Original Article

Clonidine as an adjuvant to ropivacaine-induced supraclavicular brachial plexus block for upper limb surgeries

Kalyani Nilesh Patil, Noopur Dasmit Singh

Department of Anaesthesia, Smt. Kashibai Navale Medical College and General Hospital, Pune, Maharashtra, India

Abstract

Background and Aims: Ropivacaine is a new amide, long acting, pure S-enantiomer, local anesthetic, with differential blocking effect. The addition of clonidine to local anesthetic improves the quality of peripheral nerve blocks. This study was conducted to evaluate the effect of clonidine on characteristics of ropivacaine-induced supraclavicular brachial plexus block.

Material and Methods: A total of 60 adult patients were randomly recruited to two groups of 30 each: Group I: 30 ml 0.75% ropivacaine + 1 ml normal saline. Group II: 30 ml 0.75% ropivacaine + 1 mcg/kg clonidine diluted to 1 ml with normal saline.

Results: The onset of sensorimotor block was earlier in Group II (4.36 ± 0.81 min for sensory block and 9.83 ± 1.12 min for motor block) than in Group I (4.84 ± 0.65 min for sensory block and 10.85 ± 0.79 min for motor block). The duration of both sensory and motor block were significantly prolonged by clonidine ($P < 0.001$). The duration of analgesia was also prolonged in patients receiving clonidine (613.10 ± 51.797 min vs. 878.33 ± 89.955 min). Although incidence of hypotension and bradycardia was higher in Group II when compared to Group I, it was not clinically significant.

Conclusions: Ropivacaine 0.75% is well-tolerated and provides effective surgical anesthesia as well as relief of postoperative pain. Clonidine as an adjuvant to ropivacaine significantly enhances the quality of supraclavicular brachial plexus block by faster onset, prolonged duration of sensory and motor block and improved postoperative analgesia, without associated adverse effects at the dose used.

Key words: Clonidine, ropivacine, supraclavicular brachial plexus block

Introduction

The supraclavicular brachial plexus block provides anesthesia of the entire upper extremity in the most consistent and time-efficient manner. Peripheral nerve blocks provide intraoperative anesthesia and also extend analgesia in the postoperative period without any systemic side-effects.[1]

Ropivacaine is a new amide-type, long acting, pure S-enantiomer, local anesthetic. It has differential blocking effect on motor and sensory nerve fibers. When compared to bupivacaine, motor block is often slower in onset, shorter in duration and less intense. It has lower cardiotoxicity than bupivacaine.[2]

The concurrent injection of alpha-2 adrenergic agonist drugs improves the nerve block characteristic of local anesthetics through either local vasoconstriction[3] and facilitation of C fiber blockade[4] or spinal action caused by retrograde axonal transport or simple diffusion along the nerve.[5] Clonidine is a selective alpha-2 adrenergic agonist with some alpha-1 agonist property.

The aim of our study was to assess the characteristics of supraclavicular brachial plexus block using 0.75% ropivacaine and to study the effect of clonidine as an adjuvant.

Material and Methods

After obtaining clearance from Institutional Ethics Committee, a double-blind, prospective, randomized, study was carried out on 60 patients between age group 18 and 60 years and American Society of Anesthesiologists physical status I and II,

Address for correspondence: Dr. Kalyani N. Patil,
B 12, Manasi Apartments, Behind Suvarnayug Sahakari Bank,
Bibwewadi, Pune - 411 037, Maharashtra, India.
E-mail: kalyanish19@gmail.com

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undergoing elective upper limb orthopedic surgeries. The sample size was estimated from data of previous studies, using an alpha level of 0.05 and a beta level of 0.90 to establish a desired power of 0.80.[6-8] The study was conducted in two groups of 30 patients each. The patients were randomly recruited to one of the following groups using a computer generated random number list:

- Group I: 30 ml 0.75% ropivacaine + 1 ml normal saline
- Group II: 30 ml 0.75% ropivacaine + 1 mcg/kg clonidine diluted to 1 ml with normal saline.

Patients on adrenoreceptor agonist or antagonist therapy, with known hypersensitivity to local anesthetics, bleeding disorders, preexisting peripheral neuropathy and pregnant or lactating women were excluded from the study.

Thorough preoperative assessment was done on previous day of surgery. The nature and safety of the procedure was explained and written, valid, informed consent obtained.

On arrival to the operation room, adequate fasting status was confirmed. Patients' baseline pulse rate, electrocardiogram and noninvasive blood pressure were recorded and a wide bore intravenous (IV) line established on unaffected limb and an infusion started with lactated Ringer's solution. Hemodynamic variables were measured every 5-min until the end of surgery.

The block was performed by an experienced anesthesiologist different from the one assessing the patient intra- and post-operatively. Both were blinded to the treatment groups.

The patients were administered brachial plexus block by supraclavicular approach under strict aseptic precautions. The injection site was infiltrated with 1 ml of lidocaine 2% subcutaneously. A nerve stimulator (Stimuplex, Braun, Germany) was used to locate the brachial plexus. The location end point being a distal motor response with an output lower than 0.6 mA. During injection, negative aspiration was performed every 6.5-7.0 ml to avoid intravascular injection. A 3-min massage was performed to facilitate an even drug distribution.

Sensory block was assessed by the pin prick method. Assessment of sensory block was done at each minute after completion of drug injection in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve, and musculocutaneous nerve until complete sensory blockade. Onset of sensory block was defined as a reduction of sensibility to 30% or less. Complete sensory block was considered when there was complete loss of sensation to pin prick.

Assessment of motor block was carried out by the same observer at each minute until complete motor blockade after drug injection. Onset of motor blockade was defined as reduction of muscle power to Grade 3 or less. Complete motor block was defined as complete inability to move the limb and fingers (Grade 0).

In case of block failure (surgical anesthesia not achieved even after 30-min from the anesthetic injection), the patient received general anesthesia.

Assessment of blood loss was done and fluids administered accordingly.

All patients were observed for any side-effects like nausea, vomiting, dryness of mouth and complications such as pneumothorax, hematoma, local anesthetic toxicity and postblock neuropathy in the intra- and post-operative periods. Any need for additional medication was noted.

Following operation, all patients were observed in postanesthesia care unit and received rescue analgesic (aqueous diclofenac 75 mg slow IV) on demand. The time from the end of anesthetic injection in the operated hand until the first request for postoperative rescue analgesic was recorded in each patient. The duration of sensory block was defined as the time interval between injection and complete recovery of sensation. The duration of motor block was defined as the time interval between completion of injection and complete recovery of motor power.

The statistical analysis was performed using two-independent sample *t*-test and $P \leq 0.05$ was statistically significant.

Both the groups were compared with respect to:

a. Onset of sensory block.
b. Onset of motor block.
c. Duration of sensory block.
d. Duration of motor block.
e. Duration of analgesia.
f. Occurrence of adverse effects (hypotension, bradycardia, sedation, dry mouth).

Results

There was no statistically significant difference in the demographic profile and the baseline values of hemodynamic variables between the two groups [Table 1]. One patient in the control group had block failure and was given general anesthesia. He was excluded from further statistical analysis involving block characteristics and hemodynamic changes after the block.

Significantly lower pulse rate was observed from 60 min to 180 min in the clonidine group, but was not clinically significant and did not need any intervention [Figure 1].

Mean arterial pressure dropped at 30-min and remained so until 150-min in the clonidine group [Figure 2]. No treatment was required for this fall in blood pressure. The hemodynamic parameters were comparable by 180-min.

The onset of sensory block and motor block was significantly faster in clonidine group than control group [Figure 3].

The duration of sensory block was 703.83 ± 42.90 min in clonidine group when compared to 556.38 ± 37.96 min in control group. The duration of motor block was 621.67 ± 46.76 min in clonidine group and 500.86 ± 44.58 min in control group [Figure 4]. Both were significantly prolonged in clonidine group ($P < 0.001$).

The mean time for rescue analgesia in control group was 613.10 ± 51.797 min and in clonidine group was 878.33 ± 89.955 min. Significantly prolonged duration for rescue analgesia was observed in clonidine group ($P < 0.001$).

Table 1: Demographic profile and vital signs

Patient characteristics	Control (n = 30)	Clonidine (n = 30)	P value
Age (years)	38.10±12.25	43.33±12.39	0.105
Sex (male:female)	19:11	18:12	0.896
Weight (kg)	57.03±5.86	59.87±5.22	0.053
HR (/min)	76.77±8.76	76.10±8.91	0.771
SBP (mmHg)	120.67±9.32	120.87±9.39	0.934
DBP (mmHg)	76.47±6.07	77.63±6.85	0.488
MAP (mmHg)	91.2±6.62	92.04±7.15	0.636

Values are mean ± SD = Standard deviation, MAP = Mean arterial pressure, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, HR = Heart rate

Discussion

Supraclavicular brachial plexus block is preferred for its rapid onset, reliable anesthesia and as a safe technique for any surgery in the upper extremity that does not involve the shoulder.[9] This is because the block is performed at the level of nerve trunks, where, almost the entire innervations of the upper extremity are confined to a very small surface area.[6]

Ropivacaine is a pure S(−) enantiomer, structurally related to bupivacine, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles.[10] The efficacy of ropivacaine is similar to that of bupivacaine and levobupivacaine for peripheral nerve blocks. Ropivacaine with its efficacy, lower propensity for motor block

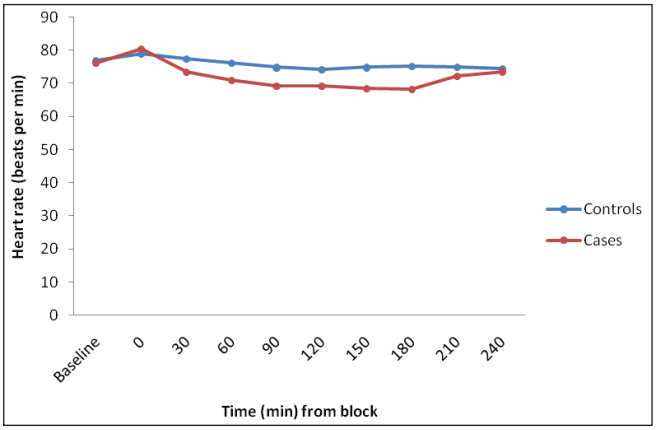

Figure 1: Comparison of mean heart rate

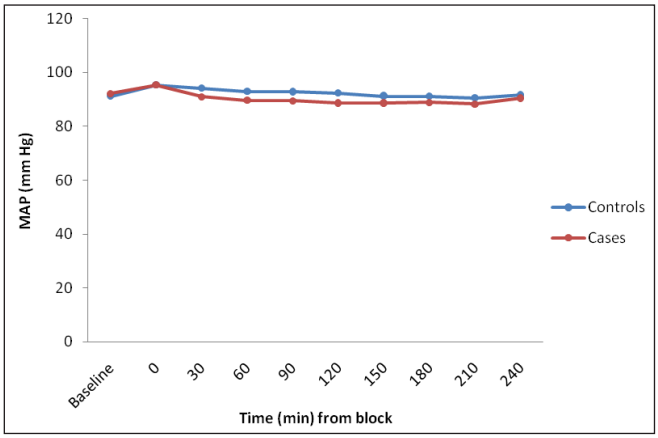

Figure 2: Comparison of mean arterial pressure

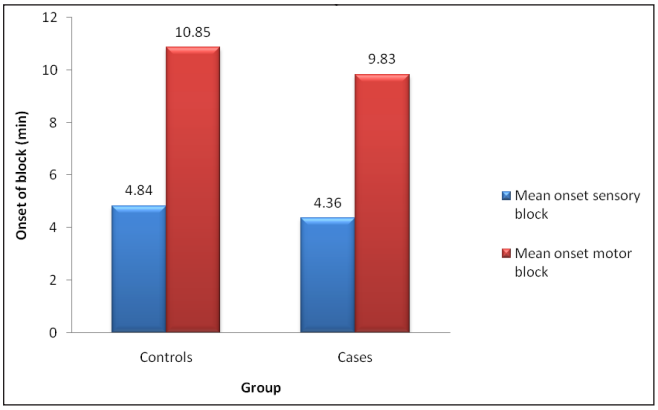

Figure 3: Mean onset of sensory and motor block

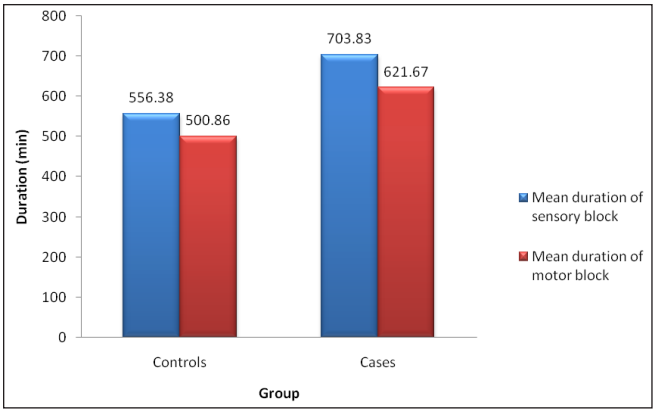

Figure 4: Mean duration of sensory and motor block

and reduced potential for cardiotoxicity and central nervous system toxicity, appears to be an important option for regional anesthesia and management of postoperative pain.[11,12]

Clonidine enhances both sensory and motor blockade of neuraxial and peripheral nerves after injection of local anesthetic solutions.[13] There have been four proposed mechanisms for the action of clonidine in peripheral nerve blocks. These mechanisms are centrally mediated analgesia, alpha-2-adrenoreceptor mediated vasoconstriction, attenuation of inflammatory response and direct action on peripheral nerve.[14] Clonidine possibly enhances or amplifies the sodium channel blocking action of local anesthetics by opening up the potassium channels resulting in hyperpolarization, a state in which the cell is unresponsive to excitatory input.[15]

In our study, the onset of sensory and motor block was significantly shortened by addition of clonidine to ropivacaine. Similar results were obtained by Singh and Aggarwal[6] In a meta-analysis of randomized trials by Pöpping *et al.*,[7] the data were heterogeneous. Five comparisons out of 11 for onset of sensory block and 2 out of 7 for onset of motor block were significant in favor of clonidine. Gabriel and Gordin. demonstrated no significant change in onset with the addition of clonidine to bupivacaine.[16]

The duration of motor and sensory block was significantly prolonged by addition of clonidine to ropivacaine in our study. This is consistent with most of the trials performed.[7,8,17,18]

Addition of clonidine to bupivacaine and ropivacaine has been shown to extend the sensory block by a few hours and increase the incidence of motor bocks.[19]

Time to first analgesic request may be regarded as a surrogate for pain intensity. Patients with moderate to severe pain are expected to request rescue analgesia earlier.[7] The prolongation of analgesia observed in our study is consistent with other trials performed at the brachial plexus[20-22] and at the popliteal fossa.[23] In the meta-analysis by Pöpping *et al.*, 13 comparisons out of 17 were significant in favor of clonidine. Clonidine prolonged the duration of postoperative analgesia by about 2-2.5 h in all tested local anesthetics.[7] Perineurally injected clonidine is thought to exert an analgesic effect through systemic absorption.

Although most of the studies have shown that clonidine prolongs the effects of local anesthetics,[7,20-22] other studies have failed to show any effect of clonidine, irrespective of the type of local anesthetic used (ropivacaine, bupivacaine and mepivacaine).[24-27]

Our study showed stable perioperative hemodynamics with the use of clonidine. Most of the studies conducted using clonidine in regional anaesthesia did not report any adverse effects.[18] However, studies by Büttner *et al.*[28] and Bernard and Macaire[17] reported the incidence of hypotension and bradycardia with the use of clonidine.

In our study, no side-effects were observed in both the groups. This could be attributed to the lower dose of clonidine used in our study. This dose provided satisfactory prolongation of block without producing significant hemodynamic compromise. 300 mcg clonidine was associated with severe hypotension in few studies.[17,29] Today, this dose is likely to be obsolete. The safe dose that has adequate analgesic properties remains to be identified.[7]

One of the limitations of our study was small sample size, but it had significantly important results, and we suggest future studies to be undertaken with a larger population size. Another issue of concern is that prolongation of motor blockade by higher dose of clonidine though is useful for long duration surgeries, but it is detrimental in outpatient settings where early mobilization is desirable.

Conclusion

Ropivacaine 0.75% used in brachial plexus block is well tolerated and provides effective surgical anesthesia as well as relief of postoperative pain. Clonidine as an adjuvant to ropivacaine significantly enhances the quality of supraclavicular brachial plexus block by faster onset, prolonged duration of sensory and motor block and improved postoperative analgesia, without associated adverse effects.

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