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Randomized Controlled Study of Comparison between Intrathecal Isobaric Ropivacaine 0.75% with Hyperbaric Bupivacaine 0.5%

Murugraj Shivkumar[1], Aher Pranjali Y[2], N Selvarajan[3], Suhedhar Rajesh[4]

[1]Consultant, [3]Professor and Head, Department of Anesthesia, Kovai Medical Center and Hospital, Coimbatore, Tamil Nadu 641014, India. [2]Assistant Professor, [4]Professor and Head, Department of Anesthesia, Shri Bhausaheb Hire Govt Medical College, Dhule Maharashtra 424001, India.

Abstract

Introduction: A number of clinical studies suggest that spinal anesthesia may be superior to general anesthesia for certain surgical procedures. *Aim:* To compare the duration, density of motor blockade, cephalad spread of sensory anesthesia and intra-operative hemodynamic instability between the both Groups. *Method:* This prospective, randomised, double blind study was conducted in 60 ASA Grades I & II patients of either sex in the age range of 20–60 *years* undergoing elective lower abdominal and lower limb surgery. The patients were randomly divided into two equal Groups. The hemodynamic parameters like ECG, NIBP, SpO_2, adverse effects and duration of surgery were monitored and recorded. Anesthesia assessed by Modified Bromage scale and bilateral loss of sensation to pin prick. The data was analysed using SPSS 20. *Results:* The maximum cephalad spread of sensory level was significantly lower in Ropivacaine Group (T 5.70 ± 1.055) than Bupivacaine Group (T 4.93 ± 0.828). The Grade IV motor block by Bromage scale after 3 *minutes* of intra-thecal injection was seen in 24 (80%) of bupivacaine group compared to 4 patients (13.7%) in ropivacaine group with statistical significance ($X^2 = 26.786$). There were highly significant incidence of intra-operative hypotension in bupivacaine group (17) than ropivacaine (7 patients). No significant differences in hemodynamic variables like bradycardia and arrhythmia. *Conclusion:* Isobaric ropivacaine as mean of providing less motor block, early ambulation and causes less hypotension when compared with bupivacaine.

Keywords: Bupivacaine; Intrathecal ropivacaine.

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Introduction

Spinal anesthesia, also called spinal analgesia or Sub-arachnoid Block (SAB), is a form of regional anesthesia involving injection of a local anesthetic into the cerebrospinal fluid (CSF) through a fine needle. Central neuroaxial blockade is the most widely used form of regional anesthesia today. Spinal anesthesia is one of the commonly used anesthetic technique for lower abdominal and lower limb surgeries. It is a safe, inexpensive and easy-to-administer technique which also offers a high level of post-operative satisfaction with good pain relief to the patients. The technique is simple, has rapid onset and is reliable. The risk of general anesthesia including mishaps due to

Corresponding Author: Aher Pranjali Y, Assistant Professor, Department of Anesthesia, Shri Bhausaheb Hire Govt Medical College, Dhule, Maharashtra 424001, India.

E-mail: aherpranjali@gmail.com

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airway management are avoided by this technique. A number of clinical studies[1] suggest that spinal anesthesia may be superior to general anesthesia for certain patients of surgical procedures. The endocrine-metabolic response to surgery is blunted when spinal anesthesia is employed compared to the response during General Anesthesia (GA).[1]

Bupivacaine, an amide compound, the most widely used drug for spinal anesthesia presently, its advantages compared to lignocaine being long duration of action and differential sensory-motor block.[2] But it is associated with some adverse cardiac effects like arrhythmias and central nervous system toxicity,[3] prolonged duration of sensory and motor blockade requiring a need to overcome these problems. However, with time a number of deaths from cardiac arrest were reported in association with regional anesthesia using bupivacaine. All deaths appeared to be caused by accidental intravenous injection of bupivacaine. These deaths, and subsequent recommendations of the United States Food and Drug Administration (FDA) provided the impetus to develop a safer drug. It was possible that a less fat soluble drug than bupivacaine would be less cardiotoxic.[4]

The identification of optically active isomers of the mepivacaine family led to the selection of ropivacaine, a pure S-(-) enantiomer, whose toxicology was selectively and extensively studied before its introduction on the market in 1996.[5] Ropivacaine, structurally resembling bupivacaine, with a propyl group on the piperidine nitrogen atom of the molecule is a relatively new amino-amide local anesthetic agent. It has various advantages like early onset and shorter duration of action and having lesser cardio toxicity as compared to bupivacaine.[6]

The present study was undertaken to determine clinical efficacy of ropivacaine over bupivacaine.

Aim and Objectives

1. To compare the duration, density of motor blockade produced by equal volume (*3 ml*) of equipotent doses of isobaric ropivacaine (0.75%) with hyperbaric bupivacaine (0.5%) when administered intrathecally.
2. To assess the height of sensory level or maximum cephalad spread between the groups.
3. To evaluate the intra-operative hemodynamic instability produced between the two drug groups.

Materials and Methods

A randomized control, double blind study was conducted in tertiary-care institute over *2 yr* after obtaining approval of the institutional ethical committee. Total 60 patients belonging to both sex coming for elective surgical procedures, orthopedics and gynecological procedures lasting less than *3 hours* under spinal anesthesia at our center during the period of *Jan 2011–Feb 2012*, were enrolled. The informed written consent of patient was taken. The study patients were selected after thorough assessment of their hemodynamic status. All the patients were ASA Gr 1 and 2 and aged between *20 and 60 years*. Our study included 35 males and 25 females.

Exclusion Criteria

Patient refusal, any contraindication for spinal anesthesia, combined spinal and general anesthesia, pregnancy and patchy or failed spinal anesthesia.

All patients were pre-medicated orally with Tab Pantoprazole *40 mg* and Alprazolam *0.25 mg* the previous night and *2½ hours* before surgery. In the receiving room an 18 G intracath was inserted and an infusion of Ringer's lactate solution started at *2 ml/kg/hr*. On arrival in the operation theatre ECG, NIBP and SpO_2 were applied for monitoring. Patients were then assigned randomly into two Groups namely: Group A (*3 ml* of 0.75% ropivacaine) and Group B (*3 ml* of 0.5% bupivacaine), according to the sealed envelope method by the anesthetic team not participating in the study but the researcher and the patient were unaware of their group. Under all aseptic and antiseptic precautions lumber puncture was performed with 26 gauge Quincke spinal needle in L3-L4 space in sitting position and drug was given over a period of *30 seconds*. Soon after the injection, time is noted and patient was made supine. No tilt was given to any patient. Onset of sensory blockade is the time between induction and bilateral loss of pin prick sensation up to T10 level, checked by every *30 second* after injection. Motor blockage was assessed with modified bromage scales shows in Table 1.[7] Supplementary oxygen was given during surgery. The hemodynamic parameters were monitored for complications and side-effects which were treated as and when required. Hypotension (systolic BP < *90 mm hg*) was treated with IV fluids ± vasopressors-Inj. Ephedrine/Mephentremine *6 mg* IV bolus SOS. Bradycardia (Heart rate < *50/mt*) was treated with Inj. Glcopyrrolate *0.02 mg/kg* IV bolus SOS. Motor blockade assessment was

done till surgery completed and continued every *15 minutes* till the patient completely recovers. Post-operatively duration of sensory blockade (regression up to L1 dermatome) was noted. Highest level of sensory blockade noted in each patient. In post-operative period Pulse, BP, Respiration, SpO_2, Cardiac monitoring (ECG) were observed were recorded at intervals of *15 min*, *30 min*, *1 hr*, *11/2 hr*, *2 hr, 3 h*, *4 hr*, *5 hr*, *6 hr*, *12 h* & *24 h*. Post-operative complication and side effects like nausea, vomiting, dryness of mouth, sedation, respiratory rate, desaturation, hypotension, bradycardia, neurological deficit, headache, etc. were noted and treated accordingly. Statistical Analaysis was done with SPSS and data was expressed as mean (standard deviation) for continous variables and proportion for qualitative variables. Student's *t* - test was used to test the statistical significance for quantitative variables and Chi-square or fisher exact test for qualitative variables. $p < 0.05$ was considered statistically significant.

Table 1: Grading according modified Bromage Scale

Grade	Criteria	Degree of block
I	Free movement of legs and feet	Nil (0%)
II	Just able to flex knees with free movement of feet	Partial (33%)
III	Unable to flex knees, but with free movement of feet	Almost complete (66%)
IV	Unable to move legs or feet	Complete (100%)

Results

Table 2 shows distribution of the demographic data like age, weight, height, (t - test) and Table 3 shows distribution according to sex, ASA (Chi-square test) in general, are comparable between both groups and there was no statistically significant difference (p – value > 0.05). Mean duration of surgery in Group A was *48.17 ± 19.49* and in Group B was *57.67 ± 34.16 minutes*, which is statistically non-significant (p - value = 0.191).

Table 2: Demographic data according to Age, Weight, Height

	Group A		Group B		*p* - value	*t* - value
	Mean	SD	Mean	SD		
Age	38.37	10.5	37.7	11.91	0.230	0.819
Weight	66.13	9.06	64.33	10.26	0.720	0.474
Height	164.27	6.96	163.07	7.85	0.627	0.533

Table 3: Distribution of patient according to gender and ASA Grading

	Sex		ASA Grading	
	Male	Female	I	II
Group A	17 (56.7%)	13 (43.3%)	21 (70%)	24 (80%)
Group B	18 (60%)	12 (40%)	9 (30%)	6 (20%)

$\chi^2 = 0.069$ $\chi^2 = 0.800$

Table 4 summarizes, thorasic level of sensory block in Group A was T4.93 ± 0.828 while in Group B was T5.70 ± 1.055 which was significant (*t* - test value = 3.131, *p* - value = 0.003).

Table 4: Cephalad spread of sensory level

	Group A	Group B
Mean	4.93	5.70
SD	0.828	1.055

p - value = 0.003, *t* - value = 3.131

Shows in Table 5 summarizes, Bromage score (Grade III & IV) after 3 minutes of intra thecal injection between two. In Group A, Grade IV of motor block is seen in 24 patients (80%) which is higher compared to 4 patients (13.3%) in Group B. This result is highly significant as Chi-square value is 26.786, p - value is 0.000. Table 6 illustrates, the total duration of motor block was *228* and *220 minutes* for Group A and Group B respectively. There was no statistically significant difference. Table 7 summarizes incidence of adverse events in both Group. The observed incidence of adverse events was significant for hypotension and vomiting as both were more in Group A. Hypotension is seen in 17 (56.7%) patients of Group A while 13 (43.3%) patients doesn`t had it. In Group B, hypotension was observed in 7 (23.3%) patients and 23 (76.7%) patients does not had hypotension. 9 patients in bupivacaine Group had intra-operative nausea/ vomiting compared to 1 patient in ropivacaine group and was found to be statistically significant ($p < 0.05$). While bradycardia and ventricular arrthymias were found to be non-significant. Incidence of bradycardia is similar between two Groups. 9 patients in each Group had bradycardia and who were treated with anti-cholinergics. Intra-operative arrhythmias, were seen in only 2 patients of bupivacaine group and no patient of ropivacaine group had it.

Table 5: Bromage Score after *3 minutes*

	Group A	Group B
Grade III	6 (20 %)	26 (87.3%)
Grade IV	24 (80%)	4 (13.7%)

$\chi^2 = 26.786$, $p = 0.000$

Table 6: Total duration of Motor Block in minutes

	Mean	SD
Group A	228	32.09
Group B	220	27.67

p - value = 0.305, *t* - value = 1.034

Table 7: Incidence of Adverse Events

Adverse Event		Group A	Group B	*p* - value	Chi-square value
Hypotension	Present	17 (56.7%)	7 (23.3%)	0.017	6.994
	Absent	13 (43.3%)	23 (76.7%)		
Nausea/Vomiting	Present	8 (26.7%)	1 (3.3%)	0.026	6.405
	Absent	22 (73.3%)	29 (96.7%)		
Bradycardia	Present	9 (30%)	9 (30%)	1	0.000
	Absent	21 (70%)	21 (70%)		
Ventricular Arrythamias	Present	2 (6.7%)	0 (0%)	0.492	2.069
	Absent	28 (33.3%)	30 (100%)		

Discussion

As practice of modern medicine focuses increasingly on day care surgical procedures, spinal anesthetics should provide short-acting and adequate anesthesia without compromising early ambulation and discharge from the day surgery unit. The risk of general anesthesia including mishaps due to airway management are avoided by this technique. Ropivacaine could have potential in this area. It was demonstrated that the significantly faster onset and regression of sensory block was seen with intrathecal bupivacaine and opioids, however, significantly shorter motor block duration with intrathecal ropivacaine might be advantageous because it allowed a faster discharge, and or early recognition of any neurologic complications. Ropivacaine is a local anesthetic with lower cardiotoxic potential than racemic bupivacaine. The majority of published data on ropivacaine concerns its use in the epidural space.

Present study was undertaken to compare isobaric ropivacaine and hyperbaric bupivacaine. In humans, ropivacaine has been shown to be effective in providing intrathecal anesthesia for patients undergoing THR,[8] TURP[9] and lower abdominal and lower limb surgery.[10,11]

Sensory level/Maximum cephalad spread

In our study maximum cephalad spread is assessed after *3 minutes* of injection of drug by using loss of sensation to pinprick. In bupivacaine Group (A) the mean sensory level was T-4 to T-6 (4.93 ± 0.828) which is higher when compared to ropivacaine Group (B) where the mean level was T-5 to T-8 (5.70 ± 1.055). The following studies agreed with our result and it shows bupivacaine level was higher than ropivacaine Group. A study by Koltka k *et al*.[12] reported spread of sensory block was higher in bupivacaine than ropivacaine. This is in contrast with the study conducted by Jean-Marc Malinovsky *et al*.[13] [Mean level for Bupivacaine: T-7 & Ropivacaine:T-9], Whiteside *et al*.[14] [Mean level for Bupivacaine:T-5 & Ropivacaine:T-7] had higher sensory level in bupivacine group.

Motor block after 3 minutes of injection

After *3 minute* of injection, Grade IV (complete motor block) is seen in 24 patients (80%) of bupivacaine Group (A) while seen in 4 patients (13.7%) of ropivacaine Group (B). Rest 26 patients (76.3%) of ropivacaine Group (B) attained Grade III of Bromage score. This difference was statistically significant since $p < 0.05$. This score was comparable with the study by Mantouvalou *et al*.[15] & Erturk E *et al*.[16] which report onset of motor block was significantly faster in bupivacaine group. Whiteside *et al*.[14] in 2003 compared the clinical efficacy of hyperbaric ropivacaine with that of the commercially available hyperbaric preparation of bupivacaine. They observed that time to peak motor blockade was delayed in the Ropivacaine Group (*20 min*) as compared to Bupivacaine Group (*15 min*), $p < 0.001$.

Total duration of motor block

In our study total duration refers to the time after intra-thecal injection to the complete recovery of the

patients from motor block. In bupivacaine Group (A) the mean duration was *228 minutes* whereas in ropivacaine Group (B) it was *220 minutes*. Which non-significant (*p* - value = 0.305). Same observations seen in studies of Gautier PE *et al*.,[17] Jean-Marc Malinovsky *et al*.[13] and Kessler P *et al*.[18] compared isobaric ropivacaine and bupivacaine, which showed similar motor blockade between the two Groups. Sanchez *et al*. in 2009 compared the effects of intrathecal Isobaric Ropivacaine (IR) *vs* Isobaric Bupivacaine (IB) in a dose ratio of 3:2 in non-ambulatory urologic and orthopedic surgery. 117 patients scheduled for surgery were randomized and assigned in a double-blind fashion to receive either *15 mg* of IR (*n* = 58) or *10 mg* of IB (*n* = 59). They concluded that the motor blockade was longer in the IB Group (*266.5 + 29.5*) compared to the IR Groups (*226.4 ± 22.3 min*), $p < 0.001$. We found the duration of motor blockade to be prolonged with bupivacaine when compared with ropivacaine.

Hemodynamic parameters

Hypotension: In our study, there was a significant incidence of hypotension in bupivacaine Group (A) compared to ropivacaine Group (B). 17 patients (56%) of bupivacaine group has hypotension which is higher when compared to 7 patients (23%) of ropivacaine group ($p < 0.05$). This is consistent with the study conducted by Lopez-soriano F *et al*.,[19] Whiteside *et al*.,[14] Mantouvalou *et al*.[15] & Erturk E *et al*.[16] In their studies it is shown that there is increased incidence of hypotension and higher requirements of vasoactive drugs in bupivacaine group than in ropivacaine group of patients. This can be attributed to the higher cephalad spread of hyperbaric bupivacaine causing more sympathetic blockade than isobaric ropivacaine. Mehta V, Gupta R, Wakhloo, *et al*.[20] compared intrathecal administration of isobaric bupivacaine (*15 mg*) and ropivacaine (*15 mg*) undergoing lower limb surgery. They found that, there was slight decrease in mean heart rate and arterial blood pressure over *30 minutes* after anesthesia which was statistically non-significant. Mac Namee, McClelland, S. Scott *et al*.[21] studied isobaric ropivacaine *5 mg/ml* (*3.5 ml*) and isobaric bupivacaine *5 mg/ml* (*3.5 ml*) for major orthopedic surgery.

Nausea/Vomiting: In our study, 8 patients of bupivacaine group had intra-operative nausea/ vomiting compared to 1 patient of ropivacaine group which was significant ($p < 0.05$). The increased incidence of nausea/vomiting in Group B can be explained due to higher incidence of hypotension and maximum cephalad spread. The study by Mantouvalou *et al*.[15] showed occurrence of nausea/ vomiting is equally distributed between the two groups, thereby not agreeing with our study.

Bradycardia and Arrhythmia: In our study, incidence of bradycardia is similar between two groups. 9 patients in each group had bradycardia and who were treated with anti-cholinergics. This is in contrast with the study done by Kessler P *et al*.,[18] Boztug N *et al*.,[22] and Koltka k *et al*.[12] which reported lower incidence in ropivacaine but no significant bradycardia between the two groups. (bupivacaine and ropivacaine). Regarding intra-operative arrhythmias, only 2 patients in bupivacaine group had ectopics and no patient of ropivacaine group had it. Though it was not statistically significant.

Conclusion

From our study it was shown that:

1. The maximum cephalad spread or height of sensory level was significantly lower in ropivacaine group;
2. After *3 minutes* of injection, motor block was denser in bupivacaine group than ropivacaine group with statistical significance;
3. There was no significant difference in the total duration of motor blockade;
4. Incidence of hypotension is higher in bupivacaine group compared to ropivacaine group;
5. Nausea/vomiting is more pronounced in bupivacaine group.

Although the onset of motor blockade was denser in bupivacaine group, the total duration of motor blockade was similar between the groups. Hence, we conclude that 0.75% isobaric ropivacaine produces similar duration of motor blockade with stable hemodynamics, as compared to 0.5% hyperbaric bupivacaine.

Key massage: Ropivacaine has lower cardiotoxic potential than bupivacaine.

Conflict of Interest: None.

Source of support: None.

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