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Randomized controlled clinical comparative study of isobaric ropivacaine 0.75% (22.5mg) versus isobaric bupivacaine 0.5% (15mg) in intrathecal Anaesthesia

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Abstract
Aim: To assess, subjectively as well as objectively whether ropivacaine 0.75% (22.5 mg) can replace bupivacaine 0.5% (15 mg) as a long acting local anaesthetic agent in patients undergoing lower abdominal surgery under intrathecal anaesthesia.
Material and method: Hemoglobin, Packed Cell volume, Bleeding time, Clotting time, Renal function test Blood sugar, Liver function test, ECG, Chest x-ray and platelet count were done. Patients who satisfied the inclusion criteria were explained about the nature of the study and the anesthetic procedure. Written informed consent was obtained from all patients included in the study. In the Operation theatre appropriate equipment for airway management and emergency drugs were kept ready. Patient was shifted from the premedication room to Operation theatre. The horizontal position of the operating table was checked and the patient was placed on it.
Result: The mean duration of segmental height (Thoracic segment) of pain and temperature in group "R" was 10.2 ± 1.85 and for group "B" was 7.98 ± 1.523. By using 2 independent sample t-tests, P-value was 0.00. Since the P-value is <0.05, there is significant difference between onset of loss of sensation to pain and temperature in group "R" and group "B". The mean duration of segmental height (Thoracic segment) of touch and pressure in group "R" was 7.92 ± 1.98 and for group "B" was 5.60 ± 1.34. By using 2 independent sample t-tests P-value was 0.00. Since the P-value is <0.05, there is significant difference between segmental height (Thoracic segment) in touch and pressure in group "R" and group "B".
Conclusion: Bupivacaine has higher cephaled spread and longer duration of sensory analgesia than ropivacaine. The duration of motor blockade was similar with the two drugs

Keywords: Bupivacaine, local anaesthetic, ropivacaine

Introduction
Intrathecal anaesthesia is an important and most common technique used in practice of anaesthesia for surgeries in the lower part of the body, over the last century. The duration of surgery and quality of anaesthesia mainly depends on the specific local anaesthetics used. The benefits of spinal anaesthesia for any surgical procedure below the level of T4 requiring a sensory loss with or without motor blockade not requiring a secured airway or mechanical ventilation, are most evident in the postoperative phase.Although spinal anaesthesia is considered a simple procedure with a high margin of safety, it is not entirely free from risks. The severe neurological complications associated with spinal anaesthesia and other central blocks may be due to the neurotoxic effects of local anaesthetics, direct neural tissue injury caused by a needle or catheter and spinal cord compression by an epidural hematoma or abscess (Alahuhta 2001) [1-3]. Although major complications are rare, they can be devastating to the patient and the anesthesiologist. For this reason, the patients must be postoperatively followed closely to detect potentially treatable sources of neurologic injury (Horlocker & Wedel 2000) [4, 5].
A newly introduced long acting amide linked local anaesthetic, bupivacaine congener structurally similar to bupivacaine called `ROPIVACAINE` introduced since 1996. It is less lipid-soluble than bupivacaine and is reported to be 20% less potent than bupivacaine at equal doses (Polley *et al.* 1998) [6, 7]. Ropivacaine produces less motor blockade and is of shorter duration than bupivacaine (Scott *et al.* 1995, Markham & Faulds 1996, Zaric *et al.* 1996) [8, 9]. Ropivacaine in equipotent doses has been shown to be virtually indistinguishable from bupivacaine for clinical anaesthesia without any obvious advantages (Atanassoff *et al.* 2001) [10].The present clinical comparative study is carried out with the aim to assess, subjectively as well as objectively whether ropivacaine 0.75% (22.5 mg) can replace bupivacaine 0.5% (15 mg) as a long acting local anaesthetic agent in patients undergoing lower abdominal surgery

under intrathecal anaesthesia.

Material and method

This proposed study was carried out as a prospective, randomized clinical trial in patients in the Department of Anaesthesia, Krishna Institute of Medical Sciences, Karad, Maharashtra, after getting approval from Ethics committee. This study was conducted at the Krishna Institute of Medical Sciences and Hospital, Karad between 24 months from October 2009 and August 2011. This study was done after Ethical committee approval and written informed consent obtained from all the patients included in this study.

Hemoglobin, Packed Cell volume, Bleeding time, Clotting time, Renal function test Blood sugar, Liver function test, ECG, Chest x-ray and platelet count were done. Patients who satisfied the inclusion criteria were explained about the nature of the study and the anesthetic procedure. Written informed consent was obtained from all patients included in the study. In the Operation theatre appropriate equipment for airway management and emergency drugs were kept ready. Patient was shifted from the premedication room to Operation theatre. The horizontal position of the operating table was checked and the patient was placed on it. Noninvasive blood pressure, SpO_2, ECG leads were connected to the patient. Pre operative base line systolic and diastolic BP, PR, SpO_2 and RR were recorded. The anesthesiologist performed the SAB and made observations in all the patients involved in the study. Under aseptic precautions a midline lumbar puncture was performed at L3-L4 interspaces using a 25G Quincke needle in lateral recumbent position. Following free flow of clear CSF, anesthetic solution was injected slowly in both the groups. Then patient was placed in supine position. The time of intrathecal injection was considered as 0 and following parameters were observed. Sensory block was assessed by loss of sensation to pinprick using 23G sterile needle. The assessment was started immediately after intrathecal injection and continued every 15secs till loss of pinprick sensation at L2 level. Onset of sensory block was taken as the time from intrathecal injection to loss of pinprick sensation at L2. At 30mins interval after SAB the dermatome level of sensory block was noted and this was considered as the maximum level of sensory block. The level of sensory block at the end of surgery noted and there after assessment was carried out at 15mins interval till return of pinprick sensation to L2 dermatome. Duration of sensory block was taken as the time from SA injection to return of pinprick sensation to L2.

The categorical factors are represented by the number and frequency (%) of cases. The continuous variables are represented by measures of central frequency (like mean, median and mode) and deviation (SD and Range). The statistical analysis was done by using 2 independent sample student's t-test, Mann-Whitney test and Fisher's exact test. P-value <0.05 was considered statistically significant.

Result

This study was conducted at the Krishna institute of medical sciences and hospital, KARAD between October 2009 – August 2011. This study was done after institutional ethical committee approval and written informed consent obtained from all the patients included in this study. Proposed work was done in a comparative controlled clinical study manner carried out on patients posted for elective lower abdominal surgery. In the present study, 100 patients of ASA I and II grade were divided randomly in to two groups:

The mean duration in the onset of loss of sensation to pain and temperature in group "R" was 2.6 ± 0.70 and for group "B" was 2.3 ± 0.55. By using 2 independent sample t-tests, P-value was 0.01. Since the P-value is <0.05, there is significant difference between onset of loss of sensation to pain and temperature in group "R" and group "B". The mean duration for onset of loss of sensation to touch and pressure in group "R" was 5.0 ± 1.60 and for group "B" was 4.5 ± 1.30. By using 2 independent sample t-tests P-value was 0.07. Since the P-value is >0.05 there is significant difference between onset of loss of touch and pressure in group "R" and group "B" this signifies that there is statistically significant difference in onset of sensory block for pain and temperature when we compare drug isobaric Ropivacaine and isobaric bupivacaine.

The mean duration in the onset of loss of sensation to motor blockade in group "R" was 8.73 ± 1.30 and for group "B" was 7.75 ± 1.20. By using 2 independent sample t-tests, P-value was 0.00. Since the P-value is <0.05, there is significant difference between onset of loss of sensation to pain and temperature in group "R" and group "B". In group "R" and group "B" there were 50 patients in each group, 2 patients in each group did not achieve any motor blockade so excluded from the statistical analysis. The mean duration of segmental height (Thoracic segment) of pain and temperature in group "R" was 10.2 ± 1.85 and for group "B" was 7.98 ± 1.523. By using 2 independent sample t-tests, P-value was 0.00. Since the P-value is <0.05, there is significant difference between onset of loss of sensation to pain and temperature in group "R" and group "B". The mean duration of segmental height (Thoracic segment) of touch and pressure in group "R" was 7.92 ± 1.98 and for group "B" was 5.60 ± 1.34. By using 2 independent sample t-tests P-value was 0.00. Since the P-value is <0.05, there is significant difference between segmental height (Thoracic segment) in touch and pressure in group "R" and group "B".

Discussion

The subarachnoid block has occupied an important place in the anesthetic practice since the time it is known. It provides efficient analgesia and adequate muscle relaxation and thus imparts optimal operating conditions in the patient. Subarachnoid block is a commonly used anaesthetic technique for lower abdominal and lower limb surgery. Since many decades 'bupivacaine' a long acting local anesthetic is being used by practicing clinicians for surgeries in the lower part of the body. Bupivacaine has been in clinical use since 1963. Bupivacaine is a pipecoloxylidides, is an amide local anaesthetic. It has got a Pk of 8.1 which is highly lipid soluble and 95% protein bound which makes it a long acting and potent amide local anaesthetic. Bupivacaine is clinically available as racemic mixture of the enantiomers.

Ropivacaine is a pipecoloxylidides amide local anaesthetic. It has got a Pk of 8.1 and 92% protein bond which is less lipid-soluble than bupivacaine and is reported to be 20% less potent than bupivacaine at equal doses (Polley *et al.* 1998) [11, 12].

Ropivacaine is a long-acting, enantiomerically pure (S-enantiomer) amide local anesthetic, with a low lipid solubility which blocks nerve fibers involved in pain transmission (A δ and C fibres) to a greater degree than those controlling motor function (A β fibres). Ropivacaine produces less motor blockade and is of shorter duration than bupivacaine (Scott *et al.* 1995, Markham & Faulds 1996, Zaric *et al.* 1996) [13-15]. Ropivacaine in equipotent doses has been shown to be virtually indistinguishable from bupivacaine for clinical

anaesthesia without any obvious advantages (Atanassoff *et al.* 2001) [16]. Ropivacaine was approved for a new route of administration, the intrathecal route, in the European Union in February 2004.

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. It produces effects similar to other local anesthetics via reversible inhibition of sodium ion influx in nerve fibers. Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibers, resulting in a relatively reduced motor blockade and has a greater degree of motor sensory differentiation. The reduced lipophilicity is also associated with decreased potential for central nervous system toxicity and cardiotoxicity. Thus, it is a favorable local anaesthetic for day care surgeries and associated with earlier post-operative mobilization than bupivacaine. A very important advantage of ropivacaine over bupivacaine is less cardiovascular toxicity but the duration of action of ropivacaine in intrathecal anaesthesia is approximately 50% to 67% than that of the bupivacaine.

These studies concluded that for gynecological, urological and minor orthopedic surgery, the spread of anesthesia was variable, the duration of analgesia and motor block were longer in the 22.5 mg group and the intensity of motor block was lower in the 15 mg group.

Two other double-blind randomized studies described the use of intrathecal ropivacaine in patients scheduled for total hip arthroplasty. In the first study, patients received 2.5 ml of a plain solution of ropivacaine of either 7.5 mg/ml or 10 mg/ml (18.75 mg or 25 mg). In the second study, 3.5 ml of plain ropivacaine 5 mg/ml or 3.5 ml of plain bupivacaine 5 mg/ml were compared. *Ropivacaine versus bupivacaine for orthopedic surgery* Gautier *et al.* published on the use of intrathecal ropivacaine or bupivacaine for ambulatory knee arthroscopy. They found that ropivacaine 12 mg produced a sensor and motor block almost comparable to the block with bupivacaine 8 mg. Lower doses of ropivacaine (8 or 10 mg) produced significantly lower quality of intraoperative analgesia, as assessed by the patient. Higher doses of ropivacaine (14 mg) significantly increased the time to void, while sensor and motor block were comparable to the 12 mg group. No signs of transient radicular irritation (TRI) were noted. When isobaric ropivacaine 0.5% was compared to bupivacaine 0.5% by Delfino *et al.* [19], there were no significant differences regarding the upper sensory block level or the time to achieve it. However, the time of onset of non-stimulated pain at the surgical site and the duration of motor block were significantly shorter in the ropivacaine group. As a conclusion, when compared to bupivacaine at the same dose, spinal ropivacaine 15 mg (5 mg/ml) allowed for good analgesia and motor block for surgical purposes.

Total duration of motor blockade was similar in the groups, no difference in hemodynamic effect, Cephalad spread of sensory block was higher with bupivacaine in our present study. Which is in accordance with Malinovsky *et al.* [17] *who* compared 100 patients scheduled for transurethral resection of bladder or prostate receive either isobaric ropivacaine (15 mg) and isobaric bupivacaine (10 mg). Concluded that 15 mg of intrathecal ropivacaine provided similar motor and hemodynamic effects but less potent anesthesia than 10 mg of bupivacaine for endoscopic urological surgery.

M. Mantouvalou *et al.*compared 15 mg of isobaric bupivacaine, 15 mg of isobaric ropivacaine, 15 mg of isobaric levobupivacaine intrathecally in lower abdominal surgery. Who stated onset of motor block was significantly faster in the bupivacaine group compared with that in the ropivacaine group, which is in accordance with our present study. Ropivacaine presented a shorter duration of both motor and sensory block than bupivacaine and levobupivacaine, which is not in accordance due to dosage of 22.5 mg in our present study.

Mcnamee *et al.* [18] demonstrated a lower degree of motor block with 7.5 mg/ml compared to 10 mg/ml, and Mcclelland *et al.* [18] showed that 17.5 mg ropivacaine (5 mg/ml) produced a similar efficacy and tolerability profile compared with bupivacaine 17.5 mg, although there was a shorter duration of sensory and motor block after ropivacaine administration. No neurotoxic effects were observed in any of these studies, which is not in accordance due to dosage of 22.5 mg in our present study. The efficacy and tolerability of ropivacaine for spinal anesthesia in orthopedic surgery have been demonstrated in several studies.

Conclusion

This study concludes that intrathecal 15 mg of isobaric bupivacaine is more potent local anaesthetic than 22.5 mg of isobaric ropivacaine. Bupivacaine has higher cephaled spread and longer duration of sensory analgesia than ropivacaine. The duration of motor blockade was similar with the two drugs. However the haemodynamic effects were comparable in both the drugs. Isobaric Ropivacaine 22.5 mg does not offer any advantage in this study over Isobaric bupivacaine 15mg intrathecally.

Conflict of interest: No conflict of interest

References

1. Standl *et al.* Sap velocity and canopy transpiration in a sweetgum stand exposed to free-air CO2 enrichment (FACE) New Phytologist. 2001; 150:489-49.
2. Alon *et al.* SVM tissue classification using expresssion data Bioinformatics-Furey-Vol. 16 no. 10200-pages 906-914
3. Seppo Alahuhta The frequency of neurological complications of central blocks due to infection are very low. Acta Anaesthesiol Scand. 2001; 45:290-293,10.
4. Horlocker TT, Wedel DJ. Neurologic complications of spinal and epidural anesthesia. Reg Anesth Pain Med. 2000; 25:83-98.79.
5. Savarese JJ, Covino BG. Basic and clinical pharmacology of local anesthetic drugs. In: Anesthesia, Miller RD, ed. vol.2., 2nd ed. New York: Churchill Livingston, New York, Edinburgh, London, Melbourne, 1986, 986-7,985-1013.
6. Hampl *et al.* Anesthesia. and Pain Management. Hampl. *et al.* 1149. Transient. Neurologic. Symptoms. After Spinal. Anesthesia. 1995; 81:1148-53.
7. Polley *et al.* Ropivacaine is 40% less potent than bupivacaine for labor epidural analgesia. The greater lipid solubility of bupivacaine becomes more apparent in the intrathecal space. J Anaesth. 1998; 45:289-292.
8. Scott, Lee A, Fagan D *et al.* Acute toxicity of ropivacaine compared with that of bupivacaine. Anesth Analg. 1995; 69:563-9.
9. Markham & Faulds *et al.* Ropivacaine. A review of its pharmacology and therapeutic use in regional anesthesia. Br J Anesth. 1996; 76:300-307.46.

10. Atanassoff *et al*. Ropivacaine in equipotent doses has been shown to be virtually indistinguishable from bupivacaine for clinical anaesthesia without any obvious advantages
11. Hansen TG, Morton NS, Cullen PM, *et al.* Plasma concentrations and pharmacokinetics of bupivacaine with and without adrenaline following caudal anaesthesia in infants. Anesth Analg. 1987; 66:995-998.55.
12. Knudsen ES, Wang JY. Department of Biology and Center for Molecular Genetics, University of California. Mol Cell Biol. 1997; 17(10):5771-83.
13. Tucker *et al.* Pharamacokinetics OF LOCAL Anaesthetics. Br. J. Anaesth. 1986; 58(7):717-731.
14. Knudsen K, Beckman Suurkul M, Blomberg S, SJovall J, Edvardsson N. Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. Br J Anaesth. 1997; 78:507-14.
15. Scott DB, Lee A, Fagan D *et al.* Acute toxicity of ropivacaine compared with that of bupivacaine. Anesth Analg. 1989; 69:563-9.
16. Pitkanen M, Feldman HS, Arthur GR, Covino BG. Chronotropic and inotropic effects of ropivacaine, bupivacaine, and lidocaine in the spontaneously beating and electrically paced isolated, perfused rabbit heart. Reg Anesth. 1992; 17:183-92.
17. Malinovsky *et al.* Intrathecal Anesthesia: Ropivacaine Versus Bupivacaine Anesth Analg. 2000; 91:1457-60.
18. McNamee *et al.*, Parks L, McClelland A, Scott S, Spinal anaesthesia: comparison of plain ropivacaine 5 mg ml±1 with bupivacaine 5 mg ml±1 for major orthopaedic surgery. Br J Anaesth. 2002; 89:702±6.