



Original Research Article

Comparison of levobupivacaine alone and levobupivacaine with dexmedetomidine in supraclavicular brachial plexus block: A prospective randomized clinical trial

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ABSTRACT

Introduction and Aim: Supraclavicular brachial plexus block is the most suitable mode of anaesthesia for various upper limb surgeries. Dexmedetomidine added to local anaesthetics shortens the onset time and prolongs the duration of block and post-operative analgesia in the brachial plexus block. However, there remains limited knowledge of its analgesic efficacy and duration in peripheral nerve and nerve plexus blockade.

Materials and Methods: This prospective randomized double-blinded study was conducted with 60 patients of ASA physical status class I/II, scheduled for elective unilateral upper limb surgery. Patients were randomized into 2 groups of 30 each. All patients in Group L received a brachial plexus block with 29 ml of 0.5% levobupivacaine + 1ml of normal saline. Group LD received 29 ml of 0.5% levobupivacaine + 1ml of dexmedetomidine 1ml(100mcg). The primary objectives were the onset and duration of sensory and motor block.

Results: The onset of sensory and motor block was earlier in Group L (12.4 ± 3.1 min and 20.5 ± 3.8 min) than Group LD (15.9 ± 2.7 min and 22.1 ± 3.2 min), (P = 0.0000 and 0.0801). The duration of sensory and motor block was longer in Group LD (1198.0 ± 48.5 min and 1178.3 ± 41.4 min) than Group L (710.3 ± 87.3 min and 688.7 ± 86.6 min), (P = 0.0000). The duration of analgesia was longer in Group LD (1222.0 ± 49.2 min) than Group L (726.3 ± 91.1 min), (P < 0.0001).

Conclusion: Dexmedetomidine added with levobupivacaine prolongs the duration of sensory as well as motor block in brachial plexus block using the supraclavicular technique with haemodynamic stability.

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1. Introduction

Supraclavicular brachial plexus block is a most suitable mode of anaesthesia for various upper limb surgeries, due to its effectiveness in terms of better margin of safety in high-risk patients, cost-effective, adequate post-operative analgesia with faster recovery, early mobilization, reduced incidences of post-operative thromboembolic and various other complications. The supraclavicular approach gives the most effective block for upper extremity and is carried out at the level of trunks of brachial plexus. The plexus is blocked where it is most compact i.e. at the middle of brachial plexus, resulting in a homogenous spread of anaesthetic

throughout the plexus with a fast onset and complete block.¹

A variety of local anaesthetic has been used for the brachial plexus block. Levobupivacaine is a local anaesthetic with long-duration having similar pharmacology to bupivacaine however, it has a wider safety margin and was shown to possess less cardiotoxicity in comparison with bupivacaine.² Dexmedetomidine, a selective α_2 -adrenoceptor agonist has been used as an adjuvant during regional and local anaesthesia.³ Several studies have shown the efficacy of adding dexmedetomidine to local anaesthetic procedures, such as subarachnoid, epidural, and caudal injections. Dexmedetomidine added to local anaesthetics shortens the onset time and prolongs the duration of block and post-operative analgesia in brachial plexus block.⁴⁻⁸ However, there remains limited knowledge of its analgesic

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efficacy and duration in peripheral nerve and nerve plexus blockade. Therefore, the present study was designed to investigate the efficacy of dexmedetomidine as an adjuvant with levobupivacaine. The primary objectives were the onset and duration of sensory and motor block while secondary objectives were the duration of analgesia, haemodynamic changes, and complication if any.

2. Materials and Methods

This prospective randomized double-blinded study was conducted at Mahatma Gandhi Medical College and Hospital, Jaipur after obtaining permission from the institutional ethics committee. Written informed consent was obtained from all the patients enrolled in the study. All the patients were explained about the procedure, the drug, the advantage, and the disadvantages and that they have the right to deny. Those denying the consent were not included in the study.

Sixty patients aged 18-70 years belonging to the American Society of Anaesthesiologists (ASA) physical status class I/II and scheduled for elective unilateral upper limb surgery (mid humerus to the entire forearm) were enrolled in the study. Exclusion criteria were patients with severe renal, hepatic, respiratory and cardiac disease, neurological deficits involving brachial plexus, psychiatric illness, intake of sedatives, antipsychotics, and antiepileptic drugs, any bleeding disorder or patient on anticoagulants; obesity and drug allergy. Likewise, pregnant, lactating females were excluded from the study.

All the enrolled patients were randomly divided into two equal groups using a computer-generated list. The group assignment was enclosed in an opaque and sealed envelope to ensure adequate concealment of allocation sequence. The sealed envelope was opened only by an anaesthesiologist who was not involved in the study but according to randomization prepared the drug solution. The anaesthesiologist responsible for performing the block procedure and observing the study outcomes was blinded to the treatment group. Anaesthesiologist responsible for data collection was also unaware of the group allocation. Patients were assigned randomly to one of the two equal groups. Group L (levobupivacaine group) received 0.5% levobupivacaine (150 mg) 29 ml + normal saline 1 ml. Group LD (levobupivacaine + dexmedetomidine group) received 0.5% levobupivacaine (150 mg) 29 ml + dexmedetomidine (100mcg) 1 ml.

All the patients were visited and evaluated thoroughly on the day before the surgery. The 10 cm visual analogue scale (VAS) (0, no pain and 10, worst possible pain) and paraesthesia were explained to the patients and attempts were made to alleviate the anxiety of the patient. All the patients received oral alprazolam 0.5 mg night before surgery.

On the day of surgery, standard 5 leads ECG, non-invasive blood pressure and pulse oximetry were attached and baseline parameters were recorded. Venous access was secured using an 18 G cannula on the dorsum of the limb opposite to that undergoing surgery. Supplemental oxygen was administered to all the patients through a nasal cannula at 4 L/min. For block performance, the patients were placed supine with the head turned 45 degrees to the contralateral side. The arm to be anaesthetized was adducted, and the hand extended along the side towards the ipsilateral knee as far as possible. A sand bag was placed beneath the shoulder. The midpoint of the clavicle was identified and marked. The posterior border of the sternocleidomastoid was palpated easily when the patient raised the head slightly. Thereafter, palpating the belly of the anterior scalene muscle moving towards interscalene groove with the fingers, a mark was made at approximately 1.5 to 2.0 cm posterior to the midpoint of the clavicle. By palpating the subclavian artery at this site, the landmark was confirmed. Under all aseptic precautions, the local site was prepared. After appropriate preparation, skin wheal was raised at the entry point with 2% xylocaine solution 2ml, 22-gauge needle was inserted at the point of entry above the midpoint of clavicle in the backward-inward-downward (BID) direction. The point of paraesthesia in the forearm was elicited and was the site for injection. After a negative aspiration for air or blood, the study drug was deposited.

Assessment of sensory and motor blockade was done for every 5 min post block performance till 30 min and then at an interval of 30 min post-surgery till the first 12 hours, thereafter assessment was done at every hour until the block had worn off completely. For assessment of sensory loss, we employed a pin-prick test using a 3-point scale: 1- no block, 2-loss of sensation to pin-prick, and 3-loss of touch sensation. Evaluation of motor blockade was done by the ability to freely flex the elbow and hand as 0- full range of flexion/extension movement against resistance in hand and arm, 1- ability to move against gravity but inability to move against resistance, 2- presence of flicker of movement in hand but absence of flicker of movement in arm and 3- no movement possible (complete motor block).

The onset of sensory blockade was defined as the time period between the point of end of injection of drug and evidence of sensory blockade by attainment of loss of sensation to pin-prick or by a pin-prick response score of 2. The onset of motor blockade was defined as the time period between the point of the end of injection of drug and attainment of complete motor paralysis of wrist and hand. The duration of the sensory block was defined as the time period between the appearance of a grade-1 block on pin-prick to the point to regression from complete grade-3 sensory block to grade-1 block on pin-prick. The duration of motor blockade was defined as the time point between the maximum motor blockade and point of complete movement

of wrist and fingers. Duration of analgesia was evaluated as the time period between the onset of sensory blockade and the first dose of analgesic administered to the patient. A complete block was considered when grade- 3 sensory anaesthesia with a grade- 3 motor block was achieved and only these patients were considered for further study. Patients with a sensory block of grade- 1, 2 or motor block of grade- 0, 1 and 2 were considered as block failure and were converted to general anaesthesia and hence were excluded from further analysis.

Post-operative pain assessment was done using a visual analogue scale (VAS) (0-no pain to 10- worst possible pain) for every hourly until the block lasted. Post-operative heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) were recorded for every two hourly for the first six hours and thereafter for every four hourly till the need for rescue analgesia. Rescue analgesia was provided using an intramuscular injection of diclofenac sodium 75 mg when VAS \geq 4. The time interval between the attainment of complete sensory block and the request for the first analgesic was recorded as the duration of analgesia.

The incidence of complications (bradycardia, hypotension, respiratory depression, etc.) was also recorded. Bradycardia was defined as a reduction in heart rate by 20% from the baseline value or an absolute heart rate $<$ 50 beats per min; which was treated by IV bolus of atropine 1 ml. Hypotension was defined as a decrease in blood pressure by 20% from the baseline or an absolute mean blood pressure $<$ 60 mmHg; which was treated by administration of IV crystalloids (200 ml bolus) or incremental dosage of mephentermine 3 mg IV.

2.1. Statistical Analyses

Assuming, a 30 min difference in prolongation of sensory analgesia and taking the power of study at 90% by keeping type I error ($\alpha = 0.05$) and type II error (β) at 0.1, the sample size was calculated at 28 patients in each group. We enrolled 30 patients in each group for better validation of study results.

Statistical analysis was performed using SPSS, version 19.0 for Windows statistical software package (SPSS Inc, Chicago, IL, USA). Chi-square test was applied for age, sex, and ASA grades. Unpaired t -test was applied for other demographic data, haemodynamic parameters, onset and duration of sensory/motor blockade, and duration of analgesia. P - value was considered significant if $<$ 0.05 and highly significant if $<$ 0.001.

3. Results

A total of sixty patients were enrolled in our study and none were excluded as shown in the consort chart [Figure 1]. Demographic data, systolic, diastolic, mean

arterial pressure, heart rate, sensory and motor block onset time and block duration, duration of analgesia (time to rescue analgesia), and complications were recorded for each patient.

Patients between the two groups were demographically comparable [Table 1]. The onset of sensory and motor block was earlier in Group L (12.4 ± 3.1 min and 20.5 ± 3.8 min) than Group LD (15.9 ± 2.7 min and 22.1 ± 3.2 min) and the difference were statistically significant ($P = 0.0000$ and 0.0801). The duration of sensory and motor block was longer in Group LD (1198.0 ± 48.5 min and 1178.3 ± 41.4 min) than Group L (710.3 ± 87.3 min and 688.7 ± 86.6 min), and the difference were also statistically significant ($P = 0.0000$). The duration of analgesia was longer in Group LD (1222.0 ± 49.2 min) than Group L (726.3 ± 91.1 min), and the difference is statistically significant ($P < 0.0001$) [Table 2].

The haemodynamic parameters (heart rate, systolic, diastolic and mean blood pressure) were well maintained within the presumed range of significant variation, i.e., 20% from baseline throughout the surgery. There was no significant difference in haemodynamic parameters in both the groups at any time point [Tables 3, 4, 5 and 6].

In the Group LD, one patient had hypotension and two patients had an episode of bradycardia. None of the patients of either group had arrhythmia, convulsions, nausea, vomiting, respiratory depression or pneumothorax [Table 7]. Out of the total thirty participants included in each study group, none had to be dropped off.

4. Discussion

In our study, we observed that the addition of dexmedetomidine to levobupivacaine although significantly prolonged the onset time for both sensory and motor block but it also prolonged the offset time for both sensory and motor block. Therefore, the duration of post-operative analgesia was also prolonged. Additionally, there were no significant haemodynamic fluctuations or complications with the addition of dexmedetomidine.

The onset, spread, duration, and quality of anaesthesia depends upon the type of local anaesthetic agent, concentration, dose, volume, and physical modifications. Levobupivacaine is the S-enantiomer of bupivacaine and has less neural and cardiac toxicity than bupivacaine. Hence, is currently the closest to the ideal neural blocking agent; however, a large volume of drug is required for adequate block.⁹

There are many adjuvants that are widely used like clonidine, fentanyl, tramadol, midazolam, ketamine, verapamil, etc. Dexmedetomidine has peripheral analgesic action [16] and thereby can potentially increase the onset and duration of sensory and motor block as well as analgesia.

Table 1: Distribution of demographic data among the studied groups

Parameters	Mean±SD		
	Group L (n=30)	Group LD (n=30)	
Age (years)	36.9±14.5	33.9±11.3	0.3857*
Sex (%)			
Male	18 (60)	18 (60)	1*
Female	12 (40)	12 (40)	
Weight (kg)	66.8±7.7	69.7±6.7	0.1296#
Duration of surgery (min)	118±7.4	121±5.6	0.0819#
ASA grade (%)			
I	19	18	0.606*
II	11	12	

*Chi-square test; #Unpaired t-test. n – Number of patients; SD – Standard deviation; ASA – American Society of Anesthesiologists

Table 2: Comparison of block outcomes in between the groups

Parameters		Group L (n=30)		Group LD (n=30)		P*
		Mean	SD	Mean	SD	
Onset of	Sensory block	12.4	3.1	15.9	2.7	< 0.0001
	Motor block	20.5	3.8	22.1	3.2	0.083
Duration of	Sensory block	710.3	87.3	1198	48.5	< 0.0001
	Motor block	688.7	86.6	1178.3	41.4	< 0.0001
Duration of analgesia		726.3	91.1	1222	49.2	< 0.0001

*Unpaired t-test. SD – Standard deviation.

Table 3: Comparison of heart rate in different time interval in between groups

Heart Rate	Group L		Group LD		P*
	Mean	SD	Mean	SD	
Baseline	83.9	7.2	84.5	5.6	0.7341
Immediately after block	83.7	6.7	81.9	6.2	0.2935
5 min after block	82.5	5.8	82.4	4.1	0.9187
10 min	82.2	6	84.6	3.6	0.0675
20 min	84.1	4.5	83.7	5.2	0.7909
30 min	83	4.6	83.8	3.8	0.4642
1 hour	83.7	4.2	81.8	14.4	0.5086
3 hours	83.4	4.9	84.7	2.1	0.1928
6 hours	85.2	2.5	85.9	2.5	0.242
12 hours	83.6	4.5	84.4	3.5	0.4445
24 hours	84.8	3.2	85.9	3.3	0.2096

*Unpaired t-test. SD – Standard deviation

Table 4: Comparison of SBP in different time interval in between groups.

	Group L		Group LD		P*
	Mean	SD	Mean	SD	
Baseline	130.2	7.6	128	4.6	0.1802
Immediately after block	129.3	7.1	129.8	5.3	0.774
5 min after block	125.9	7.7	124.4	4.8	0.3612
10 min	128.6	7.8	127.9	5.4	0.6876
20 min	127.4	7.6	128.5	5.5	0.5233
30 min	130.5	9.2	129.6	5	0.6536
1 hour	128.9	5.7	127.3	4.4	0.2285
3 hours	126.8	6.5	128.3	6.3	0.3678
6 hours	127.9	6.9	128.7	4.5	0.5968
12 hours	127.5	6.4	126.9	5.4	0.7288
24 hours	124.3	6.3	126.1	4.9	0.2211

*Unpaired t-test. SBP – Systolic blood pressure, SD - Standard deviation

Table 5: Comparison of DBP in different time interval in between groups

DBP	Group L		Group LD		P*
	Mean	SD	Mean	SD	
Baseline	85.6	2.8	85.9	2.9	0.7216
Immediately after block	84.4	4.7	84.1	4.2	0.7953
5 min after block	82.6	4.7	79.4	9	0.0957
10 min	82.3	5.9	80.7	6.6	0.3289
20 min	81.6	6.3	80.1	5.9	0.3451
30 min	80.2	8.9	79.7	4.2	0.7818
1 hour	82	2.9	81.5	7.3	0.7286
3 hours	80.8	7.9	80.6	6.4	0.9146
6 hours	79.8	5.3	81.1	4.1	0.2924
12 hours	78.5	8.5	81.8	6.4	0.0973
24 hours	75.3	7.4	74.2	4	0.4515

*Unpaired t-test. DBP – Dystolic blood pressure, SD - Standard deviation

Table 6: Comparison of MBP in different time interval in between groups

MBP	Group L		Group LD		P*
	Mean	SD	Mean	SD	
Baseline	97.6	3	98.2	2.6	0.4112
Immediately after block	94.9	4.2	96.1	3	0.2079
5 min after block	97	4.6	94.4	6.2	0.0689
10 min	95.6	4.4	96.4	4.8	0.5037
20 min	94.8	5.2	96.3	4.6	0.2514
30 min	93.2	7.8	92.3	3.4	0.5646
1 hour	95	2.8	96.8	5.1	0.0955
3 hours	94.8	6.3	93.2	5.1	0.2841
6 hours	98.5	3.1	99	3.2	0.5593
12 hours	94.8	5.6	96.8	4.1	0.1203
24 hours	91.7	5.5	91.5	3	0.8772

*Unpaired t-test. MBP – Mean blood pressure, SD - Standard deviation

Table 7: Distribution of complications

Complications	Group L	Group LD
Bradycardia	0	2
Hypotension	0	1
Nausea/Vomiting	0	0
Arrhythmia	0	0
Convulsion	0	0
Respiratory depression	0	0
Patchy block	0	0
Pneumothorax	0	0

In a meta-analysis by Abdallah and Brull,¹⁰ and several randomized trials conducted by Biswas et al.,¹¹ Esmoglu et al.,¹² and Kaur et al.¹³ dexmedetomidine was used as an adjuvant to the local anaesthetic agent for blocking the brachial plexus. It was reported that the addition of dexmedetomidine decreased the block onset time, increasing the overall duration of both motor and sensory effects, and prolonged post-operative analgesia. These results were similar to the results of our study.

Recently, Kaygusuz et al.¹⁴ analyzed the use of dexmedetomidine 1 µg/kg with 0.5% levobupivacaine

in patients requiring axillary brachial plexus block and reported a statistically significant reduction in onset of sensory block time, an increased duration of sensory and motor block effect, and extended time to rescue analgesic administration. In our study using dexmedetomidine 100 µg with 0.5% levobupivacaine, we also observed a similar effective profile of dexmedetomidine.

Ammar et al.¹⁵ and Agarwal et al.,¹⁶ compared bupivacaine alone and with dexmedetomidine and reported an increase in onset and duration of sensory and motor blockade, duration of analgesia, with decreased VAS pain

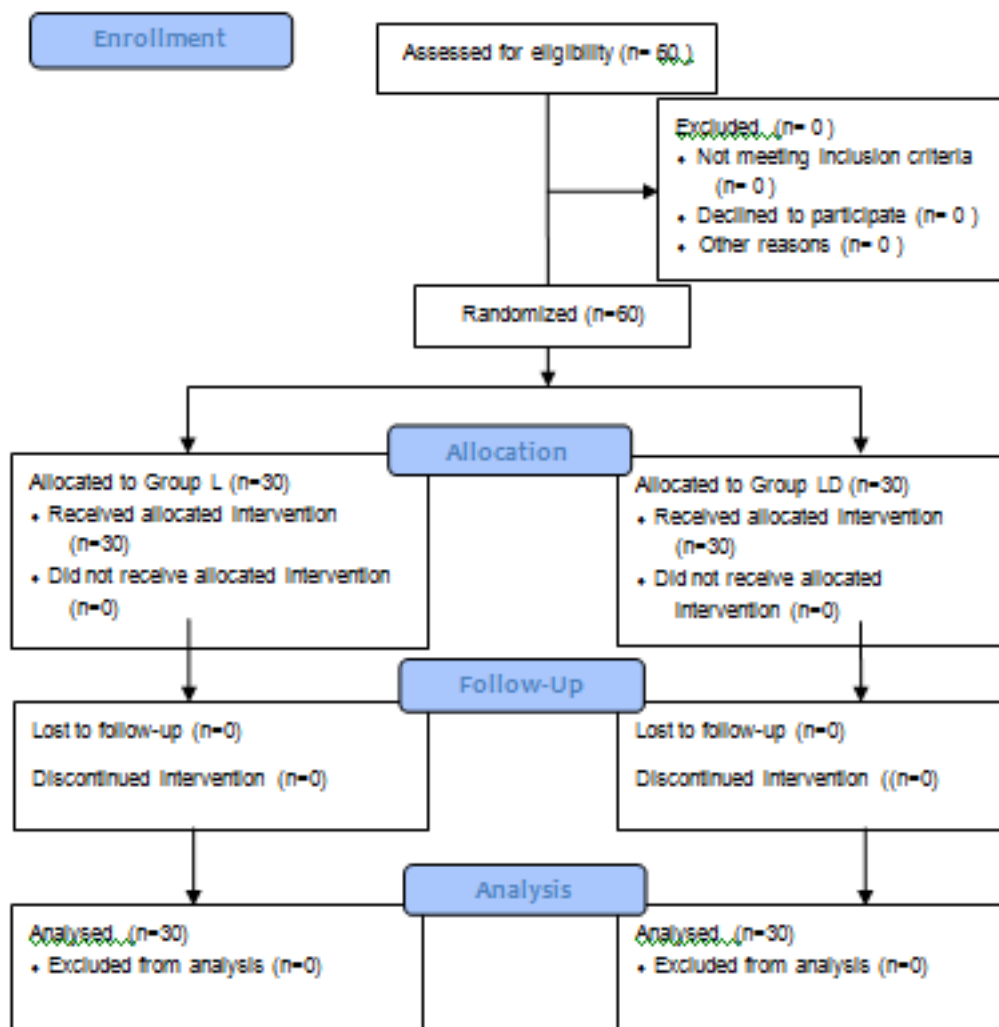


Fig. 1: Consort flow diagram

scores, and augmented supplemental opioid demands.

Dexmedetomidine in an increased dosage may be responsible for complications such as hypotension, bradycardia, anxiety and sedation.^{15,16} Among the complications, hypotension was seen in 1 patient which was treated appropriately with doses mephentermine 3 mg IV bolus. Two patients of Group LD had an episode of bradycardia and both of them responded well to atropine. The reduction in blood pressure was due to the central sympathetic outflow inhibition. The alpha-2 receptors of the presynaptic region are also excited by dexmedetomidine, thereby reducing the release of norepinephrine and leading to hypotension and bradycardia. In our study, no significant complications among both groups were observed.

The major limitation of our study was the inability to analyze biochemically the blood concentration of dexmedetomidine and levobupivacaine, which would have

supported our observations. Further randomized trials need to be conducted to validate the findings of our study.

We conclude that dexmedetomidine added with levobupivacaine prolongs the duration of sensory as well as motor block in brachial plexus block using the supraclavicular technique with haemodynamically stability.

5. Source of funding

None.

6. Conflict of interest

None.

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