

Comparative Study of Varying Doses of Dexmedetomidine Combined with Levobupivacaine in Supraclavicular Brachial Plexus Block: A Randomized Double-Blind Prospective Study

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ABSTRACT

Background: Regional anesthesia is a recommended technique for upper and lower limb surgeries with better postoperative profile. The ideal dose of dexmedetomidine for brachial plexus block is a matter of debate. Few studies compared the effect of different doses of dexmedetomidine.

Aims and Objectives: This study was carried out to evaluate 50 µg or 100 µg of dexmedetomidine added to 0.5% levobupivacaine, with regard to the duration of analgesia.

Materials and Methods: 120 patients undergoing upper limb surgeries under supraclavicular brachial plexus block were randomly allocated into two groups. Group LD50 (n=60) received 29 ml of 0.5% levobupivacaine plus 50 µg of dexmedetomidine diluted in 1 ml of normal saline. Group LD100 (n=60) received 29 ml of 0.5% levobupivacaine plus 100 µg of dexmedetomidine diluted in 1 ml of normal saline. Duration of analgesia was the primary outcome observed.

Results: The duration of analgesia was significantly prolonged in group LD100 when compared to LD50 group (P = 0.001). Significantly fewer patients in group LD100 required rescue analgesia.

Conclusion: Dexmedetomidine 100 µg used for brachial plexus block showed quicker onset and prolonged duration of sensorimotor blockade and analgesia, but had higher incidence of bradycardia and sedation.

Key words: Anaesthesia, Brachial plexus block, Dexmedetomidine, Levobupivacaine

INTRODUCTION

Considerable research has been conducted over years in order to determine the ideal local anesthetic (LA) drug. An ideal drug should have a fast sensory onset, differential offset, with an earlier offset of motor than sensory blockade, enabling early ambulation/movements with prolonged analgesia. Several combinations of LAs and adjuvants such as tramadol, sufentanil, clonidine, and fentanyl have been employed in the search for near ideal agent, which remains elusive. Currently, levobupivacaine

(S(-)-enantiomer of bupivacaine) with favorable clinical profile and lesser cardiotoxicity when compared with racemic bupivacaine is being favored LA for regional block. [1-3]

Dexmedetomidine, an α_2 -receptor agonist, with α_2/α_1 selectivity 8 times than that of clonidine has also been reported to improve the quality of intrathecal and epidural anesthesia when used along with LA as adjuvant. [4,5]

The present study was conducted with the primary aim of assessing the

duration of analgesia of two different doses of dexmedetomidine, 50 and 100 µg added to 0.5% levobupivacaine, in patients posted for upper limb surgeries under supraclavicular brachial plexus block.

MATERIALS AND METHODS

After obtaining institutional ethics committee approval, We carried a randomized double blind controlled study on 120 patients of ASA PS I/II belonging to either sex, aged 18-50 years weighing between 50 - 70 kgs scheduled for elective upper limb surgeries of mid arm and fore arm after obtaining written informed consent. The study was done in the department of anesthesia at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana state, India, from March 2016 to March 2018.

Inclusion Criteria:

Patients undergoing elective upper limb surgeries of mid arm and fore arm

Exclusion Criteria:

1. Patients allergic to the drugs being used,
2. Patients with cardiac disease, hepatic or renal impairment, neuromuscular disorders, uncontrolled hypertension or diabetes mellitus, pregnancy, coagulopathy

A total of 120 patients were included in the study and randomly allocated to two groups (Group LD50 and Group LD100) by a computer-generated randomization chart. Group LD50 (n=60) received 29 ml of 0.5% levobupivacaine plus 50 µg of dexmedetomidine diluted in 1 ml of normal saline. Group LD100 (n=60) received 29 ml of 0.5% levobupivacaine plus 100 µg of dexmedetomidine diluted in 1 ml of normal saline.

Procedure:

Preoperative evaluation with complete history, clinical examination and routine investigations were carried out on all the patients. Intravenous (IV) access was established using an 18-gauge cannula. Sedation was provided by IV administration of midazolam 1 mg and fentanyl 30 µg before the block. Sensory and motor

blockade were assessed for every 2 minutes after completion of injection till 30 minutes and then for every 30 minutes until the block had completely worn off.

For sensory loss assessment, we used pinprick test with a 3-point scale: 0-no block, 1-analgesia (loss of sensation to pinprick) and 2 -loss of touch. Motor blockade was evaluated by the ability to flex the elbow and hand as: 0 - full flexion/extension movement in hand and arm against resistance, 1 - movement against gravity but not against resistance, 2 - flicker of movement in hand but not in arm and 3 - no movement (complete motor block). Onset of sensory blockade was defined as the interval between the end of injection and sensory blockade evidenced by loss of sensation to pinprick or by a score of 1 on pinprick response. Onset of motor blockade was the interval between the end of injection and complete motor paralysis of wrist and hand.

The duration of sensory blockade was defined as the time interval between sensory blockade and reappearance of the pinprick response. The duration of motor blockade was defined as the time interval between maximum motor blockade and complete movement of wrist and fingers. Duration of analgesia was taken as the time interval between the onset of sensory blockade and the first dose of rescue analgesic given to the patient. Post-operative pain was assessed using VAS (0 - no pain to 10 - worst pain) for every hour till the block lasted. Post-operative heart rate (HR), systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP) and SpO₂ were recorded for every 2 hours for the first 6 hours and thereafter for every 4 hours till the need for rescue analgesia. Rescue analgesia was provided with injection diclofenac sodium 75 mg intramuscularly when VAS \geq 3 cm. The time between the complete sensory block and the first analgesic request was recorded as the duration of analgesia. ^[1]

The incidence of side effects (bradycardia, hypotension and sedation) was

also recorded. Sedation score was assessed according to the modified Ramsay Sedation scale from 1 to 6 as follows: 1 = Anxious, agitated, restless; 2 = Cooperative, oriented, tranquil; 3 = Responds to commands only; 4 = Brisk response to light glabellar tap or loud noise; 5 = Sluggish response to light glabellar tap or loud noise and 6 = No response. Bradycardia was defined as a decrease in HR by 20% from the baseline value or an absolute HR <50 beats per min; which was managed by 0.5 mg IV bolus of atropine. [6]

Statistical Analysis:

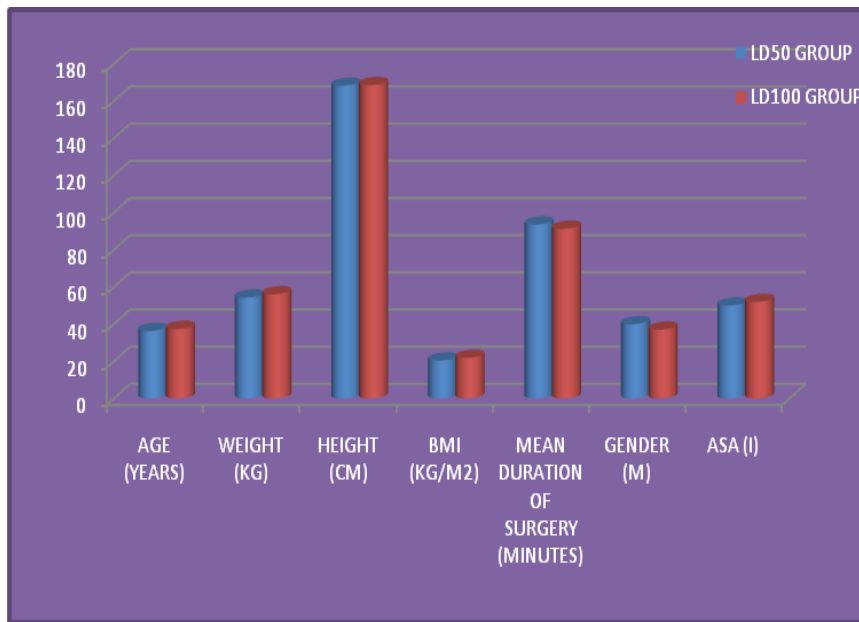
Data were expressed as mean±SD and analyzed by software SPSS Version 20 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY: USA). Chi-square test and independent two sample ‘t’-test for unpaired samples were used. A P value <0.05 was considered as significant.

RESULTS

Demographic variables were comparable with respect to age, height, weight, BMI, sex ratio, ASA physical status and the duration of surgery [Table 1 and Graph 1].

Table 1: Demographic Data

VARIABLES	LD50 GROUP	LD100 GROUP	P VALUE
AGE (YEARS)	36.3±7.20	37.4±6.63	0.3858
WEIGHT (KG)	54.3±8.1	56.1±4.2	0.1292
HEIGHT (CM)	168.3±6.2	168.6±7.1	0.8057
BMI (KG/M ²)	20.4±8.1	21.9±1.5	0.1610
MEAN DURATION OF SURGERY (MINUTES)	93.6±20.3	91.3±23.7	0.5691
GENDER (M/F)	40/20	37/23	0.547
ASA (I/II)	50/10	52/8	0.721

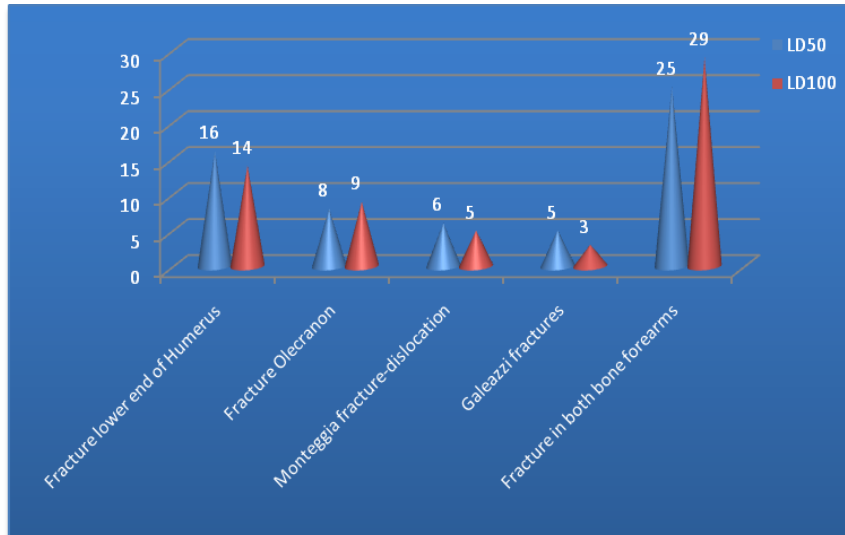


Graph 1: Demographic Data

There was no statistical significance in baseline haemodynamic parameters and type of fractures between the two groups (Table 2 and Graph 2: Table 3 and Graph 3: P > 0.05).

Table 2: Type of fractures in the patients studied

TYPE OF FRACTURE	LD50 GROUP		LD100 GROUP		P VALUE
	NO.	%	NO.	%	
Fracture lower end of Humerus	16	26.66	14	23.33	0.6749
Fracture Olecranon	8	13.33	9	15	0.7939
Monteggia fracture-dislocation	6	10	5	8.33	0.7522
Galeazzi fractures	5	8.33	3	5	0.4665
Fracture in both bone forearms	25	41.66	29	48.33	0.4646
Total	60	100	60	100	-

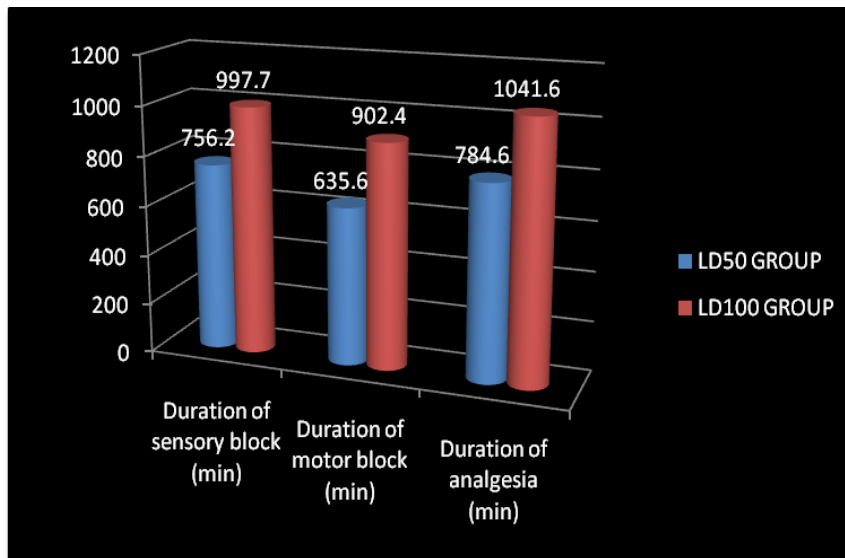


Graph 2: Type of fractures in the patients studied

Table 3: Characteristics of Blocks:

Parameter	LD50 GROUP	LD100 GROUP	P VALUE
Onset of sensory block (min)	12.8±3.2	8.2±1.7	<0.0001
Onset of motor block (min)	17.8±6.3	14.3±4.2	0.0005
Duration of sensory block (min)	756.2±138.5	997.7±102.3	<0.0001
Duration of motor block (min)	635.6±187.6	902.4±122.8	<0.0001
Duration of analgesia (min)	784.6±139.8	1041.6±140.2	<0.0001

Characteristics of block in each



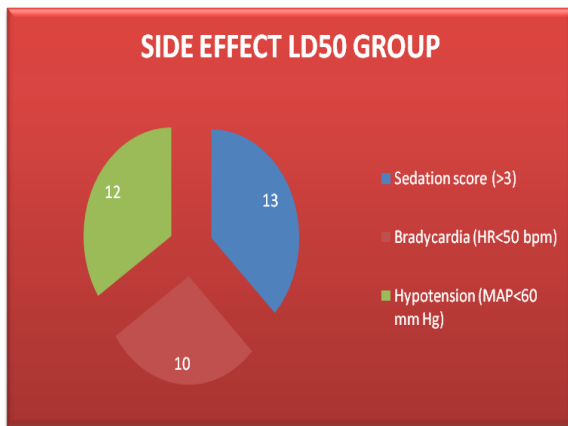
Graph 3: Characteristics of Blocks:

Rescue analgesia in the form of diclofenac sodium injection was needed in 20 patients (33.33%) in Group LD50 and 9 patients (15%) in group LD100.

The incidence of adverse effects namely sedation and bradycardia was significantly higher in group LD100 compared with group LD50 [Table 4 and Graph 4].

Table 4: Side Effects In Two Groups

SIDE EFFECT	LD50 GROUP		LD100 GROUP		P VALUE
	No.	%	No.	%	
Sedation score (>3)	13	21.66	30	50	0.0013
Bradycardia (HR<50 bpm)	10	16.66	24	40	0.0047
Hypotension (MAP<60 mm Hg)	12	20	18	30	0.2078



Graph 4: Side Effects in Two Groups

DISCUSSION

Dexmedetomidine is an α_2 -adrenoreceptor agonist with excellent analgesic properties and wide margin of safety. It has α_2/α_1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine. This high selectivity for α_2 receptors makes it more effective as a sedative and analgesic agent while minimising the unwanted effect of α_1 receptor stimulation. [1-3]

Agarwal et al compared equal doses (1mcg/kg) of clonidine and dexmedetomidine in peripheral nerve block and concluded that that dexmedetomidine is more efficient than clonidine in improving block characteristics. [7]

The mechanism by which dexmedetomidine affects the nerve block is multi-factorial. Peripherally, it acts by inhibiting the release of nor-epinephrine and also by direct effect on nerve action potential. Centrally, it acts by activation of α_2 -adrenoreceptors of locus coeruleus and by inhibiting the release of substance P. [8]

We found that addition of 100 μ g dexmedetomidine to 0.5% levobupivacaine produces longer duration of analgesia compared to 50 μ g dexmedetomidine in supraclavicular brachial plexus block. The higher dose of dexmedetomidine also hastens the onset and prolongs the duration of sensory and motor block. Fewer patients (15%) in group LD100 required diclofenac sodium injection as rescue analgesic than patients (33.33%) in group LD50.

The incidence of bradycardia was observed in more patients in LD100 group, compared to LD50 group. The higher dose of dexmedetomidine caused more sedation.

Brummett et al. found that dexmedetomidine enhanced the duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any evidence of histopathological damage to the nerve. [9]

Kosugi et al. found that high concentrations of dexmedetomidine inhibit compound action potential (CAP) in frog sciatic nerves without α_2 adrenoceptor activation. [10]

Marhofer et al compared three drug regimens with ropivacaine 0.75%, interaction of ropivacaine 0.75% with systemic dexmedetomidine or perineural dexmedetomidine on ulnar nerve block. Onset of motor block was faster, and the duration of motor block was significantly prolonged by the perineural administration of dexmedetomidine. [11]

Zhang et al. reported prolonged duration of analgesia in patients who received a higher dose of dexmedetomidine (100 μ g) in 40 ml of 0.33% ropivacaine when compared to 50 μ g of dexmedetomidine in axillary brachial plexus block. [12]

Esmaoglu et al. concluded that dexmedetomidine (100 μ g) when used as an additive to 40 ml of 0.5% levobupivacaine prolonged axillary brachial plexus block duration. [13]

Keplinger et al. assessed the dose dependency of dexmedetomidine when added to ropivacaine for peripheral nerve blockade. [14] There was a significant dose-dependent increase in the mean duration (SD) of analgesia with dexmedetomidine and the sedation was also enhanced in a dose-dependent manner. These results are similar to the results of our study. The analgesic effect of levobupivacaine in supraclavicular brachial plexus block was potentiated in a dose-dependent manner by adjuvant dexmedetomidine. In our study, fewer

patients in LD100 group required diclofenac sodium injection as rescue analgesia ($P < 0.05$). This finding correlates with the studies of Kaygusuz et al. [15]

CONCLUSION

In this double blinded comparative study, 100µg dexmedetomidine added to levobupivacaine in brachial plexus block produces a longer duration of analgesia than 50 µg. The higher dose also hastens the onset and prolongs the duration of sensorimotor blockade, but produces higher incidence of bradycardia, which requires close monitoring.

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