A comparative study of 0.5% hyperbaric Ropivacaine versus 0.5% hyperbaric Bupivacaine for spinal anaesthesia

Leena Ingale⁎, Sheetal Dalal², Santosh Ingale², N.G. Tirpude², A.S. Tarkase² and Manik C Gedam³

1Department of Anaesthesiology, Indira Gandhi Govt Medical College & Hospital, Nagpur (MS), India
2Department of Anaesthesiology, Govt Medical College & Hospital, Nagpur (MS), India
3Consultant Ophthalmoogy, PDMC, Amravati (MS), India

⁎Correspondence Info:
Dr. Leena Ingale
Department of Anaesthesiology,
Indira Gandhi Govt Medical College & Hospital, Nagpur (MS), India
E-mail: drleenaingle@gmail.com

Abstract
Aims and Objective: Aim of the present study was to compare the clinical efficacy of 0.5% hyperbaric solutions of ropivacaine versus bupivacaine in terms of characteristics of spinal blockade, haemodynamic stability, recovery profile and side effects.

Material and Method: The study enrolling 100 patients (age 20-60 years) of either sex, ASA grade I & II were randomly allocated in two groups. Group R received 3 ml of 0.5% hyperbaric ropivacaine with glucose 8.33% and Group B received 3 ml of 0.5% hyperbaric bupivacaine with glucose 8%. After induction, we studied the various parameters of subarachnoid block, hemodynamic variables, recovery and side effects.

Result: Hyperbaric ropivacaine had late onset of sensory blockade, equal time to reach maximum dermatome level, early regression and shorter total duration of sensory blockade as compared to bupivacaine. Ropivacaine shows late onset of motor blockade, less degree and total duration of motor blockade as compared to bupivacaine. Ropivacaine was more hemodyamically stable as compared to bupivacaine. Both the sensory and motor blocks were subject to a more rapid recovery with ropivacaine compared with bupivacaine. Hyperbaric ropivacaine was not associated with any side effects intra and postoperatively.

Conclusion: 3 ml of hyperbaric solution of ropivacaine 0.5% with glucose 8.33% can produce predictable and reliable spinal anaesthesia for a wide range of surgical procedure.

Keywords: Hyperbaric, Ropivacaine, Bupivacaine, haemodynamic stability, subarachnoid block

1. Introduction
The primary aims of anesthesia are to render adequate pain relief, thereby permitting the performance of surgical procedures without stress and discomfort. Since the introduction of spinal anesthesia in 1898 by Dr. August Bier, who described the intrathecal administration of cocaine, spinal anesthesia is preferred over general anesthesia, particularly in surgical procedures of lower abdomen and lower limbs [1]. Spinal anesthesia has the definitive advantage that profound nerve block can be produced in a large part of the body by the relatively simple injection of a small amount of local anesthetic. However the greatest challenge of the technique is to control the spread of that local anesthetic through the cerebrospinal fluid (CSF) to provide the block that is adequate (in both extent and degree) for the proposed surgery but without producing unnecessarily extensive spread and so increasing the risk of complications[2].

Bupivacaine has been in clinical use as local anesthetic for more than 30 years and is available commercially as a racemic mixture containing equal proportions of the S (-) and R (-) isomers. It is being extensively used and produces an adequate sensory and motor blockade [3]. However bupivacaine is also associated with a number of side effects, including motor weakness, urinary retention, cardiovascular and central nervous system toxicity. In particular, there have been reports of death attributable to bupivacaine induced cardio-toxicity in adults after accidental intravenous injection[4]. These adverse effects have prompted a search for new drugs with lesser toxicity.

Ropivacaine is a new long acting amino-amide local anesthetic. It was synthesized simultaneously with bupivacaine by Ekenstam almost 50 years ago and was launched in 1996, being the first pure S (-) - enantiomeric local anesthetic to be clinically introduced. The reason for introducing ropivacaine was the need for a long acting local anesthetic that is less cardio toxic than bupivacaine[5].
Ropivacaine produces a greater degree of differential block at low concentration and a property of producing frequency [6] dependent block offers considerable clinical advantage in providing analgesia with minimum motor blockade [7]. Looking at this property, in the past year ropivacaine has been one of the most studied drug, used in ambulatory spinal anesthesia, but ropivacaine has not offered clear advantage over bupivacaine about reliability, side effects or faster recovery [8]. It is approximately half as potent as bupivacaine in spinal anesthesia when used in hyperbaric solution [9]. Hyperbaric ropivacaine produced more predictable and reliable sensory and motor block, with faster onset than a plain solution. Plain solution of ropivacaine is associated with a less favorable pattern of block [10]. A hyperbaric solution produces motor block in a larger area of body, but it can sometimes produces cardiac arrest and therefore anesthesiologist prefer using isobaric solutions that are less dangerous, the former are used only when a limited block is required, because in this case they are effective and do not produce side effects[11].

The present study was designed to compare the clinical efficacy of hyperbaric solution of ropivacaine (0.5 %) with that of hyperbaric bupivacaine (0.5 %) in spinal anesthesia. The ropivacaine solutions were prepared aseptically immediately before injections (by adding 2 ml of injection ropivacaine 0.75% plus 1 ml glucose 25%) while the hyperbaric bupivacaine solutions were commercially available.

2. Material and Method

After obtaining institutional ethical committee approval and patients written informed consent, this randomized double blind study was conducted with 100 patients belonging to ASA grade I & II of either sex, age between 20-60 years posted for different surgical operations on abdomen, genitourinary region and on lower extremity. Patients with hypertension, who are hemodynamically stable with antihypertensive therapy and non IHD patients were included in study. Whereas patients with uncontrolled hypertension, IHD, psychiatric and neurological disorder, known allergy, sensitivity to local anaesthetics, contraindication to spinal anaesthesia, such as infection at the site of lumbar spine, septicemia, platelet disorders and clotting abnormalities, were excluded from the study. A detailed history of any major diseases and previous operative procedure elicited. A detailed pre-anesthetic evaluation including history, thorough general and systemic examination and all relevant investigations were done for all the patients. One hundred selected patients were randomly divided into two equal groups of 50 patients each by a lottery method (picking random lots from a sealed bag). All patients were blinded to spinal medication administered. Senior resident who do not participating in study prepared all medications. After obtaining subjects weight and according to randomization, the volume to be injected in spinal block was prepared in syringe with label indicating only the serial number of the patients. The residents observing the patient intra-operatively and in the recovery room were blinded to the drugs administered. All patients were kept NBM (nil by mouth) for 4-6 hours before surgery.

On operation table, standard multipara monitors were applied to the patient and baseline parameters like pulse rate, blood pressure, respiratory rate and SPO2 were recorded. A good intravenous line was secured with IV cannula and preloading was done with 10 ml /kg ringers lactate solution. All patients were premedicated with ranitidine 1 mg/kg, ondansetron 0.08 mg/kg, and midazolam 0.02 mg/kg intravenously. Under all aseptic precautions, patients were positioned in a left lateral decubitus position with the neck and knees flexed on the chest. The skin over lumbosacral area was prepared with betadine solution and draped with sterile towels. Lumber puncture was done in L3 – L4 or L4-L5 interspace with 23 gauge Quincke spinal needle. After obtaining free, clear and continuous flow of cerebrospinal fluid bupivacaine group was injected with 3 ml 0.5% of hyperbaric bupivacaine in 8% glucose and ropivacaine group was injected with 3 ml of 0.5% of hyperbaric ropivacaine in 8.3% glucose. The patients were turned immediately on their back and sensory analgesia was assessed by pinprick at every two minutes interval up to 30 minutes.

The following readings were noted for assessment of sensory blockade.
1) Time of onset of sensory block;
2) Maximum cephalic spread
3) Time to maximum cephalic spread;
4) Two segment regression time 5) Total duration of sensory block

The characteristics of motor block were assessed by following observations
1) The degree of motor blockade was assessed by Bromage scale.

Table 1: Bromage scale

| Grade | Criteria                                      |
|-------|----------------------------------------------|
| 0     | Able to raise the whole limb at hip          |
| 1     | Able to flex knee but unable to raise the lower limb at hip |
| 2     | Able to flex the ankle but unable to flex knee |
| 3     | No movement of lower limb                    |

2) Time to maximum degree of block i.e. Bromage grade 3
3) Time to complete regression

After achieving the adequate level of anaesthesia, surgeons allowed to operate. The time of beginning of surgery was noted. Intra-operatively, patients were closely monitored for pulse rate, systolic and diastolic blood
pressure, respiratory rate and SPO2 at induction, 2, 5, 10, 15, 20, 25, 30, 45, 60 minutes.

The following interventions were made and were noted as needed:

- Any hypotension (>30% fall from basal blood pressure) was treated with injection mephentermine 7.5 mg and with loading Ringer lactate solution.
- Bradycardia (pulse rate below 60 beat / minute) was treated with IV injection of atropine 0.6 mg.
- Analgesics and sedatives were supplemented when required.
- General anaesthesia given if no level of anaesthesia were achieved.
- All patients received adequate intravenous fluids.

Time of completion of surgery was noted and duration of surgery was calculated. In recovery room pulse rate, blood pressure, respiratory rate and SPO2 were monitored at arrival, 15, 30, 45, and 60 minutes with help of BIS multipara monitor. Time taken for regression below L1 and duration of motor block (Bromage scale up to 0) was noted. The total duration of sensory block and motor block defined as interval from intrathecal administration to point of complete regression of sensory block or to the point in which the Bromage score was back to zero. The patients were shifted to ward with written instruction to withhold any analgesic or sedative in postoperative period, unless the patients complained of moderate pain and to note down first time of micturition. Patients were watched for side effects like nausea, vomiting, pruritus, hypotension, bradycardia, drowsiness, respiratory depression (respiratory rate < 10 breaths/minute).

### Table 1: Demographic data and duration of surgery

| Variables                  | Group R          | Group B          | p-value |
|----------------------------|------------------|------------------|---------|
| Age (years)                | 42.5±15.65       | 40.8±15.36       | 0.81    |
| Height (cm)                | 159.2±7.24       | 161.2±7.49       | 0.73    |
| Weight (kg)                | 58.0±6.86        | 58.0±7.98        | 0.94    |
| duration of surgery (min)  | 75.7±30.36       | 85.1±32.28       | 0.98    |

The most common surgery performed in both the groups was herniorrhaphy, (Group ‘R’= 36% & Group ‘B’= 32%). Other type of surgery performed was appendicectomy, hydrocele repair, DHS, split skin grafting, I & D, orchidectomy, anatomical repair, excision of cyst, OR with plating, implant removal, SPCL, VH, TAH, TL, colonoscopy, freyers prostatectomy, TBW and polypectomy.

Both the groups were compare regarding characteristics of subarachnoid (sensory and motor) blockade were depicted in Table 2.

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

| Characteristics (min)     | Group R          | Group B          | p-value |
|---------------------------|------------------|------------------|---------|
| Onset of sensory block    | 7.1±2.75         | 3.0±1.48         | 0.00    |
| Time to Maximum Cephalic spread | 16.16±4.34       | 17.1±4.63        | 0.29    |
| Two segment regression time | 71.4±13.36       | 82.4±11.88       | 0.00    |
| Total duration of sensory block | 143.5±23.61      | 199±42.19        | 0.00    |
| Onset of motor block      | 11.28±5.00       | 7.22±1.94        | 0.00    |
| Total duration of motor blockade | 96.7±41.31      | 160±31.99        | 0.00    |

Hyperbaric ropivacaine shows late onset of sensory blockade, equal time to reach maximum dermatome level, early regression and shorter total duration of sensory blockade as compared to hyperbaric bupivacaine. Hyperbaric ropivacaine shows late onset of motor blockade, less degree and total duration of motor blockade as compared to hyperbaric bupivacaine, still adequate for the projected surgery. Both the sensory and motor blocks were also subject to a more rapid recovery with hyperbaric ropivacaine compared with hyperbaric bupivacaine.

The pulse rate, systolic blood pressure and diastolic blood pressure showed fall from 5 minutes onward, but fall was transient and were easily controlled by use of IV atropine 0.6 mg and mephentermine 7.5 mg with intravenous fluids. Only six patients from ropivacaine group and 15 patients from bupivacaine group developed significant lowering of systolic blood pressure and two patients from ropivacaine group and four patients from bupivacaine group developed significant bradycardia. Throughout the course of anaesthesia, good hemodynamic stability was maintained in both groups, (Figure 1).
Figure 1: Showing intra and post operative pulse rate (PR), systolic blood pressure (SBP) and diastolic blood pressure (DBP)

When SPO\textsubscript{2} monitoring was done with BIS multipara monitor, we observed 100% SPO\textsubscript{2} most of the times and difference was not statistically significant. Thus in present study, none of the patients in both groups showed any evidence of significant respiratory distress or desaturation.

The incidence of side effects was comparable in both groups. Intraoperative nausea and vomiting were found in both groups, but they were of mild intensity and never distressing and not required any treatment. No side effects found in recovery room. Mean time of first micturition was 252.65 ± 45.83 minutes in ropivacaine group and was 356 ± 84.85 minutes in bupivacaine group and the difference was highly significant.

4. Discussion

Bupivacaine is long acting local anaesthetic agent of choice for lower limb and lower abdominal surgeries. It binds strongly to cardiac sodium channels leading to a prolonged inhibition of normal conduction. Animal’s studies\cite{12} have proved that accidental intravascular bupivacaine results in arrhythmias, cardiac depression and cardiac arrest. Ropivacaine is one of a group of local anaesthetic drugs, the pipercoxyllidides. Mepivacaine and bupivacaine both are well known members of this group. Ropivacaine is the first local anaesthetic manufactured as a pure S-enantiomer in order to take the advantage of the decreased cardio toxicity of the S configuration. However several recent studies have described the use of ropivacaine for spinal anaesthesia and it has been suggested that ropivacaine has shorter duration of action than bupivacaine. In addition, some studies have shown that glucose containing hyperbaric ropivacaine and hyperbaric bupivacaine for elective surgeries under spinal anaesthesia.

We found no significant difference between two groups as regards the demographic profile (age, sex, weight, height) and duration of surgery. Time of onset of sensory block was observed in both the groups to compare the onset of sensory analgesia. In our study sensory block was suitable to maximum patients in ropivacaine group and to all in bupivacaine group. Patients receiving 0.5% hyperbaric ropivacaine had late onset of sensory blockade than those who received 0.5% hyperbaric bupivacaine and difference between the two groups was statistically significant. The onset of pinprick analgesia at T10 was significantly rapid with bupivacaine. Usually time for maximum cephalic spread depend on baricity of solution, dose of drug, tilt of table and position of patients etc. Present study showed no significant difference as regard to mean time to maximum cephalic spread. Mean height of sensory block i.e. mean maximum cephalic dermatome level was T5 in group R and T6 in group B,(P> 0.05). Also the mean time of two segment regression in group R was 71.4 ± 13.36 minutes and in group B was 82.4 ± 11.88 minutes. Duration of regression was more rapid in group R compare to in group B,(P< 0.05). Total duration of sensory block was shorter in group R (143.5 ±23.61 minutes) than group B (199 ± 42.19 minutes). This difference in two groups was statistically highly significant. Our findings regarding sensory blockade were accordance with different studies\cite{10,13-22}.

The motor block was inadequate to many patients in group R and adequate to all in group B and total 8 patients in group R required general anaesthesia. The onset of motor block was delayed in group R than in group B and the difference found was statistically highly significant. This difference may be due to lesser lipid solubility of ropivacaine which causes this drug to penetrate the large myelinated A
fibers more slowly than the more lipid soluble bupivacaine. Consideration with quality of motor block ropivacaine gave a lesser degree of motor block than bupivacaine. 44 (88%) out of 50 patients developed grade three block, 6 (12%) patients developed grade two block with bupivacaine. Whereas 24 (48%) out of 50 patients developed grade three block, 12 (24%) patients developed grade two block, 9 (18%) patients developed grade one block and 5 (10%) patients developed grade zero block i.e. no motor block with ropivacaine. In present study, patients who developed grade one block, out of 9 patients, in 3 patients the level of spinal block was sufficient for the planned operation not required any supplementation of analgesia, one patient of SPCL given injection propofol 25-100 μg/kg/min infusion and to 5 patients given general anaesthesia. Those patients developed grade zero blocks, out of 5, in two patients the level of spinal block was sufficient for the planned operation had no need to give supplementation of analgesia, 3 patients given general anaesthesia. The difference in two groups was statistically significant. This is general agreement that ropivacaine has less potent effect on motor nerves. We found highly significant difference in two groups as regards to the duration of motor block, group R (96.7± 41.31 min) show shorter duration than group B (160 ± 31.99 min). Our results regarding the motor blockade were agreement with various studies [10,13-19,21-26].

Present study shown that, in spite of slight hypotension in both group but there was no significant difference between both groups as regards hemodynamic stability. Mean pulse rate in group R was 76.68±9.96 beats/minute and in group B was 82.96±9.85 beats/minute at induction, which was comparable in both groups. It is clear that after spinal anaesthesia mean pulse rate was decreased from 5 minutes onwards intraoperatively in both groups. Low pulse rate was exhibited by most patients during spinal anaesthesia was explained by predominance of Bainbridge reflex. Venous pooling in periphery decrease the stimulation of volume receptors in right atria this decrease outflow resulting in fall of pulse rate. After spinal anaesthesia mean systolic and diastolic blood pressure was decreased from 5 minutes onwards in both groups intraoperatively and postoperatively, but difference between two groups was statistically significant. This result correlates with different studies [15,17,19-22,25,27-29]. The statistical analysis of arterial oxygen saturation values for two groups at early and late intraoperative and postoperative period respectively (reading of later four periods taken as mean readings) shows that there was no statistically significant difference in two groups at these five periods.(P>0.05). Thus in present study none of the patients in both groups showed any evidence of significant respiratory distress or desaturation.

No side effects were seen in 42 (84%) patients of group R and 35 (70%) patients of group B i.e. side effects were seen in more number of patients in group B than in group R, this difference was statistically significant. As regards to time of first micturition, present study shows that patients in ropivacaine group were able to pass urine sooner than those in the bupivacaine group. Mean time of first micturition was 252.65 ± 45.83 minutes in ropivacaine group and 356 ± 84.85 minutes in bupivacaine group (P < 0.001).

Compare with studies done by Whiteside et al[17], Luck et al[22]and Kallio et al[20].

5. Conclusion

We concluded that ropivacaine 0.5% in glucose 8.33%, which is hyperbaric relative to cerebrospinal fluid, can provide predictable and reliable spinal anaesthesia as compared to commercially available hyperbaric bupivacaine. The key issue was difference in the clinical profile of block (onset, extent, suitability for surgery, duration) produced, not the relative potencies of the two drugs.

This suggest that ropivacaine may be suitable for short procedures where a rapid return of ambulatory function is desirable, such as in the day case setting, where its recovery profile could confer a distinct clinical advantage.

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