Original Research Article

A comparative study of the analgesic effect between ropivacaine alone and ropivacaine with clonidine through supraclavicular brachial plexus block in upper limb surgical procedures

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Abstract

Background: Peripheral nerve blockade has become an essential and growing part of anaesthesia. Only few studies are available regarding use of ropivacaine with adjuvant clonidine for modification of block but with equivocal results. Hence the present study was planned to evaluate the effect of adding clonidine to ropivacaine in supraclavicular plexus blockade for upper limb surgical procedure. **Materials & Methods:** This prospective randomized single blind placebo controlled clinical study was done in a tertiary medical college, Kolkata between Jan 2012 and July 2013. Patients of either sex of ASA physical status I or II age groups 18-65 years undergoing elective upper limb surgery under supraclavicular brachial plexus block. This study was designed to conduct for prolonging the duration of postoperative analgesia with 25 ml 0.75% ropivacaine along with 30µgm clonidine and 25 ml 0.75% ropivacaine in two groups of patients subjected for upper limb surgery. Two groups were compared for duration of analgesia, onset and duration of sensory and motor blockade. It also studied hemodynamics changes and adverse effects. The degree of sedation was evaluated by using the University of Michigan Sedation Scale [UMSS of o to 4]. **Results:** The duration of sensory block was 9.2±0.21 hrs and 6.1±0.17 hrs respectively in group 1 and group 2 ($p<0.001$). All the patients in group 1 and 2 requiring rescue analgesic were 10.1±0.17 and 7±0.13 respectively. Thus, ropivacaine with clonidine provided earlier onset and peak of sensory effect with comparable duration of post operative analgesia when compared to ropivacaine with normal saline. The mean onset time of motor block was 10.9±0.56 min and 10.8±0.41 min ($p<0.51$) and duration of 8.1±0.21 hrs and 5.1±0.15 hrs ($p<0.001$) in group 1 and group 2 respectively. **Conclusion:** Thus, ropivacaine with clonidine gave long time of blockade in duration of sensory and motor blockade and also in time requiring for the rescue analgesia by giving injection tramadol.

Keywords: Peripheral nerve blockade, supraclavicular brachial plexus block, ropivacaine, clonidine, sensory and motor blockade, analgesia

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Introduction

Peripheral nerve blockade has become an essential and growing part of anaesthesia. It offers an excellent alternative for patients who are hemodynamically compromised or too ill to tolerate general anaesthesia. In addition very good postoperative analgesia can also be provided [1, 2]. The supraclavicular brachial plexus block is a popular nerve block for elbow, forearm, wrist and hand surgery. Supraclavicular approach to brachial plexus blockade has the advantages that the drug is delivered at the level of the trunks which is the most compact part of the brachial plexuses [3]. So success rate are high with rapid onset and dense anaesthesia. Ropivacaine is an amino amide local anesthetic, which is structurally similar to bupivacaine. The decreased cardiovascular and central nervous system toxicity makes ropivacaine interesting alternative to bupivacaine in procedures requiring large doses of local anesthetic [4]. In order to have early onset and prolonged duration of peripheral nerve block, certain drugs have been added to local anesthetics. Clonidine is one such drug that appears to have a distinct benefit when administered as an adjuvant without major side effects [5, 6]. Only few studies are available regarding use of ropivacaine with adjuvant clonidine for modification of block but with equivocal results. Hence the present study was planned to evaluate the effect of adding clonidine to ropivacaine in supraclavicular plexus blockade for upper limb surgical procedure.

Aim and objectives

This study was designed to conduct for prolonging the duration of postoperative analgesia with 25 ml 0.75% ropivacaine along with 30µgm clonidine and 25 ml 0.75% ropivacaine in two groups of patients subjected for upper limb surgery. Two groups were compared for duration of analgesia, onset and duration of sensory and motor blockade. It also studied hemodynamics changes and adverse effects.

Material & methods

This prospective randomized single blind placebo controlled clinical study was done in a tertiary medical college, Kolkata between Jan 2012 and July 2013. Patients of either sex of ASA physical status I or II age groups 18-65 years undergoing elective upper limb surgery under supraclavicular brachial plexus block.

Inclusion Criteria

- Peripheral single injection nerve or brachial plexus block by supraclavicular approach
- Adult undergoing surgery without GA
- Reporting on intraoperative and/or postoperative pain outcomes and /or drug related adverse effects

Exclusion Criteria

- Patient undergoing GA or having an additional neuraxial block
- Continuous local anesthetic administration or repeated injections
- Intravenous regional anaesthesia (Bier's block)
- Age less than 18 years
- Peribulbar block
- Cardiac, renal and hepatic disease
- Chronic treatment with calcium channel blocker
- Bleeding disorder local and systemic infection
- Inability to comprehend the numeric rating scale for pain assessment
- Any neurological disorder

Duration of analgesia was taken as the outcome measure of interest for the purpose of sample size calculation. It was estimated that 28 subjects would be required per group in order to detect a difference of 30 min in this parameter between the two groups with 80% power and 5% probability of type I error. This calculation assumed SD of 40 min for the duration of analgesia. The recruitment target was being kept at 35 subjects per group to offset any potential loss of evaluable subjects. Written consent from all participants was taken before enrolment in the study. Complete preanesthetic check was performed in each including history taking, physical examination, airway assessment and routine preoperative investigations. None of the patients were given any solid food overnight, but each was encouraged to take clear fluids until 2 hrs before induction of anaesthesia. The patents did not receive any premedication. Once a patient was brought into the operation theatre, standard monitoring should setup, including noninvasive arterial blood pressure, heart rate and pulse oximeter. An i.v. cannula was inserted and infusion started with lactated Ringer's solution. Haemodynamic variables (NIBP, HR, SPO2) was measured 10 min before block placement and then

at 0, 2, 5, 10, 20, 30 and 60 min during the surgery. All 70 patients were allocated in two groups- Group I received 25 ml of 0.75% ropivacaine along with 30 µgm clonidine and group II received only 25 ml of 0.75% ropivacaine with normal saline. A 23 G nerve stimulator needle was directed in a caudal, slightly medial, and posterior direction. If the first rib was encountered, the needle was systematically walked anteriorly and posteriorly along the rib until the plexus was located. On localization of branchial plexus, negative aspiration for blood was performed before incremental injections of the total solution. Now sensory and motor blocks on the operated limb were evaluated at 0, 2, 5, 10, 20, 30 and 60 min after the completion of anesthetic injection by one of the physicians who were unaware of the drug combination administered. Sensory block was assessed by pinprick discrimination (with 22G hypodermic needle) and motor block was evaluated by asking the patient to move the forearm against resistance and to flex the forearm. A pinprick sensation on the contralateral arm was scored as 100 points. Patients were requested to compare pinpricks in the primary innervation areas of the respective nerves in the anesthesized arm with the contralateral arm as reference. The scale ranged from 100 points (full sensation) to 0 points (no sensation). Brachial plexus block was considered successful by Vester-Andersen's criteria [7] when at least two out of four nerve territories (radial, ulnar, median, and musculocutaneous) were effectively blocked. Onset of sensory block was defined as a reduction of sensibility to 30% or less while onset of motor block was defined as the time from the end of anesthetic injection to loss of pinprick sensation along the distribution of the ulnar and radial nerves along with inability to circumrotate the thumb of the concerned limb. Noninvasive arterial blood pressure, heart rate and haemoglobin oxygen saturation monitoring was done throughout the procedure. The degree of sedation was evaluated by using the University of Michigan Sedation Scale [UMSS of o to 4] [8]. Following operation, all the patients was observed in postoperative care unit and received rescue analgesic as soon as they complained of any pain by tramadol 100 mg I.V., repeated if necessary.

Results

All the patients (n=70) had completed the study. Patient characteristics (age, height and weight) were comparable in both the groups [Table 1]. Sex and ASA grade distribution is shown on [Table 2, 3].

Table 1: Demographic variables of study participants

Variable	Group 1 (Mean±SD)	Group 2 (Mean±SD)
Age (Yr)	38.4±9	39.6±10.69
Weight (Kg)	54.3±8.09	55.8±8.22
Height (Cm)	162.5±6.74	160.6±6.78

No statistically significant difference (unpaired t test) [p>0.05] [Table 1].

Table 2: Demographic variable (sex) of study participants

Variable	Male (%)	Female (%)
ROPICLONI (Group I)	25 (71.43%)	10 (28.57%)
ROPI NS (Group II)	20 (57.14%)	15 (42.86%)

Fisher's exact test 2-tailed p=0.318.

Table 3: Comparison of categorical variables between Group I and II (ASA distribution)

Variable	ASA II	ASA III
ROPICLONI (Group I)	31 (88.57%)	4 (11.43%)
ROPI NS (Group II)	32 (91.43%)	3 (8.57%)

Fisher's exact test 2-tailed p<1.000

Table 4: Sensory, motor blockade and duration of analgesia characteristic in Group I and II

Variable	Group I (Mean±SD) [UQ-LQ]	Group II (Mean±SD) [UQ-LQ]	P value
Sensory			

Onset (min)	5.0±0.17 (5.0-5.0)	5.0±0.17 (5.0-5.0)	<1.0
Duration (hrs)	9.2±0.21 (9.0-9.3)	6.1±0.17 (6.0-6.20	<0.001
Motor			
Onset (min)	10.9±0.56 [11-11]	10.8±0.41 [11.0-11.0]	<0.5
Duration (hrs)	8.1±0.21 [8.4-8.0]	5.1±0.15 [5.2-5.0]	<0.5
Duration of analgesia	10.1±0.15 [10.2-10.0]	7.0±0.13 [7.0-6.9]	>0.001

The table 4 shows the sensory and motor characteristics of the block. The mean onset of time of sensory block was 5±0.17 min in both the groups (p<1), in group 1 and group 2. In both group 1 and 2, all patients developed onset of sensory block within 5 min and in an around. All the patients with successful block had loss of pin prick sensation over the dermatome of radial, median and ulnar nerve over hand before skin incision. The duration of sensory block was 9.2±0.21 hrs and 6.1±0.17 hrs respectively in group 1 and group 2 (p<0.001). All the patients in group 1 and 2 requiring rescue analgesic were 10.1±0.17 and 7±0.13 respectively [Figure 1]. Thus, ropivacaine with clonidine provided earlier onset and peak of sensory effect with comparable duration of post operative analgesia when compared to ropivacaine with normal saline. The mean onset time of motor block was 10.9±0.56 min and 10.8±0.41 min (p<0.51) and duration of 8.1±0.21 hrs and 5.1±0.15 hrs (p<0.001) in group 1 and group 2 respectively. Thus, ropivacaine with clonidine gave long time of blockade in duration of sensory and motor blockade and also in time requiring for the rescue analgesia by giving injection tramadol.

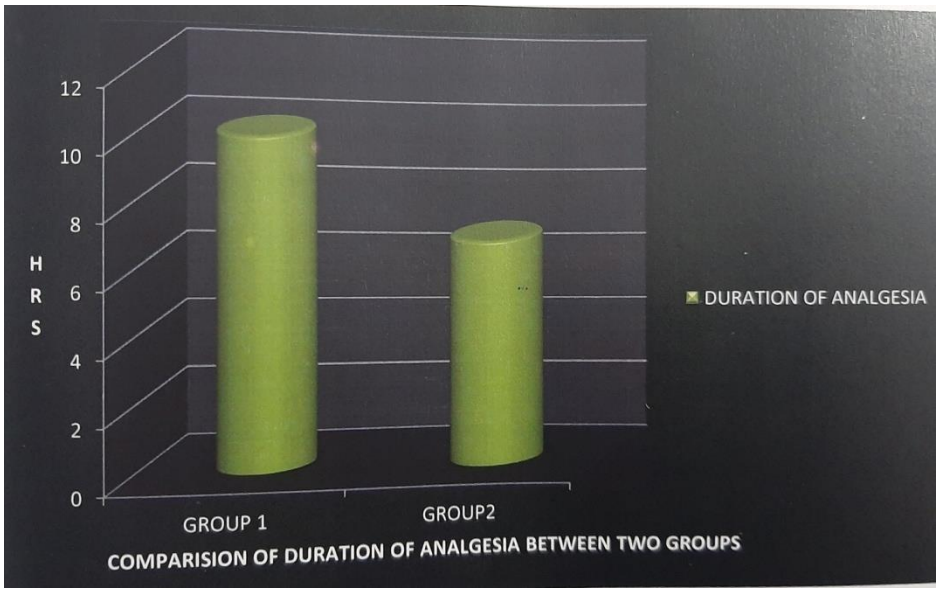

Fig 1: Distribution of mean duration of analgesia in study groups

Table 5: Mean duration in heart rate (bpm)

HR (bpm)	Group I	Group II
Pre-OP	74.7	75.6
0 Min	74.3	74.6
2 Min	73.9	75
5 Min	73.4	74.5
10 Min	72.3	74.8
20 Min	70.6	73.9
30 Min	68.8	73.5
60 Min	67.8	74

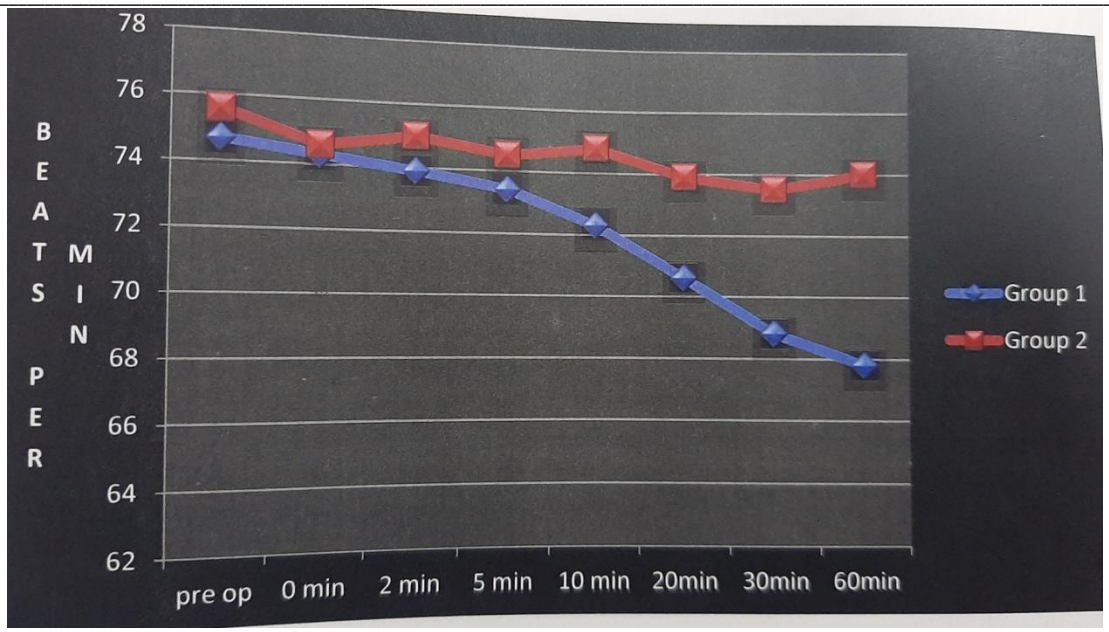

Fig 2: Mean distribution of heart rate (bpm) among study groups

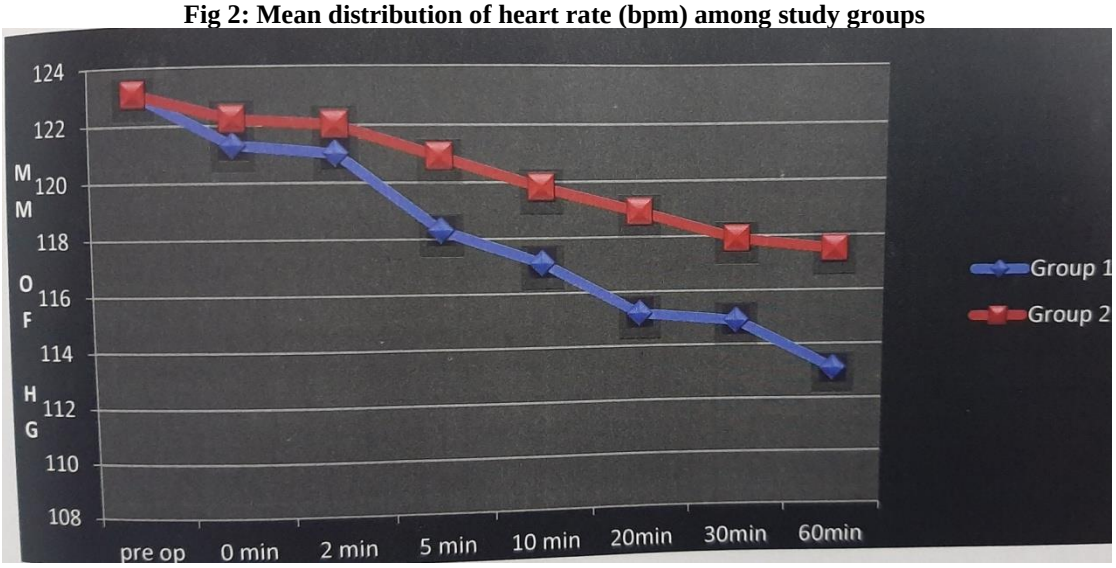

Fig 3: Mean distribution of systolic blood pressure (mm of Hg) among study groups

Table 6: Mean distribution of systolic blood pressure (mm of Hg)

HR (bpm)	Group I	Group II
Pre-OP	123.1	123.1
0 Min	121.3	122.2
2 Min	121	122
5 Min	118.3	120.9
10 Min	117.1	119.8
20 Min	115.2	118.9
30 Min	114.9	117.9
60 Min	113.1	117.5

Table 7: Mean distribution of sedation at 60 min

Variable	Sedation at 60 min (mean±SD)	P value
Group I	0.9±0.72 (1.0-0)	>0.001
Group II	0.2±0.38 (0-0)	>0.001

Haemodynamic changes and SpO2 in either group were stable [Fig. 2, 3] but some side effects were observed in either group like bradycardia and sedation which was ploted in the tables 5, 6, and 7 particularly group 1. Hypotension, nausea, vomiting, xerostomia and pruritus were the other adverse effects which were found significant in both the groups.

Discussion

The supraclavicular brachial plexus is a popular nerve block for elbow, forearm, wrist and hand surgery. The use of peripheral nerve stimulator for brachial plexus block is known to improve success rate. In the present study, technique used to block supraclavicular brachial plexus was single injection by peripheral nerve stimulator. We adopted a single injection method to reduce the risk of neural complication. Partridge et al [9] suggested that, the risk of neural complications should rise with increased number of injections.In the present study in group 1 mean onset time of sensory block was 5±0.17 min and mean onset of motor block was 10.9±0.56 min. Mean duration of sensory block and motor block was 10.9±0.56 min. Mean duration of sensory block and motor block in patients of group 1 was 9.2±0.21 hrs and 8.1±0.21 respectively.Hickey et al [10] also observed that mean onset time of analgesia ranged from 12±10.7 to 19.7±32.2 minutes as observed in different dermatome and mean motor onset time ranged from 9.1±16.5 to 41.7±45.8 minutes. However, mean duration of sensory blocks ranged from 9.2±4.2 to 10.7±2.6 hrs as observed in different dermatome and mean duration of motor block ranged from 8±3 to 10.8 ±2.7 hrs. The difference in duration of sensory block in present study and study conducted by Hickey et al [10] might be due to difference in sensory duration end point determinant. In present study group sensory block duration was taken when patient felt pinprick sensation in any one dermatome while in Hickey et al [10] study it was upto individual dermatomes. The difference in duration of motor block might be due to motor duration endpoint used to determine duration was different in both groups. In study of Hickey et al motor endpoint was paralysis of shoulder, however in present study it was paralysis of finger as most of cases had [10].Sensory onset time was 16.37±3.6 minutes in study conducted by Bertini et al, in which the earlier onset of sensory block might be due to injecting of 32 ml of drug (0.5%) in 4 divided doses in close proximity to each nerve whereas in present study the whole volume of drug was injected at single site [11].A study was conducted by El Saied et al, where sensory onset time in each nerve distribution of ropivacaine 0.75% (40 ml) alone group ranged from 14.1±0.7 to 24.6±1.7 minutes. In group where ropivacaine 0.75% (40 ml) along with clonidine 150µg was used, sensory onset time ranged from 13.6±1 to 27.7±2.5 minutes in different nerve distribution. No difference was noted for sensory onset time in two groups. Mean motor onset time for motor blockade in ropivacaine alone group was 16.3±1.4 minutes while in ropivacaine with clonidine group was 17.9±1.7 minutes, the difference being statistically insignificant. The results o present study in regards to onset of sensory block and motor block in two groups are in agreement with study of El Saied et al [12].In present study when clonidine was used in a dose of 30µg along with ropivacine (in patients of group I), it did not result in change in sensory onset time. The mean sensory onset time of ropivacaine alone group was 5±0.17 minutes and of ropivacaine along with clonidine was 5±0.17 minutes, the difference being statistically insignificant. Mean onset of motor block was also similar in both the groups in present study. In ropivacaine alone group it was 10.8±0.41 minutes and in ropivacaine along with clonidine it was 10.9±0.56 minutes. In our study the difference was being statistically insignificant.

Chakraborty et al evaluated the effect of clonidine added to bupivacaine in supraclavicular brachial plexus block for upper limb orthopaedic procedures. They concluded that addition of a small dose of clonidine to 0.5% bupivacaine significantly prolonged the duration of analgesia without producing any clinically important adverse reactions other than sedation [13].

Duma et al [14] compared the effects of clonidine added to levobupivacaine and bupivacaine on axillary brachial plexus block as well as the effectiveness of levobupivacaine alone compared with bupivacaine alone. They concluded that clonidine as an adjuvant to the long lasting local anaesthetics bupivacaine and levobupivacaine in axillary brachial plexus block exerts an uncertain and inconsistent effect, resulting in a lack of predictability and no significantly prolonged duration of action [14, 15]. We did not see any evidence of cardiovascular or central nervous system toxicity with a dose of 175 mg of ropivacaine in age

group of 20 to 60 years. Heart rate, blood pressure and oxygen saturation were not changed significantly in our study which is similar to the findings of study by El Saied et al [12] and Erlacher et al [16]. The lack of prolongation of anaesthetic effects of clonidine when combined with ropivacaine has been postulated by Erlacher et al in 2000 [17] and 2001 [16].

Clonidine is an alpha2 adrenergic agonist with a weak alpha 1 agonist activity and may produce local vasoconstriction by stimulating vascular smooth muscle alpha receptors. Studies have been performed in volunteers to determine the effect of ropivacaine compared with bupivacaine and lidocaine on cutaneous blood flow after injection of 0.1 ml. Both bupivacaine and lidocaine produced bupivacaine in human skin but ropivacaine decreased skin blood flow [18]. As ropivacaine has intrinsic vasoconstricting properties not mediated by an activation of alpha2 adrenoceptors, this could have explained why the addition of clonidine did not result in any benefit [19]. However, El Saied et al [12] reported extended duration of sensory and motor blockade would be due to synergistic mechanism of action in combination with local anaesthetic ropivacaine.

No significant changes in hemodynamic variables, but side effects like sedation and bradycardia were seen in our groups. Most of the patient have sedation scale 1 and few are scale 2 according to UMSS in group 1 but in group 2 these are statistically insignificant at 60 min after giving single injection. In a dose finding study evaluating the minimum effective dose of clonidine required to prolong duration of analgesia after axillary brachial plexus block, Singelyn et al [20] suggested that 0.5 µg/kg clonidine should be used. At this dose, significant prolongation of analgesia was achieved without undue sedation, hypotension, or bradycardia. It has been widely demonstrated in different studies that subcutaneous or intramuscular injection of clonidine is not as effective as perineural administration [21] suggesting that the local anesthetic prolonging effect of clonidine is probably mediated locally at the neuron [22]. This may also explain the variation in response in different types of peripheral nerve blocks, probably related to the rate and extent to which the injected anesthetic solutions penetrate into the nerve [7].

Even though injecting clonidine as the sole analgesic into the brachial plexus sheath does not provide clinically relevant analgesia [15]. It has been demonstrated to inhibit the action potential of A and C fibers in de-sheated sciatic nerves [23]. Many authors favour the hypothesis that clonidine exerts its local anesthetic prolonging effect directly on the nerve fiber, as a result of complex interaction between clonidine and axonal ion channels or receptors [7, 18, 21]. Peripheral antinociception induced by clonidine has also been related to alpha 2 adrenoceptor mediated local release of enkephalin like substances [24].We selected a 30 µg dose of clonidine keeping in mind the hemodynamic adversities that might be produced. It was found that this dose provided satisfactory prolongation of the duration of analgesia without producing significant hemodynamic compromise in the patients. However, clonidine did induce greater sedation in the patients during the early part of their stay in postanesthesia care unit. Therefore, we cannot say that this is the ideal dose of clonidine as adjuvant to 0.5% ropivacaine for supraclavicular brachial plexus block. This conclusion can only be drawn after a definitive dose finding study.

Conclusion

From the observations and analyses of the present study, it can be inferred that 30 µg of clonidine may be used as an adjuvant to 0.75% ropivacaine for supraclavicular brachial plexus block so as to prolong postoperative analgesia without added problems apart from some sedation and mild bradycardia in the early postoperative period. Present study showed group I received clonidine had more time of duration of sensory and motor blockade (p value >0.001) than group II which is statistically significant.

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