American Journal of Advanced Drug Delivery

www.ajadd.co.uk

Original Article

Evaluation of Hyperbaric Spinal Ropivacaine in Lower Limb and Hip Surgery: A Comparison with Hyperbaric Bupivacaine

Dr. Feroz Ahmad Dar*[1], Dr. Neelofar Jan[2]

[1]M.D Anaesthesiology, Department of Anaesthesiology, Govt. Medical College, Srinagar, J&K, India.
[2]Medical officer, Department of Geriatric Medicine, S.K.I.M.S, Srinagar, J&K, India.

Date of Receipt- 28/11/2013
Date of Revision- 03/12/2013
Date of Acceptance- 08/12/2013

Address for Correspondence
Department of Anaesthesiology and Critical Care,
Govt. Medical College, Srinagar, J&K, India.
Tel. +91-9086806324.
E-mail: drferozhabak21@gmail.com

ABSTRACT

Objectives: In this clinical study hyperbaric ropivacaine in spinal anaesthesia for lower limb and hip surgery was evaluated and results obtained were compared with those using hyperbaric bupivacaine.
Methodology: Two hundred patients scheduled for lower limb and hip surgery were randomly divided into two groups of 100 patients each. These patients received a spinal injection of either 3ml (15mg) of 0.5% hyperbaric ropivacaine or 3ml (15mg) of 0.5% hyperbaric bupivacaine using 25G Quincke type spinal needle. The parameters studied were - onset and total duration of sensory block, onset and total duration of motor block, quality of intraoperative anaesthesia, hemodynamic alterations, and any intraoperative and postoperative complications.
Results: The mean onset of sensory block (6±1.3min vs. 3±1.1min; p value<0.05) and motor block (13±1.6min vs. 9±1.3min; p value< 0.05) was significantly slower in ropivacaine group as compared to bupivacaine group. The total duration of sensory block was significantly shorter in ropivacaine group (160±12.9min) than in bupivacaine group (260±16.1min; p value <0.05). The mean duration of motor block was also shorter in ropivacaine group compared to bupivacaine group (126±9.2min vs. 174±12.6min; p value<0.05).
Conclusion: The quality of anaesthesia was excellent in both the groups. In conclusion**,** a solution of ropivacaine (hyperbaric) can be used for spinal anaesthesia and is comparable with hyperbaric bupivacaine in terms of quality of block, but has shorter recovery profile.

Keywords: Bupivacaine; Ropivacaine; Hyperbaric; Spinal anaesthesia.

INTRODUCTION

Bupivacaine, an amino amide compound, was synthesized and introduced into the clinical practice in 1963 and proved to be a very effective long acting local anaesthetic agent. In 1979, Albright drew attention to the dangers of the longer acting local anaesthetic agents, bupivacaine and etidocaine, in case they gained accidental intravascular access[1]. However, studies in animals[2] indicate that bupivacaine, when injected intravascularly, induces a dose and rate dependent depression of drug elimination, resulting in re-entrant arrhythmias and cardiac depression, sometimes culminating in cardiac arrest. These shortcomings of this otherwise novel local anaesthetic resulted in the development of more new anaesthetic agent 'ropivacaine'. Isomers of this local anaesthetic are reported to be least toxic as compared to racemic compounds[3].

Ropivacaine, a new amino-amide local anaesthetic agent is similar in chemical structure to bupivacaine[3,4]. It is presented as a single-enantiomer and has been used extensively for the local infiltration, epidural, and peripheral blocks. Extensive clinical data have shown that ropivacaine is effective and safe for regional anaesthetics techniques such as epidural and brachial plexus block[5]. However hyperbaric ropivacaine has been little studied in intrathecal anaesthesia. The purpose of this study was to evaluate the efficacy and safety of hyperbaric ropivacaine in spinal anaesthesia and to compare it with hyperbaric bupivacaine in lower limb and hip surgeries.

MATERIAL AND METHODS

The study was performed at Govt. Medical College Srinagar, after institutional approval and after obtaining informed written consent of the patients undergoing lower limb and hip surgery under spinal anaesthesia. Inclusion criteria were age ≥ 40 and ≤ 75 years and American Society of Anesthesiologists (ASA) physical status classification I – II. Exclusion criteria were bleeding disorders, neurological, disorders, reluctance to get operated under spinal anaesthesia, local skin infection, severe back deformities, raised intracranial pressure, moderate to severe valvular lesions. The patients were divided into two groups of 100 patients each under: Group R (Ropivacaine Group): This group consisted of 100 patients who received 3ml intrathecal injection of 0.5% hyperbaric ropivacaine. Group B (Bupivacaine Group): This group consisted of 100 patients who received 3ml intrathecal injection of 0.5% hyperbaric bupivacaine. Preanaesthetic evaluation was done at least 24 hours prior to surgery. Tablet *al*prazolam 0.25mg to 0.5mg night before surgery was prescribed to the patients. Patients were advised to be nil orally from midnight before surgery. On the day of surgery, intravenous line was established on the non-dominant hand using 16G size intravenous cannula and intravenous fluid (Ringer lactate) started. The multi-channel monitor (Mindrays-BeneVeiw T8, Instromedix India) was attached and base line parameters viz pulse rate, blood pressure (systolic, diastolic & mean) ECG (lead II, V) and SpO_2 were recorded. Under all aseptic precautions, the subarachnoid blocks were performed using 25G Quincke spinal needle at L3-L4 intravetebral space. After the block, vitals were monitored every 2 minute up to 16 minutes and thereafter, every 5 minutes interval till completion of surgery. Oxygen 4L/min was administered through Hudson facemask throughout the procedure. The onset of sensory block to T10 level was taken as the time from injection of anaesthetic solution to start of loss of sensation to pin prick at T10 level. The sensory block was tested at every 2 minute intervals till the

establishment of the block and every 5minutes during surgery. Total duration of sensory block was taken as complete recovery of sensory block. After the completion of the surgery, the sensory block was tested at 15minute intervals till its complete regression. Motor block was assessed using modified Bromage scale by asking the patient to flex the limb at hip, knee, and ankle joints (Grade 0: No paralysis, Grade1: Inability to raise extended leg, can bend knee, Grade 2: Inability to bend knee, can flex ankle, Grade 3: No movement). Onset time of motor blockade was taken as the time to acquire complete motor block (grade 3) after the intrathecal injection of local anaesthetic and total duration was taken as time to regain complete recovery from motor block. Quality of intraoperative anaesthesia was assessed using "Four Grade Scale" [6] which is defined as:-

Excellent: No supplementary sedative or analgesia required.
Good: Only sedative required
Fair: Both sedative and analgesic required.
Poor: General anaesthesia and tracheal intubation required.

Bradycardia (heart rate <60 beats/min) when encountered, was recorded and treated with intravenous atropine which was administered in small incremental doses. Hypotension (systolic blood pressure <30% from baseline) when encountered, was recorded and treated with intravenous ephedrine which was administered in small incremental doses. The patients were observed for first 24 hours for nausea, vomiting and any other complications.

Data were entered and analyzed with the Graph Pad.com (version 5, 2010). Data were presented as median (range), mean or frequencies, as appropriate. Nominal patient's characteristics and the duration of surgery were compared using the Fisher's exact test. A Bonferroni correction was applied for multiple two-way testing. In all categories $P<0.05$ was considered statistically significant. Pulse and blood pressure were compared using Multiple comparison test (Dennett test), q value >2.740 considered statistically significant (p value<0.05).

RESULTS

The characteristics of the two groups were comparable in terms of age, sex, weight, gender and ASA classification (Table 1).

The mean onset of sensory block at T10 level (6±1.3min vs. 3±1.1min; p value<0.05) and motor block (13±1.6min vs.9±1.3min; p value< 0.05) was significantly slower in ropivacaine group as compared to bupivacaine group (Table. 2) (Figure.2). The mean duration of sensory block was significantly shorter with ropivacaine group (160±12.9min) than with bupivacaine group (260±16.1min; p value <0.05). The mean duration of motor block was also shorter in ropivacaine group compared to bupivacaine group (126±9.2min vs. 174±12.6min; p value<0.05) (Figure 2). The intraoperative quality of anaesthesia was excellent and similar in both groups. However it was fair in 1% in bupivacaine group and 3% patients in ropivacaine group. It was statistically insignificant between the two groups (p value>0.05). None of the patients in both the groups had poor quality of anaesthesia (Table. 2).

Hypotension was the most common side effect in both groups. There was a significant difference in the incidence of hypotension between the two groups (p value<0.05). In bupivacaine group, 66 patients (66%) developed hypotension while in ropivacaine group only 19 patients (19%) developed hypotension (Table. 2) (Figure.3). The incidence of bradycardia, nausea, vomiting and shivering during intraoperative period did not differ significantly between the

two groups (p value>0.05) (Table 2). The two groups did not differ significantly in regards as nausea and vomiting (p value>0.05).

DISCUSSION

The present study confirmes the findings of a previous studies [7,8] that a glucose-containing solution of ropivacaine can produce predictable and reliable spinal anaesthesia for a wide range of surgical procedures. However present study is in variance with the results of the two early clinical studies, which have described blocks with ropivacaine inadequate for surgery [9,10]. The variance can be because these authors have used glucose-free solutions of ropivacaine. The variation confirms that the addition of glucose to solution of ropivacaine has the same effect as with other drugs[11,12,13,14]. In present study, the hyperbaric solution of 0.5% ropivacaine was prepared aseptically by mixing 5ml of 0.75% isobaric ropivacaine (Ropin®, Neon, India) with 2ml of 25% dextrose and 0.5ml sterile water at room temperature. This gave a total volume of 7.5ml and resulting in a final glucose concentration of 6.6% in hyperbaric ropivacaine solution with specific gravity of 1.02450 at room temperature[15].

In the present study, the onset of both sensory and motor block was delayed in ropivacaine group as compared to bupivacaine group. The total duration of sensory and motor block was also shorter in ropivacaine group as compared to bupivacaine group. The present study correlates with various authors[16,17,18,19,20] who also found earlier onset of sensory block to T10 level and longer duration of sensory block with hyperbaric spinal bupivacaine compared to hyperbaric spinal ropivacaine, which was statistically significant. This may be because of higher lipid solubility and slightly higher protein binding of bupivacaine as compared to ropivacaine. Lipid solubility is important determinant of local anaesthetic activity. The onset time of conduction block is directly correlated with the lipid solubility of local anaesthetic[21,22]. Increased lipid solubility increases sequestration of local anaesthetic in myelin and other surrounding neural compartments. Thus, action is increased as absorption of local anaesthetic molecule into myelin and surrounding neural compartments creates a depot for slow release of local anaesthetic[23]. This observation may be explained by a correlation between lipid solubility and both sodium channel receptor affinity and ability to alter sodium channel conformation by direct effects on lipid cell membranes. In general, the more lipid soluble and longer acting agents have increased protein binding. The lesser lipid solubility of ropivacaine may cause this drug to penetrate the large myelinated A fibers more slowly than the more lipid soluble bupivacaine[24]. It is also postulated that because ropivacaine is less lipophilic it has a greater effect on the non-myelinated pain fibres rather than the myelinated motor fibers[25]. Although the patients' satisfaction to recovery of motor block was not assessed clinically and objectively in this study, earlier recovery with spinal ropivacaine is associated with more patient satisfaction[20,26].

We found no evidence of any late sequelae such as backache or other transient symptoms in this study and this correlates with the previous studies of ropivacaine when used in spinal anaesthesia[7,15].

In the present study, intrathecal ropivacaine produced excellent intraoperative anaesthesia, indistinguishable from spinal bupivacaine. Statistically the difference in quality of anaesthesia was insignificant between the two groups. The present study correlates with those of Osama-Al-Abdulhadi *et al*[26] and J.F Luck *et al*[27] who also found statistically insignificant difference in quality of anaesthesia between ropivacaine and bupivacaine when given intrathecally.

Hypotension was the most common side effect in both groups. There was a significant difference in the incidence of hypotension between the two groups. The studies of various authors[6,28,15] supports our results of low incidence of hypotension in hyperbaric ropivacaine but the exact cause of low incidence of hypotension as compared to bupivacaine is not established. The intraoperative and postoperative complications (bradycardia, nausea, shivering, vomiting) did not differ significantly between the two groups.

CONCLUSION

A solution of ropivacaine (hyperbaric) can be used for spinal anaesthesia and is comparable with hyperbaric bupivacaine in terms of quality of block, but has shorter recovery profile.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest with the research presented in this article.

REFERENCES

1. Albright G.A. Cardiac arrest following regional anaesthesia with etidocaine or bupivacaine. *Anaesthesiology* 1979; 51: 285-287
2. Clarkson CW, Hondeghem LM. Mechanism for bupivacaine depression of cardiac conduction. *Anaesthesiology* 1985; 62: 396-405
3. Akerman B, Hellenberg, Trossvik C. Primary evaluation of local anaesthetic properties of amino amide agent ropivacaine. *Acta Anaesthesiol Scand* 1988; 32: 571-578
4. Mc Clure JH. Ropivacaine. Br J Anaesth 1996; 76: 300-7
5. McClellan KJ, Faulds D. Ropivacaine, update of its use in regional anesthesia. *Drugs* 2000; 60: 1065-93
6. Chapter in a book: Ian McConache, J. McGeachie and Janet Barrie. "Regional AnaesthesiaTechnique". In: Wylie and Churchill Davidson, editors. A practice of anaesthesia. 7th edition, chapter-37, p-609
7. Whiteside J, Burke D, Wildsmith JAW. A comparison of 0.5% ropivacaine (5% glucose) with 0.5% ropivacaine (1% glucose) when used to provide spinal anaesthesia for elective surgery. *Br J Anaesth* 2001; 86: 241-4
8. Schiffer E, Van Gessel E, Gamulin Z. Influence of sex on cerebrospinal fluid density in adults. *Br J Anaesth* 1999; 83: 943-4
9. Van Kleef JW, Veering BT, Burm AGL. Spinal anaesthesia 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
10. Wahedi W, Nolte H, Klein P. Ropivacaine in spinal anaesthesia. Anaesthesist 1996; 45: 737-4
11. Bannister J, McClure JH, Wildsmith JAW. Effect of glucose concentration on the intrathecal spread of 0.5% bupivacaine. *Br J Anaesth* 1990; 64: 232±4
12. Chambers WA, Edstrom HH, Scott DB. Effect of baricity on spinal anaesthesia with bupivacaine. *Br J Anaesth* 1981; 53: 279-82
13. Logan MR, McClure JH, Wildsmith JAW. Plain bupivacaine: an unpredictable spinal anaesthetic agent. *Br J Anaesth* 1986; 58: 292-6
14. Sanderson P, Read J, Littlewood DG, McKeown D, Wildsmith JAW. Interaction between baricity (glucose concentration) and other factors

influencing intrathecal drug spread. *Br J Anaesth* 1994; 73: 744-6
15. C .J. Chung, S.R. Choi, K.H.Yeo, H.Park, S.Lee, and Y.J.Chin. Hyperbaric spinal Ropivacaine for caesarean delivery: A comparison to hyperbaric Bupivacaine. Anesth Analg 2002; 56:453-458
16. Engin Erturk, Cigdem Tutuncu, Ahmet Eroglu, Merih Gokben. Clinical Comparison of Ropivacaine and Bupivacaine, Both with 20 µg Fentanyl, in Spinal Anaesthesia for Major Orthopaedic Surgery in Geriatric Patients. *Med Princ Pract* 2010; 19:142-147
17. Bigat, Zekiye; Boztug, Neval; Karsli, Bilge; Cete, Nihan; Ertok, Ertugrul. Comparison of Hyperbaric Ropivacaine and Hyperbaric Bupivacaine in Unilateral Spinal Anaesthesia. *Clinical Drug Investigation*:2006; 26: 35-41
18. Züleyha Kazak, Meltem Mortimer, Sumru Sekerci. spinal anaesthesia with hyperbaric solutions of ropivacaine, levobupivacaine or bupivacaine in major orthopedic surgery. *Turkiye Klinikleri Journal Med Sci* 2010; 30 (2):731-7
19. Lada Kalagac Fabris ,Livija Sakic, Katarina Sakic Zdravcevic.Unilateral spinal anesthesia with low dose bupivacaine and ropivacaine: hypobaric or hyperbaric solutions with fentanyl for one-day surgery? Periodicum Biologorum vol. 115, no 2, 197–202, 2013.
20. U Srivastava, K Joshi, A Gupta, Y Dwivedi, H Anand, A Kannaujia, S Pilendram. Comparison Of Intrathecal Hyperbaric Ropivacaine And Bupivacaine For Caesarean Delivery. *The Internet Journal of Anesthesiology*. 2012 Volume 30 Number 4.
21. Gissen AJ, Covino BG, Gregus J. Differential sensitivity of fast and slow fibers in mammalian nerve. Anesth Analg 1982 ;61: 561
22. Taheri S, Cogswell LP , Gent A, *et al*. Hydrophobic and ionic factors in the binding of local anesthetics to the major variant of human alpha1-acid glycoprotein. *J Pharmacol Exp Ther* 2003; 304:71
23. Covino BG. Pharmacology of local anaesthetic agents. *Br J Anaesth* 1986; 58:701–716
24. Rosenberg PH, Kytta J, Alila A. Absorption of bupivacaine, etidocaine, lignocaine and ropivacaine into N-heptane, rat sciatic nerve and human extradural and subcutaneous fat. *Br J Anaesth* 1986; 58:310–4.
25. Beaulieu P, Babin D, Hemmerling T. The pharmacodynamics of ropivacaine and bupivacaine in combined sciatic and femoral nerve blocks for total knee arthroplasty. Anesth Analg 2006; 103: 768-774
26. Osama Al-Abdulhadi, Diane Biehl, Bill Ong.and Abdulaziz Boker. Hyperbaric spinal for elective cesarean section. Ropivacaine vs Bupivacaine. Middle *East J Anesthsiol* 2007; 19:385-39
27. J. F. Luck, P. D. W. Fettes and J. A. W. Wildsmith. Spinal anaesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. *Br J Anaesth* 2008; 101: 705–10
28. White side JB, Bruke D, Wildsimth 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):304-308.

Table 1. Patient Demographics

Parameter	Bupivacaine group	Ropivacaine group
Age (years)	58.5±8.5	56.4±10.11
Weight (kg)	59.4±9.2	57.3±9.4
Male/female	55/45	60/40
Duration of surgery (hr)	112±8.5	108±7.8
ASA Status (I/II)	65/35	69/31

Values are expressed as mean ± standard deviation (SD) or no. of patients

Table 2. Characteristics of spinal anaesthesia and frequency of adverse effects

Parameters	Bupivacaine group	Ropivacaine group	Significance
Sensory block			
Onset at T10 (min)	3±1.1	6±1.3	P value <0.0001
Total duration of sensory block (min)	260±16.1	160±12.9	P value <0.0001
Motor block			
Onset of motor block (min)	9±1.3	13±1.6	P value <0.0001
Total duration of motor block (min)	174±12.6	126±9.2	P value <0.0001
Quality of intraoperative anaesthesia			
Excellent (%)	90	92	
Good (%)	9	5	P value <0.4068
Fair (%)	1	3	
Poor (%)	0	0	
Intraoperative side effects			
Hypotension (%)	66	19	P value <0.0001
Bradycardia (%)	5	9	P value <0.4068
Nausea (%)	20	11	P value >0.05
Vomiting (%)	3	1	P value >0.05
Shivering (%)	16	10	P value >0.05
Postoperative side effects			
Vomiting (%)	3	2	P value >1.00

Values are expressed as mean ± standard deviation (SD) and no. of patients or percentage (%)

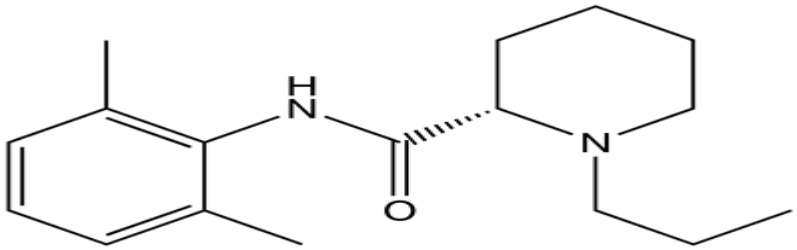
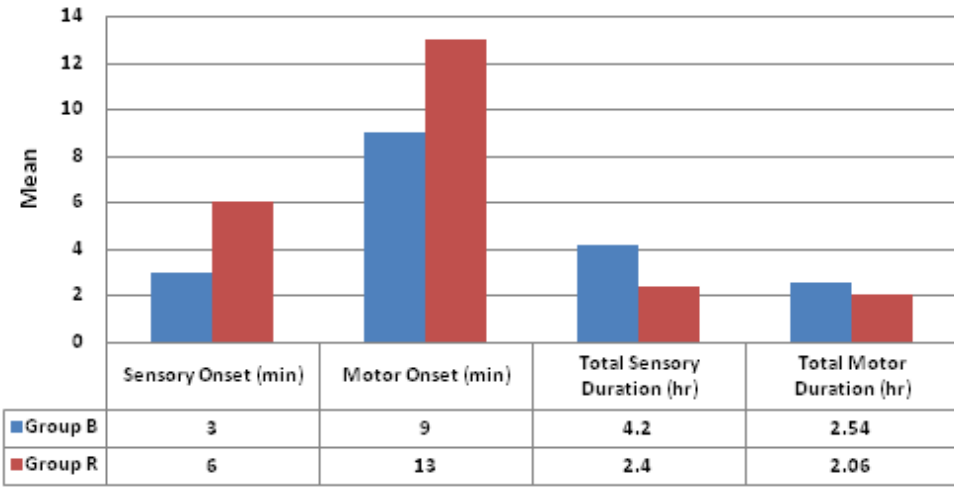


Figure 1. Ropivacaine Hydrochloride



	Sensory Onset (min)	Motor Onset (min)	Total Sensory Duration (hr)	Total Motor Duration (hr)
Group B	3	9	4.2	2.54
Group R	6	13	2.4	2.06

Figure 2. Comparison of quality of blocks in two groups

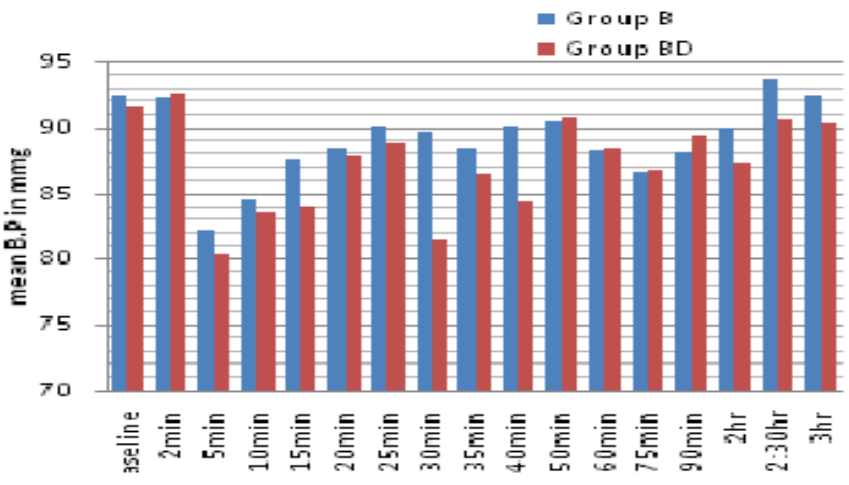


Figure 3. Mean blood pressure at different time intervals between the two groups