

A prospective randomized double blind comparative study of 0.5% ropivacaine and 0.5% bupivacaine in brachial plexus block with supraclavicular approach in upper limb surgeries using peripheral nerve locator

Shalaka S. Nellore¹, Devangi A. Parikh^{2*}

^{1,2}Associate Professor, Dept. of Anaesthesia, Lokmanya Tilak Municipal Medical College & Hospital, Sion, Maharashtra

***Corresponding Author:**

Email: sdevangi10@gmail.com

Abstract

Introduction: Racemic Bupivacaine is a commonly used local anesthetic. Ropivacaine, an enantiomerically pure stereo-isomer of Bupivacaine is now available in India. Previous studies have proved the suitability of Ropivacaine for neural blockade by different routes. Aims: Our prospective, randomized, double blind study aimed to compare 0.5% Ropivacaine with 0.5% Bupivacaine for nerve-locator aided Supraclavicular Brachial Plexus Anesthesia in terms of onset, duration and quality of anesthesia.

Materials and Method: 62 ASA I & II patients undergoing upper limb surgeries received 3mg/kg of 0.5% Ropivacaine or 0.5% Bupivacaine by Nerve locator aided Supraclavicular Brachial Plexus Block.

Results: Group Ropivacaine had an earlier onset of analgesia, sensory and motor blockade (4.61 ± 2.19 , 7.03 ± 3.37 , 11.00 ± 5.85 minutes) as compared to Group Bupivacaine (7.58 ± 3.47 , 12.35 ± 8.20 & 18.87 ± 9.26 minutes) with p values of < 0.001 , $= 0.001$ and 0.001 respectively. Duration of analgesia, sensory and motor blockade was shorter in Group Ropivacaine (444.2 ± 190.3 minutes, 457.0 ± 174.3 , 404.4 ± 137.6 minutes) than Group Bupivacaine (662.9 ± 262.6 , 650.7 ± 273.8 , 640.8 ± 218.1 minutes) with p values of < 0.001 , 0.002 and < 0.001 respectively.

Conclusion: We found that Ropivacaine in Supraclavicular Brachial Plexus Anesthesia had a faster onset, equivalent degree of sensory-motor blockade and faster recovery than Bupivacaine. 3mg/kg of both drugs showed no adverse effects. Thus 0.5 % Ropivacaine is a safe substitute for 0.5 % Bupivacaine in brachial plexus blocks with special use in ambulatory surgeries.

Keywords: 0.5% Ropivacaine, 0.5% Bupivacaine, Brachial Plexus Block, Peripheral Nerve locator

Introduction

Racemic Bupivacaine is an amide local anaesthetic which has been most widely used for a number of years. Ropivacaine, an enantiomerically pure stereo-isomer of Bupivacaine is a new long-acting, amide local anaesthetic, with a high pKa and low lipid solubility. It is considered to block sensory nerves to a greater degree than motor nerves.⁽¹⁾ Improved postoperative analgesia, opioid-sparing effect and reduced recovery time, have led to widespread acceptance of a variety of regional nerve blocks for upper extremity surgeries.⁽²⁾ Various controlled clinical studies have demonstrated that Ropivacaine may be a suitable choice for neural blockade i.e. brachial plexus anesthesia, sciatico-femoral, lumbar plexus block, intrathecal anesthesia, epidural analgesia, caudal route analgesia etc.^(3,4,5,6,1,7,8)

Lignocaine: Bupivacaine combinations are commonly used in brachial plexus block to obtain fast onset, adequate sensory-motor anesthesia and post-operative analgesia. However combinations may dilute the respective drugs leading to compromised efficacy while adding to the cumulative toxicity. Ropivacaine with its reported similar onset,⁽⁴⁾ longer duration of action and relatively lower cardiovascular toxicity profile⁽⁹⁾ as compared to Bupivacaine may prove an appropriate substitute. However, if the efficacy of the new local anesthetic is not adequate then substitution for Bupivacaine may not be appropriate.

Paresthesia technique of the nerve blocks have higher chances of the neurological injury as compared to nerve locator aided block. Moreover, motor fibers have a lower electrical threshold than sensory fibers, thereby avoiding the patients' discomfort of paresthesia technique.

The objective of our prospective, randomised, double blind clinical study was to evaluate the comparative local anesthetic efficacy of Ropivacaine and Bupivacaine in Indian population with special reference to brachial plexus block using a peripheral nerve locator, and to note the incidence of side effects if any.

Materials and Method

The study was carried out after approval of the Institutional Ethics Committee. A written, informed consent was obtained from 62 ASA grade I and II patients between 18 and 65 years scheduled for elective surgery of upper extremity (upper arm, elbow, fore arm, wrist, hand and fingers). The patients were randomly divided into two equal Groups, Group R (Ropivacaine) and Group B (Bupivacaine) on basis of computer generation randomisation scheme. The investigator, surgeon as well as the patient were blinded to the drug used for Brachial Plexus block. Each patient received 3mg/ kg of 0.5% of either drug as per randomisation. Pregnant women, lactating mothers, patients with

unstable medical conditions, with known allergy and chronic opioid users were excluded.

On arrival in the operation theatre, adequate starvation was confirmed and monitoring was commenced with noninvasive arterial blood pressure, cardioscope and pulse oximeter. Intravenous access was secured with a 20 G cannula in the non-operative limb. 2-4 ml/kg/hour of continuous infusion of Ringer's lactate was administered. No premedication was used so as to avoid confounding the findings of our study.

The brachial plexus block was performed by the investigator using supra-clavicular approach. The patient was placed supine with head turned away from the side to be blocked and operative arm adducted. Block was given using a peripheral nerve stimulator with a 50 cms, 21G, short-bevelled, teflon coated needle (Stimuplex, B Braun, Germany). The needle was advanced 2cm posterior to the mid point of the clavicle, in the interscalene groove, just behind the subclavian artery, in a caudad, medial and posterior direction. Needle placement was considered optimal when a motor response in the form of wrist and/or finger flexion at a current of 0.3 to 0.5 mA with a frequency of 1-2 HZ was obtained. 3 mg/ kg of drug solution of 30-45 ml was injected slowly into the nerve sheath with intermittent aspiration to avoid intra-vascular injection. 3ml of the total calculated drug volume was infiltrated into the substance of coracobrachialis for the musculocutaneous nerve and 2 ml was injected subcutaneously in the area innervated by the intercostobrachial nerve. The start time for clinical assessment was the completion of injection.

The innervation areas of ulnar, median and radial nerves were tested. Assessment was done every 2 minutes until there was surgical anesthesia and complete motor block. Non invasive arterial blood pressure and heart rate were measured 5, 10, 15, 30 & 60 minutes after injection and as per routine theatre protocol thereafter. ECG and SpO₂ were continuously monitored.

The following parameters were assessed

- Onset of analgesia was taken as the time at which patient does not feel sensation to cold ether swab, perceives touch but not pain to pin prick with 22 G hypodermic needle in the innervation areas of dermatomes.
- Onset of surgical sensory block/ anesthesia was taken as the time at which patient feels loss of sensation of pin-prick.
- Onset of motor blockade was the time at which the patient was unable to move the upper limb against gravity at any of its joints.
- Total duration of analgesia was from its onset till the patient started complaining of pain.
- Total duration of sensory and motor blocks were calculated upto their respective resolutions. Total duration of sensory blockade was calculated till recovery to temperature sensation while that of

motor blockade up to movement at either wrist/elbow/shoulder joint. Patients were also asked to note complete recovery of sensation as well as motor functions which was then verified by anesthesiologist.

- The quality of anesthesia was recorded on a three point scale by the operating surgeon as 1 – Excellent, 2- Satisfactory and 3- Unsatisfactory.
- Side effects such as local anaesthetic toxicity like dizziness, auditory & visual disturbances, twitching, convulsions, arrhythmias, respiratory depression etc were watched for.

After the surgery patients were transferred to the PACU (Post-operative Anesthesia Care Unit) and evaluated every 2 hours until complete resolution of the block on the affected limb. Post-operative rescue analgesia of Injection Fentanyl 1ug/kg IV was provided on request and the time was noted.

The patients with incomplete block were given general anaesthesia and hence excluded from the study.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 15. Sample size calculation was based on a pilot study of 10 patients, with onset of motor blockade as the primary outcome. It was estimated that with a power of 90% at 5% significance the minimum required sample size should be 23 in each group, however in our study we included 31 patients in each group. Results are expressed in terms of Mean \pm S.D. Demographic data was analysed using unpaired t test and Categorical data using Pearson's Chi square test. For statistical analysis of onset and duration of analgesia, sensory and motor function unpaired t test was used, the results of which were expressed as Mean \pm S.D. For intergroup comparison for quality of Anesthesia Chi Square test was used. A P value of <0.05 was considered statistically significant.

Results

62 patients were included in this double blind study, 31 each in the Bupivacaine group and the Ropivacaine group. The two groups were comparable with respect to age, weight and male/ female ratio. (Table 1).

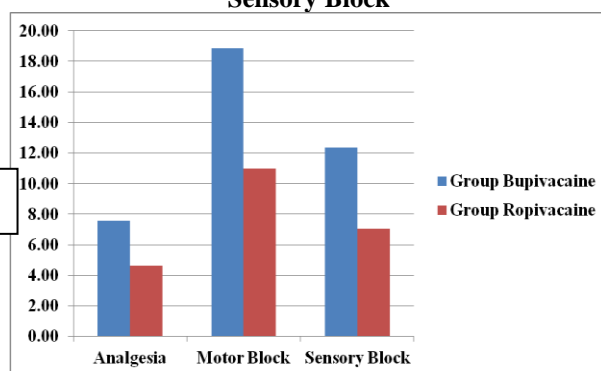
Table 1: Demographic Data

	Bupivacaine	Ropivacaine	p-value
Sex Male/ Female	22 /9	24/7	0.562
Age (Years)	39 \pm 16	34 \pm 12	0.181
Weight (kilogram)	56 \pm 11	55 \pm 9	0.508

The groups receiving ropivacaine and bupivacaine were also comparable in terms of their heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respirator rate and oxygen saturation of hemoglobin.

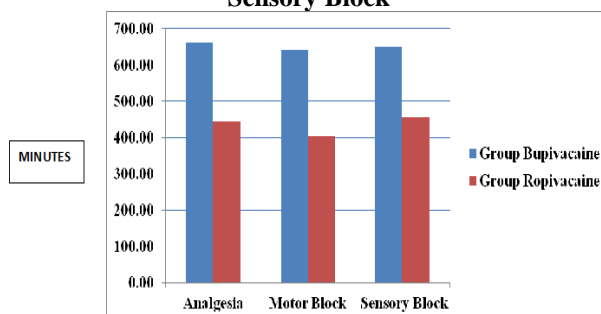
The mean onset time for analgesia for Ropivacaine was 4.61 ± 2.19 minutes which was found to be significantly shorter than that for Bupivacaine, 7.58 ± 3.47 . ($P < 0.001$) (Graph 1). The mean onset time for the sensory and motor block in case of Ropivacaine was also significantly faster as compared to Bupivacaine. Mean onset of sensory block was 7.03 ± 3.37 minutes for Ropivacaine while it was 12.35 ± 8.20 minutes in case of Bupivacaine. ($P = 0.001$) The time for mean onset of motor block was also significantly lesser with Ropivacaine; 11.00 ± 5.85 minutes, than with Bupivacaine which was 18.87 ± 9.26 minutes. ($P < 0.001$) (Graph 1)

Graph 1: Mean Onset of Analgesia, Motor Block, Sensory Block



The duration of analgesia, sensory block and motor block showed a highly significant difference between the two groups. As per the statistical analysis Ropivacaine had a significantly shorter duration than Bupivacaine. (Graph 2) The mean duration of analgesia for Ropivacaine was found to be 444.2 ± 190.3 minutes; while that for Bupivacaine was 662.9 ± 262.6 minutes ($P < 0.001$). Similarly the mean duration of sensory block was 457.0 ± 174.3 minutes with Ropivacaine whereas that for Bupivacaine was 650.7 ± 273.8 minutes; $P = 0.002$. The motor block of Ropivacaine had a mean duration of 404.4 ± 137.6 minutes while that of Bupivacaine was 640.8 ± 218.1 minutes; $P < 0.001$.

Graph 2: Mean Duration of Analgesia, Motor Block, Sensory Block



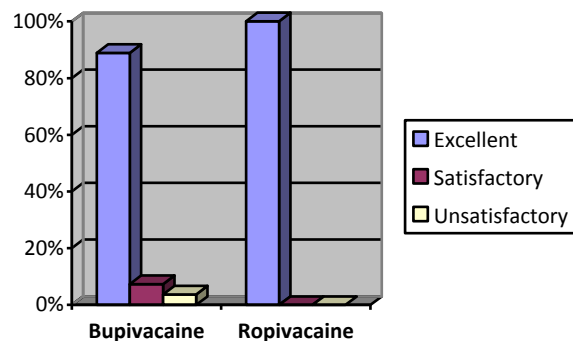
No statistically significant differences were observed among the two groups regarding the quality of anesthesia. (Table 2). Surgeon's acceptance of anesthetic technique was rated as excellent in 96.77% patients who received Ropivacaine and in 90.32% patients with Bupivacaine.

Table 2: Quality of Anesthesia

Quality of Anesthesia	Bupivacaine	Ropivacaine	p-value*
Excellent-1	28 90.32%	30 100.0%	0.496
Satisfactory-2	3 9.68%	1 3.23%	
Unsatisfactory-3	0 0%	0 0%	

The arterial pressure, heart rate & rhythm or hemoglobin oxygen saturation were comparable between the two groups. No central nervous system and cardiovascular adverse effects were observed in any of the patients.

Graph 3: Quality of Anaesthesia



Discussion

The selection of the optimal long-acting local anesthetic, its dose and concentration for supraclavicular brachial plexus block must take into consideration the available local anesthetic drugs, the time of onset, duration of blockade, and side effects of each drug and dose. A drug that has a fast onset, long duration, and lesser toxicity could be an advantage. Introduced recently, Ropivacaine, a long acting local anaesthetic, has been reported to be less toxic than Bupivacaine when compared by an intravenous infusion in human volunteers⁽¹⁰⁾ and offers a good alternative to Bupivacaine for long-acting neural blockade.

Our study of 62 patients demonstrated statistically faster onset time of analgesia, sensory and motor blockade using 0.5% Ropivacaine as compared to 0.5% Bupivacaine. The mean onset time for Bupivacaine was 3-7 minutes more than Ropivacaine. However, Hickey R et al,⁽⁴⁾ Vainionpää et al⁽¹¹⁾ and McGlade et al⁽¹²⁾ in

their comparison between 0.5% Ropivacaine and 0.5% Bupivacaine for brachial plexus block found similar onset times for both the drugs.

We found significantly shorter duration of analgesia, sensory and motor blockade with 0.5% Ropivacaine as compared to 0.5% Bupivacaine. The mean duration of analgesia, sensory and motor block in Ropivacaine was around 3-4 hours shorter than Bupivacaine. However, both the drugs were clinically effective in terms of prolonged post-operative analgesia. Contrary to our findings, Hickey R et al,⁽¹⁾ Vainionpää et al⁽¹⁰⁾ and McGlade et al⁽¹¹⁾ found no significant difference in the duration of sensory and motor block with 0.5% of Ropivacaine and 0.5% Bupivacaine when used in axillary block. The findings in the latter two studies have been attributed to the lack of block assessment between 10pm and 7am. Peña-Riverón AA et al⁽¹³⁾ also found that the duration of 0.75% Ropivacaine's analgesic effect exceeded that of 0.5% Bupivacaine by over 5 hours when given via axillary approach although both Bupivacaine and Ropivacaine provided effective postoperative analgesia. In our study, we used 0.5% Ropivacaine which may have resulted in a shorter duration of analgesia. However, H. D. Misiolek et al⁽³⁾ in his study of supraclavicular block with 0.75% Ropivacaine and 0.5% Bupivacaine found no clinically important difference in the onset and duration of blockade or quality of analgesia.

The quality of anesthesia did not differ significantly between the two groups. Anesthesia was rated as excellent in almost all (96.77%) patients in the Ropivacaine group and 92.6% of patients in Bupivacaine group. McGlade et al⁽¹²⁾ reported satisfactory analgesia in 72% patients in Ropivacaine group and 62% in Bupivacaine group. The lower percentage of satisfactory analgesia in McGlade's study could be because of involvement of anesthesia personnel relatively inexperienced with the technique and use of peripheral nerve stimulator.

Ropivacaine is believed to have a greater sensory motor separation as compared to Bupivacaine. However, the route of administration and concentration of the drug may influence the degree of sensory motor separation. The degree of motor block seen with 0.5% Bupivacaine and Ropivacaine appears to be greater with brachial plexus block than with epidural block.⁽⁴⁾ Studies have proven that differentiation between sensory and motor block appears at lower doses or concentrations of Ropivacaine.⁽¹⁴⁾ The degree of motor block was satisfactory in all of our study patients, probably because we used a dose of 3mg/kg of 0.5% Ropivacaine.

CNS adverse effects like perioral numbness and cranial nerve dysfunction (dysarthria, auditory and visual defects, paresthesiae, and abnormal taste sensation), twitching, tremors and tonic-clonic seizures usually occur at lower plasma concentrations compared

to CVS adverse effects. Cardiac toxicity beginning with negative inotropic effects and ventricular dysrhythmias⁽¹⁴⁾ usually occurs at comparatively higher plasma levels. We found no such signs with either Bupivacaine or Ropivacaine with routine clinical monitoring and assessment of neurological deficit, if any. Subtle signs of cardiovascular toxicity (eg; intra-cardiac conduction studies, echocardiography, and formal ECG analysis) were not monitored in our study. In a study by Borgeat et al⁽¹⁵⁾ using 0.5% Ropivacaine and Bupivacaine without adrenaline in interscalene block where Holter Monitoring was done, findings were similar in both the groups except for a significant prolongation of the PQ interval in Bupivacaine group. McGlade et al⁽¹²⁾ reported circumoral numbness in 1 patient receiving Ropivacaine and dizziness in one patient receiving Bupivacaine, but they were attributed to local anesthesia toxicity and were not regarded specific. No other procedure related side effects were noted in either of the groups.

Local Anesthetic (LA) toxicity is especially a concern when large doses are used as in the case of peripheral nerve blocks (PNB). However, peak plasma concentration of the local anesthetic would reach more slowly in case of a peripheral nerve block such as brachial plexus as the drug is released slowly into the blood stream.⁽¹¹⁾ Our study used a higher than routine dose i.e. 3 mg/kg of 0.5% Bupivacaine and Ropivacaine without epinephrine and demonstrated that both the drugs were equally safe in providing effective brachial plexus anesthesia. Similar results have been noted in the studies by Hickey et al⁽⁴⁾ and McGlade et al⁽¹²⁾ where doses upto 3.1mg/kg of both the drugs have been used. We did not determine plasma concentrations of either drug but in a pharmacokinetic trial conducted by Vainionpää et al⁽¹¹⁾ with 3.13 mg/kg of 0.5% Ropivacaine and 3.07 mg/kg of 0.5% Bupivacaine in axillary plexus block, peak plasma concentrations measured were 1.40mg/L and 1.45 mg/L respectively and no patients showed any signs of toxicity. In a human volunteers' study by Scott et al⁽¹⁰⁾ where upto 150mg of Ropivacaine and Bupivacaine were administered as an intravenous infusion (10mg/min), mild toxic symptoms were observed and peak plasma levels of 1-2 mg/L were noted. In a similar study by Knudsen K et al⁽⁹⁾ where upto 250 mg of the same drugs were administered intravenously, Ropivacaine showed a higher tolerated dose as compared to Bupivacaine. Misra⁽¹⁶⁾ and colleagues found no clinical signs and symptoms of Bupivacaine toxicity with either 0.5% Bupivacaine with/ without adrenaline 3 mg/kg body weight in combined femoral 3 in 1 and sciatic nerve blocks.

The concentration of the administered solution may also influence LA pharmacokinetics, because a higher extra- to intravascular space difference may facilitate absorption. In clinical practice, the choice and concentration of long-acting local anesthetics are only

partially defined.⁽¹⁷⁾ In a study evaluating the local anesthetic efficacy of Ropivacaine, Nolte et al⁽¹⁸⁾ reported that plain Ropivacaine is optimally effective at concentrations between 0.5% and 0.75%. Klein et al⁽¹⁷⁾ compared and demonstrated similar efficacy of onset and duration between 0.5% Ropivacaine, 0.75% Ropivacaine and 0.5% Bupivacaine when injected in equal volumes for interscalene block. Studies using higher concentrations 0.75% - 1% Ropivacaine have demonstrated varied results with Andrea Casati et al⁽¹⁹⁾ reporting faster onset with Ropivacaine and Vaghadia et al⁽²⁰⁾ reporting similar onset times. Adding adrenaline was not found to significantly improve the duration of motor or sensory anesthesia in a PNB.⁽²¹⁾ We chose to compare the same concentrations for each drug as increasing the concentration of Ropivacaine from 0.5% to 0.75% would have had differing volumes for the same weight. As the dosage of local anesthetic is increased, the probability and duration of satisfactory anesthesia increase and the time to onset of blockade is shortened. The dosage of local anesthetic can be increased by administering either a larger volume or a more concentrated solution. The volume of anesthetic solution per se probably influences the spread of anesthesia.⁽²²⁾

In this prospective double blind randomized study of Ropivacaine and Bupivacaine in the concentration of 0.5% and a dose of 3mg/kg for Supraclavicular brachial plexus block we found that Ropivacaine had a faster onset of action, faster recovery and an equivalent degree of motor block but shorter duration of analgesia than Bupivacaine. Both the drugs were equally safe with respect to adverse effects. Thus we conclude that (0.5%) Ropivacaine may be a suitable alternative to 0.5% Bupivacaine for supraclavicular brachial plexus block. Ropivacaine with its lesser duration of motor blockade and adequate post operative analgesia may be recommended for day case surgery.

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