

## A study to evaluate the effectiveness of Bupivacaine (0.5%) versus Ropivacaine (0.5%, 0.75%) in patients undergoing upper limb surgery under brachial plexus block

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### Abstract

This randomized double-blind study compared the efficacy of 0.5% ropivacaine, 0.75% ropivacaine, and 0.5% bupivacaine for supraclavicular brachial plexus block in upper limb surgeries. Sixty ASA grade I and II patients were randomly allocated into three groups of 20 patients each. Group I received 30 ml of 0.5% ropivacaine, Group II received 30 ml of 0.75% ropivacaine, and Group III received 30 ml of 0.5% bupivacaine.

The primary outcomes assessed were onset and duration of sensory and motor blockade, dermatomal sparing, and duration of analgesia. Secondary outcomes included pain scores, analgesic consumption within 24 hours, hemodynamic parameters, and adverse effects. Results demonstrated that both concentrations of ropivacaine produced a significantly faster onset of sensory and motor block compared to bupivacaine ( $p < 0.05$ ). However, the duration of sensory and motor blockade was shortest with 0.5% ropivacaine ( $p < 0.001$ ). Dermatomal sparing and postoperative pain scores were comparable among all groups. The total requirement for rescue analgesia was significantly lower in the 0.75% ropivacaine group ( $p < 0.001$ ). Hemodynamic stability and incidence of complications were similar across all groups. The study concluded that 0.75% ropivacaine provided superior block characteristics and reduced postoperative analgesic requirements without increasing adverse effects.

**Keywords:** Bupivacaine, Ropivacaine, Supraclavicular brach

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### INTRODUCTION

Peripheral nerve blocks have become important in clinical practice because of their role in postoperative pain relief, shortening of patient recovery time and avoiding adverse effects of general anaesthesia.(1,2) Brachial plexus block is a technique of choice employed by most of the anaesthesiologists for upper limb surgeries. Bupivacaine is one of the most commonly used local anesthetic agents in clinical use for more than 30 years.(3,4) It has been associated with cardio toxicity when used in high concentration or when accidentally administered intravenously.(5,6) Commercial preparation of bupivacaine is available as a racemic mixture of two stereo-enantiomers dextro and levo bupivacaine & is well known for its longer duration of action. Bupivacaine has 1.5- 2.5 folds lower convulsive threshold when compared to ropivacaine. It is cardio toxic due to its high protein binding and lipid solubility.(7) Because of potential risk of cardio toxicity with bupivacaine, newer local anesthetic agent ropivacaine was developed for regional anaesthetic blocks and for management of postoperative pain.(8)

Ropivacaine is a new long acting amino-amide local anaesthetic agent. It is a monohydrate of the hydrochloride salt of 1- propyl- 2',6'

pipecoloxylidide & is prepared as a pure s-enantiomer. It differs from bupivacaine in substitution of propyl for butyl group on the piperidine group. Such changes in molecular formulation hoped that ropivacaine would modulate potential cardio toxic effect and also improves sensory & motor block profiles.(9)

This study was conducted to evaluate the efficacy of different concentrations of ropivacaine 0.5% & 0.75% as compared to 0.5% bupivacaine when given through supraclavicular brachial plexus block in our setup in patients undergoing upper limb surgery.

### Material and Methods

The present study was conducted on 60 adult patient's (18-60 years) of ASA physical status I and II undergoing elective surgery for upper extremity through supraclavicular brachial plexus block. After approval from the hospital ethics committee, an informed consent was taken from all the patients. Exclusion criteria considered were-previous nerve deformity or brachial plexus injury, severe liver or kidney disease, patients having opposite side pneumothorax or collapsed lung, patients posted for bilateral upper limb surgeries, hypersensitivity to

amide local anesthetics, local infections, coagulopathies & uncooperative or unwilling patient. The patients were randomly allocated into three groups of 20 each. The present study was done in a double blind manner by making 60 coded slips. The person performing the procedure and carrying out the observations was blinded to the drug solution injected. The drug solution was prepared in three separate syringes which were partially covered. Brachial plexus block was performed via supraclavicular route.

Group I(n=20)- received 30 ml of 0.5% Ropivacaine. Group II(n=20)- received 30 ml of 0.75% Ropivacaine. Group III(n=20)- received 30 ml of 0.5% Bupivacaine.

A detailed preanesthetic checkup was performed a day before surgery. Details pertaining to the patient's clinical history, general physical and systemic examinations and basic routine investigations were obtained and patients were kept fasting overnight. Patients were explained in their own vernacular language about the brachial plexus block and linear visual analogue score using a 10 centimeter line, where 0 denoted "no pain" while 10 "worst pain imaginable". All patients were given tablet alprazolam 0.5mg orally on the night before surgery and two hours prior to the surgery with sips of water.

In the operating room, intravenous line with 20 G cannula was secured and an infusion of ringer lactate was started. All the monitors (NIBP, ECG, SpO<sub>2</sub>) were attached and the readings were taken as baseline recordings. For supraclavicular approach, the patient was placed in supine position with the head turned away from the side to be blocked. The arm to be anaesthetised was adducted and the head was extended. The medial and lateral borders of the clavicle were identified as the first rib generally lies beneath the midpoint of clavicle. The landmark was confirmed by sliding down the fingers in the interscalene groove till the arterial pulsation of subclavian artery was felt. A skin wheal was then raised 0.5 to 1 cm posterior to the midpoint of clavicle and a 22-gauge, short bevelled Visual analogue scale (VAS) nerve stimulating needle was inserted in a caudad, slightly medial and posterior direction. The needle was connected to the negative lead of the nerve locator, preset in the motor testing mode with a current setting of 2-3 mA and the patient's arm was observed. When the patient got a distal contraction of the upper limb, the current was reduced to 0.6 mA. After observing the contractions at this reading, the drug solution was injected.

Sensory block was assessed by loss of sensation to pin prick using a 22 gauge blunt hypodermic needle every minute using Hollmen scale-

1. Normal sensation of pin prick.
2. Pin prick felt as sharp pointed but weaker compared with the same area in the other limb.
3. Pin prick recognised as touch with blunt object.
4. No perception of pin prick.

A sensory block of scale 3 was considered as endpoint for the start of surgery. Onset of sensory block was taken as time from injection of drug to Hollmen sensory scale of 2. Duration of sensory block was taken as time elapsed between performing the block to regression of sensory block to scale of  $\leq$  2.

Motor block was assessed using Hollmen scale-

1. Normal muscle action.
2. Slightly weak muscle action.
3. Very weak muscular action.
4. Complete loss of muscle action.

The test was performed every minute till scale 2. A motor block of scale 3 was considered as endpoint for the start of surgery. Onset of motor block was taken as time from injection of drug to Hollmen motor scale of

2. Duration of motor block was time elapsed between performing block to regression of motor scale to lower degree.

Sparing of dermatomes was noted and supplementation given with incremental doses of inj midazolam (0.05 mg/kg) and inj ketamine (0.5 mg/kg). When the patient still complained of pain, general anaesthesia was given and the patient was excluded from the study.

Postoperative pain was assessed by Visual analog scale (VAS) at 2hrs, 4hrs, 6hrs, 8hrs, 10hrs, 12hrs, 18hrs and 24hrs after surgery. Whenever VAS score reached  $>$  4, rescue analgesia was given in the form of intravenous tramadol 100mg. Time to first dose of tramadol and the total doses required for post operative analgesia during 24 hrs was noted. In addition to this, total duration of analgesia which was the time interval from administration of the drug in supraclavicular brachial plexus block to time of first dose of rescue analgesia was also noted.

## Discussion

Brachial plexus blockade is the cornerstone of the peripheral nerve regional anesthesia practice of most anesthesiologists. This compactness of brachial plexuses may explain its historical reputation for providing short latency and complete, reliable anesthesia for upper extremity surgery.(10)

Bupivacaine is a well established long acting regional anaesthetic agent and remains the most widely used local anaesthetic in regional anaesthesia. However, reports of its cardiovascular toxicity such as life threatening ventricular tachycardia and cardiac arrest has prompted the search for a new and safer local anaesthetic drug.[11] A drug with fast onset, long duration with minimal toxicity profile could be an advantage. Ropivacaine is a long acting regional anaesthetic that is structurally related to bupivacaine and has come up recently into practice. It is a pure S(-) enantiomer, unlike bupivacaine which is a racemate.(12) Ropivacaine has been extensively used in animal studies indicated that it is less cardiotoxic than equivalent doses of bupivacaine.(13) Comparison of physicochemical properties of

ropivacaine and bupivacaine suggest that ropivacaine will have similar onset and duration time but that might be less potent in action.(14,15) Theoretically, ropivacaine offers a high level of sensory block and lesser motor block as compared with bupivacaine.(16) However, the replacement of widely used bupivacaine with ropivacaine will depend on relative cardiotoxicity of ropivacaine and the relative anaesthetic potency of ropivacaine in humans. The first aspect is difficult to study because of ethical issues. However, the relative potencies of the two drugs can be studied and our study focuses on that.

The patients were comparable demographically on the basis of age, sex and ASA grading and duration of surgery. Ropivacaine (0.5% & 0.75%) produced much quicker onset of sensory block than bupivacaine 0.5% but the onset was comparable between both concentrations of ropivacaine. Similar results were shown by Bertini et al,(9) Victoria et al(17) comparing 0.5% and 0.75% ropivacaine with 0.5% bupivacaine in axillary brachial plexus block. They concluded that the ready for surgery time was significantly shorter with both the ropivacaine groups than with bupivacaine group but the onset was comparable between both the concentrations of ropivacaine.

Our results were in contrast to studies done by Hickey et al,(18) Vainionpaa et al(19) and Raeder et al.(20) They concluded that all the groups were comparable in mean onset of sensory blockade. This variation in results could be due to differences in methodology between the studies that make accurate comparisons difficult. Despite these studies, recent researches showed a significant most fast onset time both in upper and lower extremity blocks using ropivacaine.

In our study, the mean time interval from performance of block to regression of sensory level to a lower degree was significantly more with patients receiving 0.5% bupivacaine than 0.75% ropivacaine and 0.5% ropivacaine. Our results coincide with Cox et al(21) who concluded that 0.5% bupivacaine has a significant longer duration of block than 0.5% ropivacaine and 0.25% ropivacaine. Another study conducted by Raeder et al(20) observed that 0.75% ropivacaine (11hr) had a shorter duration of sensory block than 0.5% bupivacaine (12 hr). Hickey et al(18) found that 0.5% bupivacaine and 0.5% ropivacaine had an average duration of sensory block of 9-11 hrs. The probable reason for these variations in duration of sensory blockade was due to different parameters deciding the duration. Some studies did not clearly differentiate between the duration of sensory blockade and first oral narcotic use.

Ropivacaine (0.5% & 0.75%) produced quicker onset of motor block than bupivacaine (0.5%) but the onset was comparable between both the concentrations of ropivacaine. A study done by Klein et al(22) showed that the mean onset of motor block between 0.5% and 0.75% ropivacaine and 0.5% bupivacaine was between 7 and 9 mins. Another study done by Hickey

et al(18) found a similar onset time for motor block between 0.5% ropivacaine and 0.5% bupivacaine. These differences may be accounted to the fact that in our study, accurate needle localization was determined by

motor response to a nerve stimulator compared with elicitation of paraesthesia, as used in other studies.

Patients receiving 0.5% ropivacaine had shortest duration of motor block compared to patients receiving 0.75% ropivacaine and 0.5% bupivacaine.

This was in accordance with results of Bertini et al who revealed that duration of motor block for ropivacaine 0.5% and 0.75% was significantly less than bupivacaine 0.5%.(9) However, studies done by Hickey et al and Vainionpaa et al showed similar duration of block.(18,19) The variation in the data obtained were different from other studies as the endpoints for onset and duration of motor block were different among investigators.

The reduced intensity and quicker recovery of motor block with ropivacaine in comparison to bupivacaine has been repeatedly proven by many authors.(10) The lesser motor blockade of ropivacaine in comparison to bupivacaine can be explained by its lesser lipid solubility and myelin sheath penetration, thereby causing selective action on A-delta and C fibres that carry pain rather than A-beta fibres which are involved in motor function.(23) This greater degree of differential block with ropivacaine at low concentrations has a clinical advantage in providing analgesia with minimal motor block. This property of ropivacaine holds definitive advantage in situations like labour analgesia and postoperative pain management where early ambulation is desirable.(24) All the three groups were comparable in dermatomal distribution of the anaesthetic drug and need of supplementation was similar statistically among all the three groups.

The duration of analgesia was taken as the time interval between the administration of block till the first dose of tramadol(100 mg) given intravenously when the VAS score was more than 4. These results though statistically significant, were however clinically insignificant. We, therefore, concluded that on an average the three groups provided analgesia for a duration of 10-12 hrs. This is in accordance with the results produced by Klein et al,(22) Raeder et al(20) and Bertini et al(9) showing that ropivacaine and bupivacaine have a similar duration of analgesia of around 11 hours.

The postoperative VAS scores were similar in all the three groups except for the reading at 60 mins which was lowest in ropivacaine 0.75% as compared to ropivacaine 0.5% and bupivacaine 0.5% which imply that the analgesic requirement was earlier in ropivacaine 0.5% and bupivacaine 0.5%. The total amount of tramadol requirement postoperatively was noted which revealed higher requirement in 0.5% ropivacaine group and 0.5% bupivacaine and it was less in 0.75% ropivacaine group. Furthermore, total number of top ups were also more in ropivacaine

0.5% and bupivacaine 0.5% as compared to ropivacaine 0.75%.

There were no significant differences between ropivacaine group (0.5%, 0.75%) and bupivacaine 45-year-old gentleman presented with high-grade intermittent fever associated with chills for a duration of 10 days along with yellow discoloration of eyes and high colored urine for 3 days. There was no significant past medical, surgical, drug history or any history of addictions. There is no history of recent travel and cattle exposure. On examination he was febrile and icteric. Abdominal examination revealed tender hepatomegaly with splenomegaly, rest systemic examination was normal.

On admission investigation done revealed Hemoglobin – 11.2 g/dL, Total Leucocyte Count

## DISCUSSION

*Histoplasma capsulatum* is a dimorphic fungus. It is most common cause of endemic mycosis in developing countries. It is a self-limited and asymptomatic disease in immunocompetent individuals but remains a frequent cause of opportunistic infection in patients with compromised immune status. Liver involvement as a part of disseminated histoplasmosis is well known. However, liver infection as a primary manifestation of histoplasmosis without evidence of primary lung involvement is rare. [1] While histoplasmosis is endemic in certain regions in the world including North and South America, Africa and parts of Asia, it is considered rare in India. Given the appropriate clinical context, histoplasmosis should be considered in both immunocompetent and immunocompromised patients, regardless of pulmonary symptoms in non-endemic as well as endemic areas. [1,2]

Patients with isolated hepatic histoplasmosis usually present with nonspecific symptoms, such as fever, fatigue, nausea, vomiting, weight loss, and elevation of liver enzymes. They may present with stigmata of chronic liver disease, portal hypertension, ascites, and/or varices. These features may be due to chronic parenchymal liver injury resulting from histoplasma. The full spectrum of hepatic manifestations of this disease is unknown but spans the range in the literature from mildly abnormal liver enzymes to severe icteric cholestasis with fever and pain. [3-5] Laboratory values are highly variable for this disease. High total bilirubin is usually associated with a concomitant rise in direct bilirubin, and GGT is significantly elevated as demonstrated. [6] A liver biopsy is often obtained in conjunction with serum and urine antigen studies to establish the diagnosis. GMS and PAS-D stain are useful for visualizing *Histoplasma* organisms in tissues. The early lesions in the tissue specimen contain a large number of macrophages and lymphocytes, with occasional epithelioid cells and multinucleated giant cells. [7]. The agents most commonly used for the treatment of histoplasmosis are amphotericin B and itraconazole.

group (0.5%) regarding hemodynamics and adverse effects such as nausea, vomiting, haematoma formation and bruising [8] however Isavuconazole has also demonstrated efficacy against histoplasmosis. [9].

## DISCUSSION

Both ropivacaine and bupivacaine were equally effective for brachial plexus block in patients undergoing upper limb surgeries. However, Ropivacaine 0.75% is more effective in terms of early onset of sensory and motor block, better quality of anaesthesia intraoperatively and analgesia postoperatively as evident by lesser use of number of top ups postoperatively without any side effects. Due to its better cardiotoxic profile, it has also an important edge over bupivacaine for its use in brachial plexuses and other regional blocks where the potential for intravascular injection exists.

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