Print ISSN: 2319-2003 | Online ISSN: 2279-0780

IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20162600

Research Article

A double blind prospective study of effect of intrathecal ropivacaine 0.75% and bupivacaine 0.5% for lower limb orthopedic surgery in young patients

Prasad M. Sule*, Shakuntala Basantwani

Department of Anesthesia, LTMMC and GH, Sion, Mumbai, Maharashtra, India

Received: 17 July 2016
Accepted: 22 July 2016

***Correspondence to:**
Dr. Prasad M. Sule,
Email: prasadsule.gmcl@gmail.com

ABSTRACT

Background: Subarachnoid block is among the most versatile regional block available today. It is a very old and well established anesthetic technique that is simple to perform and has a high success rate and a good safety profile. The aim of the present study was to compare the characteristics of spinal block, adequacy of anaesthesia and side effects using intrathecal ropivacaine 0.75% and bupivacaine 0.5% in young patients undergoing lower limb orthopaedic surgery.
Methods: 60 adult patients of either sex (aged 18 to 60 years) were studied, ASA grade I and II were randomly assigned into two anaesthetic groups. Group X: received 3.5 ml of 0.75% isobaric ropivacaine and group Y: received 3.5 ml of 0.5% hyperbaric bupivacaine. After induction, the various parameters of intrathecal block and adequacy of anaesthesia were studied.
Results: 0.75% isobaric ropivacaine had late onset of sensory and motor blockade as well as shorter duration of analgesia and anaesthesia with similar quality of block as compare to 0.5% bupivacaine. There was no significant change in the cardiovascular response to subarachnoid block. In present study, no adverse effects were noted in any of the patients in any group.
Conclusions: Isobaric ropivacaine at the concentration of 0.75% can be safely used as an alternative to 0.5% hyperbaric bupivacaine as long acting local anaesthetic in intrathecal block.

Keywords: Intrathecal, Ropivacaine, Bupivacaine, Lower limb orthopedic surgery, Sensory and motor blockade, Analgesia, Anaesthesia

INTRODUCTION

Subarachnoid block is among the most versatile regional block available today. It is a very old and well established anesthetic technique that is simple to perform and has a high success rate and a good safety profile. It has emerged as a viable alternative to general anaesthesia for a variety of infraumbilical, perineal and lower limb surgeries. This technique grew safer over the decades as our understanding of the anatomy and physiology as well as the characteristics of the drugs used for spinal anaesthesia improved. Adding to the safety of the technique was the advent of newer molecules of local anaesthetics that is being investigated for use in spinal anaesthesia.

The drugs used for spinal subarachnoid block are lignocaine and bupivacaine etc. But recently bupivacaine 0.5% heavy was the only drug used for spinal anaesthesia after the discontinuation of lidocaine's intrathecal use. Bupivacaine is amide local anaesthetic and it has dense sensory and motor action with long duration. However in an editorial Dr. Albright reported six cases of sudden cardiovascular collapse immediately after presumed accidental intravascular injection of bupivacaine and etidocaine despite negative aspiration test and also postulated that cardiopulmonary resuscitation in contrast to lidocaine ,might be difficult, if not impossible.[1] He also presented a further 'tally' of 15 maternal deaths after extradural injection.[2]

Hence the above mentioned events prompted clinical research for a local anesthetic which has a clinical profile similar to bupivacaine but with less or no cardiovascular and central nervous system toxicity. As solutions of bupivacaine contain equal amounts of R(+) and S(-) enantiomers, advancements in technology have allowed the development of solutions containing only one enantiomer that have similar physicochemical properties but different clinical effects.[3] In 2009 ropivacaine another amino amide local anaesthetic having all the advantages but less the cardio and CNS toxicity of bupivacaine has been introduced in India. Ropvacaine is unique amongst this group in that it is prepared for clinical use as the pure s-enantiomer rather than a racemic mixture.[4-6] It is long acting amide local anaesthetic agent, eliciting nerve block via reversible inhibition of sodium influx in nerve fibres. It is less likely to cause severe cardiac arrhythmias than bupivacaine and has been associated with greater central nervous system tolerance. This improved safety profile likely reflects its lower lipid solubility or its availability as a pure S(-) isomer, as opposed to bupivacaine raecemic mixture. Clinically adequate doses of ropivacaine with its efficacy, lower propensity for motor block and reduced potential for CNS toxicity than bupivacaine appears to be an important option for regional anaesthesia for lower limb surgery.

The principal goal of the study was to evaluate efficacy and feasibility of isobaric ropivacaine 0.75% and comparing it with hyperbaric bupivacaine 0.5% in spinal anaesthesia for lower limb orthopaedic surgery.

METHODS

After approval of ethics committee of LTMMC and LTMGH, Sion and written informed consent, 60 adult patients of either sex, ASA grade I and II with age 18 to 60 years and weight between 40 to 80 kg were included in this prospective randomized double blind study and scheduled for elective or emergency lower limb orthopedic surgery (i.e. repair of fracture of tibia-fibula, tarsal, metatarsals and patella). Patients unwilling for spinal anaesthesia, with ASA grade ≥ III, patients having contraindications for spinal anaesthesia and long duration of surgeries i.e. repair of fracture of femur, THR, TKR were excluded from the study. Sixty selected patients were divided into two equal groups of 30 patients each. The local anaesthetic was provided in non-identified syringes, labelled with the patient's serial number, prepared by another anaesthesiologist, not related to this study. The randomization was done by doing the computerized chart and selecting one of them blindly. Group X: received 3.5 ml of 0.75% isobaric ropivacaine and group Y: received 3.5 ml of 0.5% hyperbaric bupivacaine. A detailed pre-anaesthetic evaluation including history, thorough clinical examination and all relevant investigations were done for all the patients.

On the operation table, after the placement of routine non-invasive monitors, vital parameters were recorded before giving spinal anaesthesia. A good intravenous line was established with 20 gauge indwelling cannula. All patients were preloaded with 10ml/kg crystalloid. Equipments and drugs necessary for resuscitation and general anaesthesia administration were kept ready. Under all aseptic precautions, lumbar puncture was done in L3-L4 inter-space in left lateral position with 25 G spinal needle. After negative aspiration of blood, the proposed drug was injected as per the group allotment. The time of injection was noted and the patients were made supine with the table horizontal. Sensory block was assessed by pinprick every minute till 30 minutes and then every 15 minutely. If the level of analgesia was inadequate, then the regimen was switched to general anaesthesia and patient was excluded from the study. If sensory level went above T4 and patient became breathless then patient was intubated and was ventilated and such patient was excluded from study. All episodes of local anesthetic toxicity or hemodynamic changes requiring anaesthesiologist intervention were recorded as adverse events. After evidence of successful motor block surgery was performed. All the patients received oxygen by means of nasal prongs at 2L/min. Patients did not receive any analgesics during the procedure. In case of prolonged surgeries, GA was given as the effect of subarachnoid block seemed to weaning off (patient complains of pain at the site of operation).

The spinal block characteristics were assessed with parameters like onset of sensory blockade, highest level of sensory blockade (by pin prick method), onset of motor blockade (by modified Bromage scale) and duration of sensory and motor blockade, quality of block, intraoperative vital signs and discomfort, were noted in all patients.

Statistical analysis

All the observations were recorded and student's t test was applied to test statistical significance between the means of the groups. The chi square test was used to find dependencies between the two groups. A value of $P < 0.05$ was considered statistically significant.

RESULTS

The demographic profiles of the patients and mean duration of surgical procedures were comparable between two groups and difference was statistically not significant, (Table 1). The male: female ratio (53.3: 46.7) was similar in both the groups. As shown in Table 2, the onset of sensory blockade in group X was 9.4±2.63 min whereas in group Y was 4.2±1.16 min which was statistically significant ($P < 0.05$). Highest sensory level achieved was T6 in both the groups. The duration of sensory blockade in group X and in group Y was 203±24.52 min and 219.5±15.99 min respectively, ($P < 0.05$). Also the Table 2 shows that onset of motor blockade in group X was 6.47±3.04 min while in group Y was 3.57±1.45 min and the duration of motor blockade in group X and in group

Y was 185.5±9.79 min and 184±9.41 min respectively (P <0.05) difference was statistically significant. There was no statistically significant difference observed in quality of sensory and motor blockade in both groups.

Table 1: Demographic data and duration of surgery.

Variables	Group X	Group Y	P-value
Age (years)	35.8±12.47	33.73±9.02	0.564
Weight (kg)	58.83±6.39	58.40±0.309	0.759
Duration of surgery (mins)	115.5±27.33	116±27.55	0.74

Table 2: Summary of results regarding characteristics of subarachnoid (spinal) blockade.

Characteristics (min)	Group X	Group Y	p-value
Onset of sensory block	9.4±2.63	4.2±1.16	0.001
Duration of sensory block	203±24.52	219.5±15.99	0.001
Onset of motor block	6.47±3.04	3.57±1.45	0.001
Duration of motor block	180±22.63	211±20.06	0.003

Though there was fall in heart rate, systolic, diastolic and mean arterial pressure in both the groups and this was clinically insignificant. No statistically significant difference between two groups in terms of haemodynamic parameters at different time intervals was found (Figure 1).

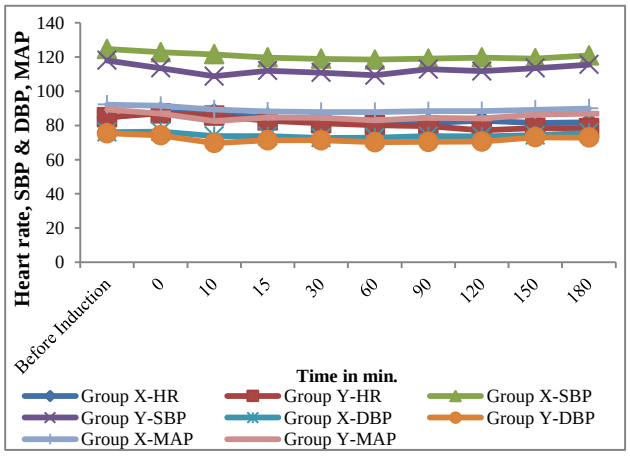

Figure 1: Comparison of haemodynamic parameters between two groups.

Neither a single patient complained of any side effects nor any sign of CNS toxicity, CVS toxicity or any allergic reaction visible in both the groups during the study period. There was complete resolution of nerve block and no signs of any neurological dysfunctions noted up to 72 hours in any patients.

DISCUSSION

Spinal anaesthesia using local anaesthetic is a well known technique for lower limb/below umbilical surgeries as it has distinct advantages over general anaesthesia including reduced stress response and improved post-operative pain relief. It would probably maintain its place in developing countries because of its simplicity, minimal skill requirement, rapidity of onset, economy and minimal post-operative complications. Because of the technical challenges in identifying the epidural space and the toxicity associated with the large doses of local anaesthetics needed for epidural anaesthesia, spinal anaesthesia was the dominant form of neuraxial anaesthesia well into the 20th century.[7] The goal of spinal anaesthesia is to instil the desired medications into the cerebrospinal fluid (CSF). The sensory motor block produced requires smaller doses of local anaesthetics (hence, local anaesthetic toxicity is rarely a concern) and is often more dense in character.

Traditionally, bupivacaine has emerged as the most commonly used drug for spinal anesthesia. However, since it has undesirable effects such as hypotension, bradycardia, prolonged duration of motor paralysis, cardiotoxicity and central nervous system toxicity, there led to the identification of long acting pure S-enantiomer of ropivacaine.[8-12] Ropivacaine, as compared to bupivacaine, has lower potential for cardiac and central nervous systemic toxic effects and shows greater differentiation between sensory and motor blockade with hemodynamic stability.[13] Ropivacaine is nearly identical to bupivacaine in onset, quality and duration of sensory block, but it produces lesser duration of motor blockade, has a better safety profile.[14] This was very helpful for short duration surgeries as well as for early ambulation. Hence, there was a need for this study to compare its safety and efficacy with bupivacaine for lower limb orthopaedic surgery. On the basis of literature review, we use 3.5 ml (26.25) of 0.75% of isobaric ropivacaine as a study dose which was nearly equal to ED95 to achieve T7 sensory level as shown by Khaw et al.[15,16] It was found that this dose of ropivacaine was adequate for intrathecal use for lower limb surgeries. This dose was successful in 100% patients and no one patient was required any sedation.

In present study, both the groups were comparable with respect to age, weight and sex (P <0.05). The demographic data being comparable has no influence on outcome of the study. The onset of sensory block was defined as time taken from injection of study drug in subarachnoid space till T10 blockade and difference was found to be statistically significant (P <0.05). Also onset of motor block was defined as time taken from injection of study drug in subarachnoid space till Grade 1 of Bromage Scale. Difference in the onset of motor blockade

in both groups was also found to be statistically significant (P <0.05). These findings of present study are similar with the findings stated by Van KJW et al, Delfino et al, Whiteside et al, Neval Boztuğ et al, Kallio H et al and Singh JB et al.[17-22] The duration of sensory blockade was defined as time elapsed between injection of study drug and return of the pin prick sensation whereas duration of motor blockade was defined as time between drug injections to complete return of motor power with movement of all lower limb joints. It was found that longer duration of sensory and motor blockade in bupivacaine group as against in ropivacaine group and difference was statistically significant (P <0.05). The findings correlate with the different studies.[17-19,21-26] The average highest level of sensory blockade which was achieved by giving either 3.5 ml of 0.75% isobaric ropivacaine or 3.5 ml of 0.5% hyperbaric bupivacaine was compared. The average highest level of sensory blockade in both the groups was T6 which was comparable (P=0.879). Similar results were observed by various authors in their studies.[17,19-21,23,26]

No significant change in heart rate in ropivacaine group was found but there was significant fall in heart rate after 60 minutes of the induction in bupivacaine group by paired 't' test. The maximum fall in heart rate was 7% at 120 minutes in bupivacaine group while it was 3% at 60 minutes in ropivacaine group. Though this fall in heart rate in bupivacaine was statistically significant, it was clinically insignificant and atropine treatment was not required in any patient. In case of systolic blood pressure there was statistically significant fall from 10 to 150 minutes after induction in bupivacaine group and from 15 to 150 minutes in ropivacaine group by paired 't' test. The maximum fall in systolic blood pressure was 7.8% at 10 minutes in bupivacaine group as against 4.9% at 60 minutes in ropivacaine group. But this fall was clinically insignificant in both groups and treatment with ephedrine was not required in any patient. There was statistically significant fall in diastolic pressure from 10 to 120 minutes after induction in bupivacaine group and at 60 minutes in ropivacaine group by paired 't' test and there was not statistically significant difference in fall in diastolic blood pressure between ropivacaine and bupivacaine group. The maximum fall in diastolic blood pressure was 7.6% at 10 minutes in bupivacaine group while it was 4.3% at 30 minutes in ropivacaine group. However this fall in diastolic blood pressure in individual group was clinically insignificant and ephedrine was not required in any patient. When mean blood pressure was compared there was statistically significant fall from 10 to 120 minutes after induction in bupivacaine group and from 15 to 120 minutes in ropivacaine group. The maximum fall in mean blood pressure was 7% at 120 minutes in bupivacaine group while it was 3% at 60 minutes in ropivacaine group. However this fall in mean blood pressure was clinically insignificant in both groups and treatment with ephedrine was not required. However, in other studies no significant defference was foud in haemodynamics in both ropivacaine and bupivacaine groups when given intrathecally.[18-20,23-25]

In present study no rescue analgesia was required in any of the patients in any group and quality of anesthesia obtained was adequate with both the groups. No signs of central nervous system toxicity (like restlessness, anxiety, incoherent speech, lightheadedness, dizziness, blurred vision, tremors, drowsiness, convulsions) or cardiovascular system toxicity (hypotension, bradycardia, hypertension, tachycardia, vasovagal reaction, arrhythmias like extra-systoles, atrial fibrillation, ST segment changes and myocardial infarction); severe allergic reactions (rash, itching, difficulty in breathing, tightness in the chest, swelling of the mouth, face, lips or tongue); nausea; vomiting noted in both groups. There was complete resolution of subarachnoid block and no signs of any neurological dysfunction or transient radicular irritation were noted up to 72 hours in any patients. Patients in isobaric ropivacaine group mobilize sooner than in hyperbaric bupivacaine group in post-operative period however we have not studied hospital stay of the patients in both the groups.

CONCLUSION

Based on the results obtained from present study, it was concluded that isobaric ropivacaine at the concentration of 0.75% can be safely used as an alternative to 0.5% hyperbaric bupivacaine as long acting local anesthetic in intrathecal block. The study recommend that 0.75% isobaric ropivacaine was associated with late onset of sensory and motor blockade; shorter duration of analgesia and anaesthesia with similar quality of block as 0.5% bupivacaine and with less CNS, CVS toxicity, local neurotoxicity. It has also added advantage of early mobilization in post-operative period than bupivacaine.

ACKNOWLEDGEMENTS

The authors would like to thank the department of anaesthesiology, surgery, other staff of operation theatre and administration of LTMMC and LTMGH, Sion, Mumbai, (M.S.), for permission to study and providing facility to carry out the work

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Stewart J, Kellett N, Castro D. The central nervous system and cardiovascular effects of levobupivacaine and ropivacaine in healthy volunteers. Anesth Analg. 2003;97:412-6.
2. Knudsen K, Beckman S, Blomberg S, Sjovall J Edvardsson N. Central nervous and cardiovascular effect of I.V. infusions of ropivacaine, bupivacaine

and placebo in volunteers. Br J Anaesth. 1997;78:507-4.
3. Bardsley H, Gristwood R, Baker H, Watson N, Nimmo W. A comparison of the cardiovascular effects of levobupivacaine and racemic bupivacaine following intravenous administration to healthy voiunteers. Br J Clin Pharmacol. 1998;46:245-9.
4. Stienstra R. The place of ropivacaine in anesthesia. Acta Anaesthetic Belg. 2003;54:141-8.
5. Stefania L, Simone DC, Andrea C. Pharmacology, toxicology and clinical use of new long acting local anaesthetics ropivacaine and levobupivacaine. Acta Biomeis. 2008;79:92-105.
6. Kuthiala G, Chaudhary G. Ropivacaine: a review of its pharmacology and clinical use. Indian J Anesth. 2011;55:(2)104-10.
7. Corning JL. Spinal anesthesia and local medications of the cord. N Y Med J. 1885;42:483.
8. Hodgson PS, Neal JM, Pollock JE, Liu SS. The neurotoxicity of drugs given intrathecally (spinal). Anesth Analg. 1999;88:797-809.
9. Barash PG, Cullen BF, Stoelting RK editors. Clinical Anaesthesia; Lippincott Williams and Wilkins.4th edition; Philadelphia;2001:451-466.
10. Hiller A, Rosenberg PH. Transient neurological symptoms after spinal anaesthesia with 4% mepivacaine and 0.5% bupivacaine. Br J Anaesth. 1997;79:301-5.
11. Hampl KF, Schneider MC, Drasner K. Toxicity of spinal local anaesthetics. Curr Opin Anaesthesiol. 1999;12:559-64.
12. Ruetsch YA, Boni T, Borgeat A. From cocaine to ropivacaine: the history of local anesthetic drugs. Curr Top Med Chem. 2001;1:175-82.
13. Wille M. Intrathecal use of ropivacaine: a review. Acta Anaesthesiol Belg. 2004;55:251-9.
14. Mcconachie I, Mcgeachie J, Barrie J. Regional anaesthetic techniques. In: Thomas EJ, Knight PR, editors.Wylie and Churchill Davidson's - A Practice of Anesthesia. London: Arnold;2003;599-612.
15. Ying YL, Warwick D. Ngan K, Hang KC, Chi LS, Tony G. Spinal ropivacaine for lower limb surgery: a dose-response study. Anesth Analg. 2007;105:520-3.
16. Khaw KS, Ngan KWD, Wong EL, Liu JY, Chung R. Spinal ropivacaine for cesarean section: a dose-finding study. Anesthesiology. 2001;95:1346-50.
17. Van KJ, Veering B, Burm A. Spinal anesthesia with ropivacaine: a double-blind study on the efficacy and safety of 0.5% and 0.75% solutions in patients undergoing minor lower limb surgery. Anesth Analg. 1994;78:1125-30.
18. Delfino J, Pontes S, Gondim D, Do VN. Isobaric 0.5% bupivacaine and 0.5% ropivacaine in spinal anesthesia for orthopedic surgery: a comparative study. Rev Bras Anesth. 1999;49(3):160-4.
19. Whiteside JB, Burke D, Wildsmith JAW. Comparison of ropivacaine 0.5% (in glucose 5%) with bupivacaine 0.5% (in glucose 8%) for spinal anaesthesia for elective surgery. Br J Anaesth. 2003;90(3):304-8.
20. Neval B, Zekiye B, Bilge K, Nurdan S, Ertugrul E. Comparison of ropivacaine and bupivacaine for intrathecal anesthesia during outpatient arthroscopic surgery. J Clinic Anesth. 2006;18:521-5.
21. Kallio H, Snall EVT, Tuomas CA, Rosenberg PH. Comparison of hyperbaric and plain ropivacaine 15mg in spinal anaesthesia for lower limb surgery. British J Anaesthesia. 2004;93(5):664-9.
22. Singh S, Singh VP, Jain M, Gupta K, Rastogi B, Abrol S. Intrathecal 0.75% isobaric ropivacaine versus 0.5% heavy bupivacaine for elective cesarean delivery: a randomized controlled trial. J Pak Med Students. 2012;2(2):75-80.
23. Mcnamee DA, Mclelland AM, Scott S, Milligan KR, Westman L, Gustafsson U. Spinal anaesthesia: a 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.
24. Şahin A, Çomlekci M. The comparison of hyperbaric bupivacaine and ropivacaine usage in spinal anesthesia at hip and lower extremity surgery. J Contemp Med. 2013;3(1):36-41.
25. Gautier P, De KM, Van SA, Poth N, Lahaye B, Fanard L, Hody J. Intrathecal ropivacaine for ambulatory surgery a comparison between intrathecal bupivacaine and intrathecal ropivacaine for knee arthroscopy. Anesthesiology. 1999;91:1239-45.
26. John ONW, Thomas DMT, Pak OL, Kin FT, Ning WC, Chao ST. Comparison of the effect of two different doses of 0.75% glucose-free ropivacaine for spinal anesthesia for lower limb and lower abdominal surgery. Kaohsiung J Med Sci. 2004;20(9):423-30.

Cite this article as: Sule PM, Basantwani S. A double blind prospective study of effect of intrathecal ropivacaine 0.75% and bupivacaine 0.5% for lower limb orthopedic surgery in young patients. Int J Basic Clin Pharmacol 2016;5:1798-1802.