The Effects of Two Different Doses of Clonidine as Adjuvant to Ropivacaine in Supraclavicular Brachial Plexus Block- A Randomized Controlled Study.

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ABSTRACT

Background: Several clinical studies have shown that clonidine prolongs sensory motor blockade when used with bupivacaine but ideal doses of clonidine on ropivacaine is not well defined and to evaluate the effect of two doses of clonidine on ropivacaine, for supraclavicular brachial plexus blockade. **Methods:** In a prospective randomized double blind study supraclavicular brachial plexus blockade were performed in 80 patients using 35 ml ropivacaine (0.5%). Group A (n=40) had 2 µg/kg clonidine and in Group B (n=40) 1 µg/kg clonidine added to ropivacaine. Sensory and motor blockade was assessed every 5 min till 30 min and at 15 min interval thereafter. **Results:** Mean sensory onset time in group A was 10.42 ± 5.5 min and in group B was 15.83 ± 6.51 min, which was statistically significant. Patients of group A had a mean motor onset time 14.35 ± 7.8 min and patients of group B had a mean motor onset time 18.53 ± 7.61 min, the difference being statistically significant. Mean duration of sensory block in group A was 484.13 ± 63.1 min and in group B was 390.83 ± 72.63 min, which was statistically significant. Patients in-group A had a mean duration of motor block 550 +60.1 min and patients in group B had a mean duration of motor block 430.43+68.5 min, which was statistically significant. **Conclusion:** The addition of clonidine in dose of 2 µg/kg to ropivacaine for brachial plexus blockade, increases the onset and duration of motor and sensory block significantly.

Keywords: Ropivacaine, Clonidine, brachial plexus.

INTRODUCTION

Brachial plexus block provides both intraoperative anaesthesia and postoperative analgesia without any systemic side-effects.[1] Ropivacaine has lower lipid solubility and have produced less central nervous system toxicity and cardiotoxicity than bupivacaine for which it is gaining popularity over bupivacaine for peripheral nerve blocks.[2] There has always been a search for ideal adjuvant to local anaesthetics for regional nerve block that prolong the analgesia with lesser adverse effects.[3] Several clinical studies have shown that clonidine can prolong the duration of analgesia when used in combination with local anaesthetic agents like bupivacaine.[4] Previous studies on the effect of adding clonidine to ropivacaine has shown conflicting result in different nerve blocks. Some study shows potentiation of block and some study show no impact.[5] As further research is required on this ,we planned to evaluate the effect of adding different doses of clonidine to ropivacaine in supraclavicular brachial plexus block.

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MATERIALS AND METHODS

Following approval from the local hospital ethics committee, we conducted this study in the department of anaesthesiology and critical care, SCB medical college, hospital from October 2014 to July 2015. Eighty patients of American Society of Anaesthesiologists (ASA) grade I or II posted for hand or forearm surgery were recruited to a prospective randomised, double blind, study.

Exclusion criteria were patients of age <18 yr or >60 yr, patients receiving anticoagulants, patients with history of hypertension, peripheral neuropathy and hypersensitivity to local anaesthetic agents.

Details of the anaesthetic technique and the study protocol were fully explained to patients during pre-anaesthetic check-up and informed written consent was obtained from each patient. Relevant investigations were performed as required. Before the procedure, visual analogue scale (VAS) on 0-10 cm. was explained to the patient for the assessment of pain where 0 denotes no pain and 10 denotes worst pain.

Patients, randomly allocated by computer generated randomization list divided into two groups A and B Group A (n=40) - ropivacaine 0.5% (35 ML) with 2 µg/kg clonidine (2 ml)

Group B (n=40) - ropivacaine 0.5% (35 ML) with 1 µg/kg clonidine (2 ml by adding 1 ml normal saline)

Identical syringes were loaded with 1 ml of either group A or B and labelled by the anaesthesiologist, not involved in nerve block.

On arrival in the operation room, baseline heart rate, blood pressure and oxygen saturation were recorded and monitored throughout the procedure. An intravenous line was secured in the unaffected limb and Ringer's lactate was started. All the patients received brachial plexus block through the supraclavicular approach by an experienced anaesthesiologist using nerve locator. Following negative aspiration, 35 mL of a solution containing local anaesthetic combined with clonidine or normal saline was injected. A 3-min massage was performed to facilitate an even drug distribution. Sensory block was assessed by the pinprick method. Assessment of sensory block was done at every 5 minutes after completion of drug injection in the dermatomal areas corresponding to the median nerve, radial nerve, ulnar nerve and musculocutaneus nerve till complete sensory blockade. Sensory onset was considered when there was a dull sensation to pin prick with a 23G needle along the distribution of any of the above-mentioned nerves. Complete sensory block was considered when there was complete loss of sensation to pin prick

Sensory block was graded as-[6]

Grade 0: Sharp pin felt

Grade 1: Analgesia, dull sensation felt

Grade 2: Anaesthesia, no sensation felt.

Assessment of motor block was carried out by the same observer at each 5 minute till complete motor blockade after drug injection. Onset of motor blockade was considered when there was Grade 1 motor blockade. Peak motor block was considered when there was Grade 2 motor blockade. Motor block was determined according to a modified Bromage scale for upper extremities on a 3-point scale.[7]

0 – normal motor function with full extension and flexion of elbow, wrist, and fingers,

1–decreased motor strength, with ability to move only fingers,

2–complete motor block with inability to move elbow, wrist, and fingers.

The block was considered incomplete when any of the segments supplied by median, radial, ulnar and musculocutaneus nerve did not have analgesia even after 30 min of drug injection. These patients were supplemented with intravenous fentanyl (1 μg/ kg) and midazolam (0.02 mg/kg). When more than one nerve remained unaffected, it was considered a failed block. In this case, general anaesthesia was given .Patients were monitored for haemodynamic variables such as heart rate, blood pressure and oxygen saturation every 15 min after the block intraoperatively and every 60 min post-operatively. Sedation of patient was assessed by the Ramsay Sedation Score.[8]

Assessment of blood loss was done and fluid was administered as per the loss. The intra- and post-operative assessment was done by an anaesthesiologist who was unaware of the drug used. Patients were assessed for the duration of analgesia as per visual analogue scale of 0 to 10. The visual analogue scale was recorded post-operatively every 30 min till the score of 5. The rescue analgesia was given in the form of inj. IV paracetamol at the visual analogue scale of 5 and the time of administration was noted. All patients were observed for any side effects like sedation, nausea, vomiting, dryness of mouth and complications like pneumothorax, haematoma, local anaesthetic toxicity.

The duration of sensory block was defined as the time interval between the end of local anaesthetic administration and the complete resolution of anaesthesia on all nerves. The duration of motor block was defined as the time interval between the end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm.

Statistical analysis

Results are expressed as mean ± standard deviation. Chi-square test was applied for non-parametric data. Parametric data were analysed by Unpaired T–test. Statistical analysis was performed by SPSS (Version 16). P-value was considered significant if <0.05 and highly significant if <0.001.

RESULTS

There was no statistically significant difference between the demographics (age, sex, height, weight, ASA grade, duration of surgery).Also there was no statistical significance in baseline parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean atrial pressure and oxygen saturation [Table 1]. Eighty patients were studied. Of these two patients were excluded from each group for incomplete / failed block to whom general anesthesia was administered.

Table 1: Distribution of subject according to demographic profile and vital signs.

	Group A	Group B	P value
Age (year)	30.6+10.2	32.5+9.6	0.3936
Sex ratio (M/F)	32/8	30/10	0.7895
Weight (kg)	60.4+11.42	61.2+10.64	0.7467
Height (cm)	162+12.64	164.3+11.68	0.4006
ASA Grade (I/II)	30/10	32/8	0.7895
Duration of Surgery (min)	92.6+28.4	91.8+29.6	0.9022
Base line heart rate (BPM)	79.2+14.4	80.4+13.8	0.7046

Base line SBP (mm of Hg)	126.0+8.9	124.4+9.1	0.4290
Base line DBP (mm of Hg)	78.3+8.4	77.6+7.6	0.6970
Base line MAP (mm of Hg)	91.6+7.8	92.1+8.2	0.7807
Base line SPO$_2$ (%)	97.2+1.4	97.6+1.2	0.1740

Parametric data expressed as mean+standard deviation, categorical data (sex) expressed as frequency (%) using Chi-square analysis. P<0.05: Statistically significant. ASA= American society of anaesthesiologists, BPM=Beats per minute, SBP=Systolic blood pressure, DBP=diastolic blood pressure, MAP=mean arterial pressure, SPO2= oxygen saturation
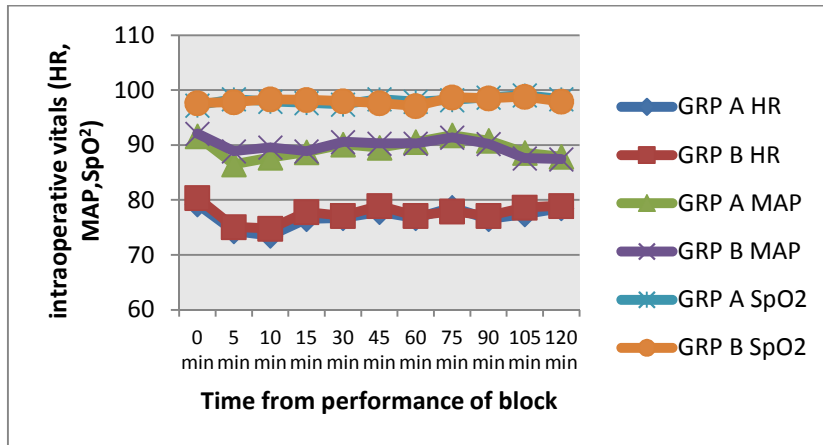

Figure 1: Comparison of intraoperative vitals (heart rate, mean arterial pressure, and oxygen saturation) in between Group A and Group B.
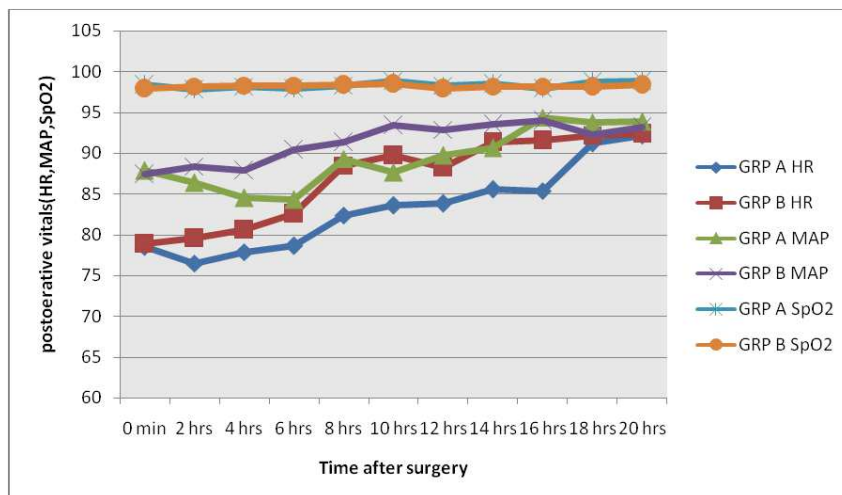

Figure 2: Comparison of postoperative vitals (heart rate, mean arterial pressure, and oxygen saturation) in between Group A and Group B.

No statistical difference was noted in the hemodynamic parameters (mean HR, MAP, SpO$_2$) before and after giving the block, throughout the surgery and postoperatively [Figure 1, 2].

The onset of block was earlier in group A patients, that was 10.42+5.5 min for sensory block and 14.35 ± 7.8 min for motor block than those in group B 15.83 ± 6.51 min for sensory block and 18.53+7.61 min for motor block, which was statistically significant ($P < 0.05$) [Table 2] [Figure 3].

Table 2: Characteristics of sensory and motor block in group A and group B.

	Group A Mean ±SD	Group B Mean ±SD	P value
Onset of sensory block (min)	10.42+5.5	15.83+6.51	0.0002
Onset of motor block (min)	14.35+7.8	18.53+7.61	0.0171
Duration of sensory block (min)	484.13+63.1	390.83+72.63	0.0001
Duration of motor block (min)	550 +60.1	430.43+68.5	0.0001
Duration of analgesia (min)	586+56.6	465.6+62.3	0.0001

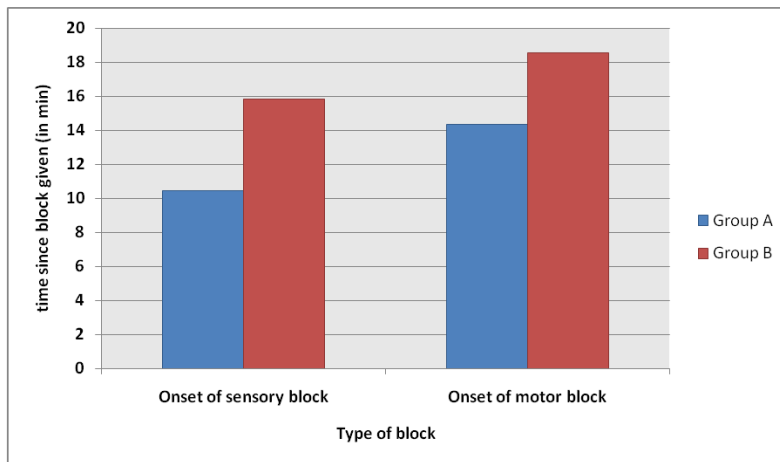Data expressed as mean + standard deviation. P<0.05= statistically significant

Figure 3: Comparison between Group A and Group B for time of onset for sensory and motor block.
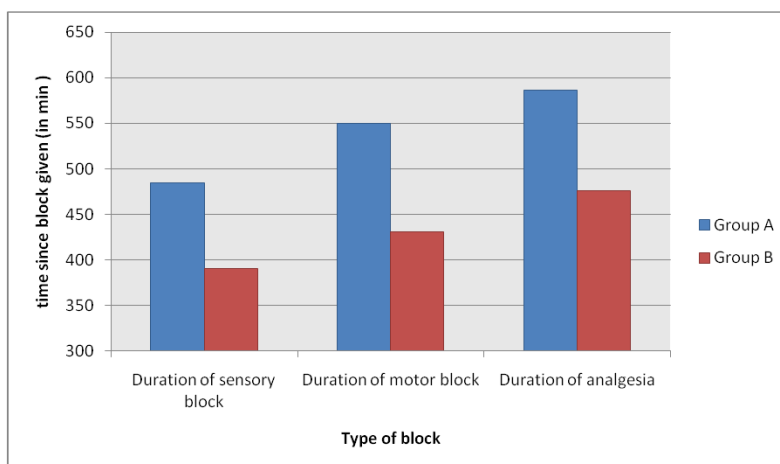

Figure 4: Comparison between Group A and Group B for duration of sensory, motor block and analgesia.

Mean duration of sensory block in-group A was 484.13 ± 63.1 min and in-group B was 390.83 ± 72.63 min. Patients belonging to group A had a mean duration of motor block 550 ± 60.1 min and group B had a mean duration of motor block 430.43 ± 68.5 min, which was statistically significant. [Table 2] [Figure 4]. Postoperative analgesia lasted 586 ± 56.6 min in-group A and 465.6 ± 62.3 min group B which was also statistically significant ($P < 0.05$).

Sedation score of patients in-group A (42.5%) were higher than those in-group B (15%) intraoperatively and postoperatively and this was statistically significant ($P < 0.05$).

DISCUSSION

The analgesic properties of clonidine when administered intrathecally or epidurally as adjuvant have been well demonstrated.[9] They are attributed to its α_2-agonist properties. Its action on large no α_2 receptors present in the central nervous system, at loecus coeruleus and dorsal horn of the spinal cord, is the main mechanism of centrally mediated sedation and analgesia.[10] Specific peripheral effects of clonidine appear less obvious because α_2-adrenoreceptors are not present on the axon of the normal peripheral nerve.[10] It has been postulated that clonidine improved the duration of postoperative analgesia only when used as an adjuvant to intermediate-acting local anaesthetics and that it was not worthwhile to combine it with long-acting local anaesthetics. Two reviews have addressed this issue.[11,12]

Murphy et al.[11] analyzed randomized trials that investigated the usefulness of a variety of adjuvants, including clonidine added to local anaesthetics for brachial plexus block. On the basis of data from six trials (349 patients), they concluded that clonidine in doses up to 150 µg increased the duration of postoperative analgesia with minimal adverse effects. McCartney *et al.*[12] reviewed 27studies (1,385 patients) using clonidine as an adjuvant in low doses to local anaesthetics for a variety of peripheral nerve blocks. They concluded that clonidine was beneficial only when added to intermediate-acting local anaesthetics.

In this randomized, double-blinded trial, we compared two doses of clonidine as an adjuvant to ropivacaine in supraclavicular brachial plexus block, and found that there was significant decrease

in onset and increase in duration of sensory and motor blockade in the clonidine group A in comparison to B group. In the present study in group A (clonidine- 2 µg/kg) mean onset time of sensory block was 10.42+5.5 minutes and In group B (clonidine- 1 µg/kg) it is 15.83+6.51 min. Mean onset of motor block was 14.35+7.8 minutes in group A and 18.53+7.61 min in group B [Table 2] . Mean duration of sensory block and motor block in patients of group A was 484.13+63.1 minutes and 550 +60. 1 minute respectively [Table 2]. Mean duration of sensory block and motor block in patients of group B was 390.83+72.63 minutes and 430.43+68.5 minutes respectively. The difference in both the groups is statistically significant. Postoperative analgesia lasted 586+56.6 min in-group A and 465.6+62.3 min group B which was also statistically significant (P < 0.05). The results of present study in regards to onset of sensory block and motor block are in agreement with study by Antonucci S and its duration of sensory motor blockade in-group A are in agreement with study of El Saied et al.

Antonucci S[13] evaluated effects of tramadol used as adjuvant in brachial plexus block and compared with clonidine and sufentanil. He used ropivacaine for block and concluded that tramadol as adjuvant provides a significative reduction of onset time of sensory motor block and also provides a prolongation of anesthesia and analgesia with a quality of block similar that obtained with clonidine and sufentanil

El Saied *et al*,[14] conducted a study in which axillary brachial plexus blockade was performed in 50 patients using 40 ml ropivacaine 0.75 %. Group (A) had 150 µg clonidine and Group (B) 1 ml normal saline added to the local anaesthetic. There was no difference in onset of sensory motor blockade. They concluded that the addition of 150 µg of clonidine to ropivacaine, for brachial plexus blockade, prolongs motor and sensory block and analgesia, without an increased incidence of side effects.

Giovanni Cucchiaro et al.[15] evaluated the effects of clonidine on the duration of sensory and motor block and analgesia time in 215 children who underwent a variety of peripheral nerve block including brachial plexus block and concluded that the addition of clonidine to bupivacaine and ropivacaine can extend sensory block by a few hours, and increase the duration of motor blocks

Casati et al[16] added low dose clonidine to ropivacaine(0.75%) in sciatic-femoral nerve block for foot surgery. They found that addition of 1 µg /kg clonidine to 0.75% ropivacaine prolongs the duration of postoperative analgesia by 3 h, with only a slight and short-lived increase in the degree of sedation and no hemodynamic adverse effects

Casati et al[17] has done a prospective, randomized, double-blind study in which he evaluated the effects of adding 1 µg/kg clonidine to 20 ml of ropivacaine 0.75% for axillary brachial plexus anesthesia. They concluded that adding 1 µg/kg clonidine to 20 ml of ropivacaine 0.75% for axillary brachial plexus anesthesia provided a 3-hour delay in first analgesic request postoperatively, without clinically relevant effects on the degree of sedation and cardiovascular homeostasis.

Danelli G et al[18] evaluated the effects of adding 50 µg clonidine to 150 mg ropivacaine for superficial cervical plexus block in patients undergoing elective carotid endarterectomy. They opined that adding 50 µg clonidine to 150 mg ropivacaine for superficial cervical plexus block shortened the onset time and improved the quality of surgical anaesthesia.

Mehdi Trifa et al[19] added clonidine to ropivacaine in axillary plexus block in 60 patients of 1-6 yr age group. They concluded that ropivacaine (0.2%) 0.4 ml/kg for axillary plexus block provides sufficient postoperative analgesia in children scheduled for forearm or hand surgery. The addition of clonidine increased the time to first analgesia request.

Marhofer D et al[20] evaluated Dexmedetomidine as an adjuvant to ropivacaine in peripheral nerve block. Profound prolongation of ulnar nerve block was detected with perineural dexmedetomidine when added to 0.75% ropivacaine

Brummett CM et al[21] found that dexmedetomidine when added to ropivacaine in peripheral nerve block caused approximately a 75% increase in the duration of analgesia

The above studies show that selective α_2-adrenoceptor agonist like clonidine or dexmedetomidine when added as adjuvant to ropivacaine in different peripheral nerve blocks potentiates the sensory motor blockade. The mechanism is not clear. Probably peripherally, α_2-agonists produce analgesia by reducing release of nor epinephrine and causing α_2-receptor-independent inhibitory effects on nerve fibre action potentials. Centrally, α_2-agonists cause analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neurone and by activation of α_2-adrenoceptors in locus coeruleus.[5] So the action of clonidine would then more likely be via a synergistic mechanism of action in combination with the local anesthetic resulting in the prolonged effect.

There are few studies, which did not found any impact of clonidine when added to ropivacaine in peripheral nerve blocks.

Erlacher W et al[22] in 2000 studied the efficacy of clonidine on ropivacaine in axillary plexus block. They found that there was no significant impact on onset/duration of sensory and motor blockade in clonidine group

Erlacher W. et al[23] in 2001 evaluated clonidine as adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary plexus block and opined that clonidine prolonged both sensory and motor blockade of mepivacaine and bupivacaine but not ropivacaine

Jaiswal et al[24] evaluated the effect of adding clonidine (150 μg) to ropivacaine (0.5%) for axillary plexus blockade among 60 patients and found that addition of clonidine (150 microgram) is of no benefit in the onset and duration of both sensory and motor block. This is the only study, which goes against finding of all other studies.

CONCLUSION

In conclusion, clonidine in dose of 2 μg/kg added to ropivacaine is an attractive option for improving the quality and duration of supraclavicular brachial plexus block in upper limb surgeries. Clonidine in supraclavicular brachial plexus block not only hastens the onset, but also prolongs the duration of sensory motor blockade, and provides a longer pain-free period without significant hemodynamic alterations. As it has more sedative potential, it can reduce patient anxiety and provide optimal intraoperative and postoperative patient comfort.

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