

## A COMPARATIVE STUDY OF EFFECTS OF CLONIDINE ADDED TO ROPIVACAINE VERSUS PLAIN ROPIVACAINE DURING SUPRA CLAVICULAR BRACHIAL PLEXUS BLOCK.

Birbal Baj<sup>1</sup>, Vandana Tyagi<sup>2</sup>, R.S. Chaudhri<sup>3</sup>, Anand Derashri<sup>4</sup>

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**ABSTRACT: BACKGROUND:** Brachial plexus block provides minimal systemic impairment & excellent localized postoperative analgesia for upper extremity surgery. Local anaesthetic agents such as lignocaine, bupivacaine & ropivacaine are widely used along with adjuvant to improve the quality, onset & duration of block and to decrease postoperative analgesic requirement and systemic side effects. Adjuvant like  $\alpha$ -2 agonist (clonidine), acetylcholinesterase inhibitors, opioids etc. are been added to LA's. Clonidine is an imidazoline derivative with  $\alpha$ 2-adrenergic agonistic activity. There has been seen a potentially clear synergism between clonidine & ropivacaine in various regional block anaesthesia. **AIM:** To compare the efficacy of Clonidine as adjuvant to Ropivacaine for Supraclavicular brachial plexus block. **METHODS AND MATERIAL:** This double blind randomized controlled study was done in Mahatma Gandhi Medical College & Hospital, Jaipur. A total of 60 ASA Grade I to IV patient were taken & randomly allocated into 2 groups comprising 30 patients in each. Group I (control group) included patients which were given 30 ml of 0.75% ropivacaine (225 mg) and Group II (study group) included patients which were given 30 ml of 0.75% ropivacaine (225 mg) with 0.4 ml (60 $\mu$ g) clonidine. Sensory function was tested using pinprick and motor with concomitant inability to move the wrist and hand and the first analgesic request was noted. Postoperatively the pain was measured using VAS score (0 to 10). **Statistical Analysis:** Results were expressed as mean and standard deviation. P value of <0.05 was considered statistically significant. **RESULTS:** The mean VAS was found lower in group II when pain was first reported and at 5, 6 & at 9 hr than group I. Duration of sensory block analgesia lasted longer in group II which were given clonidine along with LA. There was no statistically significant difference in onset time, in degree of sedation, and other hemodynamic variables. **CONCLUSIONS:** It can be postulated that clonidine produces longer analgesia time when used as an adjuvant to Ropivacaine for Supraclavicular brachial plexus block.

**KEYWORDS:** Adjuvant, brachial plexus block, clonidine,  $\alpha$ -2 adrenoreceptors.

**INTRODUCTION:** Local anaesthetics are the commonest agents used for brachial plexus block, but their relatively short duration of action may lead to early analgesic intervention in the post operative period.<sup>1,2</sup> A number of adjuvants to local anaesthetics have been used for regional blocks to prolong the intraoperative as well as postoperative analgesia.<sup>3,4</sup>

Clonidine, a selective partial  $\alpha$ -2 adrenergic agonist, is known to increase both sensory and motor blockade of local anaesthetics.<sup>5,6</sup>

The aim of the present study was to evaluate the effect of clonidine as an adjuvant to ropivacaine on duration of sensory and motor block, adequacy of analgesia and associated side effects if any.

**MATERIALS AND METHODS:** The study was approved by the hospital ethical committee and informed consent from all the participants was obtained. Sixty patients of either sex above the age of 18 years belonging to American Society of Anaesthesiologists (ASA) physical status I to IV scheduled for upper limb surgeries were included in the present study. Patients on cardiovascular medications, history of hypersensitivity to clonidine or ropivacaine, and conditions that preclude regional blocks were excluded from the study. The study was carried out prospectively in a double-blinded randomized manner.

All patients were examined preoperatively, and details regarding clinical history and general physical examination recorded. All routine investigations carried out and informed written consent was obtained. During the pre-anaesthetic visit, every patient was familiarized with linear visual analog scale (VAS 0=no pain and 10= worst imaginable pain). Patients were kept fasting for 6 hours and premedicated with oral alprazolam 0.5mg the previous night. In the operating room, after the establishment of intravenous (IV) line and attachment of standard monitors [non-invasive blood pressure (NIBP), electrocardiography (ECG), and pulse oximetry (SpO<sub>2</sub>) ], basal parameters were recorded. An intravenous access was secured in contralateral arm with a wide bore cannula (18G) and intravenous RL infusion was established. Oxygen delivered by a face mask @ 2-3L/min. Premedication/sedation was deliberately avoided to minimize interference during assessment of the quality of block and also to evaluate the post operative pain relief.

The patients were randomly allocated to one of the two groups (n=30 each) and administered 30ml of the coded drugs. Group II received 30ml of 0.75% ropivacaine and clonidine 60µgm. The volume of solution was kept constant to 30ml by adding saline where ever needed. The study drug was prepared by a fellow anaesthesiologist who was not involved in the study. Under all aseptic precautions, supraclavicular brachial plexus block was performed. A paresthesia technique was used for localization of the brachial plexus. A negative aspiration for blood was performed before each incremental injection of 5ml to a total volume of 30ml of drug solution was given. Compression to neurovascular sheath was maintained for at least five minutes following performance of the block to avoid haematoma formation and to minimize distal spread of the mixture.

The time of completion of the injection was taken as the baseline for time interval measurements (0 min) and vital parameters were monitored again at 5, 10, 20, 30, 60, 180, 360, 720 min and later at 24 hours after completion of the block injection.

Evaluation for sensory and motor blockade onset was carried out every minute till first 30 minute and at 60 minute and then hourly for duration and regression for next 24 hours or till the effects lasted whichever was earlier. No intraoperative sedatives were used.

Bradycardia was defined as pulse rate <50bpm and treated with injection Atropine 0.6mg IV. Hypotension was defined as mean blood pressure <55 mm Hg and treated with incremental doses of IV mephentermine 6mg. Respiratory insufficiency was defined as respiratory rate of less than 10 breath / min or an oxygen saturation of less than 92% managed with O<sub>2</sub> and ventilation accordingly.

**RESULTS:** Data of all 60 patients enrolled in the study were included the analysis. The age, weight, height, ASA status and duration of surgery of the patients were comparable in both the groups (Table 1).

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The onset time and the duration of sensory, motor block as well as duration of analgesia were recorded and analyzed (Table 2).

The mean VAS was comparable in both groups in postoperative period till first 4 hours. It was found that VAS was lower in group II at 5 hr, 6 hr & at 9 hr.

The mean VAS when pain was first reported in group I was  $0.96 \pm 1.71$  and in group II was  $0.86 \pm 1.67$  which was lower than group I (p value = 0.8135). (fig. 1).

The mean sedation scores were comparable in both groups at different time intervals. It was found that the sedation score was higher in clonidine group II at 10 & 20 min, but the difference was statistically insignificant.

As far as adverse effect of drug is concern, nausea and headache separately were seen in 5.3% of total study patients. Drowsiness occurred more in clonidine group II but the difference of mean sedation score was statistically insignificant in between group. A total of 18.34% inadvertent vascular puncture occurs during block placement, but the difference in between groups was statistically insignificant.

Hemodynamic parameters showed that the mean arterial blood pressure at baseline for group I and II were  $97.76 \pm 11.97$  mm Hg and  $98.02 \pm 12.04$  mm Hg, which were comparable. Although there was significant fall in the MAP from 30min onwards with comparison to basal MAP in both the groups, but when the changes in MAP were compared in between the groups, they were found to be statistically insignificant. (fig.2)

The mean pulse rate of group I after giving block varied from a minimum of  $80.43 \pm 12.0$  per min or 6<sup>th</sup> hour to a maximum of  $84.75 \pm 13.38$  per min. The mean pulse rate in group II after giving block varies from a minimum of  $74.32 \pm 11.92$  per min at 1<sup>st</sup> hour to a maximum of  $82.79 \pm 11.62$  per min. (fig.3)

Although there was significant fall in the pulse rate from 10 min onwards in clonidine group II in comparison to basal rate of that group. But, throughout the period the two groups were comparable with respect to mean change in pulse rate from baseline at all time intervals, and the difference among two groups was statistically insignificant.

|  | Group I     | Group II    | p-value* |
|--|-------------|-------------|----------|
| Age (years)<br>(Mean±SD)               | 37.90±17.81 | 37±14.62    | 0.8313   |
| Weight (kg)<br>(Mean±SD)               | 60.77±9.36  | 61.23±6.32  | 0.8217   |
| Height (cm)<br>(Mean±SD)               | 165.48±6.95 | 166.32±7.15 | >0.05    |
| ASA I:II                               | 19:6        | 20:5        | >0.05    |
| Duration of surgery (min)<br>(Mean±SD) | 75.97±22.66 | 76.43±20.81 | >0.05    |

Table 1: Patient Characteristics

\* significant difference between two groups p value >0.05 was considered statistically insignificant.

|                           | Group I      | Group II     | p-value |
|---------------------------|--------------|--------------|---------|
| Onset of sensory block    | 15.17±5.09   | 14.71±3.70   | 0.70    |
| Onset of motor block      | 24.38±6.44   | 24.46±7.27   | 0.9629  |
| Duration of sensory block | 422.50±87.75 | 551.07±84.09 | 0.001*  |
| Duration of motor block   | 403.39±87.91 | 533.75±84.36 | 0.001*  |
| Duration of analgesia     | 442.14±86.47 | 576.96±81.45 | 0.001*  |

Table 2: Characteristics of analgesia sensory & motor block

\* significant difference between two groups p value <0.001 was considered statistically significant.

**DISCUSSION:** Surgical stress and pain elicit a consistent and well defined metabolic response involving release of neuroendocrine hormones and cytokines, which lead to myriad of detrimental effects.

Regional anaesthesia besides reducing neuroendocrine stress response, also reduces myocardial work and oxygen consumption by reducing heart rate, arterial pressure and left ventricular contractility. To improve the outcome of surgery, it is necessary to extend into the postoperative period all the advantages of the regional anaesthesia.

Parkhouse and Coworker<sup>7</sup> found that during the first 48 hours postoperatively the pain was maximum and declined after that. It has been emphasized that anesthetic technique should be designed in such a way that it will provide residual analgesia in the postoperative period so that immediate postoperative period would be pain free.

Brachial plexus regional anaesthesia has been a main stay of the anaesthesiologist's armamentarium since Hall<sup>4</sup> first reported the use of cocaine to block upper extremity nerves in 1884. Though several approaches have been described for brachial plexus block, the supraclavicular approach still retains its wide popularity, since it provides short latency and the most complete and reliable anaesthesia (Brown DL 1993).

Adjuvants are added to local anesthetics to improve quality, onset and duration of block and decrease postoperative analgesic requirement and systemic side effects.<sup>11</sup>

The role of alpha agonist in the management of postoperative pain is established. The discovery of  $\alpha$ -2 adrenoceptors on primary afferent terminal (both at peripheral and spinal endings), on neuron in the superficial laminae of the spinal cord and within several brainstem nuclei implicated in analgesia, supports the possibility of analgesic action of alpha agonist at peripheral, spinal and brainstem site.<sup>10, 12, 20</sup>

Preferential nerve blockade of C-fibers by alpha agonist is also known.<sup>15</sup> Also the possible enhancement or amplification of sodium channel blockade action of local anaesthetic, by opening up of potassium channel leading to hyper-polarization of cell is one of the virtues by which alpha agonists act.<sup>10, 12, 20</sup>

It has been established that combined administration of local anaesthetic and clonidine into the brachial plexus ensures a more even, adequate and durable anaesthesia during surgery and post operative period without major side effects, but opinion differs on the incidence of the side effects, particularly the possibility of bradycardia, hypotension and sedation.<sup>20</sup> However, there are limited studies using clonidine as an adjunct to ropivacaine in supraclavicular block.<sup>10</sup> Considering the above facts the present study was planned.

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We observed that the mean time of onset of sensory and motor block was earlier in clonidine group as compared to plain ropivacaine group, though the difference was not statistically significant. Our findings were similar to those of the study conducted by Giorgio Danelli et al<sup>21</sup> and Chakraborty et al<sup>18</sup>. It is believed that when clonidine is added to local anaesthetic mixture, it has synergistic action resulting in earlier onset of nerve block when compared with plain local anaesthetic.

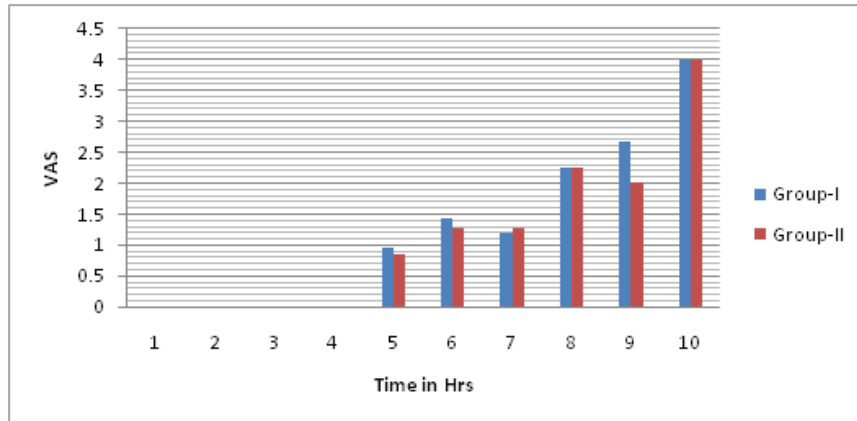


Fig.-1 Mean VAS

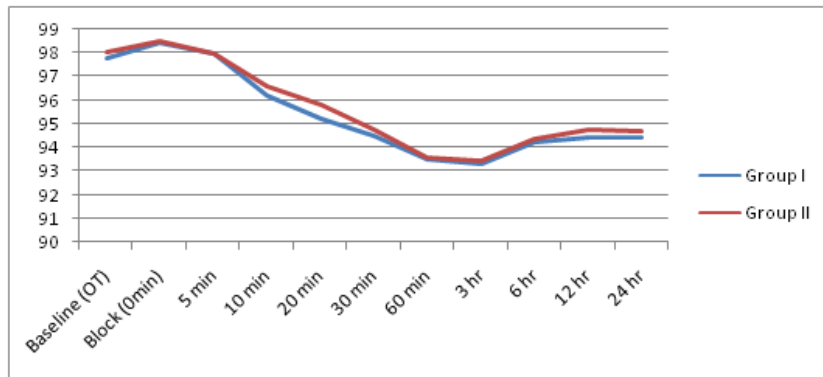


Fig.-2: Mean Arterial Pressure

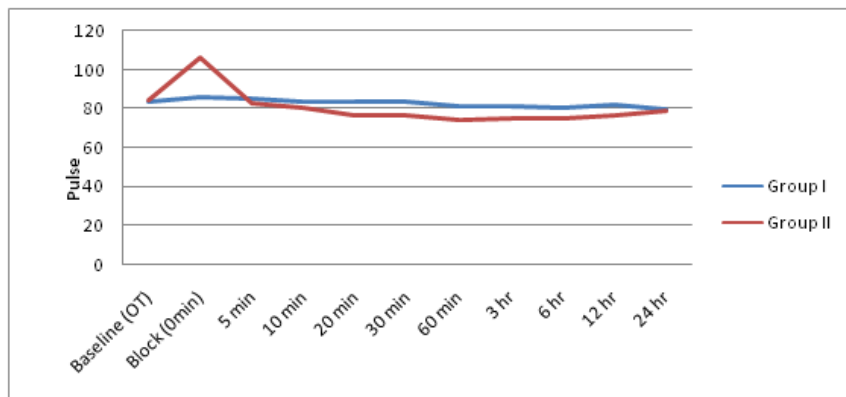


Fig. 3: Mean Pulse Rate

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The mean duration of sensory block in clonidine group II was significantly prolonged ( $p < 0.001$ ) in compare to plain ropivacaine group I. These findings are consistent with previous studies (El Saied et al<sup>14</sup>, Giovanni and Arjuman Ganesh<sup>17</sup>, Eledjam et al<sup>11</sup>).

The mean duration of motor block was significantly longer in clonidine group than ropivacaine group ( $p < 0.001$ ) similar findings were observed by El Saied et al<sup>14</sup>, Chakraborty et al<sup>18</sup> and Daniel M, Popping et al<sup>19</sup> with different duration.

The difference in the duration observed in various studies can be explained by the difference in the strength and volumes of drug used in these studies. Probable explanation for all this inconsistency regarding onset and duration may relate to inter-patient variation in the study population, anatomy of the plexus sheath & difference in the spread of local anaesthetics in the plexus sheath depending upon the block technique.

The duration of analgesia in group II was significantly longer than group I ( $p$  value  $< 0.001$ ).

El Saied et al<sup>14</sup>, Casati A et al<sup>20</sup>, Andrea Casati and Luca Magistris<sup>15</sup>, Giorgio Danelli et al<sup>21</sup>, Chakraborty et al<sup>18</sup>. Studies are in consistence with this study.

Mean VAS scores in postoperative period till 4 hrs, were comparable in both groups. Clonidine in group II prolonged the requirement for rescue analgesia indicating good postoperative analgesia than group I.

All hemodynamic parameters were comparable, although after giving block the mean pulse rate in clonidine group was low as against mean pulse rate in plain ropivacaine group at all time intervals, but was statistically insignificant. No patient in any group suffered bradycardia. However, when the changes in mean blood pressures were compared between the groups, they were found comparable, and no patient in any group had hypotension. Sinelyn, FJ. et al<sup>9</sup> and Murphy, D.Bet al<sup>10</sup> did not find any significant hypotension/bradycardia whereas Bernard JM<sup>7</sup> et al and Gaumann DM et al<sup>14</sup> observed significant hypotension.

Apart from only some incidence of vascular puncture during block placemen, we did not in counter any vascular complications and no other significant postoperative complications observed in the study. Drowsiness occurred more in patients of clonidine group when compared to plain ropivacaine group; however mean sedation score in between group was comparable. Nausea & headache separately were seen in 5.3% of total patients. But the incidence of these adverse effects in between groups was found to be statistically insignificant.

To conclude, the clonidine when added to ropivacaine for brachial plexus block has almost same onset time of both sensory and motor block as compared to plain ropivacaine but increases the duration of both sensory and motor blockade. Duration of analgesia was significantly increased by clonidine when added to ropivacaine in brachial plexus block. Clonidine exhibits sedative effect in some of the patients. This effect is at time, beneficial for the patients undergoing surgery under regional block. Though statistically insignificant, addition of clonidine results in more intraoperative hemodynamic stability. Both clonidine and ropivacaine do not cause any major side effects in anaesthesia techniques. Thus, this study shows that clonidine 60 $\mu$ g added to ropivacaine 0.75% in an appropriate technique has low side effect profile with considerable therapeutic benefit and enhances the quality of supraclavicular brachial plexus block.

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## **AUTHORS:**

1. Birbal Baj
2. Vandana Tyagi
3. R.S. Chaudhri
4. Anand Derashri

## **PARTICULARS OF CONTRIBUTORS:**

1. Associate Professor, Department of Anaesthesiology, Mahatma Gandhi Medical College & Hospital, Jaipur.
2. Post Graduate Trainee, Department of Anaesthesiology, Mahatma Gandhi Medical College & Hospital, Jaipur.
3. Professor, Department of Anaesthesiology, Mahatma Gandhi Medical College & Hospital, Jaipur.

4. Medical Officer, Department of Anaesthesiology, Mahatma Gandhi Medical College & Hospital, Jaipur.

## **NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Birbal Baj,  
D-702, Ashadeep,  
Green Avanie, Goner Road,  
Jagatpura, Jaipur,  
Rajasthan, India.  
Email – drvandanatyagi@gmail.com

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