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A Double-blind Randomized Clinical Study to Compare the Effects of Levobupivacaine Alone and with Dexmedetomidine in Brachial Plexus Block by Axillary Approach

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Abstract

Background: For regional nerve blocks, a combination of dexmedetomidine with local anesthetic like levobupivacaine has shown improved effectiveness by extending the duration of analgesia and reduction in postoperative analgesic requirement. This study was undertaken to evaluate the effectiveness and efficacy of levobupivacaine alone and levobupivacaine with dexmedetomidine in axillary brachial plexus block. *Materials and Methods:* We included 70 patients of ASA category I, II, and III, posted for elective hand and forearm surgeries and randomly assigned them into two groups to receive either 24 ml 0.5% Inj.levobupivacaine and 1 ml normal saline (Group L) or 24 ml of 0.5% Inj.levobupivacaine and 1 mcg/kg of Inj.dexmedetomidine diluted to 1 ml with normal saline (Group LD). *Results:* In Group LD the onset of sensory block (16.13 ± 4.001 min) and motor block (18 ± 3.889 min) was significantly shorter compared to that of Group L. Duration of sensory block in Group LD was 677.25 ± 99.54 min and in Group L was 494.38 ± 70.64 min and the difference was clinically significant ($p < 0.001$). Duration of motor block in Group LD was 710.88 ± 87.32 min and in Group L was 526.25 ± 70.229 min and was clinically significant. Duration of analgesia in Group L was 576.88 ± 76.306 min and that in Group LD was 764.38 ± 110.275 min. There was a significant change in hemodynamics in Group LD as compared to that in Group L. *Conclusion:* Levobupivacaine along with sdexmedetomidine provides faster onset of anesthesia with extended duration of analgesia. It offers efficacious and trouble-free method of anesthesia and better analgesia in postoperative period for hand and forearm surgeries.

Keywords: Axillary block; Dexmedetomidine; Peripheral nerve block; Levobupivacaine.

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Introduction

Regional anesthesia provides long-lasting and effective anesthesia at specific sites. Brachial plexus block is being used as a primary and sole anesthetic technique to facilitate painless surgery. It can be used for management of postoperative pain and chronic pain conditions.

Usually for upper limb surgeries, brachial plexus block is used regularly as regional anesthetic technique. Various approaches like interscalene, supraclavicular, infraclavicular and axillary are used. Among these, axillary approach to the brachial plexus block is popular because of its ease of access, safety of administration and reliable block. It is indicated in surgeries involving forearm and hand.

Levobupivacaine is a newer, long-acting local anesthetic agent having pharmacokinetic properties similar to bupivacaine. Various study

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trials have shown its wider safety and minimal myocardial toxicity in contrast to bupivocaine. The efficacy of local anesthetic is improved by addition of adjuvant thereby enhancing the onset of action, increasing the duration of action, and prolonging postoperative analgesia.

Dexmedetomidine which is used as an adjuvant to local anesthetics is a selective alpha-2 adrenoreceptor agonist. It is assumed to hasten the onset of action, prolong the duration of action, and postoperative analgesia.

The aim of the study was to compare the effects and efficacy of levobupivacaine alone and levobupivacaine with dexmedetomidine in axillary brachial plexus block for hand and forearm surgeries in terms of onset of sensory and motor block, duration of sensory and motor block and duration of analgesia.

Materials and Methods

Following Ethical Committee approval in our institution Subbaiah Institute of Medical Scinces and Hospital, Shimoga, 70 patients undergoing elective hand and forearm surgeries were randomized using closed envelope technique. Patients between the ages of 18 and 60 belonging to physical status of ASA I, II and III were included. Patients with weight <45 kg, pregnant patients, allergy to levobupivacaine or dexmedetomidine, coagulation abnormalities and infection at block site were excluded.

All patients underwent pre-anesthetic evaluation; written informed consent was obtained. All patients were kept nil by mouth 6 hours prior to surgery, tablet alprazolam 0.5 mg was given the night before the surgery, and premedicated with Inj. ranitidine 50 mg and Inj.perinorm 10 mg 2 hr before surgery. Baseline readings of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2) were noted. Under all aseptic precautions, operative limb was positioned. Axillary block was performed by using 40 mm length 26G, short beveled, stimulating needle using nerve stimulator. Once the limb was positioned, the pulsation of axillary artery was felt in the upper one-third of the arm. 1 ml of inj. lignocaine 2% was injected subcutaneously just above and below the pulsation. By starting the stimulation with current intensity at 2.5 mA, location of each nerve was done. Then current intensity was decreased slowly to a minimum of 0.5 to 0.6 mA by changing direction of the needle to obtain the desired appropriate response. 6 ml of the drug solution was injected for each nerve (ulnar, radial, musculocutaneous and median nerve) after negative aspiration for blood.

Group L: Received Inj.levobupivacaine (0.5%) 24 ml and 1 ml of normal saline.

Group LD: Received Inj.levobupivacaine (0.5%) 24 ml and Inj. dexmedetomidine 1 mcg/kg diluted to make a volume of 1 ml with normal saline.

The anesthetist involved in preparation of drug combinations was blinded for study groups. Inj. dexmedetomidine 1 mcg/kg diluted to make volume of 1 ml with normal saline. Time of drug admistration was noted.

After giving the block hemodynamic parameters like HR, MAP, SBP, DBP, SpO_2 were noted every five min for the first 20 min, every 15 min for first 1 hour thereafter and every half an hour later on till sensory block regression. Sensory block was assessed by pinprick sensation using 22G needle in various dermatome of respective nerves using a three-point scale.

Motor block was assessed by ability to oppose, abduct and adduct the thumb for median, radial and ulnar nerve respectively and ability to flex the elbow for musculocutaneous nerve.[1]

The time of onset for sensory and motor block was noted separately. Level of blockade was assessed every five min for the initial 20 min intraoperatively and then every 15 min postoperatively till the resolution of sensory and motor functions. During postoperative period, time for requirement of primary analgesic was noted.

Surgery was started after 30 min of giving the block to ease the evaluation of sensory and motor block. If there was incomplete loss of pinprick sensation in the ulnar, radial, musculocutaneous and median nerve distribution with minimal motor block 25 min after the local anesthetic injection, intravenous (IV) midazolam 2 mg, and fentanyl 2 mcg/kg IV were given. If patients complained of pain despite supplemental analgesia with fentanyl, general anesthesia was administered and they were excluded from the study.

The time gap between the local anesthetic drug administration and full sensory block was taken as sensory onset time. Duration of sensory block was defined as time taken for complete resolution of the sensory block in all dermatome.

The time gap between drug administration and complete motor block was taken as motor block onset time. Time for recovery of complete motor activity in the hand and forearm was taken as duration of motor block.

Visual analog scale (VAS) was used for assessment of pain postoperatively. When VAS score >4, Inj.paracetamol 1 gm iv infusion was given and the time of requirement of first analgesic was noted.

Any untoward effects like desaturation (SpO_2 less than 94%) was treated with supplemental oxygen through face mask. Fall in BP more than 20% from baseline was treated by the IV fluids if required iv vasopressors were also used. Bradycardia with heart rate of less than 50 beats/min was treated with atropine 0.6 mg iv. Any other untoward side effects were recorded.

Statistical analysis

Statistical analysis of data was done using Statistical Package for the Social Sciences (SPSS) Version 20.0 software. Independent Student *t*-tests were used to compare qualitative demographic variable and surgical time between two groups. Chi-square test was used to compare gender distribution in two groups. Data is considered as statistically significant if *p* value is less than 0.05. For outcome data with continuous variables and to measure the variation in outcome independent Student *t*-tests were used for statistical analysis.

Results

Demographic Data

As shown in Table 1, there was no statistical difference between the two groups in regards to age, weight, gender distribution and duration of surgery with a *p* value of 0.65, 0.696, 0.639, 0.32, respectively.

Chi-square test was used for American Society of Anesthesiologist (ASA) category distribution. The difference was statistically insignificant ($p = 0.577$).

Onset of sensory and motor block

As shown in Table 2, the onset of sensory block in Group LD (16.13 min) was earlier compared to Group L (19.05 min) and mean onset time of motor block in Group LD was 18 min compared to 23.13 min in Group L which was statistically significant ($p \leq 0.001$).

Duration of sensory block, motor block and analgesia

As shown Table 2, the mean duration of sensory block, motor block and analgesia was significantly prolonged in Group LD as compared to that in Group L which was statistically significant ($p \leq 0.001$).

Hemodynamic data

Heart rate

There was a statistically significant fall in heart rate between 25 min and 105 min in Group LD compared to Group L ($p < 0.05$). But there was no clinically significant bradycardia requiring treatment (Fig. 1).

Systolic blood pressure

There was a statistically significant fall in systolic blood pressure between 10 min and 480 min in Group LD compared to that in Group L ($p < 0.05$). But it was not significant clinically as none of the patients required vasopressors (Fig. 2).

Diastolic blood pressure

There was a statistically significant fall in diastolic blood pressure in Group LD compared to Group L between 10 min and 420 min ($p < 0.05$). But it was not significant clinically as none of the patients required vasopressors (Fig. 3).

Oxygen saturation

As shown in Figure 4, there was no fall in the oxygen saturation in either group.

Table 1: Demographic Data

Variables	Mean ± SD		*p* value
	Group L	Group LD	
Age	41.15 ± 15.22	39.5 ± 16.23	0.652
Weight	60.9 ± 5.945	60.33 ± 7.11	0.696
Gender			
Male	22	24	0.639
Female	13	11	
ASA			
I	15	16	0.557
II	19	16	
III	1	3	
Duration of Surgery (in min)	81.42 ± 17.23	85.98 ± 22.14	0.32

SD-Standard Deviation, ASA-American Society of Anesthesiologist

Table 2: Results Showing Onset of Sensory and Motor Block.

Variables	Mean ± SD (in min)		*p* value
	Group L	Group LD	
Onset of Sensory Block	19.5 ± 3.889	16.13 ± 4.001	<0.001
Onset of Motor Block	23.13 ± 3.37	18 ± 3.889	<0.001

Table 3: Results Showing Duration of Sensory Block, Motor Block and Duration of Analgesia

Variables	Mean ± SD (in min)		*p* value
	Group L	Group LD	
Duration of Sensory Block	494.38 ± 70.64	677.25 ± 9.54	<0.001
Duration of Motor Block	525.25 ± 70.23	710.88 ± 87.32	<0.001
Duration of Analgesia	576.88 ± 73.330	764 ± 110.23	<0.001

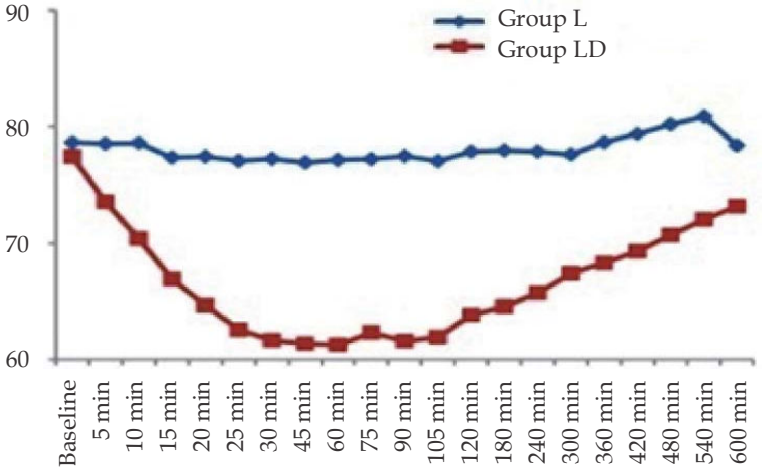

Fig. 1: Graph showing variation in the heart rate in both the groups

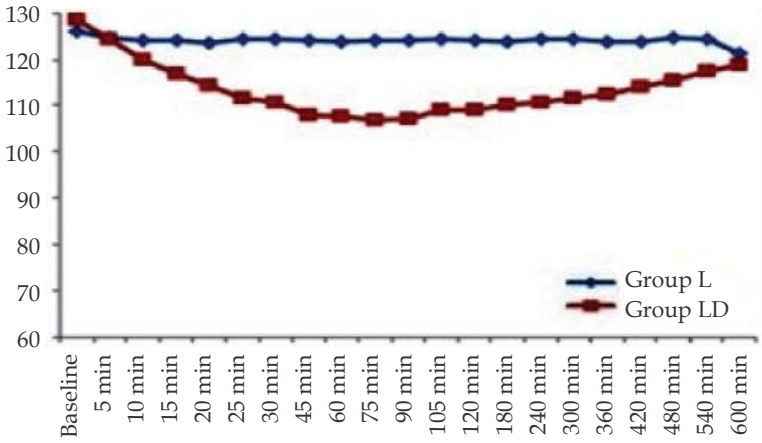

Fig. 2: Graphs showing variation in the systolic blood pressure in both the groups.

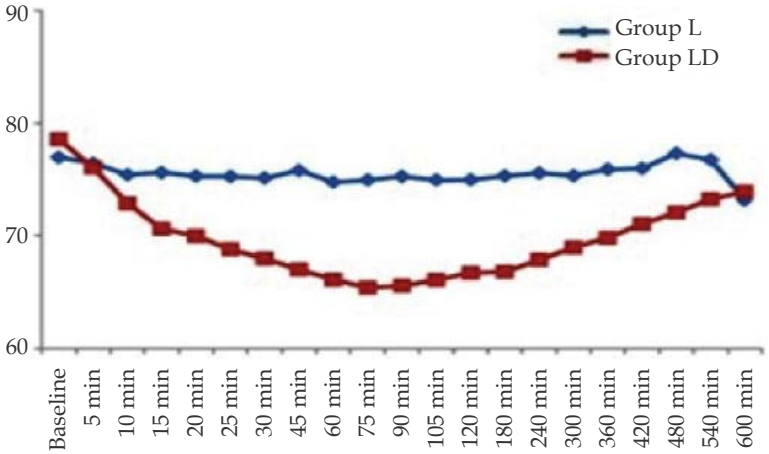

Fig. 3: Graphs showing variation in the diastolic blood pressure in both the groups

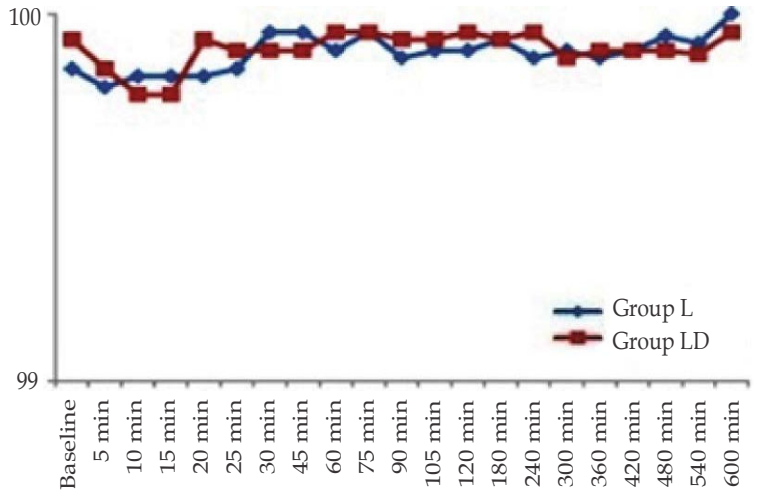

Fig. 4: Graphs showing variation in the oxygen saturation in both the groups

Discussion

The most commonly performed regional nerve block for surgeries on hand and forearm is the brachial plexus block. It offers many advantages over general anesthesia. Many complications like pneumothorax, vascular injuries which are common in interscalene, supraclavicular and infraclavicular brachial plexus block are less common in axillary brachial plexus block. Various anesthetic drugs have been used for axillary brachial plexus block. Different studies have compared bupivacaine, ropivacaine and levobupivacaine in brachial plexus block for upper limb surgery. Levobupivacaine is a good substitute for bupivacaine. Compared to ropivacaine, levobupivacaine provides a significantly longer duration of analgesia.[1] The long duration of sensory block associated with good analgesia and lesser cardiotoxicity than bupivacaine makes levobupivacaine a better choice for upper extremity blocks.

Local anesthetics along with adjuvant for axillary brachial plexus block intensify and extend the duration of block and analgesia.

Various parameters in demographic profile were comparable in both the groups. No patients in either group were excluded from the study.

In our study, we found that the mean onset time of sensory block was 16.13 ± 4.0 min in Group LD which was earlier and statistically significant ($p < 0.001$) than that in Group L which was 19.5 ± 3.8 min, and mean onset time of motor block was 18 ± 3.8 min in Group LD which was earlier andstatistically significant ($p < 0.001$) than that in Group L which was 23.13 ± 3.3 min (Table 2).

In this study, we demonstrated that addition of dexmedetomidine with levobupivacaine prolonged the duration of blockade and delayed the requisite for rescue analgesics (Table 3). Peripherally, alpha 2 agonists produce analgesia by reducing release of norepinephrine and causing alpha 2 receptor-independent inhibitory effects on nerve fiber action potentials. Centrally, alpha 2 agonists produce analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activation of alpha 2 adrenoceptors in the locus coeruleus.[2-3]

Abosedira[4] in his study compared the effect of adding either clonidine or dexmedetomidine to lidocaine during Bier's block and reported that adding dexmedetomidine to lidocaine during Bier's block provides better quality of anesthesia, tourniquet tolerance, and reduced intraoperative and early postoperative analgesic requirement than the addition of clonidine.

Brummett *et al.*[5] in their study showed that perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat

Brummett *et al.*[6] in their study showed that perineural injection of dexmedetomidine added to ropivacaine causes dose dependent increase in duration of thermal antinociception in sciatic nerve block in rats and also found that on histopathological examination of myelin sheath was normal in both groups, in the same study also showed dexmedetomidine acts peripherally by causing hyperpolarization of nerve fiber and preventing the nerve from subsequent depolarization from resting membrane action potential. Kosugi *et al.*[7]

concluded dexmedetomidine reduced amplitude of compound action potential without stimulating alpha-2 adrenergic receptors.

The effectiveness of peripheral dexmedotomedine for analgesia has been recognized. This effect is dose dependent (not mediated by central action).

Very few studies on humans have been conducted to know the effects of α_2 agonists in peripheral nerve block. However various studies have showed that dexmedetomidine can be used safely in spinal anesthesia and IV regional anesthesia.[8–10] With this background, we determined the effects of addition of dexmedetomidine with levobupivacaine in axillary brachial plexus block. Although dexmedetomidine has an α_2/α_1 selectivity ratio that is eight times higher than that of clonidine, an equipotent comparative study of both the drugs in peripheral nerve block was conducted by Sudheer *et al.*[11] and it demonstrated that dexmedetomidine as adjuvants to levobupivacaine in supraclavicular brachial plexus block shortened the onset time of both sensory and motor blockade. It also prolonged the duration of sensory and motor blockade as well as duration of analgesia when compared to clonidine.

Erlacher *et al.*[12] concluded that the addition of clonidine has a different impact on mepivacaine, bupivacaine and ropivacaine in terms of onset and duration of block and found that ropivacaine has vasoconstrictor properties. Addition of alpha-2 adrenergic agonist did not change the quality of sensory or motor blockade. Masuki *et al.*[13] suggested that dexmedetomidine induces vasoconstriction via alpha-2 receptors in the human forearm (around the site of injection) which might delay the absorption of local anesthetics thus prolonging their effects. Agarwal Sandhya *et al.*[14] in their study showed that dexmedetomidine prolongs the effect of bupivacaine in supraclavicular brachial plexus block.

Swami *et al.*[15] in their study showed that there was considerably enhanced duration of sensory and motor block of brachial plexus when dexmedetomidine was added to bupivacaine and the quality of block was comparable to that when clonidine was used as adjuvant. Prolongation of duration of blockade by dexmedetomidine reduced postoperative pain and requirement of post operative analgesics.

In our study none of the patients required sedation in group LD which can be explained by the fact that there is some amount of systemic absorption of dexmedetomidine.[16] Alpha-2 agonists act on dorsal horn neurons inhibiting the release of substance P in pain pathway and activate alpha-2 adrenergic receptors in locus coeruleus to produce sleep.

Limitation of study was the lack of facility for ultrasound guided blocks which could have helped us to reduce the volume and dosage of levobupivacaine, the block performance time and the number of needle passes. Though clonidine is preferred because of its low cost and is commonly used as an adjuvant compared to dexmedetomidine, we acknowledge that more study trials are essential to establish the cost-effectiveness and efficacy of dexmedetomidine compared to clonidine as an adjuvant in peripheral nerve blocks.

Conclusion

Dexmedetomidine used as an adjuvant to levobupivacaine provides more rapid onset of anesthesia and prolongs the duration of analgesia in axillary brachial plexus block and also provides expedient, simple, efficient anesthesia and painless postoperative period for foream and hand surgeries.

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