ORIGINAL RESEARCH PAPER

Anesthesiology

KEY WORDS: Supraclavicular brachial plexus block, Dexmedetomidine, Clonidine, Levobupivacaine

A COMPARATIVE EVALUATION OF THE ADDITION OF CLONIDINE AND DEXMEDETOMIDINE TO LEVOBUPIVACAINE FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN UPPER LIMB ORTHOPAEDIC SURGERIES.

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ABSTRACT

Background: Adjuncts to local anaesthetics for brachial plexus block may enhance the quality and duration of analgesia. Clonidine, an Alpha-2 adrenergic agonist, is known to produce antinociception and enhance the effect of local anaesthetics when given epidurally, intrathecally or in various peripheral nerve blocks. Levobupivacaine is a local anaesthetic drug belonging to amino amide group. It is the s.enantiomer of bupivacaine. Levobupivacaine has a greater margin of clinical safety with respect to both CVS AND CNS effects as compared to racemic bupivacaine. Dexmedetomidine, a selective 2-adrenoceptor agonist, has been used as an adjuvant during regional and local anesthesia.

Objective: We conducted this study to assess the effect of Clonidine or dexmedetomidine, added to Levobupivacaine in brachial plexus block by supraclavicular approach. The endpoints were evaluation of onset, duration of sensory and motor block and duration of analgesia.

Methods: A prospective, randomized, single blinded study was conducted on total n=60 American Society of Anaesthesiologists (ASA) I or II adult patients undergoing upper limb surgeries under supraclavicular brachial plexus block. Patients were randomly divided into three groups. Patients in first group L (n = 20) were administered 29mL of 0.5% Levobupivacaine (L) plus 1 ml NS and second group L+C (n= 20) were given 29mL of 0.5% levobupivacaine (L) with clonidine (C) 1µg/kg. And group L+D (n=20) were given 29 ml of 0.5% levobupivacaine with dexmedetomidine (D) 1µg/kg. The onset time and duration of sensory and motor blockade were recorded. Haemodynamic variables (i.e., heart rate, noninvasive blood pressure, and oxygen saturation), sedation scores and rescue analgesic requirements were recorded for 24 hrs postoperatively.

Results: The onset of sensory and motor block was significantly faster in Group L+D compared to Group L+C and L ($P < 0.05$). Rescue analgesic requirements were significantly less in Group L+D compared to Group L+C and L ($P < 0.05$). Haemodynamics and sedation scores did not differ between groups in the post-operative period.Conclusion: Dexmedetomidine(1µg/kg) in combination with 29mL of levobupivacaine (0.5%) hastened onset of sensory and motor block, and improved postoperative analgesia when used in brachial plexus block, without producing any adverse events.

INTRODUCTION

Supraclavicular brachial plexus block is a very popular mode of anaesthesia for various upper limb surgeries, due to its effectiveness in terms of cost and performance, margin of safety and good post operative analgesia .A variety of adjuvants have been studied for brachial plexus blockade.

Levobupivacaine is a local anaesthetic drug belonging to amino amide group. It is the s.enantiomer of bupivacaine. Previous studies have shown levobupivacaine to have a greater margin of clinical safety with respect to both CVS and CNS effect compared with racemic bupivacaine.[1,2,3,4]

Dexmedetomidine, a selective α2-adrenoceptor agonist, has been used as an adjuvant during regional and local anesthesia.

Clonidine, an imidazoline alpha -2 adrenergic receptor agonist is mainly used as an antihypertensive agent. Alpha-2 receptors mediate sedation, analgesia and sympatholysis. Clonidine is known to produce antinociception and enhances the effect of local anaesthetics when administered intrathecally, epidurally and in peripheral nerve block. Clonidine produces this effect by modulating pain pathway through presynaptic alpha-2 adrenergic receptors. It also produces sedation by acting on pontine locus ceruleus where highest density of alpha-2 receptors are present.

The aim of this this study was to evaluatethe addition of clonidine and dexmedetomidine to levobupivacaine for supraclavicular brachial plexus block in upper limb orthopaedic surgery. The effects studied in terms of Onset and duration of sensory and motor blockade, Haemodynamic variables ,Sedation score intra and post-operatively and reqirement of rescue analgesics in post operative period.

Methodology:

60 patients ranging from 20 to 50 years, planned for upper limb surgery

under supraclavicular were included in the study.Written Informed consent was obtained from enrolled patients.

Inclusion criteria were
ASA Class I & II,
Age between 20 to 50 years,
SBP 100- 139mm of Hg, DBP : 60-89mm of Hg,
Male and Female patients
Exclusion criteria
patients refusing to give consent,
Patients with history of bleeding disorders
Patients with local infection at the site of block
Patients with documented neuromuscular disorders
Patients with respiratory compromise
Patients with known allergy to local anaesthetic drugs
ASA grade III and IV patients
Patients with heart block.

We performed routine **Investigations like** Hb%, TLC, DLC, BT, CT, Urine routine microscopy, RBS, Blood urea and serum creatinine, Chest x-ray, ECG, HIV, HBsAg.

A prospective, randomized, single blinded study was undertaken . 60 patients posted for upper limb surgeries under supraclavicular block were assigned in 3 groups, each containing 20 patients. All the patients received injection Midazolam 0.05mg/kg before the procedure. Control group - Group-L: Received 29 ml Levobupivacaine (0.5%) +1ml NS, Study group - Group L+C: Received 29ml of mixture of Levobupivacaine (0.5%) and Clonidine (1µg/kg).

Group L+D: Received 29 ml of mixture of Levobupivacaine(0.5%) and Dexmedetomidine (1µg/kg).

ONSET OF ACTION: SENSORY & MOTOR BLOCKADE; Sensory block was evaluated by a Hollmen Scale Score. The findings were recorded at an interval of 2 min till a complete sensory block was sensation of pinprick. The onset of motor block was evaluated based on the Modified Bromage Scale.Pain was assessed by visual analogue scale for pain .

1 The visual analogue scale (VAS) consists of a line, usually 100 mm long, whose ends are labelled as the extremes ('no pain' and 'pain as bad as it could be'); the rest of the line is blank. The patient is asked to put a mark on the line indicating their pain intensity (at the present time, over the past week, or over the past 2 weeks, etc.). –

2 Sedation score described by University of Michigan Sedation Scale(UMSS) would be used to assess sedation.1 – Awaked & Alert. 2 – Minimally Sedated: tired/sleepy, responding to verbal stimulus. 3 – Moderately Sedated: somnolent/sleeping, responding to mild physical stimulus. 4 – Deeply Sedated: deep sleep, responding to moderate to severe physical stimulus. 5 – Unarousable.

The distance between that mark and the origin is measured to obtain the patient's score. Sometimes descriptive terms, such as 'mild', 'moderate' and 'severe', or numbers are provided along the scale for guidance, as shown below, and the scale is then referred to as a graphic rating scale.

MODE OF SELECTION OF CASES: Random Sampling technique
Statistical data analysis: Data will be analyzed by using ANOVA test.

RESULT:
Sixty patients ASA I and II of either sex aged between 20-50 years, posted for upper limb surgeries under supraclavicular brachial plexus block were selected for the study. The study was undertaken to evaluate the efficacy of Clonidine (1µg/kg) and dexmedetomidine (1µg/kg) as adjuvant to levobupivacaine (0.5%) in comparison with plain levobupivacaine (0.5%) for brachial plexus block by supraclavicular approach. The minimum age of the patient was 20 years and the maximum age was 50 years. The mean age of the patients in group L was 32.50 ± 10.440, in group L+C was 32.50 ± 7.214 years and in group L+D was 35.10 ±8.854. Age incidences between three groups were comparable.

Onset of sensory and motor block :
The mean onset of sensory block (group L, 13.50 ± 0.607 min, group L+C, 10.55 ± 1.317 min and group L+D 6.85 ± 0.745) and motor block (group L, 16.55 ± 0.605 min; group L+C, 15.00 ± 0.973 min, and group L+D 13.25 ± 0.550 min) was significantly faster in group L+D than in group L and L+C ($P < 0.001$). The duration of analgesia (group L, 11.10 ± 1.373 hrs, group L+C, 13.75 ± 1.118 hrs, group L+D 15.55 ± 0.605 hrs) was also longer in group L+D than in group L+C and L. The duration of motor block (group L+D 13.85 ± 0.366 hrs, group L+C, 11.70 ± 0.657 hrs and group L 9.10 ± 1.373 hrs) was also longer in group L+D than in group L+C and L. All three groups shows statistically significant difference ($P < 0.05$). [Table-1&2]

Table No. 1. showing the onset of sensory block in different groups (n=20)

DESCRIPTIVE TABLE

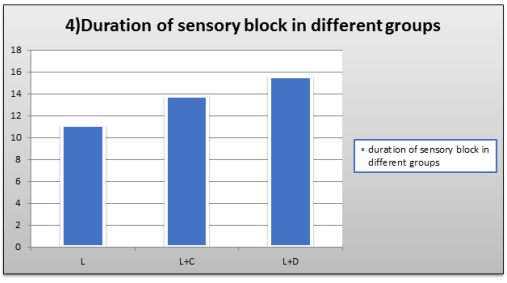
GROUPS	Mean	Std. Deviation	Std. Error	ANOVA	
				F value	P value *
L	13.50	.607	.136	250.631	<0.001
L+C	10.55	1.317	.294		
L+D	6.85	.745	.167		
Total	10.30	2.895	.374		

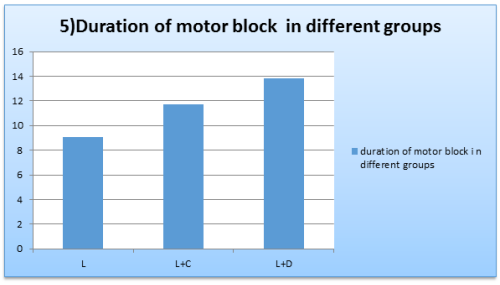
Table No. 2. showing onset of motor block in different groups (n =20)

DESCRIPTIVE TABLE

GROUPS	Mean	Std. Deviation	Std. Error	ANOVA	
				F value	P value*
L	16.55	.605	.135	101.220	< .001
L+C	15.00	.973	.218		
L+D	13.25	.550	.123		
Total	14.93	1.539	.199		

Duration of sensory and motor block :
The mean duration of analgesia (group L, 11.10 ± 1.373 hrs, group L+C, 13.75 ± 1.118 hrs, group L+D 15.55 ± 0.605 hrs) was also longer in group L+D than in L+C and L. The mean duration of motor block (group L+D 13.85 ± 0.366 hrs, group L+C, 11.70 ± 0.657 hrs and group L 9.10 ± 1.373 hrs) was also longer in group L+D than in group L+C and L. This difference was statistically significant ($P < 0.05$).





The mean duration of motor block in group L+D was 13.85 ± 0.366 hours, in the group L+C was 11.70 ± 0.657 hours and in group L was 9.10±1.119. The statistical analysis by ANOVA test showed that the difference between duration of motor block in group L+D was significantly longer when compared to group L ($P < 0.001$).

Rescue analgesic requirements: In post op 24 hours
The total number of rescue analgesics used in the form of i/v diclofenac 75 mg. In group L+D, 100% patients required only 1 rescue analgesic dosage in post-op 24 hours. In group L+C, 90% of patients required 1 and 10% of patients required 2 rescue analgesic doses in post-op 24 hours. In group L,75% patients required 2 and 25% of patient required 3 rescue analgesic doses in post-op 24 hours.

Rescue analgesia requirement in group L was significantly higher ($P < 0.05$).

Sedation score :
In group L, all patients were awake and alert and had sedation score of 1. In group L+C, sedation corresponding to score 1 was observed in 19 patients and score 2 in 1 patient at 15 min, in 16 patient score 1 at 30min and score 2 in 4 patients in 30 min. and in 20 patient score 1 at 60min from time of injection . In group L+D 9 patients had score of 1 in 15min,score 2 in 11 patients in 15 min, In 30min score of 1 in 11 patients, score 2 in 9 patients in 30min ,and in 16 patients had score of 1 in 60min.and score 2 in 4 patients in 60 min from time of injection. None of the patients had sedation score of 3 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).

Table 3: Sedation Score

Time of Assessment	Scores	L	L + C	Chi Square Test
0 min	1	20	20	NA
	2	0	0	
5 min	1	20	20	NA
	2	0	0	
15 min	1	20	19	1.03, df= 1, p= 0.311, NS
	2	0	1	
30 min	1	20	16	4.44, df= 1, p= 0.035 S
	2	0	4	
60 min	1	20	16	4.44, df= 1, p= 0.035 S
	2	0	4	
2 hrs	1	20	20	NA
	2	0	0	
6 hrs	1	20	20	NA
	2	0	0	
12 hrs	1	20	20	NA
	2	0	0	
24 hrs	1	20	20	NA
	2	0	0	

NA- Not Applicable, HS- Highly Significant, NS- Non Significant, S- Significant

Table 4: Sedation Score

Time of Assessment	Scores	L	L + D	Chi Square Test
0 min	1	20	20	NA
	2	0	0	
5 min	1	20	20	NA
	2	0	0	
15 min	1	20	9	15.2, df= 1, p= 0.000, HS
	2	0	11	
30 min	1	20	11	11.6, df= 1, p= 0.001
	2	0	9	
60 min	1	20	20	NA
	2	0	0	
2 hrs	1	20	20	NA
	2	0	0	
6 hrs	1	20	20	NA
	2	0	0	
12 hrs	1	20	20	NA
	2	0	0	
24 hrs	1	20	20	NA
	2	0	0	

NA- Not Applicable, HS- Highly Significant, NS- Non Significant, S- Significant

Haemodynamic variables :
All three groups were comparable with regard to pulse rate, systolic blood pressure, diastolic blood pressure and O2 saturation. There was no statistically significant.

DISCUSSION

Our study of dexmedetomidine is comparable with study ofSarita S Swami, et al5 which showed 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. It enhanced the quality of block as compared with clonidine. Our study of Dexmedetomidine is also comparable with Aliye Esmaoglu6 whose observation shows that dexmedetomidine added to levobupivacaine for axillary brachial plexus block shortens the onset time and prolongs the duration of the block and the duration of postoperative analgesia. The study of Amany S Ammar, Khaled M Mahmoud 7 shows that on adding Dexmedetomidine to Bupivacaine during the placement of an infra-clavicular block provides.

In our study the combination of clonidine with Levobupivacaine shows enhancement of onset of sensory and motor blockade, prolonged duration of analgesia, increases duration of sensory and motor block,which is consistent with study performed by Dr. Sidharth Sraban Routray et al 8

Santvana Kohli et al9 concluded that the higher dose of clonidine in Brachial PlexusBlock hastens the onset, prolongs the duration of sensorimotor blockade and postoperative analgesia without significant hemodynamic alterations. It also causes more sedation. Susmita Chakraborty et al10, found that that the addition of a small dose of clonidine to 0.5% bupivacaine significantly prolonged the duration of analgesia without producing any clinically significant adverse reactions other than sedation. Our study is also comparable with Pöpping DM et al[11], whose study shows that the Clonidine added to intermediate or long-acting local anesthetics for single-shot peripheral nerve or plexus blocks prolongs duration of analgesia and motor block by about 2 h, ,De Jong et al.[12] explained that large fibres require a higher concentration of local anaesthetic than small fibres. The minimal effective concentration of local anaesthetic for large (motor) fibres is greater than for small (sensory) fibres. Thus, motor function return before pain perception and duration of motor block is shorter than the sensory block.

McCartney et al.[13] found that a Bupivacaine and Clonidine combination prolonged postoperative analgesia compared to a Bupivacaine alone when administered for various peripheral nerve blocks. Eledjam J.J et al.[14], showed Clonidine is an attractive alternative to epinephrine to prolong duration of analgesia in supraclavicular brachial plexus block. Hutschala. D et al.[15], found lower plasma concentration of Clonidine after brachial plexus block which strongly suggested its local effect on peripheral nerves. Clonidine produces this additive effect on local anaesthetics by its action on the presynaptic alpha-2 receptor complexes present on 80 peripheral nerves.

In our study, the number of patients who required rescue analgesia and the mean number of supplemental analgesic boluses required were also significantly lower in patients in Group L+D as compare to group L+C and group L. Similar observation was made in the above mentioned study by Sarita S Swami, et al 5. The prolonged analgesia in Group L+C could be due to the action of Clonidine by inhibiting action potential of A & C fibers in peripheral nerves as demonstrated by Gaumann et al.16 Many authors favor the hypothesis that Clonidine exerts its local anesthetic-prolonging effect directly on nerve fibers, as a result of complex interaction between Clonidine and axonal ion channels or receptors.

In our study, sedation scores were higher in patients in group L+D compared to group L+C and L in[15] min after injecting the drug, until 60 min after injection, This may have been due to partial vascular uptake of Clonidine, and its transport to the central nervous system where it acts and produces sedation. The limited duration of sedation could be explained by the fact that Clonidine is highly lipophilic and diffuses faster into the blood vessels. Though mean sedation score in group L+D was higher as compared to group L+C and L (P < 0.05), we did not observe clinically significant sedation in patients in group L. No patient experienced airway compromise or required airway assistance. In conclusion, dexmedetomidine 1 µg/kg when added to 29mL of levobupivacaine 0.5% for supraclavicular brachial plexus block, speeds the onset of sensory and motor blocks (P < 0.05). The

combination produces improved analgesia, resulting in a prolonged effect and reduced requirements for rescue analgesics.

CONCLUSION

From our study, we conclude that, the addition of dexmedetomidine(1µg / kg) as an adjuvant to levobupivacaine (0.5%) has following effects; Faster onset of sensory block, Faster onset of motor block, Longer duration of sensory block, Longer duration of motor block, Less number of rescue analgesics in post-op 24 hours, Comfortable sedation intra operatively without any need for airway assistance, No significant difference in haemodynamic variables i.e., pulse rate, systolic BP, diastolic BP and O2 saturation.

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