

**COMPARATIVE STUDY OF ROPIVACAINE (0.75%) ALONE VS. ROPIVACAINE (0.75%) WITH CLONIDINE (1MCG/KG) IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCKADE**

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**ABSTRACT**

**Context:** Brachial plexus block provides post-operative analgesia in addition to intra Operative anaesthesia without any systemic side effects. Ropivacaine is a Local Anaesthetic belonging to amino amide group. Clonidine is a selective alpha – 2 Adrenergic agonist. It acts as an adjuvant to Local Anaesthetics for regional anaesthesia.

**Aims:** To evaluate the effect of Clonidine as an adjuvant to local anaesthetic Ropivacaine on onset as well as duration of sensory & motor blockade and quality of analgesia. **Methods and Material:** 60 adult patients falling in age group of 20 to 60 years undergoing upper limb surgery under supraclavicular brachial plexus blockade using peripheral nerve stimulator were included in the study. These patients were randomly allocated to two groups, each group with 30 patients. **Group1:** 25 ml 0.75% Ropivacaine + 2 ml normal saline. **Group2:** 25 ml 0.75% Ropivacaine mixed with Clonidine at dose of 1 mcg/kg which had been diluted to 2 ml with normal saline. Vitals, Sensory and motor blockade and VAS scores were recorded. Results were analyzed using Unpaired Student t- test.

**Results:** Onset of sensory and motor block was significantly earlier and duration of analgesia and motor blockade was prolonged with lower VAS Scores in group 2. **Conclusions:** Addition of Clonidine to Local Anaesthetic leads to faster onset, prolonged duration of both sensory and motor block and better postoperative analgesia following supraclavicular brachial plexus block.

**KEYWORDS:** Ropivacaine; Clonidine; Supraclavicular Brachial Plexus Block, Peripheral Nerve Stimulator.

**INTRODUCTION**

Regional Anaesthesia offers an excellent alternative for patients undergoing upper limb who are compromised hemodynamically or General Anaesthesia can be troublesome. Brachial plexus block provides post-operative analgesia in addition to intra operative anaesthesia without any systemic side effects. Ropivacaine,<sup>[1]</sup> is a Local Anaesthetic belonging to amino amide group, which can be used as an alternative to Bupivacaine with an advantage of proven safety profile on CVS and CNS. Clonidine is a selective alpha – 2 adrenergic agonist.<sup>[2,3,4]</sup> It acts as an adjuvant to Local Anaesthetics for regional anaesthesia by increasing sensory as well as motor blockade action of L.A.<sup>[5]</sup>

**Aims:** This study was taken up to evaluate the effect of clonidine as an adjuvant to local anaesthetic Ropivacaine on

1. Onset as well as Duration of sensory & motor blockade.
2. Adequacy of analgesia
3. Hemodynamic variables (HR, BP, RR)
4. Effectiveness of pain relief post operatively using VAS score.
5. Any side effects.

**MATERIALS AND METHODS**

60 adult patients falling in age group of 20 to 60 years, belonging to either sex, weighting between 50 to 70 kilograms, having physical status as per American Society of Anesthesiologists grade 1 or 2 were included in the study. These pts had to undergo hand or forearm

surgery under supraclavicular brachial plexus blockade using peripheral nerve stimulator. These patients were randomly allocated to two groups, each group with 30 patients.

**Group1:** 25 ml 0.75% Ropivacaine + 2 ml normal saline.

**Group2:** 25 ml 0.75% Ropivacaine mixed with Clonidine at dose of 1 mcg/kg which had been diluted to 2 ml with normal saline.

Patient with age <20 and >60 years, diseases of Central Nervous System, Cardio Vascular system, weighing <50 kg and >70 kg, having psychiatric disorder, bleeding disorders,

hypersensitivity to L.A., any abnormality in the local area and chronic drug abuse were excluded from our study.

### Method

After taking due clearance from Ethical Committee and informed written consent, patients were kept fasting for 6 hours and provided anxiolysis with Tab. Alprazolam 0.5mg the previous night. On the day of surgery in the operating room, intravenous line was established in the contralateral arm using 18 G green cannula and i.v. infusion with RL infusion was started. Standard monitoring with non-invasive blood pressure, electrocardiography, and pulse oximetry was started and basal parameters were recorded. Sedative premedication was avoided to minimize interference in assessment of grading of block and also post-operative pain relief. The total volume of drug to be injected was 27 ml. Supraclavicular brachial plexus blockade was performed using B Braun Peripheral Nerve Stimulator model HNS 12.

**Nerve Stimulator Guided Nerve Block:** was performed taking care of strict aseptic precautions

- Initial frequency was set at 1 Hz. Negative electrode was connected to a port in the needle and Positive one to ECG electrode placed near the ipsilateral shoulder.
- 50 mm long insulated needle was taken. 2mA current strength was set and then we observed for twitching in the fingers. Twitching of all fingers was taken as a satisfactory motor response.
- Current strength was gradually reduced to 0.5 mA and twitching in fingers monitored
- Continuously. Before each incremental injection of 5ml a negative aspiration for blood was
- Performed to avoid intravascular injection of drug. Total 27 ml of drug solution was administered to each patient.
- Care was taken that if on decreasing the current strength, finger twitch disappeared, then the
- Needle position was readjusted to re-elicite the response and the procedure was repeated.

**Sensory function** was tested on a 3 point pain scale using pin prick with a 25G needle.

1. Sharp sensation
2. Blunt sensation
3. No sensation

**Motor block** was assessed by using modified Bromage Scale

- 4 Full strength in the relevant muscle groups
- 3 Strength reduction, but is able to move against resistance
- 2 Ability to move against gravity but not against resistance
- 1 Discrete movements (like trembling) of muscle group
- 0 Absence of any movements

Onset and duration of sensory (defined by pin prick test 3 to 1) and motor block (modified Bromage Scale 0 to 4) and 1st analgesic request was noted.

### Post-operative observations

Patient was assessed every 15 min till the complete regression of sensory and motor block.

When VAS =4, all patients received Inj Diclofenac 75mg intramuscular and time was recorded and study ended here.

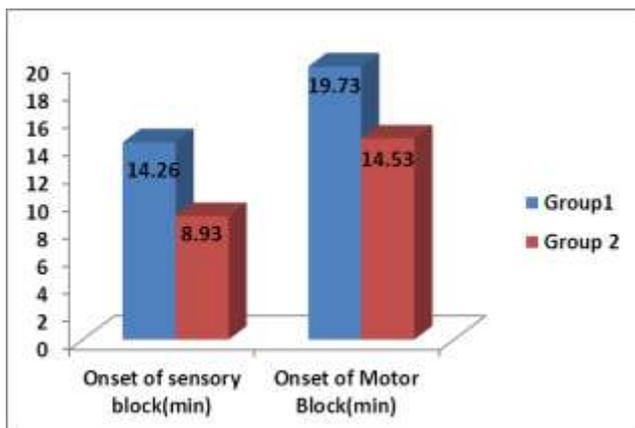
### Statistical analysis

Mean and standard deviation were calculated. Onset as well as duration of both sensory and motor blockade was noted down. Also, duration of analgesia and hemodynamic parameters were monitored and recorded. Unpaired Student t- test was used for testing the significance of the two groups. Analysis of observations was performed using SPSS statistics software (VERSION 16). P-value was considered Non-Significant if >0.05, Significant if <0.05, Mod significant if <0.01 and Highly Significant if <0.001.

### RESULTS

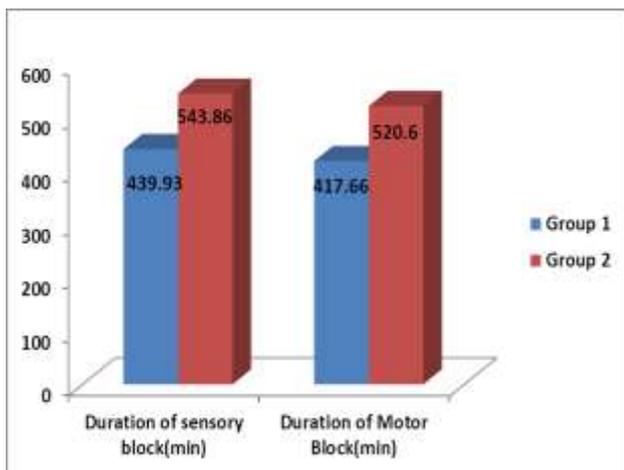
The demographic profile consisting of age, sex, height, weight, ASA grade, duration of surgery was similar in both control as well as cohort group. Baseline vitals like heart rate, systolic, diastolic and mean blood pressure and oxygen saturation were also found to be statistically similar in both groups. Average weight of Group 1 pts was 62.54 kg and in Group 2 pts was 63.26kg. Sixty four patients were studied initially. Two patients were excluded from each group for incomplete/ failed block to whom general anaesthesia was administered.

The onset of both sensory and motor block was earlier in clonidine treated patients i.e. 8.93 min for sensory and 14.53 min for motor block versus 14.26 min for sensory block and 19.73min for motor block. This aspect was found to be statistically significant (P<0.05) (Table 3), (Fig. 1).



**Fig. 1: Comparison of Onset of Sensory and Motor Block.**

Mean duration of sensory block was 439.93 min in control group and 543.86 min in group 2. Mean duration of motor block was 417.66 min in Group I patients while in Clonidine treated patients mean duration of motor block was 520.60 min, which was found to be statistically significant. ( $P < 0.05$ ) (table 3) (fig. 2).



**Fig. 2: Comparison of Duration of Sensory and Motor Block.**

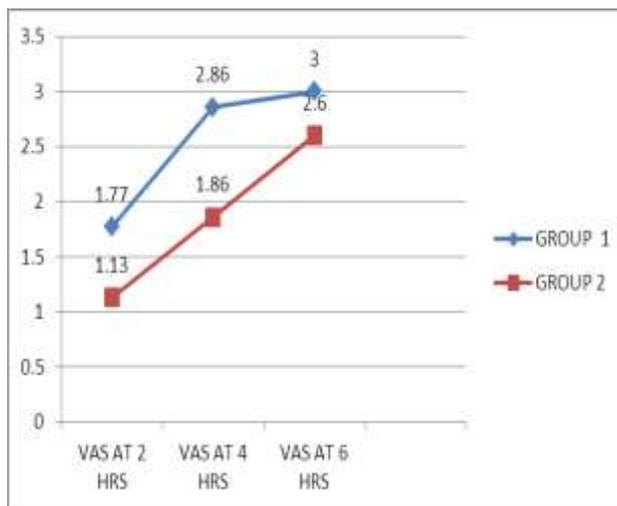
**Table 1: Comparison of Post-Operative HR in group 1 and group 2.**

	Group 1	Group 2	P-value	Interpretation
Post -op HR at 4 hrs	88.93	85.33	<0.01	Mod significant
Post -op HR at 8 hrs	94.73	88.40	<0.001	Highly Significant
Post -op HR at 12 hrs	93.5	95.1	0.056	Non-significant

**Table 2: Comparison of Post-Operative MAP in group1 and group 2.**

	Group 1	Group 2	P-value	Interpretation
Post-op MAP at 4 hrs	95.43	90.80	<0.001	Highly Significant
Post-op MAP at 8 hrs	98.50	95.20	<0.05	Significant

In the present study we found a significant decrease in onset and prolongation in duration of both sensory and motor blockade in Group 2 versus Group 1. In this randomized, double-blinded trial in group 2 (clonidine treated) mean onset time of sensory block was 8.93 minutes and in group 1 (saline treated) was 14.26 min.



**Fig. 3: Comparison of Post-Operative Vas Scores In Group 1 and Group 2.**

**DISCUSSION**

Adjuvants like neostigmine, hyaluronidase, opioids, tramadol and dexamethasone have been reported to prolong the duration of analgesia when used with local anaesthetic in peripheral nerve blocks.<sup>[6,7]</sup>

Casati *et al.*<sup>[8]</sup> performed sciatic-femoral nerve block for foot surgery by adding clonidine in dose of 1 µg /kg to ropivacaine (0.75%). They found that duration of postoperative analgesia increased by 3 hrs. No significant hemodynamic effects were noticed.

So sensory blockade onset becomes faster by adding clonidine in our study. The study by **Erlacher** showed that adding clonidine did not change the time of onset of block, this aspect was not in accordance to our study.[9] Mean duration of sensory and motor block in patients of group 2 (clonidine) was 543.86 minutes and 520.60

minutes respectively (table 3, fig.2). Mean duration of sensory block and motor block in patients of group 1 (saline) was 439.93 minutes and 417.66 minutes respectively. The difference in both the groups is statistically significant unlike study by **Erlacher**.<sup>[10]</sup>

Postoperative analgesia lasted 567.13 min in group2 and 461.93 min in group 1 which was also statistically significant (P <0.001). The results of this study with reference to onset of sensory as well as motor block are in agreement with study by **Antonucci S.**<sup>[2]</sup> and its duration of sensory motor blockade in group 2 are in consensus with study of **El Saied et al.**<sup>[11]</sup> Post-operative vitals like HR and MAP at 2 to 8 hrs. showed significant relationship with simultaneously observed VAS score among Group 1 and Group 2 patients. VAS scores in Group 1 at 2, 4 and 6 hrs. were 1.77, 2.86, and 3.0 respectively while in Group 2 VAS scores at 2, 4 and 6 hrs. were 1.13, 1.86 and 2.60 respectively (Figure 3). Lower VAS scores in Clonidine treated Group 2 patients with normotension and stable heart rate during 2 to 8 hrs. post operatively was perhaps related to better analgesia cover and thus comfort offered by adjuvant Clonidine.

**Table 3: Characteristics of sensory and motor block in group 1 and group 2.**

	Group 1	Group 2	P-value	Interpretation
Onset of sensory block	14.26	8.93	<0.001	Highly Significant
Onset of motor block	19.73	14.53	<0.001	Highly Significant
Duration of sensory block	439.93	543.86	<0.001	Highly Significant
Duration of motor block	417.66	520.60	<0.001	Highly Significant
Rescue Analgesia(min)	561.93	567.13	<0.001	Highly Significant
Hypotension	0	0	<0.05	Non-significant

**Jaiswal et al.**<sup>[13]</sup> found that there was no significant difference in the onset and duration of both sensory as well as motor block on adding 150mcg clonidine. Injection of alpha 2 agonists perineurally has shown to influence postoperative analgesia.

**Murphy et al.**<sup>[14]</sup> conducted six trials by adding clonidine to local anaesthetic during brachial plexus block. He concluded that clonidine increased the duration of postoperative analgesia when added in doses up to 150 µg, without any significant adverse effects.

**Table 4: Side Effects and Complications.**

Group	Hypotension	Bradycardia
1	-	-
2	-	-

**McCartney et al.**<sup>[15]</sup> after his review of 27 studies (1,385 patients) concluded that Clonidine was beneficial only when it was added to an intermediate-acting local anaesthetics. Both control as well as cohort groups showed no significant hemodynamic changes in intraoperative and postoperative period (Table 4). This is akin to antecedent studies.<sup>[11,12]</sup> but discordant to the study by **Culebras**.<sup>[16]</sup>

**This aspect was not reported in earlier studies.**

**Antonucci**<sup>[2]</sup> evaluated effects of clonidine, sufentanil and tramadol used as an adjuvant to ropivacaine in brachial plexus block. He concluded that tramadol provides a significant reduction in time of onset of both sensory and motor block. He also found that the quality and duration of prolongation of anaesthesia and analgesia was analogous to that with sufentanil and clonidine.

**Erlacher W et al.**<sup>[10]</sup> in the year 2000 studied the efficacy of clonidine as an adjuvant to ropivacaine in axillary plexus block. They didn't report any significant effect on onset or duration of sensory as well as motor blockade in clonidine group.

**El Saied et al.**<sup>[11]</sup> showed an increase in duration of analgesia from 587 minutes in control group to 828 minutes in clonidine group with a mean difference of 241 min. He added 150 µg clonidine to 40 ml of 0.75% Ropivacaine, in brachial plexus block. They also noted that there was no significant difference in time of onset of both sensory as well as motor blocks of both groups and no major side effects were noted.

In future more studied can be conducted using lower concentrations of Ropivacaine and using it as per body weight.

Strength of study was high Power of the study and prolonged post operative monitoring. There was no controversy during the study period.

The limitation of present study was small sample size and ropivacaine was not used as per body weight in kg.

The greater duration of the motor blockade as well as postoperative analgesia in clonidine treated group could be as a result of the direct action of clonidine on C and A delta fibers conduction.<sup>[18,19,20]</sup> Synergistic action of Clonidine with the local anaesthetic Ropivacaine probably also resulted in this prolonged analgesic effect.<sup>[21,22,23]</sup> Study results showed that duration of sensory block tends to last longer than motor block perhaps because large motor fibers require a higher concentration of local anesthetic than small sensory fibers. So due to the same reason motor function returns before sensory perception and thus the duration of the motor block is shorter than that of sensory block.

**CONCLUSION**

Addition of Clonidine to Local Anaesthetic leads to faster onset, prolonged duration of both sensory and motor block and better postoperative analgesia as interpreted by extended duration of analgesia and VAS, without any significant side effects following supraclavicular brachial plexus block.

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**REFERENCES**

1. Akerman B, Hellberg IB, Trossvik C. Primary evaluation of local anaesthetic properties of amino amide agent ropivacaine. *Acta Anaesthesiol Scand*, 1988; 32: 571- 87.
2. Antonucci S; Adjuvants in axillary brachial plexus blockade- Comparison between tramadol, clonidine and sufentanil. *Minerva Anesthesiol*, 2001; 67: 23–27.
3. Bernard JM, MaCaire P. Dose-range effects of clonidine added to lidocaine for brachial plexus block. *Anaesthesiology*, 1997; 87: 277-84.
4. Butterworth JF 5th, Strichartz GR. The alpha 2- adrenergic agonists clonidine and guanfacine produce tonic and phasic block of conduction in rat sciatic nerve fibers. *Anaesth Analg*, 1993; 76: 295-301.
5. Casati A, Magistris L, Beccaria P, Cappelleri G, Aldegheri G, Fanelli G. Improving postoperative analgesia following axillary brachial plexus anesthesia using 0.75% ropivacaine. A double-blind evaluation of adding clonidine. *Minerva Anesthesiol*, 2001; 67: 407- 12.
6. Damien B, Murhy, Cartney, Vincent WS; Novel analgesic adjuncts for brachial plexus block A systemic review. *Anesth Analg*, 2000; 90: 1122 – 1128.
7. David L.B. Spinal, epidural and caudal anaesthesia. In: Miller RD, editor. *Miller's Anaesthesia*. 6th ed, Vol. 2. Philadelphia: Churchill Livingstone, 2005; 1653-63.
8. Casati A, Magistris L, Fanelli G, Beccaria P, Cappelleri G, Aldegheri G, *et al.* Small- dose clonidine prolongs postoperative analgesia after sciatic- femoral nerve block with 0.75% ropivacaine for foot surgery. *Anaesth Analg*, 2000; 91: 388- 92.
9. Erlacher W, Schuschnig C, Koinig H, Marhofer P, Melischek M, Mayer N, *et al.* Clonidine as adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary, perivascular brachial plexus block. *Can J Anaesth*, 2001; 48: 522- 5.
10. Erlacher W, Schuschnig C, Orlicek F, Marhofer P, Koinig H, Kapral S; The effects of clonidine on ropivacaine 0.75% in axillary perivascular brachial plexus block. *Acta Anaesthesiol Scand.*, 2000; 44(1): 53-55.
11. El Saied AH, Steyn MP, Ansermino JM. Clonidine prolongs the effect of ropivacaine for axillary brachial plexus blockade. *Can J Anaesth*, 2000; 47: 962- 7.
12. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S. Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: A randomized, controlled study. *Br J Anaesth*, 2005; 94: 112.
13. Jaiswal R, Bansal T, Mehta S; A study to evaluate effect of adding clonidine to ropivacaine for axillary plexus blockade. *Asian Journal of Pharmaceutical and Clinical Research*, 2013; 6(3): 166-168.
14. Murphy DB, McCartney CJ, Chan VW; Novel analgesic adjuncts for brachial plexus block: A systematic review. *Anaesth Analg.*, 2000; 90: 1122–1128.
15. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anesthetic does not prolong postoperative analgesia after brachial plexus block but does induce hemodynamic changes. *Anaesth Analg*, 2001; 92: 199-204.
16. Dejong RH, Wagman IH. Physiological mechanisms of peripheral nerve block by local anaesthetics. *Anaesthesiology*, 1963; 24: 684- 727.
17. Denise J: Nerve Block In – Miller RD, editor *Miller's Anaesthesia*. 7th ed. Philadelphia, Churchill Livingstone, 2009; 1639 – 49.
18. Eisenach JC, DeKock M, Klimscha W;  $\alpha 2$  adrenergic agonists for regional anaesthesia: A clinical review of clonidine. *Anaesthesiology*, 1996; 85: 655 – 674.
19. Khasar SG, Green PG, Chou B, Levine JD. Peripheral nociceptive effects of alpha 2- adrenergic receptor agonists in the rat. *Neuroscience*, 1995; 66: 427-32.
20. Eisenach JC. Overview: first international symposium on  $\alpha$ -2 adrenergic mechanism of spinal anaesthesia. *Reg Anaesth*, 1993; 18(4S): i-vi.
21. Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effects of lidocaine on C- fiber action potential. *Anaesth Analg*, 1992; 74: 719- 25.
22. Elia N, Culebras X, Mazza C, Schiffer E, Trame'r MR: Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. *Reg Anaesth Pain Med.*, 2008; 33: 159 – 167.
23. Elliott S, Eckersall S, Fligelstone L, Jothilingam S. Does the addition of clonidine affect duration of analgesia of bupivacaine wound infiltration in inguinal hernia surgery? *Br J Anaesth*, 1997; 79: 446-9.