

Deciding the Better Dose- A Prospective Randomized Double Blind Study of Two Different Doses of Perineural Dexmedetomidine in Axillary Brachial Block

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Abstract

Background : Axillary brachial plexus block is generally regarded as the safest and reliable technique for forearm and hand surgeries. Dexmedetomidine, a potent alpha (α)-2-adrenergic receptor agonist when used as an additive in any peripheral nerve block can improve quality of block and postoperative analgesia, though uncertainty prevails regarding the dose in patients undergoing hand and forearm surgeries.

Methods: In this prospective, randomized, comparative, double blind study, 80 patients were included. Each participant fulfilling the inclusion criteria then received axillary brachial plexus block using 15cc 2% lignocaine with adrenaline (1:200000) and 0.5% bupivacaine 5cc mixed with dexmedetomidine either 0.5 $\mu\text{g/kg}$ (group A) or 1 $\mu\text{g/kg}$ (group B) in 2cc normal saline. Duration of post-operative analgesia was the primary outcome.

Result: Duration of analgesia was significantly prolonged in group B (493.77 ± 115.62 min) compared to group A (434.62 ± 45.18 min, $P < 0.01$).

Conclusion: Between the two doses of dexmedetomidine, block characteristics and analgesia obtained were better with higher dose (1 $\mu\text{g/kg}$) but chances of side effects like bradycardia increased. Hence 0.5 $\mu\text{g/kg}$ can be a better dose with improved block characteristics yet negligible side effects.

Keywords: Brachial plexus block, Dexmedetomidine Perineural, Peripheral nerve stimulator, Ultrasonography

Introduction

Axillary approach to brachial plexus is the most popular approach for forearm and hand surgeries considering its ease of administration and safety profile [1]. Adequate pain relief after these surgeries leads to early restoration of functions and facilitates timely discharges. In order to increase analgesia, dose of local anesthetics can be increased but it has been associated with prolonged duration of motor blockade leading to delayed restoration of limb movements [2]. Various adjuvants have been studied in brachial plexus block including buprenorphine, dexamethasone, magnesium sulphate etc. with the intention to prolong analgesic effect of the block [3, 4, 5]. But there exists paradoxical data about their safety and efficacy [6].

Selective alpha(α)-2-adrenergic receptor agonist like dexmedetomidine is becoming a focus of interest because of its excellent sedative, analgesic properties. It has been established that perineural addition of dexmedetomidine prolongs postoperative analgesia after brachial plexus block [1]. The optimal dose that provides prolonged analgesic benefit while minimizing associated perioperative side-effects, remains to be determined [7].

This study was done to compare the efficacy and safety of two different doses of perineural dexmedetomidine 0.5 $\mu\text{g/kg}$ and 1 $\mu\text{g/kg}$ as an adjuvant to axillary brachial plexus block performed with both ultrasound and nerve stimulator (dual guidance) in patients undergoing hand and forearm surgeries.

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Aim

Duration of analgesia was the primary objective while nerve block characteristics like onset of sensory and motor block as well as duration of motor block and side effect profile were the secondary objectives.

Material and Methods

This prospective randomized double blind study was conducted after obtaining clearance from institutional ethics committee. Eighty consenting adult patients of age 18-60 years with American Society of Anesthesiologists (ASA) physical class I and II undergoing elective forearm and hand surgery were recruited. Patients were excluded if morbidly obese, on beta blocker therapy, having baseline heart rate less than 60 or preexisting upper limb neuropathies, pregnant and lactating mothers, coagulopathy, local skin infection or allergic to any of the study drugs.

Sample size calculation: Sample size required was estimated from a similar study in which the mean duration of analgesia after brachial block was 395.90 ± 52.89 min. in Group LD 1 followed by Group LD 0.5 (327.30 ± 92.01 min) [1].

Hence by using this formula

$$n \geq \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta} \right)^2 \left(\sigma_1^2 + \frac{\sigma_2^2}{r} \right)}{(\mu_1 - \mu_2)^2}$$

n=size per group;

$\sigma_1 = 52.89$ (i.e. The SD duration of analgesia was maximum in Group LD₁ 395.90 ± 52.89 min)

$\sigma_2 = 92.01$ (i.e. The SD duration of analgesia in Group LD Group LD_{0.5} 327.30 ± 92.01 min)

$\mu_1 = 395.90$ (The Mean duration of analgesia was maximum in Group LD₁ 395.90 ± 52.89 min)

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$Z_{\alpha/2} = Z_{0.01/2} = Z_{0.005} = 2.58$ — From Z table at type I error of 5

$Z_\beta = Z_{0.10} = 1.28$ — at 90% power

N= 35.63. With 90% power, and 95% confidence limit, 36 patients were required in each group. Expecting a few drop outs, 40 patients were enrolled in each group.

Preoperatively all the patients were assessed and educated about the procedure of the regional anaesthesia and Numeric Rating Scale (NRS), where 0 was no pain and 10 was worst imaginable pain [8]. In operation theatre, after confirming adequate fasting and valid informed consent, baseline parameters like heart rate (HR), oxygen saturation (SpO₂),

five lead electrocardiogram (ECG), noninvasive blood pressure (NIBP) were recorded. An intravenous line was secured in the contralateral hand and Ringer's lactate infusion was started. Oxygen 2 lit/min was administered via nasal prongs. Intravenous injection of midazolam 0.03-0.05 mg/kg was administered for anxiolysis prior to the block.

Patients were randomly divided into two groups with the help of computer generated random numbers. Group A received perineural dexmedetomidine 0.5 µg/kg in saline to make 2cc volume along with 15 ml 2% Lignocaine with adrenaline (1:200000) and 5 ml 0.5% Bupivacaine and to make total volume 22 ml (LA mixture). Similarly, Group B received perineural dexmedetomidine 1 µg/kg in 2 cc saline with 15 ml 2% Lignocaine with adrenaline (1:200000) and 5 ml 0.5% Bupivacaine to make total volume 22 ml (LA mixture). The block was administered by an anaesthetist who had experience of performing at least 20 USG guided axillary blocks and who was blinded to the constituents of the syringes. Intra operative and post-operative readings were taken by an anaesthetist who was also unaware of the study drugs.

A scout scan in axilla using a high frequency linear array transducer (Sonosite Edge Ultrasound system with 6-13 MHz probe) identified the neural targets: Median nerve at 11-1 O'clock, ulnar nerve at 2-4 O'clock, radial nerve at 5-7 O'clock in relation to the axillary artery and musculocutaneous nerve in the fascial groove between biceps and coracobrachialis muscles.

Skin asepsis was achieved with 10% povidone iodine solution. High frequency transducer was covered with sterile polythene sheath. The PNS, was adjusted to 0.5 mA current, 1-Hz frequency and, 0.1 ms duration at the beginning of the procedure. Under local infiltration of 2% lignocaine, 22G sterile needle was advanced under ultrasound guidance in plane PNS technique and appropriate distal motor responses flexion of the forearm (musculocutaneous nerve), extension of the fingers/wrist (radial nerve), flexion of 5th metacarpophalangeal joint and flexion of wrist or other metacarpophalangeal joints (ulnar and median nerve) were the commonest endpoints for the identification of the nerves. The stimulating current was gradually decreased and the needle was repositioned until twitches were seen at 0.2-0.5 mA. The needle was gently withdrawn a little in case the twitches continued even below 0.2 mA. Local anaesthetic mixture was administered equally at all four sites after careful aspiration to rule out intravascular injection. The entire block procedure was completed with this dual technique. Both the groups were compared with respect to the onset of sensory and motor block, duration of motor block and duration of postoperative analgesia.

Sensory block evaluation was done every 2 minutes by pinprick assessment in the dermatomes of sensory distribution of the musculocutaneous, radial, ulnar and median nerves and graded using a 3-point scale [9]: Grade 0= Normal sensations, Grade 1= Analgesia (loss of pinprick sensation) and Grade 2= Loss of touch (anaesthesia). Onset of sensory block was calculated as the time from completion of injection till the achievement of grade 1 block at operative site.

Motor block was assessed every 2 minutes using Modified Bromage scale on a 3-point scale [9]: Grade 0= Normal movement of forearm, wrist and fingers, Grade 1= Decreased motor strength with ability to move fingers only, Grade 2= Complete motor block. Onset of motor block was the time from completion of injection till grade 1 motor block.

Block was considered as failed if there was no inadequate surgical anaesthesia 30 minutes after administration of block. Such patients were given supplementary anaesthesia and were excluded from the study.

Duration of Analgesia was the duration from the onset of sensory block till the time when patient reported pain with NRS ≥ 3 . Duration of motor block was calculated as the duration from the onset of motor block till the recovery of finger movements.

Surgery was allowed to commence after ensuring grade 2 sensory block in the surgical area. Hemodynamics of the patients were assessed by monitoring heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure (DBP), mean arterial pressure (MAP), SpO₂ every five minutes till 30 minutes post block, then every 15 minutes till 60 minutes and in immediate post-operative period. Heart rate if <50 /min was treated with intravenous injection of atropine 0.6 mg and hypotension (MAP <60 mm of Hg) was treated with injection ephedrine 6 mg.

Postoperative pain was assessed by NRS every hour. When the score was three or more, intravenous paracetamol 1 gm was administered as rescue analgesic and the time was noted.

Motor block was assessed every hour till the patient had complete recovery of finger movements.

Statistical Analysis

Statistical testing was conducted using SPSS Statistics 21.0 (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA). For assessing quantitative variables mean and standard deviation (SD) were used while frequency and percentages were used to analyze qualitative variables. For the data with normal distribution, comparison of quantitative variables was done using unpaired t-test. Inter-group statistical comparison of non-normally distributed continuous variables was done using Mann Whitney U test. Intergroup statistical comparison of normally distributed categorical data, Chi square test was performed. Fisher exact test was used instead when the expected frequency was less than 5. $p < 0.05$ was considered statistically significant.

Results

Out of 40 patients in each group, three patients from group A and one patient from group B were excluded from the study as they failed to achieve the required surgical analgesia (Fig 1) Both group A and group B were comparable with respect to demographic profile, ASA physical status and surgical duration (Table 1).

Mean sensory block onset in group A was 5.95 ± 2.16 min. while in group B it was 4.31 ± 1.49 min. Similarly, mean motor block onset in group A was 7.84 ± 2.24 min and group B was 6.62 ± 1.93 min. Thus, Group B showed faster onset of both sensory as well as motor block. (p value < 0.01) (Fig. 2).

Group A had mean duration of analgesia 434.62 ± 45.18 min compared to group B 493.77 ± 115.62 minutes which received higher dose of dexmedetomidine. [p value < 0.01 , Table 2]

Group A had mean duration of motor blockade 389.16 ± 44.18 min compared to 422.13 ± 46.59 min in group B. (p value < 0.01) (Fig. 2). Thus, motor blockade was significantly prolonged in patients receiving higher dose of

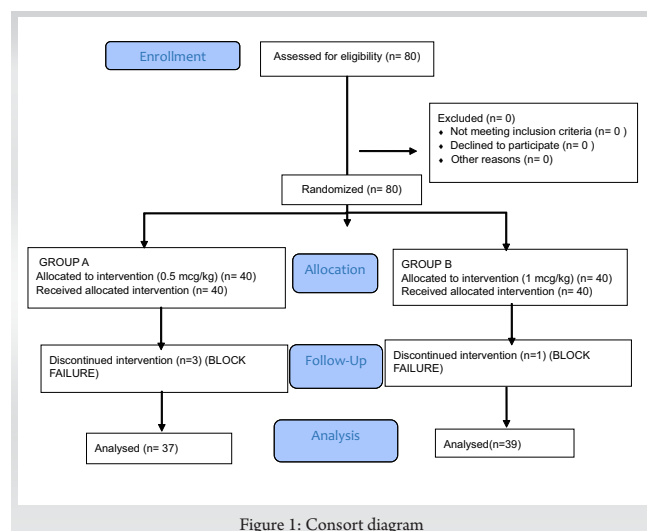


Figure 1: Consort diagram

Parameters		A (n=37)	B (n=39)	P value
Age		45.43 (SD ± 11.15)	44.82 (SD ± 15.00)	0.84
Gender	Male	21	24	0.816
	Female	16	15	
ASA	I	24	13	0.489
	II	22	17	
Weight in kg (SD)		67.7 \pm 7.5	66 \pm 12.7	
Surgery duration (min)		93.17 (SD ± 28.10)	101.8 (SD ± 35.55)	0.28

Table 1: Heart rate comparison

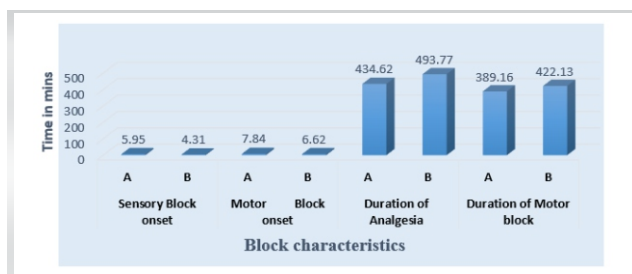


Figure 2: Comparison of block characteristics

Variables	Group	N	Mean	SD	p- value
Duration of Analgesia (mins)	A	37	434.62	45.18	<0.01
	B	39	493.77	115.62	

Table 2: Comparison of mean duration of analgesia

dexmedetomidine.

In our study, baseline mean heart rate recorded in group A was 78.08 ± 9.31 /min and in group B was 75.59 ± 8.64 /min. (p value – 0.23). Heart rate in both the groups showed a steady decline through the surgery so that at the end of 1 hour it was found to be 64.73 ± 4.25 /minute in group A and was 59.28 ± 4.62 /min in group B (p value < 0.01) (Fig. 3).

Three patients in group B had significant bradycardia (47/min, 45/min, and 45/min) which needed treatment with inj. atropine 0.6 mg unlike group A which showed stable heart rate. SBP, DBP and MAP were comparable in both group A and group B (Fig. 4).

None of the patients required treatment with ephedrine. The mean SpO_2 was maintained at 99% in all patients.

Discussion

Based on our clinical study it was evident that 1 µg/kg perineural dexmedetomidine in axillary approach to brachial plexus block under dual guidance, caused faster sensory and motor blockade compared to 0.5 µg/kg perineural dexmedetomidine. It also provided clinically and statistically significant longer postoperative analgesia. However, these advantages of using dexmedetomidine 1 µg/kg are offset by the risk of bradycardia needing treatment and prolonged motor block. Lower dose of 0.5 µg/kg provides lesser motor block and reasonably good post-operative analgesia without the risk of bradycardia.

The effect of prolongation of postoperative analgesia after upper limb surgeries has been observed with variety of doses of dexmedetomidine given as an adjuvant with LA [10, 11, and 12]. Dexmedetomidine is a potent alpha 2 adrenergic agonist. A central analgesic action in the form of a decrease in release of norepinephrine from the locus coeruleus has been

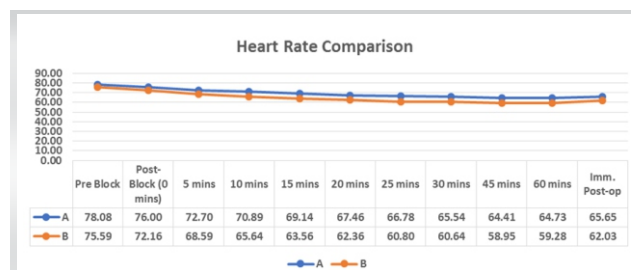


Figure 3: Heart rate comparison

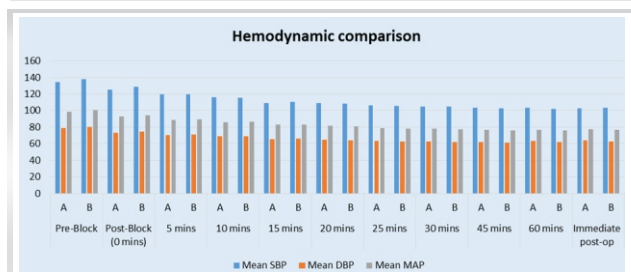


Figure 4: Comparison of hemodynamics

proposed in addition to the direct peripheral action on nerves [13]. Hai Cai et al in their systematic review and meta-analysis of 57 randomized clinical trials on perineural dexmedetomidine in brachial block suggested that addition of dexmedetomidine to local anaesthetics prolonged duration of analgesia up to five hours [7].

Local anesthetic blocks with dexmedetomidine 1 µg/kg has faster onset and prolonged duration when compared to 0.5 µg/kg and control [1, 13].

Further, precise delivery of LA mixture under dual guidance and use of bupivacaine in addition to lignocaine could be a reason for longer analgesia observed in our patients.

Hypotension and bradycardia have been reported with 100 µg dexmedetomidine added as an adjuvant to local anesthetic [13, 15]. Activation of α-2 receptors by dexmedetomidine leads to dose dependent reduction in level of plasma catecholamine (maximum 89%) leading to bradycardia and hypotension secondary to sympathetic inhibition of medullary vasomotor center. [16]. Higher doses of dexmedetomidine in the block can lead to lower heart rates as early as within 10 minutes of the block and the effect may persist for 480 minutes requiring postoperative monitoring and possible treatment with anticholinergic. [14] Hai Cai et al in their review have suggested that addition of perineural dexmedetomidine more than 60 µg was associated with bradycardia and hypotension which was not seen with dose less than 60 µg [7]. In our study, observation of stable haemodynamics were observed with perineural dose of 0.5 µg/kg dexmedetomidine.

Dual guidance, in our study allowed lower volume and dose of LA and adjuvant respectively, improved safety profile and resulted in good block success of 93% (group A) and 97% (group B). Dual guidance reduces intramuscular or intra-

neural drug deposition as well as misdistribution of the drug and hence highly recommended [17].

Limitation of the study

Post-operative assessment of sensory block in respective dermatomes could not be carried out because of the presence of plaster cast. Due to same reason, the recovery of motor blockade was also assessed from the return of only finger movements. Assessment of duration of analgesia was based on subjective perception of pain by patient. This may vary between patients due to different pain threshold between them.

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Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.

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