side effects. However, in our study due to use of ultrasound guidance for infraclavicular block, less amount of drug was adequate due to drug deposition at exact location in the vicinity of cords, which might have decreased the incidence of side effects. We suggest further multicentric large population studies with similar doses in different peripheral nerve blocks along with measurement of serum dexmedetomidine levels.

## Conclusion

From this study, we conclude that (0.25 $\mu$ g/kg) dose of dexmedetomidine is optimal, safe and effective dose as an adjuvant to 0.5% bupivacaine for ultrasound guided infraclavicular block in terms of sensory and motor onset of nerve block and duration of analgesia with minimal incidence of side effects.

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<b>Ethics:</b>	There is no ethical violation as it is based on voluntary anonymous interviews
<b>Funding:</b>	No external funding
<b>Guarantor:</b>	Dr. Sumedha Mehta will act as guarantor of this article on behalf of all co-authors.

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