Brachial Plexus Block with Ropivacaine, Effects of Added Alpha Adrenergic Agonists - Comparison between Clonidine and Epinephrine

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ABSTRACT

BACKGROUND

To improve the time of regional anaesthesia many methods have been used. Epinephrine continues to be the most commonly used drug for this purpose. We wanted to compare the effects of alpha-adrenergic agonists clonidine and adrenaline as an adjuvant to ropivacaine in blocking brachial plexus by the supraclavicular approach in patients undergoing upper limb surgeries.

METHODS

It is a prospective randomised comparative study conducted for 18 months in 40 patients randomly divided into group RA and group RC, conducted on American Society of Anesthesiology (ASA) I and II patients undergoing upper limb surgeries under supraclavicular brachial plexus block. In group RA 30 mL of 0.5 % ropivacaine with 5 microgram / mL of epinephrine was given and in group RC 30 mL of 0.5 % ropivacaine with 1 microgram / Kg of clonidine was given.

RESULTS

On comparing effects of added alpha-adrenergic agonists clonidine and epinephrine to ropivacaine for supraclavicular brachial plexus block, it was found that there was no significant difference in the onset of the sensory blockade and motor blockade in the two groups. Duration of sensory blockade was significantly more in the clonidine with ropivacaine group when compared with the epinephrine and ropivacaine. There was no significant difference in haemodynamic responses between the two groups.

CONCLUSIONS

Supraclavicular approach brachial plexus block is effective in terms of cost and performance, and the margin of safety along with good postoperative analgesia. Hence, it can be concluded that the addition of 1 µg / Kg of clonidine to 0.5 % ropivacaine in supraclavicular brachial plexus block provides a longer duration of analgesia as compared to 5 µg / mL of epinephrine added to 0.5 % ropivacaine.

KEYWORDS

Ropivacaine, Supraclavicular Brachial Plexus, Epinephrine

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DOI: 10.18410/jebmh/2021/19

How to Cite This Article:
Das PK, Vallabha R, Merugu SH, et al. Brachial plexus block with ropivacaine, effects of added alpha adrenergic agonists - comparison between clonidine and epinephrine. J Evid Based Med Healthc 2021;8(02):97-102. DOI: 10.18410/jebmh/2021/19

Submission 08-09-2020,
Peer Review 15-09-2020,
Acceptance 23-11-2020,
Published 11-01-2021.

BACKGROUND

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. According to The International Association for the Study of Pain (IASP),[1] pain is the mechanism for informing an organism of a dangerous situation. In the ancient days alcohol opium hashish was used to reduce the pain. Regional nerve blocks are advantageous over general anaesthesia as they avoid morbidity and complications associated with general anaesthesia. They reduce the hospital stay, offer postoperative analgesia and are cost-effective too. This type of anaesthesia mainly helps to achieve near-ideal operating conditions by producing muscular relaxation. Maintaining the stable intraoperative hemodynamic status and sympathetic block which reduces postoperative pain, vasospasm and oedema.[2] Hence, peripheral nerve blockade is becoming popular as comprehensive anaesthetic care and today it is the usual choice of anaesthesia for upper limb surgeries.

Brachial plexus block at the supraclavicular level provides anaesthesia for the upper limb surgeries by blocking the middle & lower part of the plexus (median nerve, radial nerve and ulnar nerve). The supraclavicular approach of brachial plexus block is one of the regional block techniques that is safer and popular among various brachial plexus block techniques.[3]

In the first half of the 20th century, where majority of local anaesthesia was amino ester compounds; their efficacy was less due to the shorter duration of action and allergic reactions and systemic toxicity. Which led to the synthesis of newer agents. With the advent of long-acting drugs, prolonged surgeries were made possible in the extremities. To overcome the delayed onset of action, varying quality of blockade and inadequate postoperative analgesia, a commonly used drug is bupivacaine 0.5 %. It is a long-acting local anaesthetic when used in high concentration or when administered intravascularly is associated with cardiotoxicity.

As with other field's, regional anaesthesia to has undergone significant developments. Both in techniques and drug availability. Ropivacaine was developed after it was noted that bupivacaine was associated with the considerable number of cardiac arrests. Ropivacaine is a new long-acting local anaesthetic drug belonging to the amino amide group. Ropivacaine and bupivacaine belong to pipecoloxylidides group of local anaesthetics. Ropivacaine is a pure S (-) enantiomer. Unlike bupivacaine, which is a racemate, has been developed for reducing potential toxicity and improving sensory and motor block profiles.[1]

Addition of adjuvants to the local anaesthetics might improve quality onset and duration of block and decrease the requirement of postoperative analgesia and systemic side effects· Opioids clonidine ketamine have been added to local anaesthetics and injected extradural intrathecally or in nerve plexuses for prolonged analgesia. Clonidine is a mixed alpha-1 and alpha-2 adrenoreceptor agonist with a predominant alpha-2 action. The addition of clonidine to local anaesthetics improved peripheral nerve blocks by reducing the onset time, enhancing the efficacy of the block during surgery and extending postoperative analgesia.

Clonidine enhances the sodium channel blockade action of local anaesthetics by opening up the potassium channels resulting in membrane hyperpolarization. A state in which cell is unresponsive to excitatory input.[4] Thus clonidine has been used as an adjuvant to local anaesthetics to prolong the duration of effect of local anaesthetic drugs. This is an attempt to study the efficacy of added alpha-adrenergic agonist to ropivacaine i.e., clonidine and epinephrine for prolongation of postoperative analgesia when used in the brachial plexus block.

METHODS

It is prospective randomised comparative study conducted for 18 months from December 2017 to November 2019 in the Department of Anaesthesia. A total of 40 patients were randomly divided into group RA and group RC and conducted on ASA I and II patients undergoing upper limb surgeries under supraclavicular brachial plexus block. This study started after the approval of the institutional ethical committee and written informed consent was obtained from the patients in their languages.

RA-30 mL of 0.5 % ropivacaine with 5 microgram / mL of epinephrine.
RC-30 mL of 0.5 % ropivacaine with 1 microgram / Kg of clonidine.

Inclusion Criteria

ASA I and II, age between 18 and 65 years, weight > 50 Kg. Patients undergoing surgery of the upper limb with the possibility of shoulder abduction for assessment of motor blockade.

Exclusion Criteria

Known allergy, local infections / sepsis, coagulation abnormalities, cardiovascular pulmonary, renal or hepatic disease. H / O significant neurological, psychiatric. neuromuscular, alcohol / drug abuse, pregnancy / lactating women, chronic analgesic therapy (other than NSAIDs; non-steroidal anti-inflammatory)**.** On adrenergic drugs peripheral neuropathy.

Patients were preoperatively assessed and the procedure was explained to the patient. Written and informed consent was obtained. And were assessed with particular attention to any contraindications. Visual Analogue Scale (VAS) for assessment of pain postoperatively was explained to the patient preoperatively.

After the arrival of the patient into the operating room intravenous access obtained in the opposite limb with a large-bore iv cannula. Standard multi-parameter monitors like a pulse oximeter. Non-invasive blood pressure and ECG were connected and baseline values were recorded.

The patients were subjected to detailed pre-anaesthetic check-up which includes thorough laboratory workup including complete haemogram, serum electrolytes, blood urea, serum creatinine and urine routine. Patients were subjected to human immunodeficiency virus (HIV) and HBsAg screening, chest X-ray and electrocardiogram (ECG) examination. Written and informed consent was obtained from the subjects. Patients were kept nil per oral for 6 hr. Premedicated with tablet alprazolam 0.5 mg night before surgery. Intravenous access secured with 20 gauze intravenous canula on the contralateral upper limb under aseptic precautions.

Patients were placed in supine position with head turned away from the side to be blocked and the ipsilateral arm adducted. The neck was prepared with povidone-iodine solution and draped with sterile towels.

After the patient was taken on the operating table intravenous access obtained in the limb opposite to that undergoing surgery with a large-bore iv cannula. Standard multi-parameter monitor. ECG, pulse oximeter, non-invasive blood pressure were connected and monitored in all the patients.

Under strict aseptic precautions, subclavian artery pulsations were felt at a point 1.5 - 2.0 cm posterior and cephalad to the midpoint of the clavicle. A skin wheal is raised with local anaesthetic cephalo posterior to the pulsations. A 22G. 5 cm short bevelled needle is introduced through the point located parallel to head and neck in a caudal and slight medial and posterior direction until either paraesthesia is elicited or the first rib is encountered.

If the needle feels the rib, it should be moved over the first rib until paraesthesia is elicited in the arm or hand. After paraesthesia is elicited. The intravascular placement of the needle is excluded by aspiration negative for blood. The needle should be kept in the same position and the drug has to be injected slowly by ruling out the intravascular injection by aspirating intermittently.

Sensory block was assessed by pinprick by using 23g hypodermic needle in skin dermatomes C4 - T2 once in every minute for initial 30 minutes and then after every 30 minutes till patient regained normal sensations and graded according to visual analogue scale.

Onset time for the motor blockade is from the end of the injection to time when the patient was unable to abduct arm at the shoulder. The effect on the following parameters were observed; onset time of motor blockade taken from the completion of injection of study drug till the patient develops motor blockade. (Lovetts Grade 1). Onset time of sensory blockade taken from the completion of injection of study drug till the patient does not feel the pin prick (visual analogue scalescore 0). Duration of motor blockade taken from the onset of motor blockade till complete recovery of motor power. (Lovett's grade 6) Duration of sensory blockade – taken from the onset of sensory blockade till the patient feels pin prick. (Visual analogue scale of 2). Level of sensory blockade: loss of pin prick sensation from T2 dermatome to C4. Level of motor blockade: shoulder movement lost = 3, elbow movement lost = 2, medial finger movements lost = 1). Quality of post-operative analgesia: number of rescue analgesics required in the first 24 hours after the injection. Patients were watched for bradycardia, convulsions, restlessness, disorientation, drowsiness, nausea, vomiting & any other complications.

Statistical Analysis

Data was analysed by entering into MS Excel 2007 version and further analysed using SPSS 20. For descriptive analysis. The categorical variables were analysed by using percentages and the continuous variables were analysed by calculating mean ± standard deviation. For inferential analysis. The numerical data was analysed using 't' test and the categorical data were analysed using the chi-square test. A p-value of < 0.05 is considered as statistically significant.

RESULTS

About 40 patients of ASA I and II posted for upper limb surgeries were enrolled in this study as study subjects. They were randomly divided into two equal groups consisting of 20 patients each. Group RC (n = 20) received 30 mL of 0.5 % ropivacaine with 1 µg / Kg of clonidine and Group RA (n = 20) received a 30 mL of 0.5 % ropivacaine with 5 µg / mL of epinephrine. The RA group age mean ± SD is 43.35 ± 5.7 and RC group is 39.80 + 10.8 and p > 0.05 so the age distribution between the two groups is insignificant.

Age Distribution		Group-RA Number (%)	Group-RC Number (%)	P-Value
Age Interval in Years	< 30	0	6 (30 %)	> 0.05
	31 - 40	12 (60 %)	3 (15 %)	
	41 - 50	5 (25 %)	10 (50 %)	
	51 - 60	3 (15 %)	1 (5 %)	
Gender	Male	9 (47.6 %)	11 (52.4 %)	> 0.05
	Female	11 (52.4 %)	9 (47.6 %)	

Table 1. Age Distribution in the Two Groups

P value > 0.05 Therefore Distribution of Age Between the Two Groups is Insignificant.

		Group-RA Number (%)	Group-RC Number (%)	P-Value
Type of Surgical Procedure	ORIF	11 (55 %)	10 (50 %)	> 0.05
	TBW	1 (5 %)	1 (5 %)	
	IF	2 (10 %)	0	
	PTDC	5 (25 %)	2 (10 %)	
	RHE	1 (5 %)	2 (10 %)	
	EF	0	5 (25 %)	
Duration of Surgery	Mean + SD	98.5 + 19.06	98.75 + 16.84	0.965

Table 2. Type of Surgical Procedure and Duration in the Two Groups

The Duration of Surgery in the Groups was not Statistically Significant (p > 0.05)

Onset of sensory blockade in the two groups was comparable and there was no statistically significant difference among the two groups. P (> 0.05).

There was no statistical significance in the onset of motor blockade (p > 0.05) in the two groups.

Patients in group RC had a longer duration of sensory blockade than patients in group RA and the difference is statistically significant. (P < 0.05)

In this study blood pressure, heart rate, oxygen saturation remained stable throughout the procedure and no statistically significant difference was observed in both groups (p-value > 0.05).

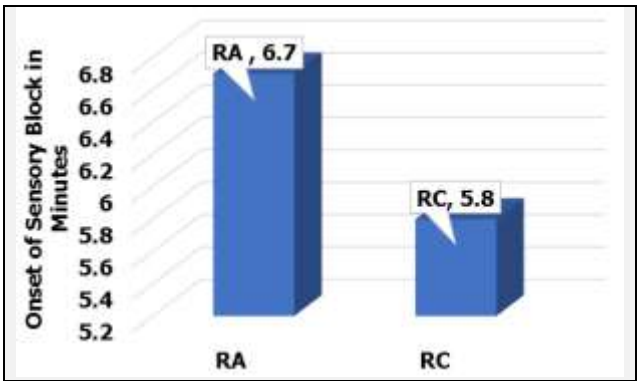

Figure 1. Onset of Sensory Blockade in Minutes and Mean Onset of Sensory Blockade in the Two Groups.

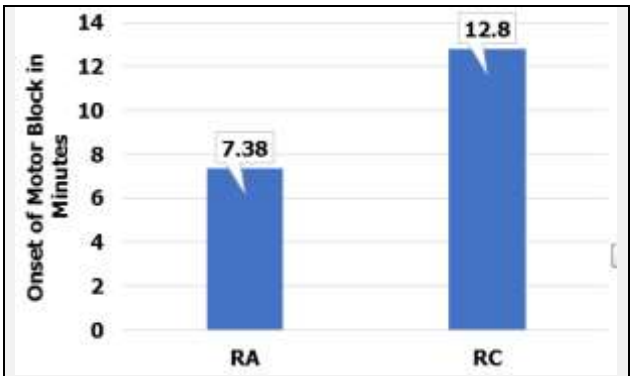

Figure 2. Mean Duration of Motor Blockade in the Two Groups

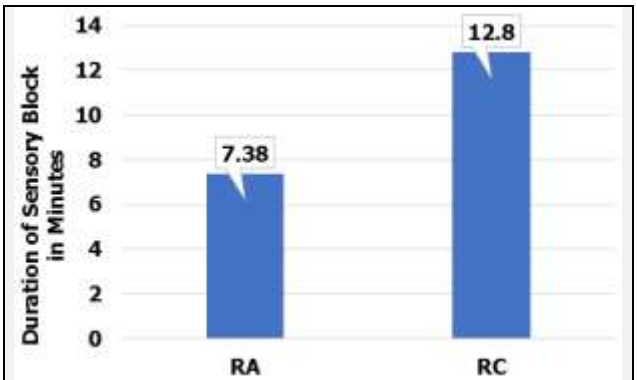

Figure 3. Duration of Sensory Blockade in the Two Groups

DISCUSSION

Brachial plexus block has become a popular technique among the anaesthetists for upper limb surgeries. This type of anaesthesia avoids the untoward effects of general anaesthesia like complications related to upper airway instrumentation. The research has also shown that this approach is an attractive approach and valid in terms of cost, performance, margin of safety and also provides good post-operative analgesia.[2] Many strategies of brachial plexus block are also described and the available literature has consistently shown that supraclavicular block is better and easiest method for anaesthesia and post-operative pain management.[3]

Ropivacaine is a long-acting amide local anaesthetic with a potentially improved safety profile as compared to bupivacaine. Historically, bupivacaine has been clinically used as it had a more prolonged duration of action. Subsequently, it was found that 'propyl' (ropivacaine) derivatives of pipecoloxylidides were less toxic than butyl derivatives (bupivacaine).[6] Human trials have demonstrated less cardiac depression and fewer central nervous system side effects when ropivacaine is injected intravenously. [7] Knudsen et al. presented data in which they compared the incidence of CNS symptoms and changes in echocardiography and electrophysiology during intravenous infusion of ropivacaine, bupivacaine and placebo. These preclinical studies showed that ropivacaine is less CNS and cardiotoxic than bupivacaine and the potential of ropivacaine to produce CNS and cardiotoxicity is also less in humans. In order to have early onset and prolonged duration of peripheral nerve block certain drugs have been added to local anaesthetics. Clonidine is one such drug that appears to have a distinct effect. Addition of adjuvant drugs to the local anaesthetic might improve quality, onset and duration of block and decrease postoperative analgesic requirement and systemic side effects.[2] Opioids clonidine ketamine have been added to local anaesthetics and injected extradurally intrathecally or in nerve plexuses for more intense and prolonged analgesia.

Clonidine enhances or amplifies the sodium channel blockade action of local anaesthetics by opening up the potassium channels resulting in membrane hyperpolarization, a state in which cell is unresponsive to excitatory input.[5]

Thus, clonidine has been used as an adjuvant to local anaesthetics to prolong the duration of effect of local anaesthetic drugs. Supraclavicular block provides anaesthesia that is said to be the most consistent in a time-efficient manner when compared with any other brachial plexus technique for the entire upper extremity (Brown et al. in their study on brachial plexus anaesthesia). [6] It is the single most effective block for all portions of the upper extremity and is performed at the division level of the brachial plexus. Perhaps this is why there is often little or no sparing of peripheral nerves if "adequate" paraesthesia is obtained. If this block is used for shoulder surgery. It should be supplemented with a superficial cervical plexus block to block the cutaneous innervation overlying the shoulder. Lanz and his colleagues in their study on the extent of blockade following various techniques of brachial plexus block demonstrated that the extent of sensory and motor blockades by using 50 mL of 0.5 % of bupivacaine by using four different techniques of brachial plexus block. The supraclavicular approach of Kulenkampff (N = 55) and the subclavian perivascular approach of Winnie (N = 56) each resulted in a homogeneous blockade of the nerves of the brachial plexus. Therefore, in this study the subclavian perivascular approach to the brachial plexus was used.[7] Cherryl et al.[8] in their comparative study of 0.25 % bupivacaine and 0.25 % ropivacaine for brachial plexus block demonstrated a higher incidence of supplementation required. Therefore, they recommended using local anaesthetics of concentration more than 0.25 % to provide brachial plexus block. Thus, in this study 0.5 % ropivacaine is used.

The demonstration of 2 receptors in the peripheral nervous system prompted recent investigations on the use of 2 receptor agonists either alone or combined with local anaesthetics for regional anaesthesia procedures like brachial plexus block. Studies have shown that the addition of 2 receptor agonist clonidine with ropivacaine produces a longer duration of postoperative analgesia. In this study, clonidine and adrenaline were added as an adjuvant to ropivacaine, and their effects were evaluated. In this study, the mean weight of the patient in group RC was 64.80 ± 7.64 Kg and in the group. RA was 64.40 ± 11.9 Kg. The onset of sensory blockade was tested by temperature testing by using ether soaked cotton in the skin dermatome C4-T2. In the study by Eledjam and his colleagues, there was no significant difference in the onset time of sensory blockade between clonidine and adrenaline group. In this study, the time of onset of sensory analgesia was 6.70 ± 1.34 minutes in group RA and 5.80 ± 1.28 minutes in group RC, the difference was not statistically significant among the two groups. In the study by Eledjam and his colleagues, there was no significant difference in the onset of sensory blockade between adrenaline and clonidine group. In this study, the onset time for the motor blockade was 4.10 ± 0.91 minutes in group RA and 3.40 ± 0.88 minutes in group RC and the difference is statistically insignificant among the two groups and it is assessed by loss of shoulder abduction. The finding that motor blockade develops before sensory blockade is consistent with the study by Winnie and Ramamoorthy. There was no difference in the time of onset of motor blockade between the two group's adrenaline with bupivacaine and clonidine with bupivacaine in the study by Eledjam and his colleagues.[9] In another study done by EL Saied AH36 and colleagues, there was no significant difference in the time of onset of the motor blockade between the clonidine groups and control groups.

In this study, the onset of sensory blockade in group RA was found to be 7.12 ± 0.63 hours and for group RC 12.69 ± 1.28 hours. Thus, the addition of clonidine to ropivacaine prolongs the duration of analgesia significantly than the ropivacaine with adrenaline group. In the study conducted by Eledjam JJ and colleagues,[9] the addition of 150 mg clonidine with 0.5 % bupivacaine conferred a mean duration of postoperative analgesia of 994.2 ± 34.2 minutes compared with 728.3 ± 35.8 minutes for 150mg of adrenaline with 0.5 % bupivacaine.

In the study done by Casati A et al.[10] the addition of clonidine provided 15.2 hours of postoperative analgesia. In the other research done by EL Saied AH et al.[36] the addition of clonidine showed a duration of sensory analgesia from 587 minutes to 828 minutes. In another study by Erlacher et al.[11] the addition of 150 mg of clonidine to 40mL of 0.5 %. bupivacaine prolonged the duration of the sensory blockade to 972 ± 72 minutes. In the study by Adnan T and colleagues.[12] the addition of clonidine to local anaesthetics prolongs the duration of sensory block significantly. In the study by Duma A and colleagues, the duration of the sensory block was more within the clonidine group.[13] They concluded the review by saying that there is a responder and non-responder behaviour within the patients in the clonidine group.

In this study, there was no statistically significant difference in the haemodynamic parameters among the two groups from the baseline. This was consistent with the observation made by EL Saied AH et al.[14] Eledjam JJ et al[9] and Casati A et al.[10]

Patients were observed for any of the side effects like bradycardia, hypotension, sedation, dry mouth, dizziness, arrhythmias and local anaesthetic toxicity and none of the patients in the two groups showed any side effects. In 1991, Eledjam J.J. and colleagues[9] none of the patients had clonidine related side effects.

In the study performed by Casati A et al.[10] clonidine pertaining side effects like sedation or haemodynamic instability aren't observed when added to the local anaesthetics. This was consistent with the observation by EL Saied AH and colleagues.[14] But in the study of 28 adult chronic renal failure patients by Adnan T et al.[12] in 2005, showed that the clonidine group had lower mean arterial pressure, heart rate and higher sedation score compared to the control groups.

CONCLUSIONS

Regional blocks are advantageous over general anaesthesia as they avoid morbidity and complications associated with general anaesthesia. Besides, they offer postoperative analgesia and are cost-effective. Hence, they are the usual choice of anaesthesia for upper limb surgeries. The supraclavicular approach of brachial plexus block has been a popular technique in the delivery of anaesthesia in patients undergoing upper limb surgeries.

Supraclavicular approach brachial plexus block is effective in terms of cost and performance, the margin of safety along with good postoperative analgesia. This technique helps in safe delivery of anaesthesia and also assures prolonged analgesia by preventing the side effects of general anaesthesia. Hence, it can be concluded that the addition of 1 µg / Kg of clonidine to 0.5 % ropivacaine in supraclavicular brachial plexus block provides a longer duration of analgesia as compared to 5 µg / mL of epinephrine added to 0.5 % ropivacaine.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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