

# Clonidine as an Adjuvant to Local Anaesthetic in Infraclavicular Brachial Plexus Block: A Randomised Clinical Trial

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## ABSTRACT

**Introduction:** Brachial plexus blocks are routinely performed to provide anaesthesia and analgesia for upper limb orthopaedic surgeries. Various adjuvants are being added to local anaesthetic solution to prolong the duration of sensory and motor blockade to ensure successful completion of long duration surgeries with adequate postoperative analgesia. Clonidine is used in varying dosages as adjuvant for peripheral nerve block.

**Aim:** To study different dosages of clonidine when used as an adjuvant in infraclavicular approach to brachial plexus block.

**Materials and Methods:** The randomised double-blind clinical study enrolled 60 American Society of Anaesthesiologists (ASA) I and II patients, between ages of 18-60 years, undergoing elective forearm orthopaedic surgery, lasting more than one hour. Based on the dose of clonidine added, the patients were distributed

to group I (75 µg); group II (100 µg) and group III (150 µg). They were compared with regard to onset and duration of sensory and motor blockade, haemodynamic parameters, quality of sedation and side-effects. The results were analysed using Statistical Package for the Social Sciences (SPSS) version 21.0.

**Results:** Demographic profile was comparable between the study groups. The onset of sensory and motor duration was faster in group III (5.8±1.65 minutes; 10.08±0.98 minutes). Also, the duration of sensory and motor blockade was highest in group III (11.02±2.33 hours; 10.44±1.45 hours). Patients in group III had significantly higher level of sedation in comparison to other groups.

**Conclusion:** Clonidine in a dose of 150 µg provides significantly longer duration of sensory and motor blockade without any adverse haemodynamic outcomes.

**Keywords:** Infraclavicular approach, Peripheral nerve block, Sensory block

## INTRODUCTION

Brachial plexus block is routinely performed to provide surgical anaesthesia in patients undergoing upper limb orthopaedic surgeries [1]. Over a period of time various approaches to block brachial plexus have been discovered. Each approach has its own advantages and shortcomings. Infraclavicular approach to brachial plexus block is a relatively new approach with limited literature pertaining to it [2,3]. Other than providing surgical anaesthesia, they also aid in providing adequate postoperative analgesia. Optimal postoperative analgesia ensures early mobilisation, decreased hospital stay and faster recovery [3]. To enhance the effect of local anaesthetic solutions, many adjuvants may be added for faster onset and prolonged duration of sensory and motor blockade [3].

Clonidine is an alpha adrenoceptor agonist which is used as adjuvant in regional anaesthesia. It has been used as adjuvant in brachial plexus nerve block in different doses [4]. While using any drug utmost care should be taken while weighing the risk benefit ratio of the drug. Clonidine is known to cause profound bradycardia and hypotension which can be a cause of concern especially in high-risk patients. Therefore, it is important to carefully titrate the dose so as to avoid any catastrophic events like haemodynamic instability, arrhythmias, over sedation, upper airway obstruction etc., [5,6].

In order to study the impact of clonidine on block characteristics this study was planned comparing three different doses of clonidine in infraclavicular nerve block. It was hypothesised that increasing the dose of clonidine would result in faster onset with prolonged duration of motor and sensory block with higher incidence of haemodynamic instability. The primary outcome was time to first rescue analgesia and the secondary outcomes were onset and duration of sensory and motor block, haemodynamics and complications.

## MATERIALS AND METHODS

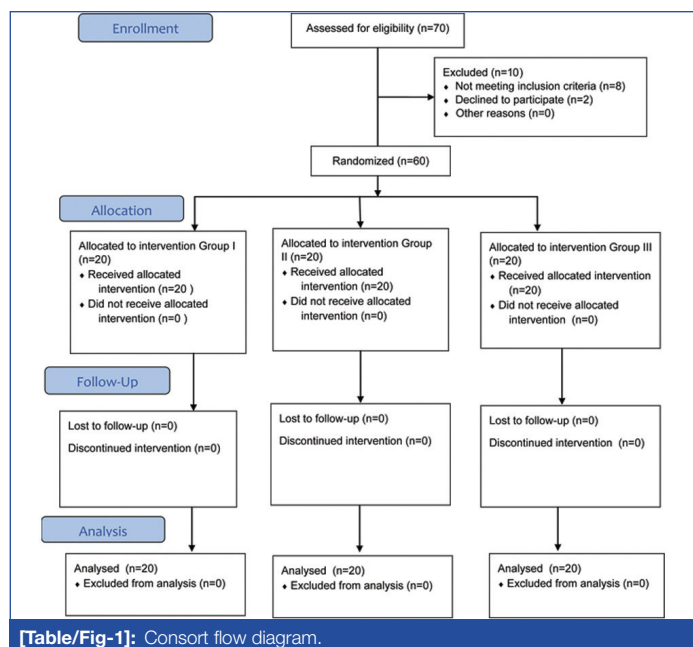
The randomised clinical study was conducted at Indian Spinal Injuries Centre, New Delhi, India, from December 2010 to December 2012 after approval from Institutional Ethics Committee (IEC). Written and informed consent was obtained from all the patients.

**Inclusion criteria:** A total of 60 patients were enrolled of ASA I and II between 18-60 years of either sex, weighing 50-70 kg undergoing elective forearm orthopaedic surgery in supine position with surgical duration lasting more than one hour.

**Exclusion criteria:** Patients with history of neurological disorders, patients on antiplatelet or anticoagulant drug therapy, infection at the injection site, documented nerve injury, allergy to study drugs, pregnant and lactating females and chronic pain syndromes were excluded from the study.

**Sample size:** Based on the study published by Juliuos SA et al., a pilot study was conducted with 10 patients in each study group wherein infraclavicular nerve block with three different doses of clonidine (75 µg, 100 µg, 150 µg) was administered to each group [7]. The mean time to first rescue analgesia were 4, 5 and 12 hours in respective groups. Considering the mean time to first rescue analgesia from the pilot study, the effect size was calculated to be 0.38. For execution of 80% power of study and 95% confidence interval using the effect size the sample size was calculated with G power statistical analysis software (version 3.1.a) using proportions obtained from the pilot study. Finally, the sample size came out to be 60 (20 in each group) with mentioned effect size.

Based on computer generated random number table, patients were allocated into three groups namely group I (clonidine 75 µg); group II (clonidine 100 µg); group III (clonidine 150 µg). The final group allocation was performed before the start of procedure [Table/Fig-1]. The number slips were sealed inside an opaque envelope which was opened by the staff nurse present at the time of procedure. The anaesthetist observing the study parameters was blinded to the group allocation.



All patients had to undergo a thorough preoperative evaluation. They were kept nil per oral for eight hours for solids and two hours for clear liquids. On the day of surgery, it was ensured that the preoperative advice was followed. Patients were shifted inside the operation theatre and standard ASA monitors (electrocardiogram, non invasive blood pressure, pulse oximetry) were applied. A 20 G intravenous cannula was secured in the non operative hand and ringer lactate was started. Patient was again explained the block technique and the methods of block assessment before starting the procedure. The sensory block was assessed using the pin prick technique (Grade I - Sharp pain; Grade II - Touch sensation only; Grade III - Not even touch sensation) [8] whereas for assessing the motor block modified bromage scale (Grade 0 - No block-total arm and forearm flexion; Grade I - Partial block-total arm and partial forearm flexion; Grade II - Almost complete block-inability to flex the arm and decreased ability to flex the forearm; Grade III - Total block-inability to flex both the arm and forearm) was used [9]. The patient was placed supine with head slightly turned towards the non operative side. Sterile painting and draping were done. The anatomical landmarks namely the medial end of the clavicle and the acromion process were palpated. The point of insertion was 2 cm medial and caudal to the coracoid process [10]. The skin over the point of insertion of block needle was infiltrated with local anaesthetic solution. A 5 cm insulated block needle connected to peripheral nerve stimulator was inserted at the point defined above. The needle directed towards the ipsilateral axillary artery at an angle of 60° to the skin plane. The point of injection was when flexion index and middle fingers can be elicited at current of 0.5-0.6 mA at 2 Hz. In case the muscle contractions persisted even at current of less than 0.4 ma, the needle was withdrawn by 1 mm to avoid intraneural injection of local anaesthetic solution. Bupivacaine (0.5%) 20 mL with 5 mL of normal saline containing the group specific study drug and dose (total 25 mL) were injected after careful repeated negative aspiration. The patient was monitored every five minutes for initial 30 minutes followed by two hourly intervals for initial 12 hours and then at 16, 24 hours after the procedure for the following study parameters.

The dermatomes supplied by radial, ulnar, median and musculocutaneous nerve were assessed. The success of the block was assessed after 20 minutes of procedure [8]. The block was considered a failure if two or more nerves were spared. It was considered incomplete if one nerve was spared. In case of incomplete block, supplemental sedation was provided in the form of propofol infusion along with fentanyl in dosages decided by the

anaesthetist in-charge for the case. Patients with failed blocks were considered for general anaesthesia and were excluded from further statistical analysis. The onset of sensory block was considered from the time of administration of block till attainment of Grade-1 sensory blockade using pin prick technique. The total duration of sensory blockade was from the time of administration of block till Numerical Rate Scale (NRS)  $\geq 4$ , postoperatively. Onset of motor block was defined as from the time of administration of block till attainment of Bromage scale 1. The total duration of motor blockade was from the time the block was administered till Bromage scale 0 was attained in the postoperative period. Intraoperative sedation was assessed using Ramsay sedation scale. Haemodynamic parameters {Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Heart Rate (HR)} and oxygen saturation were also monitored at timed intervals. All patients were observed for any complications (pneumothorax, local anaesthetic systemic toxicity, nerve injury, vascular injury).

## STATISTICAL ANALYSIS

Data was analysed with Shapiro-Wilk test for assessment of normality. Quantitative variables were compared using Kruskal-Wallis test. Qualitative variables were compared using Chi-square test. Continuous variables were compared using Analysis of Variance (ANOVA) test. Multiple comparisons between the study groups were analysed using post-hoc and Bonferonni test. The level of significant i.e., p-value was denoted as P1 when comparing group I and group II, P2 when comparing group I and group III and P3 when comparing group II and group III. A p-value  $<0.05$  was considered to be statistically significant.

Parameters	Group I	Group II	Group III	p-value
Age (years)	50 $\pm$ 6.2	51 $\pm$ 4.8	51.5 $\pm$ 3.5	0.68
Sex ratio (Male:Female)	17:3	15:5	16:4	0.55
Weight (kg)	55.6 $\pm$ 4.6	55.06 $\pm$ 3.3	57.4 $\pm$ 3.1	0.58
Duration of surgery (hours)	2.06 $\pm$ 0.5	1.98 $\pm$ 0.32	2.10 $\pm$ 0.44	0.72
ASA physical status (I/II)	19:1	18:2	19:1	0.82

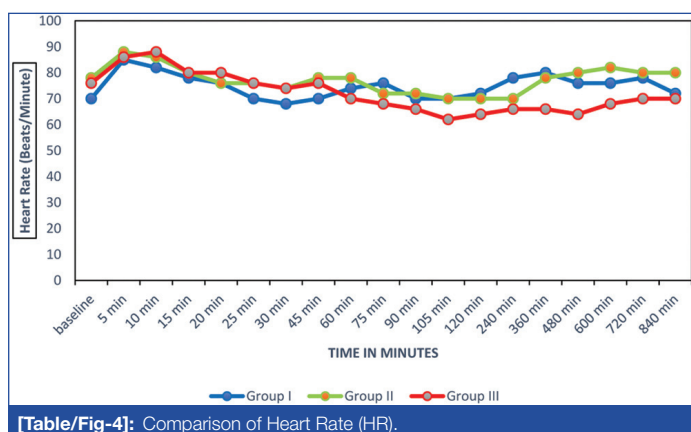
**[Table/Fig-2]:** Comparison of demographic data.  
ASA: American society of anaesthesiologists; KG: Kilograms

Parameters	Group I	Group II	Group III	p-values
Time to onset of sensory block (min)	9.05 $\pm$ 1.2	9.45 $\pm$ 1.78	5.8 $\pm$ 1.65	P1-0.57 P2-0.034 P3-0.020
Time to onset of motor block (min)	14.97 $\pm$ 2.34	13.87 $\pm$ 1.89	10.08 $\pm$ 0.98	P1-0.67 P2-0.015 P3-0.034
Total duration of sensory block (h)	3.56 $\pm$ 0.67	4.87 $\pm$ 0.56	11.02 $\pm$ 2.33	P1-0.68 P2-0.002 P3-0.0001
Total duration of motor block (h)	3.04 $\pm$ 0.64	4.06 $\pm$ 1.03	10.44 $\pm$ 1.45	P1-0.55 P2-0.003 P3-0.012
Ramsay sedation score	1.02 $\pm$ 0.34	1.67 $\pm$ 0.45	3.45 $\pm$ 0.87	P1-0.65 P2-0.023 P3-0.034
Number of successful blocks	19	19	20	P1-1.00 P2-0.045 P3-0.045
Number of failed blocks	0	0	0	P1-1.0 P2-1.0 P3-1.0
Number of incomplete blocks	1	1	0	P1-1.0 P2-0.0001 P3-0.0001

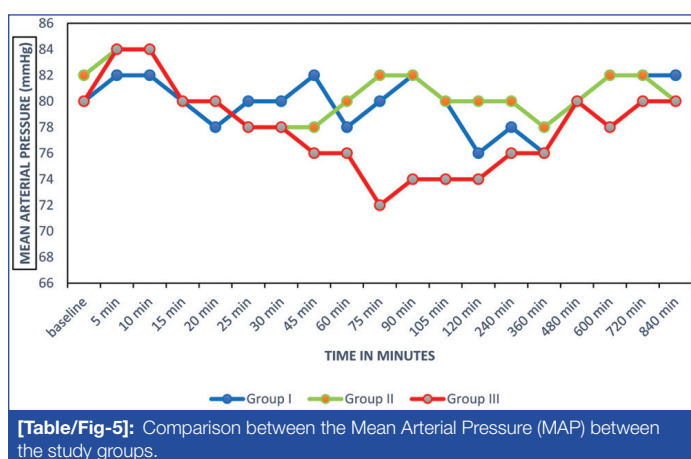
**[Table/Fig-3]:** Comparison of different study parameters between the study groups.  
Min: minutes; h: hours; p-value was denoted as P1 when comparing group I and group II, P2 when comparing group I and group III and P3 when comparing group II and group III

## RESULTS

The demographic parameters (age, sex distribution, weight, duration of surgery and ASA physical status) were comparable between the study groups [Table/Fig-2]. The time of onset of sensory and motor block was significantly faster in group III. The duration of sensory and motor block was significantly longer in group III. All patients in group III had complete block whereas one patient each in group I and group II had incomplete block. The mean sedation score was significantly higher in group III compared to other two study groups [Table/Fig-3]. The MAP and HR were significantly lower in group III compared to the other study groups though no intervention was required in any enrolled patient [Table/Fig-4,5]. No complication was observed in any patient enrolled in the study.



[Table/Fig-4]: Comparison of Heart Rate (HR).



[Table/Fig-5]: Comparison between the Mean Arterial Pressure (MAP) between the study groups.

## DISCUSSION

Clonidine is being used as an adjuvant in peripheral nerve blocks due to its role in increasing the duration and quality of analgesia following administration of block [11]. The present study compared three different doses (75 µg, 100 µg and 150 µg) of clonidine when used as an adjuvant in infraclavicular approach to brachial plexus block. In group III, clonidine was added in the dose of 150 µg which had a significant effect on the all the block characteristics. The onset of sensory and motor block was faster with prolonged duration of sensory and motor block duration with 150 µg of clonidine added as adjuvant to the local anaesthetic solution used for infraclavicular block. The duration of motor and sensory block was longer with 100 µg in comparison to 75 µg but it was not statistically significant.

The onset of sensory and motor block was significantly faster with 150 µg of clonidine in comparison to the other drug dosages. It was noticed that with increase in the dose of clonidine the time to onset of sensory and motor block became significantly shorter unlike in the study by Shah DM et al., wherein they did not find any difference in these parameters when they compared it to a control group [12]. This difference could possibly be explained by the difference in the drug (1.5% lignocaine with adrenaline

(1:2,00,000) and the volume of drug used (0.6 ml/kg) in their study. Chatrath V et al., compared clonidine (150 µg) with bupivacaine and ropivacaine and found faster onset in group with clonidine and bupivacaine which are comparable to present study findings [13].

In the current study, the total duration of sensory and motor block duration increased with increase in the dose of clonidine and was found to be significantly longer with 150 µg of clonidine when added as adjuvant to bupivacaine. The results were comparable to those observed by Chatrath V et al., using the same dose of clonidine with different local anaesthetic formulations [13]. Shah DM et al., observed longer duration of both sensory and motor block duration with clonidine in comparison to the control group [12].

While comparing the haemodynamic variables, the mean HR and MAP significantly decreased with increase in the dose of clonidine. The group with 150 µg of clonidine should statistically lower HR and blood pressure but none of the patients required any pharmacological intervention. Shah DM et al., did report hypotension with clonidine but it was not clinically significant and did not require any intervention [12]. Chatrath V et al., study results were comparable in the two groups as both groups had similar dosage of clonidine [13]. The present study also observed an increasing trend in the level of sedation with increase in the dose of clonidine. It was also noted that only one patient of failed block was observed in groups with 75 µg and 100 µg of clonidine. The reasons could be presence of septations which alter the spread of drug and thereby may affect the success rate of the block [14]. Other possible explanation for no failed block with 150 µg of clonidine could be the higher level of sedation observed in this patient cohort which could have overshadowed the patient with incomplete block. As in the previous studies, no side-effects were observed in any study group of the present study.

## Limitation(s)

The study results could have been different if the block was performed under ultrasound guidance with real-time deposition of drug under ultrasound guidance. There is still no census on the ideal volume of local anaesthetic required to ensure adequate nerve block which is one of the confounding factors for the success and other block characteristics.

## CONCLUSION(S)

It was found that with increase in the dose of clonidine the onset and duration of sensory and motor block was significantly affected. Clonidine in a dose of 150 µg provides significantly faster onset and total duration of sensory and motor block while maintaining stable haemodynamics. However, the higher sedation score observed with this dosage required vigilant monitoring.

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