Original Research Article

A Comparative Study Using Dexmedetomidine and Clonidine as Adjuvants with Levobupivacaine in Axillary Brachial Plexus Block for Upper Limb Surgeries

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Abstract

Introduction: The axillary approach to the brachial plexus is the most popular because of its ease, reliability, and safety. Blockade occurs at the level of the terminal nerves. Alpha2-agonists are mixed with local anaesthetic agents to extend the duration of spinal, extradural and peripheral nerve blocks. The aim of the study is to compare the effects of clonidine and that of dexmedetomidine as adjuvants to levobupivacaine in axillary brachial plexus block. The onset time and duration of sensory and motor block, duration of analgesia, sedation score and haemodynamic parameters were studied in both groups. **Methods:** A prospective, double blinded, randomized clinical study was conducted at Department of Anaesthesia, Kamineni Academy of Medical Sciences and Research Center on eighty ASA class I and II adult patients undergoing upper limb surgeries under ultrasound guided axillary brachial plexus block. Patients were randomly divided into two equal groups, group LD (n=40): will receive 25ml of 0.5 % of levobupivacaine +1 µg/kg dexmedetomidine, and group LC (n=40) will receive 25ml of 0.5 % levobupivacaine +1 µg/kg of clonidine. The whole solution made up to 30 ml in each group by adding sterile water for injection. Haemodynamic parameters (heart rate, non invasive blood pressure, oxygen saturation), onset time and duration of sensory, motor block, duration of analgesia and, sedation score were recorded and then compared between the groups. **Results:** There was no statistically significant difference (P>0.05) in haemodynamic parameters. Onset time of sensory and motor block were significantly faster (P<0.05), duration of sensory and motor block and duration of analgesia significantly longer (P <0.05) in dexmedetomidine group (group LD) when compared to clonidine group (group LC). The sedation scores were also better in group LD (P<0.05). **Conclusion:** Dexmedetomidine is a better adjuvant than clonidine when added to levobupivacaine in axillary brachial plexus block, as it hastens the onset time of sensory and motor block, prolongs the duration of sensory and motor blockade as well as the duration of analgesia, with better intraoperative sedation without causing any haemodynamic variations.

Keywords: Axillary brachial plexus block; clonidine; dexmedetomidine; levobupivacaine.

Introduction

"For all the happiness mankind can gain is not in pleasure but in rest from pain"- John Dryden. Regional anaesthetic techniques are as successful as general anaesthesia in alleviating pain during various surgical procedures[1]. Peripheral Nerve Block has advantages of a single shot PNB (Peripheral Nerve Block) like rapid onset, predictable and dense anaesthesia, a relatively simpler technique, good muscle relaxation, adequate postoperative analgesia and sympathetic block. The sympathetic block decreases postoperative pain, vasospasm and oedema. It also means early ambulation, early oral intake, avoiding intubation and its complications with lesser systemic side effects and fewer postoperative effects[2].

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Among the various PNB, Brachial Plexus Block (BPB) is one of the most commonly practiced blocks. The various local anaesthetics used in axillary block are quite effective but the duration of analgesia is a major limiting factor[3]. There has always been a search for adjuvants which can be added to the local anaesthetics in peripheral nerve block to improve the duration and quality of analgesia but without producing any major adverse effects. Various studies have investigated several adjuncts, including opioid, neostigmine, hyaluronidase, dexamethasone etc[4].

Since their synthesis, α-2 adrenergic receptor agonists have been used intrathecally, epidurally or as part of peripheral nerve blocks either alone or in conjunction with local anaesthetics in an attempt to prolong the duration of analgesia and to improve the quality of the block[5].

Clonidine, the older drug is a selective α-2 adrenergic agonist with some α-1 agonist property. In clinical studies, the addition of clonidine to local anaesthetic solutions has shown produce anti-nociception and enhance the effect of local anaesthetics. Clonidine produces this effect by reduction in the onset time of the block and a more efficient peripheral nerve block with longer post operative analgesia[6]. Dexmedetomidine, the newer drug, is a potent α-2 adrenoceptor agonist, and about eight-times more selective towards the α-2 adrenoceptor than clonidine. In previous clinical studies, administration of intravenous dexmedetomidine has shown to produce significant opioid sparing effects as well as a decrease in inhalational anaesthetic requirements. In humans, it has been used in various

strengths as an adjunct to local anaesthetics to prolong the duration of block and postoperative analgesia in various peripheral blocks[7].

Very few studies have compared dexmedetomidine with clonidine with respect to duration of block and postoperative analgesia especially as an adjuvant to levobupivacaine 0.5%[8]. Keeping their pharmacologic interactions and other beneficial properties, we planned a double blind prospective randomized clinical study at our institute with an aim to evaluate and compare the onset time and duration of sensory and motor blockade, duration of analgesia and sedation score by both these drugs when used in axillary brachial plexus block as adjuvants to levobupivacaine in patients undergoing upper limb orthopedic surgeries.

The Brachial plexus blocks provide a useful alternative to general anaesthesia for upper limb surgeries. They achieve near ideal operating conditions by producing complete muscular relaxation, maintaining stable intraoperative haemodynamic condition and sympathetic block.

The application of ultrasound technique for exact localization of nerves has revolutionized the regional anaesthesia field and is becoming increasingly popular as it increases success rates, shortens block onset time and reduces the number of needle insertions and complications.

Levobupivacaine is a long acting local anaesthetic, S(-)– enantiomer of racemic bupivacaine. When compared with bupivocaine it produces less vasodilation, so less hypotensive episodes, less CNS toxicity, less negative inotropic effect and less prolongation of QTc interval and hence higher toxic threshold.

Methodology

After approval of the study protocol by institutional ethical committee, this study was conducted on 80 patients of either sex, undergoing upper limb surgeries aged between 20 to 60 years under ultrasound guided axillary brachial plexus block at Department of Anaesthesia, Kamineni Academy of Medical Sciences and Research Center. Informed written consent was taken from each patient before conducting the procedure

Inclusion criteria

- ASA Class I and II
- Age between 20 to 60 years
- SBP - 100-140 mm of Hg
- DBP - 60-90 mm of Hg

Exclusion criteria

- ASA Class III and IV
- Patients with medical complications like severe anaemia, severe hypovolumia, shock, septicemia
- Abnormal CT, BT or anticoagulant therapy
- Local infection at the site of proposed puncture for axillary block
- History of drug allery to local anaethetics, clonidine, or dexmedetomidine
- Patient refusal

The procedure of the technique and the development of sensory and motor block were explained to the patient to ensure good co-operation

Technique

The technique, ultrasound guided axillary brachial plexus, was conducted in the major operation theatre.

Moniters

Pulse oxymeter

Non-invasive blood pressure monitor- on the opposite upper limb

Procedure: A prospective, randomized, double blinded study was undertaken. Eighty patients posted for upper limb surgeries under ultrasound guided axillary brachial plexus block were assigned randomly into 2 groups using „slip in the box technique", each containing 40 patients. **Group LC:** (n=40) receive 25ml of 0.5 % of levobupivacaine +1 µg/kg of clonidine, the whole solution made 30 ml by adding sterile water for injection **Group LD:** (n=40) receive 25ml of 0.5 % of levobupivacaine + 1µg/kg of dexmedetomidine, the whole solution made 30 ml by adding sterile water for injection.

Performance of Axillary Block under Ultrasound Guidance[48,49]

Patient is placed supine with head turned away from the side of the block. The arm is abducted to 90 degrees and the elbow flexed to 90 degrees. The axilla is prepared aseptically.

Scanning

High-frequency, linear probes are generally recommended (10 to 15 MHz) for imaging because the nerves are superficial (1 to 2 cm) below the skin. The most proximal location at the apex of the axilla may be the best for viewing all of the terminal branches of the brachial plexus. The probe is positioned perpendicular to the anterior axillary fold and in cross-section to the humerus at the bicipital sulcus (and at the level of the axillary pulse) to capture the transverse, or short-axis, view of the neurovascular bundle.

Appearance: In cross-section

The biceps brachii and coracobrachialis muscles are seen laterally; the triceps brachii muscle is medially, deeper than the biceps brachii muscle. The anechoic and circular axillary artery lies centrally, adjacent to both the biceps brachii and coracobrachialis muscles; it is surrounded by the nerves. The nerves appear round-tooval in short axis; generally they appear as hyperechoic masses because of the large amount of connective tissue (epi- and perineurium) interspersed within the hypoechoic nerve fascicles.

The median nerve is often located superficial and between the artery and biceps brachii muscle; the ulnar nerve is usually located medial and superficial to the artery; the radial nerve lies deep to the artery at the midline (clockwise: median, ulnar, radial, The median nerve usually lies around 9–12 o-clock position, the ulnar nerve often in the corresponding 2 o-clock position, and radial at the 5 o-clock position in relation to the axillary artery but there are many variations). The musculocutaneous nerve is commonly located in the hyperechoic plane between the biceps brachii and coracobrachialis muscles

All patients were monitored for onset and duration of motor and sensory block and duration of analgesia up to 12hrs post operatively. Sensory blockade was tested using pin prick method along the distribution of the four nerves.

Sensory block was graded as-

Grade 0= sharp pin(pain) felt,

Grade 1= analgesia, dull sensation,

Grade 2= anaesthesia, no sensation,

Statistical Analysis

All the collected data was entered in microsoft excel sheet. It was then transferred to SPSS (Statistical Package for Social Science) ver. 17 software for statistical analysis. Quantitative data were analyzed by student-s „t-test . Qualitative data were analyzed by Chi-square test. P value <0.05 was considered statistically significant.

Results

Eighty ASA class I and II patients of either sex, aged between 20-60 years, posted for upper limb surgeries under ultrasound guided axillary brachial plexus block were selected for the study. The study was undertaken to evaluate and compare the efficacies of dexmedetomidine with that of clonidine as adjuvants to newer local anaesthetic levobupivacaine in brachial plexus block by ultrasound guided axillary approach.

Table 1: Age distribution of study groups

Study groups	Mean ± SD (Years)	t* Value	P Value	Significance
Group LC	39.90±11.41	0.120	0.90	**NS**
Group LD	39.60±11.03			

The minimum age of the patient was 20 years and maximum age was 60 years. The mean of the patients in group LC was 39.90 ±11.41 years and in group LD was 39.60 ±11.03 years. Age incidences between two groups were comparable, i.e., there is no statistically significant difference in age incidences between groups as P value is more than 0.05.

Table 2: Sex distribution of study groups

Study groups	Sex					
	Male	Female	Total	X^2 Value	P Value	Significance
Group LC	24 (60%)	16 (40%)	40 (100%)	0	1.00	NS
Group LD	24 (60%)	16 (40%)	40 (100%)			

X^2 – Chi-square test, NS – Nothing Significant

Male and female population are comparable between the group LC and group LD, i.e., there was no statistically significant difference observed between the groups on the basis of gender distribution. Sex distribution among groups is similar with P=1.00.

Table 3: Patient distribution based on ASA grade

Study groups	ASA Class			X^2 Value	P Value	Significance
	I	II	Total			
Group LC	25 (62.5 %)	15 (37.5%)	40 (100%)	0.053	0.818	NS
Group LD	24 (60%)	16 (40 %)	40 (100%)			

X^2 – Chi-square test, NS – Nothing Significant

In group LC, 62.5 % of the patients and in group LD 60% of the patients were
ASA class I, where as 37.5% of patients in group LC and 40% of patients in group LD were ASA class II. Distribution of subjects based on ASA class is comparable, i.e., no significant difference was observed between the groups, as the P value is more than 0.05.

Table 4: Time for onset of sensory block (min)

Study group	Onset time	Mean difference	t*Value	P value	Significance
Group LC	8.80 ± 1.18	0.98	3.639	P<0.001	HS
Group LD	7.90 ± 1.21				

The mean time for onset of sensory block in group LC was 8.88±1.18 min and in group LD was 7.90 ± 1.21 min. The statistical analysis by student-s unpaired „t- test showed that, time for onset of sensory block in group LD was significantly faster when compared to group LC (P < 0.001).

Table 5: Time for onset of motor block (min)

Study group	Onset time	Mean difference	t*Value	P value	Significance
Group LC	13.48 ± 1.64	3.25	8.32	P<0.001	HS
Group LD	10.23 ± 1.60				

The mean time for onset of motor block in group LC was 13.48 ±1.64 min and in group LD was 10.23 ± 1.60 min. The statistical analysis by student"s unpaired „t" test showed that, time for onset of motor block in group LD was significantly faster when compared to group LC (P < 0.001).

Table 6: Duration of sensory block (min)

Study group	Duration of block (min)	Mean difference	t*value	P value	Significance
Group LC	305.60 ± 26.61	101.9	18.29	P<0.001	HS
Group LD	407.50 ± 23.07				

Patients of both groups were observed for 12 hours. The mean duration of sensory block in group LC was 305.60 ± 26.61 min and in group LD was 407.50 ±
23.07 min. The statistical analysis by student"s unpaired „t- test showed that, time for duration of sensory block in group LD was significantly longer when compared to group LC (P < 0.001).

Table 7: Duration of motor block (min)

Study group	Duration of block (min)	Mean difference	t*value	P value	Significance
Group LC	324.80 ± 24.65	82.3	16.49	P <0.001	HS
Group LD	407.10 ± 19.68				

The mean duration of motor block in group LC was 324.80 ± 24.65 min and in group LD was 407.10 ± 19.68 min. The statistical analysis by student"s unpaired
„t" test showed that, duration of motor block in group LD was significantly longer when compared to group LC (P < 0.001).

Table 8: Duration of analgesia (min)

Study group	Duration of analgesia	Mean difference	t*Value	P value	Significance
Group LC	345.92±23.77	111.58	21.16	P<0.001	HS
Group LD	457.50±23.37				

The mean duration of analgesia in group LC was 345.92 ± 23.77 min and in group LD was 457.50 ± 23.37 min. The statistical analysis by student"s unpaired „t" test showed that, duration of analgesia in group LD was significantly longer when compared to group LC (P < 0.001).

Table 9: Sedation score

Time of assessment	Scores*	Group LC (%)	Group LD (%)	X^2 Value, Significance
0 min	1	40(100)	40(100)	- No Difference
	2	0(0)	0	
	3	0	0	
5 min	1	40(100)	40(100)	- No Difference
	2	0	0	
	3	0	0	
15 min	1	32(80)	29(72.5)	X^2=0.62 P>0.05(P=0.4) (Non Significant)
	2	8(20)	11(27.5)	
	3	0(0)	0(0)	
30 min	1	25(62.5)	9(22.5)	X^2=16.02 P<0.05 (Significant)
	2	15(37.5)	25(62.5)	
	3	0	6(15)	
60 min	1	20(50)	9(22.5)	X^2=6.69 P<0.05 (Significant)
	2	17(42.5)	25(62.5)	
	3	3(7.5)	6(15)	
2 hrs	1	40(100)	40(100)	- No Difference
	2	0(0)	0(0)	
	3	0(0)	0(0)	
6 hrs	1	40(100)	40(100)	- No Difference
	2	0(0)	0(0)	
	3	0(0)	0(0)	
12 hrs	1	40(100)	40(100)	- No Difference
	2	0(0)	0(0)	
	3	0(0)	0(0)	

In both the groups patients are awake and alert and hence had sedation score 1 at 0 min, 5 min, 2hours, 6 hours and 12 hours. Whereas sedation is observed between 15 min and 60 min from the time of drug injection in both the groups.

At 15 min, in group LC, 20% of patients are sedated (with sedation score 2), where as in group LD, 27.5% of patients were sedated (with sedation score 2). **At 30 min,** in group LC, 37.5% of patients were sedated (with sedation score 2), where as 85% of patients were sedated (62.5% of patients with sedation score 2 and 15% of patients with sedation score 3) in group LD. **At 60 min,** in group LC, 50% of patients were sedated (42.5% of patients with sedation score 2 and 7.5% of patients with sedation score 3), and in group LD, 77.5% of patients were sedated (62.5% of patients with sedation score 2 and 15% of patients with 3).

None of the patients had sedation score 4 and above during the study period. Statistical analysis of sedation score by Chi-square test showed that the difference in sedation score was significant (P <0.05) at 30 and 60 min. The difference in sedation score at 15 min is not statistically significant though few subjects in both the groups were sedated (P >0.05).

Discussion

A total of 80 patients within the age group of 20-60 years were included in the study. They were randomly divided into two groups, 40 in each group. With levobupivacaine, group LC received clonidine, where as other group, group LD received dexmedetomidine. Both groups were comparable in terms of mean age, sex ratio and ASA class (P > 0.05).

There have been four proposed mechanisms for the action of clonidine in peripheral nerve blocks. These mechanisms are centrally mediated analgesia, α_2 β adrenocept or-mediated vasoconstrictive effects, attenuation of inflammatory response and direct action on peripheral nerve. The direct action of clonidine on the nerve can be explained on the basis of a study conducted by Dalle *et al.*[10], They proposed that clonidine, by enhancing activity-dependent hyperpolarisation generated by the Na/K pump during repetitive stimulation, increases the threshold for initiating the action potential causing slowing or blockage of conduction.

Kosugi*et al.*[11], examined the effects of various adrenoceptor agonists including dexmedetomidine, tetracaine, oxymetazoline and clonidine, and also an α2 adrenoceptor antagonist (atipamezole) on compound action potential (CAP) recorded from frog sciatic nerve, and found that CAPs were inhibited by $\alpha_2$adrenoceptor agents so that they are able to block nerve conduction.

Popping *et* al.[12], in their metaanalysis of randomized trials showed the beneficial effect of clonidine on the duration of analgesia with all tested local anaesthetics. There are still various studies done with clonidine as adjuvant to local anaesthetics. El Saied et al.[20], conducted a study in which axillary brachial plexus blockade was performed with addition of clonidine to ropivacaine. The study showed that addition resulted in prolongation of sensory and motor block and analgesia without increased incidence of side effects.

In another study Giovanni Cucchiaro et al.[13],evaluated the effects of clonidine on the duration of sensory and motor block and analgesia time in children who underwent a variety of peripheral nerve blocks including brachial plexus block and concluded that the addition of clonidine to bupivacaine and ropivacaine can extend sensory and motor blocks.

Dexmedetomidine and clonidine are both α_2 selective agonists. It is possible that they work in a similar manner and may indicate a class effect. A study by Brumett*et al*.[14], showed that dexmedetomidine enhances duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any damage to the nerve. The analgesic effect of peripheral perineural dexmedetomidine was caused by enhancement of the hyperpolarisation-activated cation current, which prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing.

Kousugi *et al*.[11], in their study found that high concentrations of dexmedetomidine inhibit CAPs (Compound Action Potentials) in frog sciatic nerves without $\alpha_2$adrenoceptor activation. Their result showed that dexmedetomidine reduced the peak amplitude of CAPs reversibly and in a concentration- dependent manner.

This action was not antagonized by $\alpha_2$adrenoceptor antagonists (i.e., yohimbine and atipamezole); rather, α_2 antagonists reduced the CAP peak amplitude. Clonidine and oxymetazoline, two other α_2 agonists, also inhibit CAPs. The maximum effect of clonidine was only 20%. On the other hand, adrenaline, noradrenaline and α_1 agonist phenylephrine and beta agonist isoprenaline had no effect on CAPs.

There are many human studies on brachial plexus nerve blocks, which have demonstrated that increased duration of sensory and motor blockade can be achieved by adding dexmedetomidine to local anaesthetics.

Aggarwal S et al.[15], compared the effects of adding dexmedetomidine to bupivacaine in supraclavicular brachial plexus block in fifty patients. They concluded that dexmedetomidine added as an adjuvant to bupivacaine for supraclavicular brachial plexus block significantly shortens the onset time and prolongs the duration of sensory and motor blocks and duration of analgesia. Patients in dexmedetomidine group were adequately sedated with no adverse effects except bradycardia in one
patient.

Other studies like Feroz Ahmad Dar et al.[16], evaluated the effect of adding dexmedetomidine to local anaesthetics for brachial plexus blockade in patients scheduled for elective forearm and hand surgeries. They found that sensory and motor block onset times were shorter, sensory and motor blockade durations were longer along with prolonged duration of analgesia with addition of dexmedetomidine.

Keeping these facts in mind, we decided to compare the action of two α2 agonists, i.e. clonidine and dexmedetomidine with levobupivacaine in axillary brachial plexus block, so that by increasing the duration of analgesia with a single shot block we can achieve a longer duration of post-operative analgesia without significant clinical side-effects and hence we can avoid continuous catheterization.

The result of our study shows that onset time of sensory and motor blockade was significantly faster in group LD. The duration of sensory and motor blockade and duration of analgesia were also prolonged significantly in Group LD when compared with group LC.

These results are consistant with other studies. Harshavardhana HS et al.[17], did a study aiming to test the hypothesis that dexmedetomidine produces a better analgesia, motor block and postoperative analgesia when added as an adjuvant to ropivacaine 0.5% in supraclavicular brachial plexus block compared with clonidine. They found that dexmedetomidine prolonged the duration of sensory and motor block and enhances the quality of block as compared with clonidine when used as an adjuvant to ropivacaine in peripheral nerve block and concluded that dexmedetomidine is a better adjuvant compared to clonidine.

Swami SS et al.[18], compared clonidine and dexmedetomidine as an adjuvant to local anaesthetic agent in supraclavicular brachial plexus block with respect to onset and duration of sensory and motor block and duration of analgesia. Their finding was that dexmedetomidine, when added to local anaesthetic in supraclavicular brachial plexus block enhanced the duration of sensory and motor block and also the duration of analgesia. The time for rescue analgesia was prolonged in patients receiving dexmedetomidine and also enhanced the quality of block as compared with clonidine. In our study no patients in either study group had any haemodynamic instability, bradycardia or significant hypotension. None of the patients developed any serious complications due to block procedure (large haematoma, prolonged nerve palsy, nausea, vomiting, or dry mouth).We studied clonidine and dexmedetomidine at doses of 1µg/kg, as others also have used same dosage in peripheral nerve block without any significant adverse effects.

In a study conducted by Singh S et al.[19], the effects of clonidine (150 µg) added to bupivacaine was compared with bupivacaine alone on supraclavicular brachial plexus block. No side-effects were observed in both the clonidine and the control group throughout the study period.

A study conducted by Singelyn et al.[20], reported that a minimum dose of clonidine (0.5 µg/kg) added to mepivacaine prolongs the duration of anaesthesia and analgesia after brachial plexus block and found no added advantage by exceeding the dose of clonidine to 1.5 µg/kg.

In their study Vinod Hosalli et al.[21], did a comparative study using in the dexmedetomidine and clonidine, as adjuvants 1 µg/kg each with levobupivacaine in axillary brachial plexus block. They also reported no significant side-effects during the first 24 h in the post-operative period in both the groups. In another comparative study by Karthik GS et al.[22], on supraclavicular brachial plexus block, they compared clonidine and dexmedetomidine as adjuvant with dose of 1µg/kg each to levobupivacaine. No adverse effects were observed in both the groups during both intraoperatively and postoperatively.

In our study none of the patients in both the groups required sedation and they were comfortable throughout the surgery with arousable sedative effects. But dexmedetomidine provided better arousable sedative effects when compared to clonidine. At 30 min and 60 min sedation score was significantly higher in group LD when compared to group LC. No patients in both the groups experienced airway compromise or required airway assistance. Similar observation has seen in many of the above mentioned comparative studies like those done by Swami S.S et al[23].

Conclusion

Hence when compared to clonidine(1µg/kg), dexmedetomidine (1µg/kg) is a better choice of adjuvant to local anaesthetic levobupivacaine (0.5%), in ultrasound guided axillary brachial plexus block.

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