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A PROSPECTIVE, CLINICAL COMPARATIVE STUDY BETWEEN ROPIVACAINE-CLONIDINE COMBINATION AND ROPIVACAINE PLAIN IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK WITH USG GUIDED, IN UPPER EXTREMITY SURGERY

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ABSTRACT

***Background*:** Compared to previous methods, supraclavicular brachial plexus block offers quicker onset and more reliable regional anaesthesia. We predicted that adding clonidine to ropivacaine in an ultrasound-guided supraclavicular brachial plexus block would improve the analgesia's quality and lengthen the time it lasted after surgery for patients having upper limb procedures. ***Methods*:** This study included 58 patients posted for upper limb surgeries who were randomly allocated into 2 groups of 29 each. Group R patients were given 19.8 ml of 0.75% ropivacaine + 0.2 ml normal saline and Group RC were given 19.8 ml of 0.75% ropivacaine with 0.2ml (30 µg) clonidine. Wilcoxon rank sum test, Pearson's Chi-squared test, ANOVA, were applied to find significance. ***Results*:** There is no statistically significant difference in onset of sensorimotor block between Group RC (5.93 ± 2.14 min for sensory block and 11.45 ± 3.80 min for motor block) and Group R (6.41 ± 5.57 min for sensory block and 12.72 ± 8.15 min for motor block). Both sensory and motor block duration were significantly prolonged by clonidine ($P < 0.001$). The duration of analgesia was also prolonged in Group RC 749.97 ± 82.22 min as compared to Group R 486.28 ± 90.69 min ($P < 0.001$). None of the patients in either group observed any adverse effects. ***Conclusion*:** When clonidine is used with ropivacaine for supraclavicular brachial plexus block, postoperative analgesia and sensory and motor blockade occur more quickly and last longer without any discernible side effects.

KEYWORDS: Supraclavicular block; Ropivacaine 0.75%; clonidine: USG.

INTRODUCTION

Patients undergoing surgery in the upper extremity often report postoperative pain that is intense and difficult to control. The pain itself is not only associated with patient suffering but can also lead to a number of complications that may lead to an unintended long term stay in the hospital after surgery.[1]

Upper limb surgery can be performed under general or regional anaesthesia. Regional anaesthesia has several advantages including decreased haemodynamic instability, avoidance of airway instruments, and intra-operative and postoperative analgesia. Brachial plexus block is a very reliable method of regional anaesthesia for upper limb.[2] Techniques to improve the efficacy and safety of regional anaesthesia include, nerve stimulation, percutaneous electrical guidance, ultrasound.[3]

USG has revolutionized the practice of regional anaesthesia. By real time visualising of needle entry throughout the procedure, the relationship between the anatomical structures and the needle can reduce the incidence of complications. In addition, direct visualisation of spread of local anaesthesia and provide postoperative analgesia for considerable duration as well as have a good safety profile.[4]

Ropivacaine is a long-acting amide local anaesthetic agent. It's a pure S- enantiomer with a high pKa and relatively low lipid solubility.

It produces an effect by causing reversible inhibition of sodium ion influx and thereby blocks impulse conduction in nerve fibres.[5] This action is potentiated by dose dependent inhibition of potassium channels.[6]

Ropivacaine is less lipophilic than bupivacaine and together with its stereo-elective properties contributes to having an increased threshold for cardiotoxicity and CNS toxicity than bupivacaine in animals and humans.[7,8,9] And less likely to penetrate large myelinated motor fibres. Thus, ropivacaine has a greater degree of motor sensory differentiation.

The long acting sensory and motor blockade provided by 0.5% or 0.75% of ropivacaine for hand and arm surgeries compared with bupivacaine 0.5%,[10,11,12,13,14] with well tolerated regardless of route of administration.[15]

Clonidine, an alpha 2 adrenergic agonist has sedative, analgesic, perioperative sympatholytic with cardiovascular stabilizing effect and has been tried in combination with local anaesthetic drug to enhance regional anaesthesia.[16,17]

The present study aimed to compare duration of analgesia and to compare onset and duration of motor and sensory block of 0.75% ropivacaine alone or in combination with clonidine in supraclavicular brachial plexus block for upper extremity surgeries using USG.

AIM AND OBJECTIVES

The present study aimed to compare of analgesia of 0.75% ropivacaine alone or in combination with clonidine in supraclavicular brachial plexus block for upper extremity surgeries using USG.

Primary objective: To compare duration of analgesia.

Secondary objectives: To compare onset and duration of motor and sensory block.

MATERIALS AND METHOLODOGY

After receiving approval from the institutional ethical committee 58 ASA physical status I and II patients, aged 18 to 60, of either sex, undergoing various orthopaedic surgeries on upper extremities distal to the shoulder under ultrasound guided supraclavicular brachial plexus block participated in a prospective, randomized, double-blinded study. There were two groups of 29 patients each totalling 58 patients. The study was conducted in two groups of 29 patients each between Aug 2019 and Augus2021.

Patients were randomly allotted in to two groups by computer- generated random selection. Group R patients received ropivacaine 0.75% (19.8 ml) and placebo (0.2 ml NS) whereas Group RC patients received ropivacaine 0.75% (19.8 ml) and clonidine 0.2ml.

Randomization and preparation of injecting drugs were done by an anaesthesiologist who was not an investigator and it was concealed from patients and investigators until completion of statistical analysis. The exclusion criteria of our study were ASA grade 3and 4, patients with peripheral neuromuscular disease, bleeding or coagulation disorder, allergy to local anaesthetic amides, patients refusal to technique, inability to localise the brachial plexus accurately on ultrasound, any patient taking medication with psychotropic or adrenergic analgesic or patients receiving chronic analgesic therapy other than simple analgesics.

Prior to surgery, patients received training on how to evaluate pain using a visual analogue scale. During the preoperative visit detailed patient history will be recorded and physical, systemic examination and routine lab investigation will be conducted. The anaesthesia procedure will be explained to the patient in detail. Patients will be kept fasting for a duration of 8hrs prior to the surgery. After establishing IV access on arrival in operation theatre, the RL started at the rate of 4ml/kg/h in all patients with continuous monitoring of ECG,SPO_2, PR, NIBP, and oxygen will be connected by Hudson mask at rate of 4L/min to all patients.

The supraclavicular brachial plexus block will be performed using a transportable USG with 38mm, 8-13MHz linear high frequency ultrasound transducer to obtain images of brachial plexus in the transverse and longitudinal planes. Patient lay down supine with his/her head turned to the contralateral side and the ipsilateral arm adducted gently by the assistant and the shoulder kept down with flexed elbow. After sterile preparation of the skin and USG probe, the brachial plexus will be visualised by placing the transducer in the sagittal plane in the supraclavicular fossa behind the middle third of the clavicle. Two distinct appearances of brachial plexus will be seen at the supraclavicular region, it either appeared as 3 hypo echoic circle with hyper echoic outer rings or as a grape like cluster of 5 to 6 hypo echoic circles, located lateral and superior to the subclavian artery between the anterior and middle scalene muscle at lower cervical region. The block will be performing using local anaesthetic mixture according to Group R or Group RC with a 23-gauge short bevelled echogenic needle for optimal control and visibility. The predetermined volume of 20ml of study drug solution will be administering around the brachial plexus after negative aspiration to avoid accidental intravascular needle puncture and spread of local anaesthetic drug observed in tissue plane. The multiple injection technique will be used to deposit the total amount of drug. A 3minute massage will be performed to facilitate an even drug distribution.

The sensory dermatome level analgesia of upper extremity will be assessed by pinprick test along the distribution of each nerve with 25G hypodermic needle using a 3 point scale for pain (2-sharp pain,1-blunt pain,0-no pain) and compared to same stimulation on contralateral arm.

Motor weakness will be assessed by hand grip and movement at the elbow, wrist and fingers using a modified Bromage scale. Grade 0-normal motor function with full flexion and extension of elbow, wrist and

fingers. Grade 1-decreased motor power with the ability to move the fingers only. Grade 2-complete motor block with inability to move the fingers.

Sensory block onset defined as loss of pain to pin prick (0- no pain). Motor block onset defined as reduction of muscle force to grade 2, according to modified Bromage scale.

For all patients standard ASA monitoring will be done throughout the surgery. Patients will be observed for any discomfort, nausea, vomiting, shivering, bradycardia, pain and any other side effects. Any need for additional medication noted. Any patients with unsuccessful block or patient complaining of pain in intra operative period which require general anaesthesia will be excluded from study.

Postoperative pain will be assess by using 10 point visual analogue scale, 0- no pain to 10-excruciating pain at 2,4,6,8,12 and16 h. Inj. Tramadol(50mg) will be used as rescue analgesic when VAS score reaches 5 or more in post-operative period.

Duration of analgesia was the primary outcome measure whereas onset and duration of sensory blockade, VAS pain scores, onset and duration of motor blockade and adverse drug reactions were secondary outcome measures.

RESULTS

Patient and surgical characteristics are summarized by group [Table 1]

The mean time for onset of sensory block in Group R was 6.41± 5.57min and in Group RC was 5.93±2.14min (P - 0.5), the mean time for onset of motor block in Group R was 12.72±8.15 min and in Group RC was 11.45±3.80 min (P – 0.9) [fig 1]. The total duration of sensory block in Group R was 417±74 min and in Group RC 640 ± 81min (P < 0.001), the total duration of motor block in Group R was 375.59 ± 69.00 min and in Group RC 562.24 ± 77.64 min (P < 0.001) [fig 2]. The time for first rescue analgesia was given when VAS score was 5 and above. The Mean duration of analgesia in group R was 486.28 ± 90.69 min and in group RC was 749.97 ± 82.22min (P < 0.01) [fig 3]. The VAS Score, mean heart rate and the mean systolic and diastolic pressure and the during intra and post-operative period were comparable between both the group [Figs. 4 and 5]

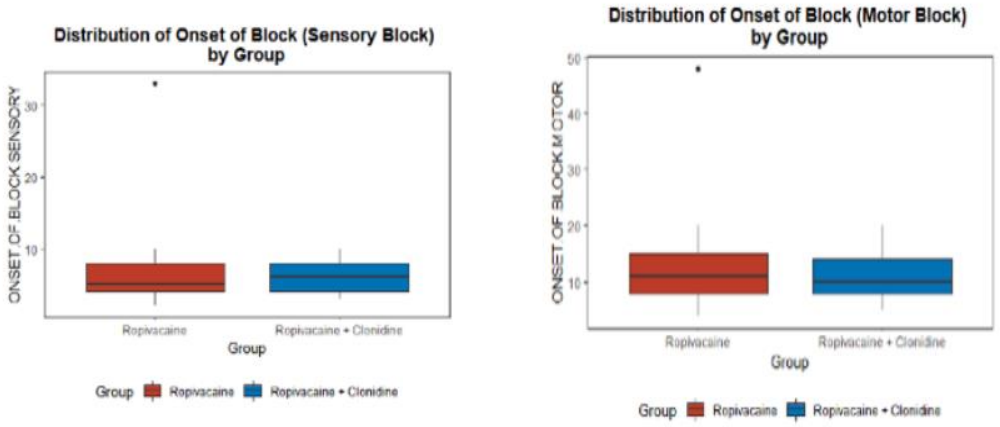

Fig. 1

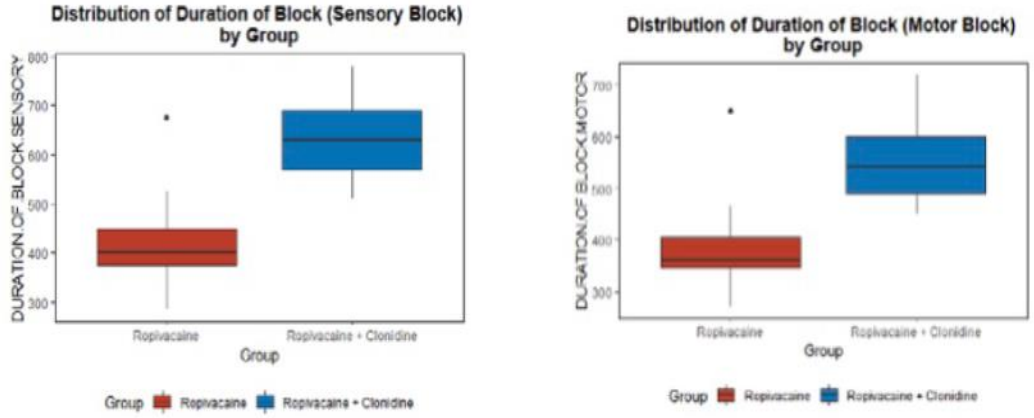

Fig. 2

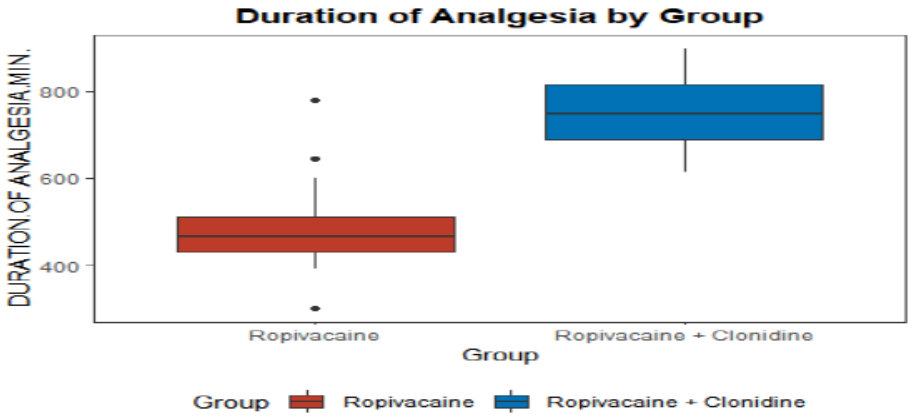

Fig. 3

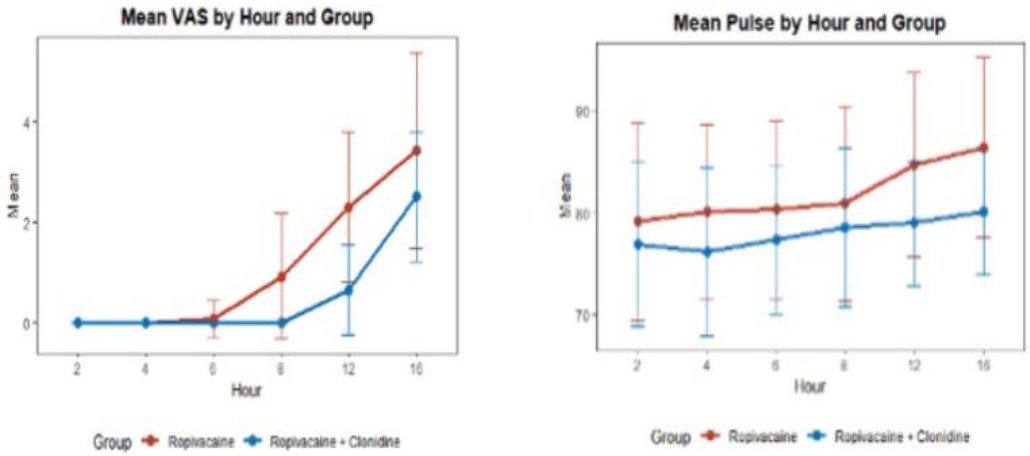

Fig. 4

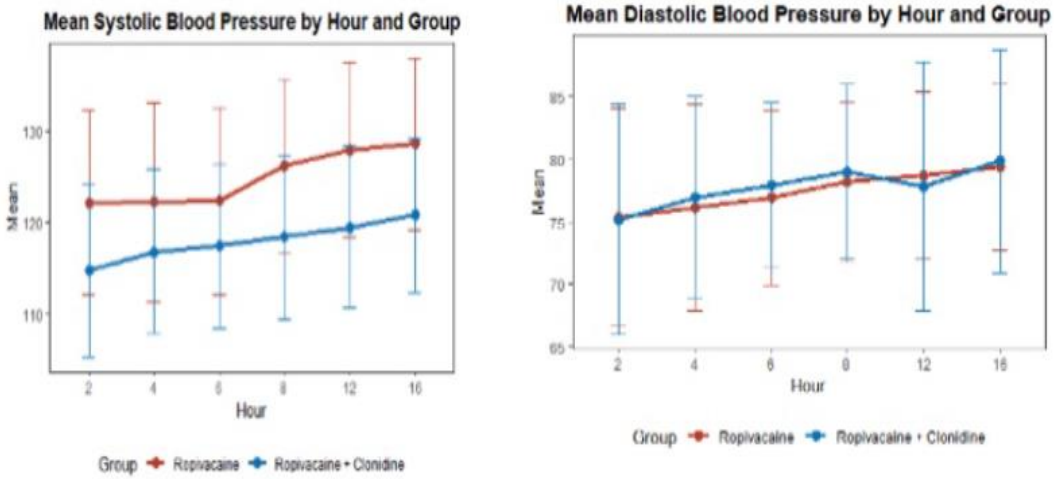

Fig. 5

Table 1

Characteristic	Ropivacaine, N = 29	Ropivacaine + Clonidine, N = 29	P-value
AGE			0.7
Mean ± SD	42.86 ± 17.88	40.24 ± 11.61	
Median (IQR)	45 (26 - 56)	38 (30 - 48)	
Range	17-80	20-60	
SEX			0.4
FEMALE	17 (59%)	14 (48%)	
MALE	12 (41%)	15 (52%)	
REGION.OF.SURGERY			>0.9
ELBOW	8 (28%)	8 (28%)	
FOREARM	21 (72%)	21 (72%)	
ASA			0.8
I	13 (45%)	14 (48%)	
II	16 (55%)	15 (52%)	

DISCUSSION

Peripheral nerve blocks are low-cost anaesthetic procedures that give excellent anaesthesia and analgesia without the need for airway equipment or the hemodynamic effects of general anaesthesia.[18] Patient satisfaction, an increasing desire for low-cost anaesthetic, and a favourable postoperative recovery profile have all contributed to regional methods expanding popularity.[19,20] For upper limb procedures, a brachial plexus block is a simple and reasonably safe treatment. Supraclavicular, Interscalene, Infraclavicular, and Axillary methods have all been utilised to block the brachial plexus. Supraclavicular Brachial plexus block is linked with quick onset and consistent anaesthesia. As a result, it is one of the most often utilised procedures for upper limb surgery.

The precise placement of local anaesthetic (LA) around the nerve structures is essential for effective regional anaesthesia. In the past, patients were treated with a nerve stimulator or a paraesthesia method, both of which depended on surface landmark detection. However, there are limits to landmark techniques: differences in nerve architecture and physiology, as well as equipment accuracy, have an impact on success rate and problems. The development of ultrasonography has solved these issues by allowing for real-time imaging of LA deposition and spread.[20] As a result, we decided to adopt an ultrasound-guided approach. Our hospital has frequently employed an ultrasound-guided supraclavicular approach for upper-limb procedures, and it has shown to be a safe technique.

When administered as a single injection, currently available local anaesthetics can give analgesia for a short duration. Various methods have been tried with the goal of prolonging the local anaesthetic action intraoperatively and beyond the operating rooms, such as continuous infusion of local anaesthetics via indwelling catheters, use of a combination of anaesthetics to

increase the volume of LA, and addition of different adjuvants in local anaesthetics.[21] Increasing the volume (dosage) of LAs can extend the duration of analgesia while simultaneously increasing the risk of systemic toxicity. As a result, LA with less side effects is favoured. Continuous catheter-based nerve blocks can extend intraoperative and postoperative analgesia, but their application takes more time, needs more skill, and is more expensive. While phase III studies of an unique sustained-release encapsulated (liposomal) formulation of Bupivacaine are now underway.[22]

Lignocaine and Bupivacaine are the most often used LAs, although both have drawbacks, such as a shorter duration of action (Lignocaine) and a higher incidence of Cardiotoxicity (Bupivacaine).[23] To solve these limitations, newer LA has been produced, such as Ropivacaine, which is 10-30% less cardiotoxic and neurotoxic than Bupivacaine and has a greater ability to block sensory fibres more quickly than motor fibres. As a result, we decided to employ Ropivacaine in our research.

Buprenorphine, Fentanyl,[24] Tramadol, Clonidine, Dexmedetomidine, Dexamethasone, Magnesium, and Midazolam[25] are some of the perineural adjuvants that have been utilised to extend the duration of analgesia of nerve blocks with varied degrees of effectiveness. Clonidine was utilised as an adjuvant to Ropivacaine in this study.

Clonidine has a synergistic effect with local anaesthetics. Clonidine appears to have better analgesic effectiveness with less side effects, according to a systematic assessment of several adjuvants for brachial plexus block.[26,27]

When injected intrathecally and epidurally, clonidine is known to cause antinociception and to improve the action of local anaesthetics. Clonidine works by acting on the Alpha 2 adrenergic receptors in the peripheral nervous system.[16,28]

Centrally mediated analgesia, 2 adrenoceptor mediated vasoconstrictive effects, attenuation of the response, and direct impact on the peripheral nerve are the four methods hypothesised. Dalle et al. proposed that clonidine increased activity by increasing the threshold for initiating the action potential, causing slowing or blockade of conduction.[29] Dependent hyperpolarization, generated by the Na/K pump during repetitive stimulation, increased the threshold for initiating the action potential, causing slowing or blockade of conduction. When added to a local anaesthetic solution, clonidine was proven to be a good adjuvant for peripheral nerve blocks, regardless of mechanism of action.

Hence an attempt has been made to assess the efficacy of Clonidine as an adjuvant to Ropivacaine (0.75%) in brachial plexus block (supraclavicular approach) in terms onset time, duration of motor and sensory block and duration of analgesia. Haemodynamic variables and rescue analgesic requirements in 2,4, 8,12 and 16 hrs postoperatively.

A total of 58 patients within the age group of 18-60 were in included in the study, 29 in each group. Out of which the mean age of group R (receiving only Ropivacaine) was 42.86 ± 17.88 years and the mean age of group RC (receiving Clonidine with Ropivacaine) was 40.24 ± 11.61years. Hence both groups were comparable in regard to age. Female ratio was greater than male ratio in both groups.

In the present study, we did not find a statistically significant difference in the onset of sensory and motor blockade between the two groups. Most authors have also reported no effect on the onset of block.[29,30,31] Onset of sensory block (Group RC 5.93 ± 2.14 min, Group R 6.41 ± 5.57min). Onset of motor block (Group RC 11.45 ± 3.80 min, Group R 12.72 ± 8.15min)

Our results showed that sensory block tended to last longer as compared to motor block which agrees with the observation by de Jong et al[32]. These authors explained that large fibres require a higher concentration of local anaesthetic than small fibres. The minimal effective concentration of local anaesthetic for large (motor) fibres is greater than for small (sensory) fibres. Thus, motor function return before pain perception and duration of motor block is shorter than the sensory block. In our study duration of motor block was prolonged when clonidine was added to Ropivacaine (group RC 562.24 ± 77.64min; group R 375.59 ± 69.00min).

In our study, the mean duration of sensory block (i.e. time elapsed from time of injection to appearance of pain requiring analgesia) was significantly higher ($P < 0.05$) in group RC than in group R. (group RC 640 ± 81min; group R 417 ± 74 min).

The beneficial effect of clonidine on the prolongation of analgesia was observed by Pöpping et al., with all tested local anaesthetics.[30] Singelyn et al., reported that a minimum dose of clonidine (0.5 µg/kg) added to mepivacaine prolongs the duration of anaesthesia and analgesia after brachial plexus block and found no added advantage by exceeding the dose of clonidine to 1.5 µg/kg.[31] Therefore, we decided to use clonidine in dose of 30 µg with 19.8 mL of 0.75% ropivacaine for supraclavicular brachial plexus block.

In our study there was a statistically significant difference in duration of analgesia between the two groups. Group RC 749.97 ± 82.22min, Group R 486.28 ± 90.69min

No patient in any of the groups exhibited significant side effects or hemodynamic variability in both groups during the perioperative period.

CONCLUSION

From our study, we conclude that, the addition of Clonidine (30 µg) as an adjuvant to Ropivacaine (0.75%) has following effects:

1. Longer duration of analgesia.
2. Longer duration of sensory block.
3. Longer duration of motor block.
4. No significant difference in haemodynamic variables i.e. pulse rate, systolic BP, diastolic BP, and O2 saturation.

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