

## CLONIDINE AS AN ADJUVANT TO LEVOBUPIVACAINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK- A RANDOMIZED DOUBLE-BLIND CONTROL STUDY

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### ABSTRACT

#### BACKGROUND

Alpha 2 agonists as adjuvants to local anaesthetics in brachial plexus blocks augment the local anaesthetic effects and reduces the analgesic requirements postoperatively. This study was designed to evaluate the analgesic effects of clonidine as an adjuvant to levobupivacaine in supraclavicular brachial plexus (SCBP) block.

#### MATERIALS AND METHODS

In a prospective randomized double-blind study, sixty patients of 20 to 60 years, American Society of Anaesthesiologists Physical Status (ASA PS) I and II scheduled for elective upper limb surgeries were randomly divided into two groups of 30 each. SCBP block was performed using peripheral nerve stimulator, Group C received 30 ml of 0.5% Levobupivacaine + 0.5 ml (50 mcg) Clonidine and Group L received 30 ml of 0.5% Levobupivacaine + 0.5 ml of Normal saline. Parameters observed were time of onset, duration of sensory and motor blockade, duration of analgesia, intraoperative haemodynamics and adverse effects.

*Statistical Analysis*- Data analysis was done using SPSS 15.0. Variables were compared using Pearson's Chi-square test for nonparametric data and Student's t test for parametric data. Statistical significance was defined as P<0.05.

#### RESULTS

Duration of sensory and motor block were longer in Group C as compared to Group L (P<0.01). Duration of analgesia was significantly longer in Group C as compared to Group L (P<0.01). No significant difference was observed in haemodynamics, side-effects and complications in either groups.

#### CONCLUSION

The addition of clonidine to levobupivacaine in SCBP block leads to faster onset, prolongs the duration of sensory and motor block and provides adequate post-operative analgesia without any adverse effects.

#### KEYWORDS

Clonidine, Levobupivacaine, Supraclavicular, Brachial Plexus Block.

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#### BACKGROUND

Brachial plexus blocks for surgeries of the upper limb have proved to be a good alternative to general anaesthesia.<sup>1</sup> They provide adequate intra-operative anaesthesia with analgesia extending to the postoperative period.  $\alpha_2$  adrenoreceptor agonists like clonidine, may enhance the quality and duration of analgesia with their perioperative sympatholytic, cardiovascular stabilizing effects with reduced anaesthetic requirements.<sup>2</sup> Considerable research has been conducted over the years in order to determine the ideal local anaesthetic drug.<sup>3</sup> Levobupivacaine, the pure S (-) enantiomer of bupivacaine has emerged to be a safer and

effective drug for regional anaesthesia with an advantage of lesser cardiac and CNS toxicity as compared to its racemic sibling bupivacaine.<sup>4</sup> The purpose of this study was to evaluate the effects of clonidine in combination with levobupivacaine on peripheral nerves during brachial plexus block in terms of the quality of block, post-operative analgesia and to detect any potential complication.

#### MATERIALS AND METHODS

A randomized prospective double blind controlled study was conducted in a tertiary care hospital from Jan 2016 to May 2017 after approval from Institutional Ethical committee. Sixty ASA PS I and II patients, between 20 to 60 years of either gender, scheduled for elective upper limb surgery were enrolled in the study. Patients who refused to give consent, with allergy to trial drugs, clavicular fracture, morbid obesity, bleeding diathesis, skin infection at the needle insertion site were excluded from the study. Sixty patients were randomly allocated into two groups of thirty patients (n=30) each using computer generated random number table. Group C received 30 ml of 0.5% Levobupivacaine (Levoanawin, Neon Laboratories, Mumbai)

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+0.5 ml (50 mcg) Clonidine (Cloneon, Neon Laboratories, Mumbai) and group L to received 30 ml of 0.5% Levobupivacaine + 0.5ml of Normal saline. Blinding was done in the following manner

1. The patients were unaware of the study drug administered
2. The anaesthesiologist performing the brachial plexus block was unaware of group allocation and drug being administered
3. The local anaesthetic solution was prepared by a different anaesthetist not involved in the study in coded transparent syringes labelled with the patients' study number. The study blinding was broken after statistical analysis. In case of emergency related to the study drug this anaesthetist was authorised to disclose the contents of the syringe to the anaesthetist performing the study.

Preoperative assessment was done on the day before surgery and written informed consent obtained. Visual Analog Scale (VAS) was explained to each patient. All patients received tab Diazepam 10 mg per oral (PO) and tab Ranitidine 150 mg PO on the night before the surgery and were fasting overnight. On arrival in the operation room, baseline heart rate, blood pressure, respiratory rate, 3 lead electrocardiogram and peripheral oxygen saturation was recorded for all patients. Intravenous line was obtained with 18-gauge cannula in the opposite limb and ringer lactate solution started. Inj. Midazolam 1 mg was given as premedication. Subcutaneous injection with 1ml of 0.5% levobupivacaine was administered at the needle insertion site. All the patients received SBP block with the aid of a nerve stimulator (Inmed Equipments Pvt. Ltd.,) connected to a 22 G, 50-mm-long stimulating needle. Stimulation frequency was set at 2 Hz, while the intensity of stimulating current was initially set to deliver 1 mA. The location end point was a distal motor response, that is, the movement of the fingers with an output current lower than 0.5 mA. Following negative aspiration, 30 ml of a solution containing the drug solution was injected. Inj. levobupivacaine 0.5% 2 ml was given to block intercostobrachial nerve to avoid tourniquet pain, if tourniquet was required.

Motor and sensory block was assessed at each minute. Onset of sensory blockade was the time taken from the completion of the injection of the study drug to the first loss of pinprick sensation in C5-T1 dermatomes using a blunt needle. The sensory blockade was assessed using Hollmen scale.<sup>5</sup> Grade 1: Normal sensation of pinprick. Grade 2: Pin prick felt as sharp pointed but weaker compared with same area in the other upper limb. Grade 3: Pin prick recognized as touch with blunt object. Grade 4: No perception of pin prick. Brachial plexus block was considered successful by Vester-Anderson's criteria when at least two out of four nerve territories (radial, ulnar, median and musculocutaneous nerves) were effectively blocked. The duration of sensory block was taken as the time interval

between the onset of sensory anaesthesia and the complete resolution of anaesthesia on all nerves.

Motor block was assessed from the completion of injection of the study drug to the maximum motor block attained. Motor block was evaluated by Bromage scale for upper extremity.<sup>6</sup> Grade 1: Able to raise the extended arm to 90° for full 2 seconds. Grade 2: Able to flex the elbow and move the fingers but unable to raise the extended arm. Grade 3: Unable to flex the elbow but able to move the fingers. Grade 4: Unable to move the arm, elbow and fingers. The block will be considered to be failed when at least two of the four nerves (median, radial, ulnar and musculocutaneous nerve) were not affected even after 30 minutes of drug injection. In this case general anaesthesia will be administered. The duration of motor block was the time interval between the end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm. At the conclusion of the procedure, quality of operative conditions will be assessed according to the following numeric scale.<sup>7</sup> Grade 4: (Excellent) No complaint from patient. Grade 3: (Good) Minor complaint with no need for the supplemental analgesics. Grade 2: (Moderate) Complaint that required supplemental analgesia. Grade 1: (Unsuccessful) Patient given general anaesthesia.

Patients were assessed for post-operative pain using VAS. Rescue analgesia was given in the form of inj. diclofenac sodium (1.5 mg/kg) intramuscular (I.M.) when VAS score > 4. The time between the end of local anaesthetic administration and the first analgesic request was noted as duration of analgesia. Patients were observed for any side effects like nausea, vomiting, dizziness, pruritis, bradycardia, hypotension, dryness of mouth, headache and complications like pneumothorax, hematoma, anaphylactic reactions and post block neuropathy in the intra and post-operative periods.

Intraoperatively hemodynamic parameters was monitored continuously and the readings were recorded every 5 min till 150 minutes. Postoperatively monitoring was done hourly for 24 hours.

Duration of analgesia was taken as the outcome measure of interest for the purpose of sample size calculation. It was estimated that 23 subjects would be required per group to detect a difference of 30 minutes in this parameter between the two groups with power of 90% and 5% probability of Type 1 error. Statistical analysis was done using student t test, chi-square test or Fischer's exact test as appropriate. The Statistical Software namely SPSS 15.0 was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. The value of P < 0.05 was considered significant.

## RESULTS

Block was successful in all the patients and all the enrolled patients completed the study. We recruited 30 subjects per group, more than the calculated sample size. In the present study, both groups were comparable with respect to the demographic profile (P > 0.05) as shown in Table 1.

Baseline Characteristics	Levobupivacaine +Clonidine(n=30)	Levobupivacaine+Saline (n=30)	P value
Age (Years)	34.20 ± 12.01	38.40 ± 9.46	0.1379
Sex (Male: Female)	23:7	24:6	0.7542
Height (cm)	166.33 ± 6.95	165.43 ± 5.77	0.5873
Weight (kg)	66.17 ± 7.72	65.27 ± 6.62	0.6299
Duration of Surgery (min)	123.50 ± 31.87	114.67 ± 25.43	0.2402

**Table 1. Comparison of Demographic and other Relevant Parameters at Baseline between the Two Groups**

After giving supraclavicular block, the mean time taken for onset of sensory block was significantly faster in group C as compared to group L. Similarly, time taken for onset of motor block was significantly faster in group C as compared to group L. Mean duration of sensory block and motor block was significantly prolonged in Group C (684.33±33.60 min and 540.33 ± 20.42 min respectively) as compared to group

L (559.33±17.01 min and 453.00 ± 25.48 min respectively) (P< 0.001). The mean time from onset of block till the first request of pain medication was 852.67 ± 24.90 min in Group C and 746.00 ± 13.80 min in Group L. This difference was highly significant (P< 0.001). Motor and sensory block characteristics of both groups are shown in Table 2.

Baseline Characteristics	Levobupivacaine +Clonidine(n=30)	Levobupivacaine+Saline (n=30)	P value
Onset of sensory Block (min)	7.57 ± 1.01	10.03 ± 0.76	0.0001
Duration of sensory Block (min)	684.33 ± 33.60	559.33 ± 17.01	0.0001
Onset of Motor Block (min)	9.87 ± 0.86	11.97 ± 0.81	0.0001
Duration of Motor Block (min)	540.33 ± 20.42	453.00 ± 25.48	0.0001
Duration of Analgesia (min)	852.67 ± 24.90	746.00 ± 13.80	0.0001

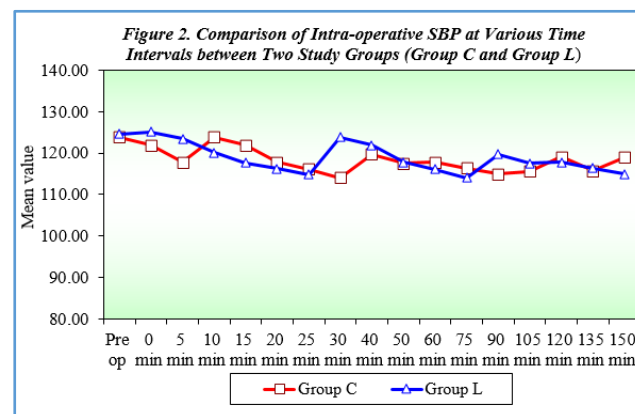
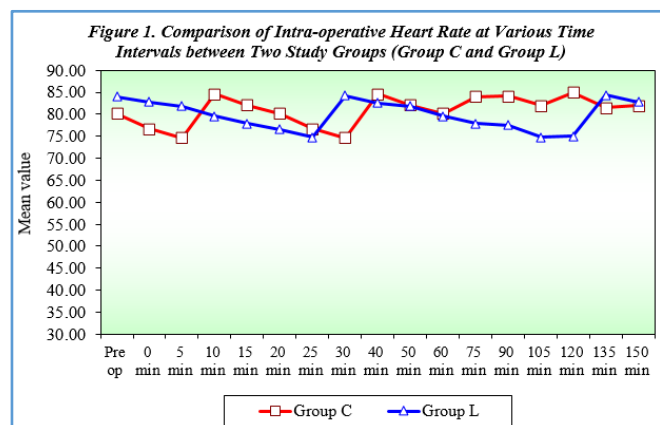
**Table 2. Time Profiles of Sensory and Motor Blocks and Duration of Analgesia in the Study Groups**

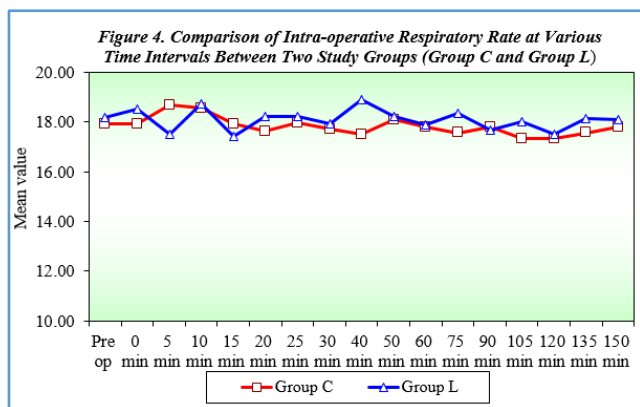
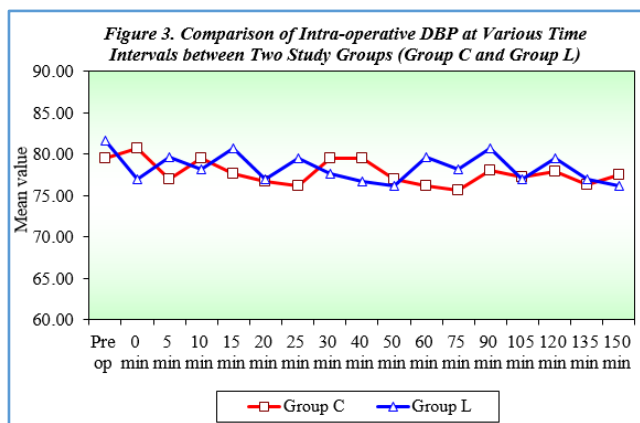
Mean duration of surgery was comparable (123.50± 31.87 min in Group C and 114.67± 25.43 min in Group L). There were no significant differences between the study groups with respect to pattern of changes in heart rate, systolic blood pressure, diastolic blood pressure, respiratory

rate intraoperatively as shown in figures 1-4. In our study only 2 patients in the Levobupivacaine group complained of nausea and had vomiting. The present study showed that the requirement of rescue analgesia was significantly lower in Group C as compared to group L at 6-12 hours (table 3).

Time of Rescue Analgesia		Group C	%	Group L	%	Total	%	P Value
0-6 hours	Yes	0	0.00	0	0.00	0	0.00	
	No	30	100.00	30	100.00	60	100.00	
6-12 hours	Yes	0	0.00	6	20.00	6	10.00	0.024
	No	30	100.00	24	80.00	54	90.00	
12-18 hours	Yes	6	20.00	12	40.00	16	26.6	0.091
	No	24	80.00	18	60.00	30	50	

**Table 3. Time of rescue analgesia in two study groups (Group C and Group L)**





**DISCUSSION**

The aim of this study was to evaluate the analgesic effects of 50 mcg of Clonidine as an adjuvant to 30 ml of 0.5% Levobupivacaine in SBB block. The supraclavicular route was preferred as the anatomical landmarks are easily identifiable, making the learning curve faster and hence better outcomes. Using a nerve stimulator, further improved the success rate of block as the drug is deposited close to the nerve sheath with less chances of vascular and neurological injuries.<sup>8</sup> Clonidine has been used as an adjuvant due to its high selectivity for alpha 2A receptors. The presynaptic activation of alpha 2A adrenoceptor in the locus coeruleus inhibits the release of norepinephrine resulting in the sedative, hypnotic effects and terminates the propagation of pain signals.<sup>9,10,11</sup> Cox et al had compared bupivacaine and levobupivacaine in brachial plexus block. They found that 0.25% levobupivacaine had slower onset, shorter maintenance and a lower overall success rate than the other two groups (0.5% levobupivacaine, 0.5% bupivacaine) with a success rate of 65 to 80% in relation to the anaesthesia technique. The study also found levobupivacaine to be more appropriate for brachial plexus block due to its lower toxic potential than bupivacaine and is expected to increase the safety margin in regional anaesthesia.<sup>12</sup> In a study by Singelyn et al, increased duration of analgesia was obtained with increasing dose of clonidine (0.2, 0.3, 0.4, 0.5, 1 µg/kg, 1.5 µg/kg). In yet another study by Singelyn, et al it was concluded that the minimum dose of clonidine required to significantly prolong the duration of analgesia after brachial plexus block with mepivacaine 1% with epinephrine, is 0.1 µg/kg (duration of

analgesia 351 ± 12 min v/s 260 ± 40 min (control Group I).<sup>13, 14</sup> In a study by Chakraborty et al, the addition of clonidine to bupivacaine significantly prolonged duration of analgesia in supraclavicular brachial plexus block.<sup>15</sup> Another study by Patil KN, the addition of clonidine to ropivacaine significantly prolonged duration of analgesia in supraclavicular brachial plexus block.<sup>16</sup> The present study shows significant prolongation of analgesia when clonidine 50mcg is added to levobupivacaine. There were no significant differences between the study groups with respect to pattern of changes in heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate intraoperatively. In a study done by Karthik GS et al, intraoperative haemodynamics remained stable in both the Levobupivacaine and Clonidine groups for supraclavicular brachial plexus block.<sup>17</sup>

**CONCLUSION**

To conclude the upper limb surgeries done under supraclavicular brachial plexus block with clonidine as an adjuvant to levobupivacaine resulted in early onset, prolonged duration of sensory and motor blockade and increased duration of postoperative analgesia as compared to levobupivacaine alone. Thus, clonidine as an adjuvant to levobupivacaine augments the local anaesthetic effects and reduces the analgesic requirements postoperatively.

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