

International Journal of Biomedical Research

ISSN: 0976-9633 (Online); 2455-0566 (Print)

Journal DOI: [10.7439/ijbr](https://doi.org/10.7439/ijbr)

CODEN: IJBRFA

Original Research Article

Comparative study of 0.375% bupivacaine and 0.375% ropivacaine in brachial plexus block via supraclavicular approach

Hetal Rathod*, Hetal Parikh and R. M. Upadhyaya

Department of Anaesthesiology, S.B.K.S. M.I. & R.C., Vadodara, Gujarat, India

***Correspondence Info:**

Dr. Hetal Rathod

E-1, Balaji Avenue, Judges bungalows road,

Near Mansi Tower, Vastrapur,

Ahmedabad, PIN – 380015

E-mail: drhetalrathod@gmail.com

Abstract

Objectives: To compare the effect of 35 ml of 0.375% bupivacaine and 35 ml of 0.375% ropivacaine in supraclavicular brachial plexus block.

Materials and Methods: In this prospective double blind study, sixty patients of ASA- I and II scheduled for upper limb orthopedic surgeries were randomly divided into Group B and Group R which received 35 ml of 0.375% bupivacaine and 0.375% ropivacaine respectively. Sensory and motor block onset & duration and duration of analgesia were evaluated statistically using unpaired t-test and p-value < 0.05 was considered significant.

Results: The sensory and motor onset (mean-minutes) was 21.13 and 25.87 in group B and was 13.3 and 21.37 in group R respectively. The duration of sensory and motor block (mean- minutes) was 480.3 and 472.8 in group R, and 472.1 and 460.2 in group B. The duration of post-operative analgesia was 504.2 minutes in Group R and 499.6 minutes in Group B.

Conclusion: Group R provided statistically significant & rapid onset of sensory and motor blockade than Group B for upper limb surgeries. There were no significant differences in duration of sensory and motor blockade, any complication or side effects. Ropivacaine may be a preferred option because of its higher therapeutic index.

Keywords: bupivacaine, ropivacaine, supraclavicular block.

1.Introduction

Regional nerve blocks are based on the concept that pain is conveyed by nerve fibers, which are amenable to interruption anywhere along their pathway. The idea that pain is conducted in the nervous system originated with the specific theory of Johannes P. Muller described in 1826. This was followed by the alternate intensity theory of Erb in 1874.[1]

Regional anaesthesia was not available when general anaesthesia was first successfully administered in 1846. It had to wait until 1855 when Rynd described the idea of introducing a solution of morphine hypodermically around a peripheral nerve. Because he did not have a needle or a syringe, he improvised by introducing a trocar and cannula into

the region and then allowing the solution to reach the nerves by gravity.[2]

It is particularly useful in out-patient anaesthesia, for patients with full stomach, for diabetic patients, associated cardiac, pulmonary, hepatic or renal damage and polytrauma. Some of the significant advantages[3] of brachial block are postoperative analgesia, early ambulation, avoidance of polypharmacy, No airway manipulation, early resumption of oral feeding and consequently decreased postoperative pulmonary, gastrointestinal and thromboembolic complications.

The supraclavicular approach to brachial plexus blockade was introduced in clinical practise in Germany by Kulenkampff in 1911.[4] Supraclavicular brachial plexus block provides

anaesthesia for surgeries around elbow, forearm and hand. As it provides dense block and also relieves tourniquet pain, this technique was chosen for upper limb surgeries in our study. Though few potential complications like pneumothorax, injury to vessels, hematoma are described with this technique, it can be minimized with proper technique and strict vigilance.

A commonly used drug for this technique is bupivacaine 0.5% which is a well established long acting local anaesthetic, which like all amide anaesthetics has been associated with cardiotoxicity when used in high concentration or when accidentally administered intravascularly.[5] As with other fields, regional anaesthesia too, has undergone major developments, both in techniques and drug availability. Ropivacaine was thus developed after it was noted that bupivacaine was associated with significant number of cardiac arrests.

Ropivacaine is a new long acting local anaesthetic drug belonging to the amino amide group[5]. Ropivacaine and bupivacaine belong to pipercolonylidides group of local anaesthetics. It is a pure S(-) enantiomer, unlike Bupivacaine, which is a racemate, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles.

1.1 Aims & Objectives

The aim is to compare 35 ml of 0.375% bupivacaine and 35 ml of 0.375% ropivacaine in brachial plexus block via supraclavicular approach.

The study was carried out with following objectives:

- To compare time of onset of sensory and motor block.
- To compare total duration of sensory and motor block.
- To compare total time duration for analgesia.

2. Materials and Methods

This prospective randomized double blind clinical study was undertaken at Dhiraj Hospital, attached to S.B.K.S. Medical Institute and Research Centre during the period from November 2012 to July 2014. The study was undertaken after obtaining ethical committee clearance as well as informed consent from all the patients.

2.1 Allocation of Groups

Sixty patients posted for elective upper limb orthopaedic surgery were randomly divided into two groups of 30 patients in each.

Group B: 35 ml of 0.375% Bupivacaine (30 ml 0.5% Bupivacaine + 10 ml of normal saline)

Group R: 35 ml of 0.375% Ropivacaine (30 ml 0.5% Ropivacaine + 10 ml of normal saline)

2.2 Inclusion Criteria

- ✓ Patients aging between 18-70 years ASA risk category I and II
- ✓ No known history of allergy, sensitivity or other form of reaction to local anesthetics of the amide type
- ✓ Patient willing to sign informed consent

2.3 Exclusion Criteria

- × ASA \geq III.
- × local skin infections at site of injection.
- × coagulopathy.
- × potent antiplatelet, or on anticoagulants.
- × allergy to the trial drugs.
- × hemidiaphragmatic paralysis on contralateral side of surgery.
- × psychological disorder.

A routine pre-anaesthetic evaluation of each case was done a day prior to surgery. Local examination of block site and airway Assessment was done. Tab. Alprazolam 0.25 mg was given on the previous night and Patients were kept nil orally 6-8 hours prior to surgery. The patients were reassured, the procedure of block was explained and a written informed consent was obtained from them. On arrival of the patient in the operation theatre, Multipara monitors were applied and baseline vitals noted. Intravenous line was secured with 18G intracath and the patients were given I.V., Fluids according to the requirement. Premedication with Inj. Ondansetron 4 mg and Inj. Glycopyrrolate 0.2 mg were given intravenously 5 minutes before giving supraclavicular brachial plexus block.

2.4 Technique

After appropriate preparation and creating a skin wheal with local anaesthetic, 23-gauge one and half inch needle was inserted at the point of entry above the midpoint of clavicle in the backward inward downward direction (BID) until paraesthesia was elicited in the forearm or hand and after negative aspiration for air or blood, 35 ml of a solution containing local anaesthetic was injected and a 3 minute massage was performed to facilitate even distribution of drug inside the sheath covering neurovascular bundle.

The double blind nature of study was maintained by keeping the anaesthesiologists who were performing the block and collecting the data kept blinded to the study drugs.

2.5 Assessment of the block

- 1. Onset of Sensory and Motor Blockade** was monitored every minute for first 10 minutes then every 5 minutes till 30 mins.

Sensory Blockade

- **Assessment of sensory block** was done after completion of drug injection in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve and musculocutaneous nerve. (i.e. C4 through T2 dermatomes)

Sensory block was measured with pin prick by using following grades

0 = No loss of sensation to pinprick

1 = Analgesia (patient feel touch but no pain on pinprick)

2 = Anaesthesia (patient even not feel touch & sensation on pin prick)

- **Onset of sensory** = Time taken from drug injection to complete ablation of sensation (sensory score 2).
- **Duration of sensory blockade** = Time of onset of block to complete return of parasthesia (sensory score 0).
- **Failed Block** = anaesthesia was not present in 2 or more peripheral nerve distributions and such patients were excluded from the study.

Motor Blockade:

- Motor block was measured at every minute for first 15 minutes and then every 2 minutes for next 45 minutes by assessing the following motor functions:

- Flexion at the elbow (musculocutaneous nerve)
- Extension of the elbow and wrist (radial nerve)
- Opposition of thumb and index finger (ulnar nerve)
- It was graded according to the following scale:
0 = no block (full muscle activity);
1 = partial block (decreased muscle activity);
2 = Complete block (no muscle activity).

Onset of motor block was considered as time from completion of injection to the inability of the patient to move his/her fingers or raises their hand.

- In case of both sensory and motor blockade, a score of two denote complete onset of block.
- The **duration of sensory blockade**, defined as the time between onset of sensory block and return of dull pain and VAS < 3, was assessed every 30 minutes postoperatively in at least 3 major nerve distributions
- The **duration of motor block** defined as the time between onset of motor block and regained ability of the patient to move his/her fingers. It was assessed every 30 minutes postoperatively.
- The **duration of analgesia**, defined as the time between onset of action and onset of pain (VAS \geq 4), was the time when patients received the first dose of analgesic in form of injection diclofenac sodium 75 mg IV.

Maximum duration of all surgeries was not more than 120 minutes.

The operation was started when full surgical anaesthesia developed. In case, patient experienced mild pain (VAS < 3) intraoperative supplementation was given with Inj. Ketamine 0.5mg/kg IV. General Anaesthesia was given to the patients with failed block and such cases were excluded from the study groups.

Intensity of post-operative pain was evaluated using VAS (visual analogue scale) with grade 0 (no pain) to 10 (worst pain). Pain score were noted at every 30 minutes initially for 2 hours and then hourly till the patient regain VAS score of 4. If score was 4 or more than 4, analgesia was judged unsatisfactory and rescue analgesia was administered in the form of inj. Diclofenac sodium 75mg IV. Evaluation was stopped and time for need of first analgesia was noted.

2.6 Statistical methods

Both groups were compared for onset and total duration of analgesia, sensory and motor blockade. All the data were filled up in proforma and were statistically analysed by applying student's unpaired t-test. The results were considered significant if P value was < 0.05.

3. Results

Both for age and weight, p-value was > 0.05, which clearly indicates that there was no statistically significant difference in the demographic profile of patients of Group B and Group R. Table 1 shows that the average age in group B was 42.4 years and in group R was 44.5 years. Youngest patient in the study group was 18 years and oldest was 80 years. The average body weight was 61.6 kg in group B and 60.40 kg in group R. Male-to-female ratio was 7:3 in group B and 19:11 in group R. Both groups had predominantly male population.

Both for sensory and motor block, p-value was < 0.0001, which clearly indicated that the difference in the time duration for the onset of sensory and motor nerves in Group B vs Group R was statistically significant. The average onset time for Sensory and motor block is shown in Table 2. The onset in Group R patients was faster for both Sensory and Motor block compared to Group B patients.

As shown in Table 3 average duration for sensory block was 472.1 mins in group B and 480.3 mins in group R. The average duration for motor block was 460.2 mins in group B and 472.8 mins in group R. The average duration for analgesia block was 499.6 mins in group B and 504.8 mins in group R. No Significant difference was observed in the duration of sensory and motor block of patients

belonging to Group B and Group R. Similar results were seen for analgesia also.

Table 1: Demographic characteristics of study population

Variable	Group B	Group R	p-value
Age (years)	42.40 ± 17.49	44.50 ± 17.33	0.8985
Weight (kg)	61.60 ± 9.18	60.40 ± 9.12	0.5357
Sex (M/F)	21(70%) / 9(30%)	19(63%) / 11(37%)	0.746

Both for age and weight, p-value was > 0.05, which clearly indicates that there was no statistically significant difference in the demographic profile of patients of Group B and Group R.

Table 2: Onset of sensory and motor block in two groups (Mins) (MEAN ± SD)

Variable	Group B	Group R	p-value
Sensory Block	21.13 ± 2.57	13.77 ± 1.92	< 0.0001
Motor Block	25.87 ± 2.64	21.37 ± 1.88	< 0.0001

Both for sensory and motor block, p-value was < 0.0001, which clearly indicated that the difference in the time duration for the onset of sensory and motor nerves in Group B vs Group R was statistically significant.

Table 3: Duration of sensory and motor block and duration of analgesia in two groups (MEAN ± SD)

Time (min)	Group B	Group R	p Value
Sensory block	472.1 ± 32.83	480.3 ± 31.89	0.3286
Motor block	460.2 ± 66.19	472.8 ± 59.67	0.4430
Analgesia	499.6 ± 32.70	504.2 ± 32.40	0.5863

No Significant difference was observed in the duration of sensory and motor block of patients belonging to Group B and Group R. Similar results were seen for analgesia.

4. Discussion

As with other fields, regional anaesthesia too, has undergone major developments, both in techniques and drug availability. One of the first local anaesthetic agents that emerged as a possible replacement for bupivacaine was ropivacaine. Ropivacaine was thus developed after it was noted that bupivacaine was associated with significant number of cardiac arrests.

The S(-) enantiomer is the principal agonist (the eutomer) because it possesses true local anaesthetic activity, whereas the R(+) enantiomer (the distomer) not only possesses less local anaesthetic activity, but greater toxicity[6] Ropivacaine is a pure S(-) enantiomer, unlike bupivacaine, which is a racemate, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles[7].

In our study, we selected to compare effectiveness of 0.375% bupivacaine with 0.375%

ropivacaine for brachial plexus block via supraclavicular approach.

It has been emphasized over the time that for making comparison between any two agents, equipotent doses should be compared. In continuous interscalene block, ropivacaine 0.2% and bupivacaine 0.15% showed comparable pain control.[8][9] When administered as a bolus interscalene block, Casati *et al* reported that ropivacaine 0.5% had similar pain relief with bupivacaine 0.5% [10], while ropivacaine 0.75% showed similar effects with bupivacaine 0.5% in the study by Hoffmann-Kiefer *et al* [11].

Hansen [12] and Nunez *et al* [13] has studied the effect of concentration of local anaesthetic solution on the ED₅₀ of bupivacaine for supraclavicular brachial plexus block and he proved that mass of local anaesthetic rather than the concentration which is the major determinant of the ED₅₀ for achieving successful block. On comparison of a small volume at high concentration with a large volume at low concentration of levobupivacaine injected in the humeral canal demonstrated that the success rate was lower in the group receiving the smaller volume at a higher concentration.

Therefore, we selected to compare higher volume (35ml) of local anaesthetic (ropivacaine versus bupivacaine) at relatively lower concentration (0.375%) than commercially available concentration (0.5%, 0.75%) for supraclavicular brachial plexus block in order to minimise the total dose to be injected and improve the safety profile which has already been used in studies performed for caudal anaesthesia, epidural anaesthesia, 3-in-1 femoral nerve block etc [10][11].

Raikwar *et al* [14] also found statistically significant difference between Ropivacaine 0.5% and Bupivacaine 0.5% with faster onset in Ropivacaine group which is similar to our study. Tripathi *et al* [15] also found faster onset with ropivacaine than bupivacaine but their onset time was shorter 11 minutes for ropivacaine and 18.46 minutes for bupivacaine that may be because of their higher concentration of drug (bupivacaine 0.5% and ropivacaine 0.5%). Hickey *et al* [16] has compared 0.25% bupivacaine and 0.25% ropivacaine in subclavian perivascular brachial plexus block and they found no difference in onset time. An onset of sensory and motor block similar to our study was also found in the result of a study conducted by Senel *et al* [16]. Onset time for sensory block with 40 ml 0.375% ropivacaine was 9.55±0.34 mins and the same for motor block was 10.8±0.38 mins [17].

Tripathi *et al* [15] also noted 8-9 hours duration of block with 0.5% bupivacaine and 0.5%

ropivacaine with $p > 0.05$ which was similar to our study. Same way, no statistically significant difference was found in duration of motor and sensory block between two groups in various studies conducted by Raikwar *et al*[14], Hickey *et al*[16], Klein *et al*[18], Casati *et al*[10] and Hickey *et al*[19]. Borgeat[8] also reported better preservation of strength in the hand and less paresthesia in fingers with 0.2% ropivacaine as compared to bupivacaine 0.15% which also reflect the inability of ropivacaine to produce adequate motor block at lower concentration. Brown *et al*[21] reported that the duration of sensory and motor block produced by equal concentration of ropivacaine may be slightly less than that of bupivacaine when used for epidural anaesthesia.

Hofmann-kiefer *et al*[11] reported similar duration of post-operative analgesia of 8 hours with use of 40 ml of 0.375% ropivacaine solution in 3-in-1 FNB which significantly reduced the post-operative morphine requirement at 12, 18, 24, and 48 hours ($p < 0.001$) which was comparable to our result. Mean duration of analgesia for ropivacaine 0.5% and bupivacaine 0.5% for brachial plexus block was found to be similar, average 13-14 hours, which was slightly greater than our study result reflecting that the higher concentration was associated with prolonged duration of analgesia.[16] Similar results were found by Raikwar *et al*[14] with use of 0.5% ropivacaine (11.8 ± 2.5 hours) and 0.5% bupivacaine (10.6 ± 1.2 hours).

The duration of analgesia in the studies conducted by Klein *et al*[18] (ropivacaine:720-900 minutes and bupivacaine:720-900 minutes), Vaghadia *et al*[7] (ropivacaine:678-858 minutes and bupivacaine:618-1026 minutes), Bertini *et al*[22] (ropivacaine: 666 ± 174 minutes and bupivacaine: 666 ± 210 minutes) and Raeder *et al*[23] (ropivacaine:720 \pm 72 minutes and bupivacaine:780 \pm 78 minutes), like ours, showed no statistically significant difference between ropivacaine and bupivacaine group for brachial plexus block ($p > 0.05$). The longer duration of analgesia in above studies compared to ours may be due to large volume of study drugs(40 ml) or due to higher concentration used.

To conclude, ropivacaine 0.375% 35 ml when used for supraclavicular brachial plexus blockade provided statistically significant rapid onset of sensory and motor blockade than 0.375% 35ml bupivacaine for upper limb surgeries. However, there were no significant differences in duration of sensory and motor blockade, any complication or side effects. Vital parameter changes were also found insignificant between two groups.

Fixed doses of ropivacaine and bupivacaine may have influenced the results in this study. However, ropivacaine may be a preferred option because of its higher therapeutic index which leads to a better safety profile over other local anaesthetic in terms of reduced CNS and cardiotoxic potential.

Acknowledgments

I am using this opportunity to express my gratitude to everyone who supported me throughout the course of this study. I would like to express the deepest gratitude to all my esteemed teachers, for their constant help support and invaluable guidance. I gratefully acknowledge the help rendered by my seniors, my colleagues and my juniors. I express my thanks to the chancellor; the dean; the medical superintendent, the research director and the registrar of S.B.K.S.M.I.R.C., Sumandeep Vidyapeeth University for allowing me to carry out this work in this institution. I am also thankful to all medical, paramedical and nursing personal for their direct or indirect contribution in making this study possible. I express my thanks to the patients for their participation and co-operation for the study, which made the study possible. Finally, I would like to pay my profound regards to almighty.

References

- [1] Prithvi Raj P. Development of Regional Anaesthesia; 3rd edition; Chapter-Historical Aspects of Regional Anaesthesia, P23.
- [2] Rynd F; Neuralgia-Introduction of fluid to the nerve; Dublin Med Press 13:167, 1845.
- [3] Cousins MJ Bridenbaugh. Neural blockade in clinical anaesthesia and pain medicine. 4th Edition.: Lippincott Williams and Wilkins; 2009.
- [4] Kullenkampff D: Anaesthesia of the brachial plexus; *Zentralbl Chir* 38:1337-1340, 1911.
- [5] Mc Clure JH. Ropivacaine. *British Journal of Anaesthesia* 1996; 76:300-7.
- [6] Raikwar Surendra, Sonal Awasya, Gupta Pankaj. "Comparative clinical evaluation of 0.5% ropivacaine and 0.5% bupivacaine for brachial plexus block via supraclavicular approach for upper limb surgeries". *Journal of Evolution of Medical and Dental Sciences* 2013; 2 (47): 9167-9173.
- [7] Vaghadia H, Chan V, Ganapathy S, Lui A, McKenna J, Zimmer K; A multicentre trial of ropivacaine 7.5 mg x ml(-1) vs bupivacaine 5 mg x ml(-1) for supra clavicular brachial plexus anaesthesia; *Can J Anaesth.* 1999 Oct; 46(10):946-51.

- [8] Borgeat A, Kalberer F, Jacob H, Ruetsch YA, Gerber C. Patient-controlled interscalene analgesia with ropivacaine 0.2% versus bupivacaine 0.15% after major open shoulder surgery: The effects on hand motor function. *Anesth Analg.* 2001; 92: 218-223.
- [9] Nishiyama T et al. Comparison of the Motor and Sensory Block by Ropivacaine and Bupivacaine in Combination with Lidocaine in Interscalene Block; *Med Arh.* 2012 Oct; 66(5): 315-317.
- [10] Casati A, Fanelli G, Albertin A, Deni F, Anelati D, Antonino FA, Beccaria P ; Interscalene brachial plexus anesthesia with either 0.5% ropivacaine or 0.5% bupivacaine.; *Minerva Anesthesiol.* 2000 Jan-Feb; 66(1-2):39-44.
- [11] Hofmann-Kiefer K, Herbrich C, Seebauer A, Schwender D, Peter K.; Ropivacaine 7.5 mg/ml versus bupivacaine 5 mg/ml for interscalene brachial plexus block---comparative study; *Anaesth Intensive Care.* 2002 Jun; 30(3):331-7.
- [12] Hansen TG. Ropivacaine: A pharmacological review. *Expert Rev Neurother* 2004; 4:781.
- [13] Nunez Aguado D, Lopez Alvarez S, Salamanca Montana ME, Janeiro Amela M, Fernandez Fernandez R, Cobian Llamas JM. Brachial plexus block with levobupivacaine at the humeral canal: comparison of a small volume at high concentration with a large volume at low concentration. *Rev Esp Anesthesiol Reanim* 2005; 52:529-35.
- [14] Raikwar Surendra, Sonal Awasya, Gupta Pankaj. "Comparative clinical evaluation of 0.5% ropivacaine and 0.5% bupivacaine for brachial plexus block via supraclavicular approach for upper limb surgeries". *Journal of Evolution of Medical and Dental Sciences* 2013; 2 (47): 9167-9173.
- [15] Tripathi D, Shah K, Shah C, Shah S, Das E et al. Supraclavicular brachial plexus block for upper limb orthopaedic surgery: a randomized, double blinded comparison between ropivacaine and bupivacaine; *The International Journal of Anesthesiology*, Nov 2012 (30): 4.
- [16] Hickey Rosemary, Hoffman Joan, Ramamurthy Somayaji. A comparison of Ropivacaine 0.5% and Bupivacaine 0.5% for brachial plexus block; *Anesthesiology*, 1991; (74): 639-642.
- [17] Senel Ahmet Can, Ukin Ozlem, Timurkaynak Alper; Clinical Study: Does the Addition of Tramadol and Ketamine to Ropivacaine Prolong the Axillary Brachial Plexus Block?; *BioMed Research International* 2014 (2014), Article ID 686287, <http://dx.doi.org/10.1155/2014/686287>
- [18] Klein SM, Greengrass RA, Steele SM, D'Ercole FJ, Speer KP, Gleason DH, DeLong ER, Warner DS.; A comparison of 0.5% bupivacaine, 0.5% ropivacaine, and 0.75% ropivacaine for interscalene brachial plexus block; *Anesth Analg.* 1998 Dec; 87(6):1316-9.
- [19] Hickey R, Rowley CL, Candido KD, Hoffman J, Ramamurthy S, Winnie AP; A comparative study of 0.25% ropivacaine and 0.25% bupivacaine for brachial plexus block; *Anesth Analg.* 1992 Oct; 75(4):602-6.
- [20] Da Conceicao MJ, Coelho L; Caudal anaesthesia with 0.375% ropivacaine or 0.375% bupivacaine in paediatric patients; *British Journal of Anaesthesia*, 1998 Apr; 80(4):507-8.
- [21] Brown DL, Carpenter RL, Thompson GE; Comparison of 0.5% ropivacaine and 0.5% bupivacaine for epidural anesthesia in patients undergoing lower-extremity surgery. *Anesthesiology* 72:633-636, 1990.
- [22] Bertini Laura, Tagariello Vincenzo, Mancini Stefania, Ciaschi Alma, Posteraro Carla Maria, Pia Di Benedetto, Martini Ornella. 0.75% and 0.5% ropivacaine for axillary brachial plexus block: A clinical comparison with 0.5% bupivacaine; *American Society of Regional Anesthesia and Pain Medicine*; 1999 (24)6:493-600.
- [23] Raeder J.C, Drosdahl S, Klaastad O, Kvalsvik O, Isaksen B., Stromskag K. E, Mowinckel P, Bergheim R, Selander D. Axillary brachial plexus block with ropivacaine 7.5 mg/ml: A comparative study with bupivacaine 5 mg/ml; *Acta Anaesthesiologica Scandinavica* 1999; 43 (8): 794-798.