

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

Anita Kumari^{1,*}, Anandini Rajput², Lakshmi Mahajan³, Ruchi Gupta⁴, Pankaj Sarangal⁵

¹Associate Professor, ^{3,5}Assistant Professor, ⁴Professor & HOD, Dept. of Anaesthesia, Sri Guru Ramdas Institute of Medical Sciences & Research, Amritsar, Punjab, ²Consultant, Corporate Hospital

***Corresponding Author:**

Email: kumarianitadr1@gmail.com

Abstract

Introduction: Brachial plexus block is the commonest form of regional anaesthesia being used for upper limb surgeries. Bupivacaine is most widely used local anaesthetic in regional anaesthesia, but its cardiotoxicity has led to the development of a new and safer local anaesthetic agent. Ropivacaine is a pure (-) enantiomer and is less cardiotoxic than equivalent concentrations of bupivacaine has recently introduced for its clinical use. The aim of this study was to evaluate the efficacy of different concentrations of ropivacaine 0.5% and 0.75% as compared to bupivacaine 0.5% in supraclavicular brachial plexus block in upper limb surgeries.

Material and Methods: A randomized double blind study was conducted on 60 adult patients of ASA grade I and II, were randomly allocated into three groups of 20 each. Group I and group II received 30 ml of 0.5% and 0.75% ropivacaine respectively and group III received 0.5% bupivacaine in supraclavicular brachial plexus block. Onset and duration of sensory and motor block, sparing of dermatomes and duration of analgesia were studied as primary outcome. VAS scores, analgesic consumption in 24 hours, hemodynamics and side effects were also evaluated as secondary outcome.

Results: Ropivacaine 0.5% and 0.75% produced quick onset of motor and sensory blockade compared to bupivacaine ($p < 0.05$). Duration of sensory and motor blockade was shortest in patients receiving 0.5% ropivacaine compared to 0.75% ropivacaine and 0.5% bupivacaine ($p < 0.001$). Sparing of dermatomes was present in all the three groups but statistically insignificant ($p > 0.05$). Pain scores in all three groups were statistically insignificant ($p > 0.05$). However, total doses of rescue analgesia required was least in group II (1.86 ± 7.86) as compared to group I (3.60 ± 8.83) and group III (3.26 ± 8.06) ($p < 0.001$). There were no significant hemodynamic changes among all the three groups. Incidence of perioperative complications were similar in all the three groups.

Conclusion: To conclude, 0.5% ropivacaine was less effective than 0.75% ropivacaine and 0.5% bupivacaine. Postoperatively although the duration of analgesia was comparable among all the three groups but the total dose of rescue analgesia required was significantly lesser in 0.75% ropivacaine than 0.5% ropivacaine and 0.5% bupivacaine. No significant adverse effects were noted in all the three groups.

Keywords: Bupivacaine, Ropivacaine, Supraclavicular brach

Date of Acceptance: 25th November, 2016

Date of Manuscript Receive: 21st October, 2016

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' piperidoxylidide & 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, SpO₂) 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)

0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
Score 0-no pain, 1-3-mild pain, 4-7-moderate pain, 8-10-severe pain

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 ≤ 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.

Hemodynamic derangements, side effects and complications such as local anaesthetic toxicity, hematoma formation, pneumothorax, phrenic nerve block or any other complication was noted and managed accordingly. After completion of the study, the results were compiled and statistically analysed using chi square test for non parametric data and ANOVA test for parametric data. Post hoc students paired t- test was applied wherever indicated using SSPS I or III software. $P < 0.05$ was considered significant and < 0.001 as highly significant. The power of our study was more than 80% taking into considerations the parameters such as onset and duration of sensory as well as motor block and duration of analgesia.

Results

Demographic data including age, sex & duration of surgery were comparable in all three groups ($p > 0.05$) (Table 1).

Table 1: Demographic data

	Group I(n=20)	Group II(n=20)	Group III(n=20)	Statistical Analysis
Age (years)	34.20±11.441	39.89±12.199	38.11±14.723	NS
Sex(F:M)	6:14	8:12	5:15	NS
Duration of Surgery (min)	85±36.778	105±21.625	101.58±19.934	NS

Data: Mean±S.D, NS: Non significant($p > 0.05$).

Sensory onset was 5.20±0.76 min in group I, 5.33±1.02 min in group II and 6.63±0.49 min in group III (Table 2). On statistical analysis, the difference was highly significant ($p < 0.001$) when group III was compared with group I and group II but on comparison between groups I & II, it was non significant ($p > 0.05$). Patients in group I had shorter duration of sensory block (378±43.96 min) as compared to group II (486.67±28.28 min) and group III (587.37±37.8 min) (Table 2). The intergroup statistical analysis was highly significant ($p < 0.001$) among all the three groups.

Table 2: Onset and duration of sensory and motor block

Time (min)	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group I vs II	Group I vs III	Group II vs III
Sensory Onset	5.20±0.768	5.33±1.029	6.63±0.496	NS	HS	HS
Duration of sensory block	378±43.962	486.67±28.284	587.37±37.836	HS	HS	HS
Motor Onset	8.30±0.657	8.17±1.043	8.95±0.405	NS	S	S
Duration of motor block	492±36.935	593.33±28.284	707.37±37.836	HS	S	S

Data: Mean±SD, HS: Highly Significant($p < 0.001$) S: Significant($p < 0.05$).

The onset of motor blockade was 8.30±0.65 min in group I, 8.17±1.04 min in group II and 8.95±0.40 min in group III. On statistical analysis, the difference was significant ($p < 0.05$) when group III was compared with group I and group II but on comparison between groups I & II, it was non-significant ($p > 0.05$) (Table 2). Patients in group I had shorter duration of motor block (492±36.93 min) as compared group II (593.33±28.28 min) and group III (707.37±37.83 min). The intergroup statistical analysis was significant when Group I was compared with group II and III (Table 2)

The C4 dermatome was spared in 18 patients in group I, 17 in group II and 15 in group III. C5 was spared in 1 patient each of group I and group III. C6 was spared in 1 patient of group II. C8 dermatome was spared in 2 patients in group II, 1 patient each in group I and group III. T1 was spared in 2 patients of group I

and 1 patient each in group II and group III. However the statistical analysis was insignificant ($p > 0.05$). Supplementation in the form of ketamine (0.5 mg/kg) and midazolam (0.05 mg/kg) was given to 3 patients in group I, 2 patients each in group II and III. On statistical analysis, the intergroup comparison was insignificant ($p > 0.05$) There were 2 block failures in group II and 1 failure in group III and were excluded from the study.

The mean duration of analgesia was prolonged in group III (631.05±17.42 min) when compared to group I (617.95±17.42 min) and was statistically significant ($p < 0.05$) but it was found statistically insignificant when compared with group II (626.22±15.88 min). This meant, when concentration of ropivacaine was increased to 0.75%, the duration increased but it was statistically insignificant compared to 0.5%

ropivacaine. However, 0.5% Bupivacaine had 0.5% (Table 3). significant longer duration as compared to ropivacaine

Table 3: Mean Duration of Analgesia

	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group I vs II	Group I vs III	Group II vs III
Duration (min)	617.950±17.421	626.22±15.887	631.056±17.146	NS	S	NS

Data: Mean±SD, NS: Non significant(p>0.05), S: Significant(p<0.05)

The mean pain scores among all the three groups were statistically insignificant till 45 minutes postoperatively (Fig. 1). At 60 min, there was an increase in VAS in group I and group III which was significant as compared to group II. Thereafter, pain scores among all the three groups were statistically insignificant postoperatively (p>0.05). Rescue analgesic requirement in group I (360±88.28 mg) and group III (326.32±80.56mg) was significantly more than group II(183.33±78.59mg). The total doses of rescue analgesia required was least in group II(1.86±.78) as compared to group I(3.60±.88) and group III(3.26±.80). This difference when compared statistically, was highly significant in group I and III when compared to group II(p<0.001) (Table 4)

Table 4: Total number of patients receiving rescue analgesia and total doses and dosage of rescue analgesia

	Group I (n=20)	Group II (n=20)	Group III (n=20)	Intergroup Comparison		
				Group I vs II	Group I vs III	Group II vs III
No. of doses	3.60±.883	1.86±.786	3.26±.806	HS	NS	S
Total dosage	360±88.288	183.33±78.591	326.32±80.568	HS	NS	HS
Total no. of patients requiring rescue analgesia	20	20	20	NS	NS	NS

Data: Mean±SD, HS: Highly significant(p<0.001), NS: Not Significant(p>0.05)

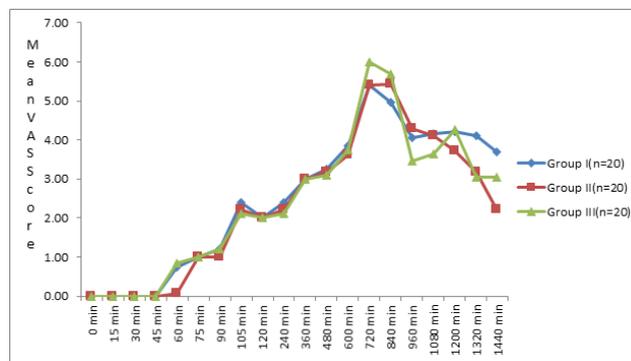


Fig. 1: Visual Analogue scale (VAS) score

The mean pulse rate and systolic blood pressure intra and postoperatively showed no statistical significant difference among all the three groups (p>0.05). The intergroup comparison of mean pulse rate and systolic blood pressure, showed statistically insignificant difference (p<0.05). However, the intragroup comparison showed few significant recordings from the baseline which were significant statistically but clinically insignificant (p>0.05%).

Adverse effects such as- hematoma formation was observed in 2 patients in group I, 3 in group II and 2 in group III. Nausea and vomiting occurred in 2 in group II and 1 each in group I and III. Postoperative paresthesias in the form of burning sensation was seen only in one patient of the group III. Bruising was seen in 2 patients in group I, 1 each in group II and III. The intergroup comparison, however, showed insignificant results statistically.(p> 0.05) (Table 5)

Table 5: Adverse Effects

Adverse Effects	Group I(n=20)	Group II(n=20)	Group III(n=20)	Statistical Analysis
Hematoma	2	3	2	NS
Pneumothorax	0	0	0	NS
Phrenic nerve block	0	0	0	NS
Nausea and Vomiting	1	2	1	NS
LA toxicity	0	0	0	NS
Postoperative paresthesias	0	0	1	NS
Bruising	2	1	1	NS

NS: Non-significant. ($p > 0.05$)

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

group (0.5%) regarding hemodynamics and adverse effects such as nausea, vomiting, haematoma formation and bruising.

Conclusion

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.

References

1. Chan VWS, Peng PWH, Kaszas Z, Middleton WJ, Muni R, Anastakis DG. A competitive study of general anaesthesia, intravenous regional anaesthesia and axillary block for outpatient hand surgery: clinical outcome and cost. *Anesth Analg*. 2001;93:1181-4.
2. Armstrong KPJ, Cherry RA. Brachial plexus anaesthesia compared to general anaesthesia when a block room is available. *Can J Anesth*. 2004;51:41-4.
3. Afekenstam B, Egnér B, Ulfendahl K, Dhuner G. Trials with carbocaine a new local anaesthetic agent. *Br J Anaesth*. 1956;28:503-6.
4. Ekbolam L, Widman B. A comparison of the properties of LAC43, prilocaine and mepivacaine in extradural anaesthesia. *Acta Anaesthesiol Scand*. 1966 (Suppl. XXI):33-43.
5. Terasaki T, Pardridge WM, Denson DD. Differential effect of plasma protein binding on its in vivo transfer into brain and salivary glands of rats. *Journal of Pharmacology and Experimental Therapeutics*. 1978;239:724-9.
6. Tucker GT. Pharmacokinetics of local anaesthetics. *Br J Anaesth*. 1986;58:717-31.
7. Jarboo K, Batra YK, Panda NB. Brachial plexus block with midazolam and bupivacaine improves analgesia. *Can J Anaesth*. 2005;52:822-6.
8. Fanelli G, Casati A, Capelleri G. A clinical comparison of ropivacaine 0.75%, ropivacaine 1% or bupivacaine 0.5% for interscalene brachial plexus anaesthesia. *Eur J Anaesthesiol*. 1999;16:784-9.
9. Bertini L, Tagariello V, Mancini S, Ciasehi A, Posteraro CM. 0.75% and 0.5% ropivacaine for axillary brachial plexus block: A clinical comparison with 0.5% bupivacaine. *Reg Anesth Pain Med*. 1999;24:514-8.
10. Neal JM, Gerancher JC, Hebl JR, Iifeld BM, McCartney CJL, Franco CD. Upper extremity regional anaesthesia: Essentials of our current understanding. *Reg Anesth Pain Med*. 2009;32:134-70.
11. Markey JR, Naseer OB, Bird DJ, Rabito SF, Winnie AP. Transient neurological symptoms after epidural analgesia. *Anesth Analg*. 2000;90:437-9.
12. Afekenstam B, Egnér B, Petersson G. Local anaesthetics: N-alkylpyrrolidine and N-alkyl piperidine carboxylic amides. *Acta Chemica Scandinavica*. 1957;1183-90.
13. Nancarrow C, Rutton AJ, Runciman WG, Mather LE. Myocardial and cerebral drug concentrations and mechanisms of death after fatal intravenous doses of

- lidocaine, bupivacaine ropivacaine in the sheep. *Anesth Analg.* 1989;69:276-83.
14. McDonald S, Liu S, Kopacz D, Stephenson CA. Hyperbaric spinal ropivacaine: A comparison to bupivacaine in volunteers. *Anesthesiol.* 1999;91:971-7.
 15. Gautier PH, De Kock M, Fanard L, Van Steenberge A. Intrathecal ropivacaine or bupivacaine for ambulatory knee arthroscopy. *Anesthesiol.* 1999;91:1239-45.
 16. Markham A, Faulds D. Ropivacaine: a review of its pharmacology and therapeutic use in regional anaesthesia. *Drugs.* 1996;52:429-49.
 17. Victoria GLR, Ana Angelica PR, Guadalerpe ZL, Beatriz SV. Clinical comparison of bupivacaine and ropivacaine for neurostimulation guided brachial plexus block by axillary approach. *Anesthesiologica.* 2009;32:7-13.
 18. Hickey R, Hoffman J, Ramamurthy S. A comparison of 0.5% ropivacaine and 0.5% bupivacaine for brachial plexus block. *Anaesthesiol.* 1991; 74:639-42.
 19. Vainionpaa VA, Haavisto ET, Huho TM. A clinical and pharmacokinetic comparison of ropivacaine and bupivacaine in axillary brachial plexus block. *Anesth Analg.* 1995;81:534-5.
 20. Raeder J, Drosdahl S, Klaastad O. Axillary brachial plexus block with ropivacaine 7.5mg/ml : a comparative study with bupivacaine 5 mg/ml. *Actaanaesthesiolscand.* 1999;87:794-8.
 21. Cox CR, Checketts MR, Mackenzie N, Scott NB, Bannister J. Comparison of (s)- bupivacaine with (RS) bupivacaine in supraclavicular brachial plexus block. *Br J Anaesth.* 1998;80:594-8.
 22. Klein SM, Greengrass RA, Steele SM. Comparison of 0.5% bupivacaine, 0.5% ropivacaine and 0.75% ropivacaine for interscalene brachial plexus block. *Anesth Analg.* 1998 ;87:1316-7.
 23. McClure JH. Ropivacaine. *Br J Anaesth.* 1996;76:300-7.
 24. Stienstra R. The place of ropivacaine in anaesthesia. *Actaanaesthesiol Belg.* 2003;54:144-8.