

A Comparative Study of Intrathecal Isobaric 0.5% Bupivacaine and Intrathecal Isobaric 0.75% Ropivacaine in Elective Lower Segment Cesarean Section

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Abstract

Objective: To compare the anesthetic efficacy of isobaric 0.75% ropivacaine with isobaric 0.5% bupivacaine in patients undergoing elective lower segment cesarean section (LSCS) under spinal anesthesia (SA) with respect to the nature of sensory block, motor block, and duration of analgesia. **Materials and Methods:** In this prospective, randomized, double-blinded study, sixty full-term parturients of American Society of Anesthesiologists Grade I–II, aged 20–35 years, scheduled for elective LSCS, were randomized into two groups namely B and R ($n = 30$). Preoperative medication regimen and anesthesia protocol followed, were uniform for all patients. Patients received 2.5 ml of either local anesthetic agent intrathecally. Hemodynamic parameters, onset and duration of sensory and motor blockade, level achieved, and side effects were compared between the two groups. Postoperative analgesia was assessed using the Visual Analog Scale scoring and also by noting the time of requirement of the first dose of rescue analgesic. Qualitative data were analyzed by Chi-square test and quantitative data were analyzed by independent sample *t*-test. **Results:** All the thirty patients in each arm completed the study without any dropouts. Baseline demographic variables, hemodynamic parameters, characteristics of sensory block (onset, time to reach peak sensory level, and duration), postoperative analgesia, and neonatal outcome were similar in both groups. However, intrathecal isobaric 0.75% ropivacaine demonstrated delayed onset ($P = 0.005$), and a significantly shorter duration ($P = 0.001$) of motor block. **Conclusion:** In view of the shorter duration of motor blockade, with similar duration of sensory blockade, hemodynamics, and postoperative analgesia, 0.75% isobaric ropivacaine (18.75 mg) is an efficient and safe alternative to bupivacaine for SA in elective LSCS.

Keywords: Cesarean section, isobaric bupivacaine, isobaric ropivacaine, subarachnoid block

INTRODUCTION

Subarachnoid block has been the gold standard for providing anesthesia in lower segment cesarean section (LSCS) with advantages such as with rapid onset of action, being easy to perform, being an effective anesthesia in mother, and with least fetal toxicity, being a few of them.^[1] Bupivacaine, a long-acting amide local anesthetic (LA), is used most commonly for spinal anesthesia (SA), both as a hyperbaric and isobaric solution.^[2] However, the major concern about the cardiotoxicity of bupivacaine led to the development of ropivacaine, a new long-acting amide LA.^[3] Ropivacaine, a pure S-enantiomer, is less cardiotoxic, has shorter duration of action, and has lesser lipid solubility than bupivacaine.^[4] Ropivacaine also exhibits differential blockade property (sensory > motor), leading to early return of motor activity and postoperative ambulation.^[5]

Various studies till date have compared the efficacy and side effect profile of equipotent doses of intrathecal hyperbaric bupivacaine and hyperbaric or isobaric ropivacaine both with and without adjuvants in different types of surgeries.^[6]

However, our novel study was undertaken with the primary aim to compare the anesthetic efficacy of intrathecal use of isobaric 0.75% ropivacaine (18.75 mg) and isobaric

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0.5% bupivacaine (12.5 mg), without adjuvants, with respect to the nature of sensory block, motor block, and duration of analgesia, specifically in LSCSs. In addition to this, our objective was also to compare the perioperative changes in vital parameters, namely heart rate (HR), respiratory rate, arterial oxygen saturation, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and the side effects, if any, of the above two study drugs.

MATERIALS AND METHODS

After obtaining approval from the institutional ethical committee and written informed consent from the patients, sixty full-term parturients of American Society of Anesthesiologists (ASA) Grade I and II, aged 20–35 years, with uncomplicated singleton pregnancy and scheduled for elective LSCS under SA, were included in this prospective, randomized, double-blinded, observational study.

Parturients unwilling to take part in the study, those having a history of hypersensitivity reactions to LA, those with cardiac or neurologic disease, those with gestational diabetes, those with hypertensive disorders of pregnancy, those with preterm gestation (<37 weeks) or multiple pregnancy, those with bleeding disorder or on anticoagulants, those with any obstetric complications, those with evidence of fetal compromise, or those with suspected fetal abnormality were excluded from the study. Patients with inadequate sensory and motor blockade and requiring conversion to general anesthesia were also excluded from the study.

All patients underwent complete preanesthetic evaluation which included thorough physical examination and baseline preoperative investigations such as hemoglobin, total leukocyte count, differential leukocyte count, blood sugar (fasting and postprandial), serum urea, creatinine, coagulation profile, and urine analysis for albumin and sugar, along with a 12-lead electrocardiography. The parturients were randomized, according to a computer-generated number, into two treatment groups of thirty each. Group B ($n = 30$) received 2.5 ml of 0.5% isobaric bupivacaine (12.5 mg), whereas Group R ($n = 30$) received 2.5 ml of 0.75% isobaric ropivacaine (18.75 mg) intrathecally. The blinding was done to the patients by not informing them the name of the drug that they received. An independent anesthesiologist, not participating in the study, prepared the drug and administered the SA, while the observations were noted by a second anesthesiologist who was blinded to the drugs used.

As per institutional protocol, tablet ranitidine 150 mg was given orally, night before and again on the morning of the planned LSCS. Anesthesia machine and airway equipment were checked, and drugs for resuscitation were kept ready before starting the procedure. The standard recommended ASA monitoring parameters were attached to the patient, and the baseline pulse rate, O_2 saturation, respiratory rate, SBP, DBP, and MAP were recorded. Similar intraoperative

anesthetic management was followed in patients of both the groups. Patients were preloaded with 10 ml/kg of ringer's lactate using 18G intravenous cannula, 15 min prior to the administration of the subarachnoid block. Subarachnoid blockade was performed aseptically, by midline approach, in the sitting position, at L2–L3 or L3–L4 spinal interspace using 27G pencil-tipped BD Whitacre spinal needle, and the study drug was administered slowly over 10–12 s. Immediately after administration of the subarachnoid block, the patients were placed in the supine position with left uterine displacement by putting a wedge under their right buttock. Surgery was started after establishment of the sensory blockade up to T4 and motor blockade score of Bromage IV.^[7] Oxygen was supplemented via Hudson face mask at a flow rate of 3 L/min throughout the procedure, and the following parameters were assessed.

Sensory block

The onset of sensory block was defined as the time between the injection of the study drug and the loss of pinprick sensation at the T10 dermatomal level. Sensory block to pin prick was evaluated bilaterally along the midclavicular line by using a short beveled 27G needle, and the assessment was done with respect to its time of onset, highest level of blockade, two-segment regression, and duration of the blockade. Sensory block was evaluated immediately after administration of the subarachnoid block, then every 1 min up to the first 10 min or up to the attainment of sensory block to T4 level, whichever came earlier. Following surgery, it was assessed every 30 min for the next 3 h and hourly thereafter up to 6 h. Duration of sensory blockade was defined as time interval from injection of the study drug to regression of sensory block to the level of T12.

Motor block

Bromage score was used to assess motor block bilaterally, with regard to its time of onset, degree of motor blockade, and duration of the blockade.

Bromage score:

- I = Able to lift extended leg at the hip, i.e., free movement of legs and feet
- II = Just able to flex the knee with free movement of feet, but not lift extended leg
- III = Unable to flex knees but having free movement of feet
- IV = Unable to move legs or feet.

Motor blockade was assessed immediately after administration of the subarachnoid block, then every 1 min up to the first 10 min or up to attainment of Bromage IV score, whichever came earlier. Following surgery, it was assessed every 30 min for the next 3 h and hourly thereafter up to 6 h. Onset of motor block was defined as the time from the completion of intrathecal injection till the attainment of Bromage IV. Duration of the motor blockade was denoted by the time taken from the onset of motor blockade (Bromage Score IV), to time when patient was able to raise legs (Bromage Score I).

Intensity and duration of postoperative analgesia

Assessment was done by the Visual Analog Scale (VAS) and also by noting the time of requirement of the first dose of rescue analgesic.^[8] For VAS scoring, a 10-cm vertical line was used, marked out in millimeters. The patient was asked to indicate a spot on the line corresponding to his or her perceived intensity of pain at the moment, assuming that the lowest point on the line (0 mm) represented zero pain, whereas the highest point (100 mm) represented the worst pain imaginable. The distance from the origin of the line to the marked spot was then recorded. A fresh VAS scoring line was used at each assessment to ensure that the patient's opinion was not influenced by the position of an earlier mark. VAS scoring was noted at hourly intervals for 6 h after administration of the block. Rescue analgesia was administered if VAS was marked at 4 cm or more, as well as on patient demand. We administered injection diclofenac (aqueous form) as rescue analgesic, at a dose of 1.5 mg/kg body weight, intramuscularly.^[9] Total rescue analgesia requirement was also recorded.

Intraoperative and postoperative vital parameters and side effects

SBP, DBP, MAP, HR, respiratory rate, and SpO₂ were recorded immediately after subarachnoid block (0 min), thereafter at 1 min, 3 min, 5 min, 10 min, and then every 10 min up to 30 min, and every 30 min up to 180 min, followed by every 60 min up to 6 h after the block. Duration of surgery was also noted in all patients.

Decrease in the mean arterial BP more than 20% of the preoperative value was considered as hypotension and was treated with rapid infusion of 200 ml of crystalloids and incremental doses of 6-mg intravenous injection mephentermine.^[10] HR <50/min was considered as bradycardia and managed by immediate administration of 0.6-mg intravenous atropine.^[11] Respiratory rate <10/min and/or SPO₂ <90% were considered as respiratory depression which was treated with oxygen supplementation and assisted ventilation.^[12]

The condition of neonate was evaluated by the attending pediatrician by the assessment of Apgar scores at 1 and 5 min after delivery.^[13] Occurrence of any maternal side effects such as nausea, vomiting, and shivering was observed, recorded, and managed accordingly. Nausea and vomiting were managed with ondansetron 8 mg intravenously.

The sample size was decided based on a pilot study with ropivacaine, which indicated that approximately 17 patients should be included in each group in order to detect a 30-min difference in mean duration of motor blockade between the groups with type 1 error of 0.01 and power of 90%.^[14] Considering the above study as reference and using the power of study of 90% with 5% probability of α (type I) error, the sample size of our study was calculated to be 28.57 in each group. Further assuming a 5% dropout rate and for ease of calculation, we included thirty patients in each group.^[15] All raw data of the study parameters were entered into a Microsoft

Excel spread sheet and analyzed using IBM SPSS (Version 20.0, IBM Corp., Armonk, New York City, USA) software. Continuous variables were presented as mean $\pm$ standard deviation and categorical variables as number and percentage. Qualitative data were analyzed by Chi-square test, whereas quantitative data by independent sample *t*-test, and *P* < 0.05 was considered statistically significant.

RESULTS

Seventy-two patients were screened, of whom 12 were excluded because of violation of the inclusion criteria or lack of confidence in understanding and handling the VAS pain scoring. Sixty patients were randomized to receive the study drugs and thereafter completed the study without any exclusion or dropout. The patient disposal has been depicted in the Consolidated Standards for Reporting Trials style flow diagram in Figure 1.

The collected data were presented as mean $\pm$ standard deviation and subsequently subjected to intergroup analysis. Patients' demographic variables (age, height, weight, ASA physical status, and duration of surgery) and the neonates' Apgar score (at 1 min and 5 min) were comparable and statistically insignificant, as illustrated in Table 1.

MAP decreased in both the groups, with the maximum recorded fall being 12.56% in Group B between 3 and 10 min and 11.85% in Group R between 3 and 5 min after the subarachnoid block. The comparison was statistically insignificant, and none of the patients had hypotension as per the definition [Figure 2]. There was not much variation in the HR compared to the baseline in both the groups [Figure 3]. Adequate level of sensory analgesia was achieved in all patients before surgery. The mean time of onset of sensory block was 4.20 ± 0.805 min in Group B and 4.33 ± 0.844 min in Group R. The comparison of mean time of sensory block to reach the highest sensory level (Group B: 8.60 ± 1.589 min, Group R: 9.0 ± 2.034 min), two-segment regression of block (Group B:

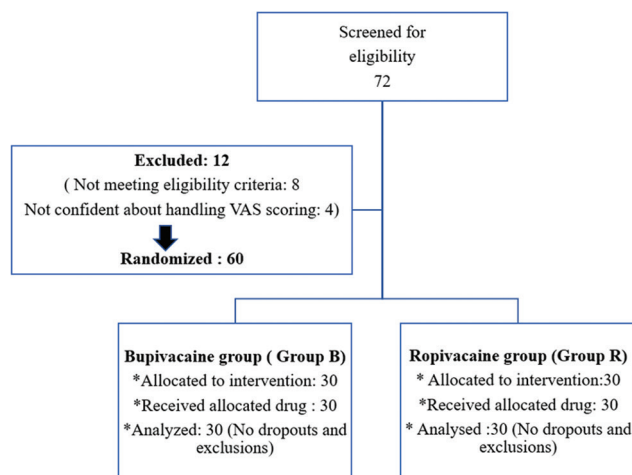


Figure 1: Flowchart showing patient disposal in the study

79.33 $\pm$ 6.915 min; Group R: 78.10 $\pm$ 6.960 min), and total duration of sensory block (Group B: 176.15 $\pm$ 9.255 min; Group R: 173.50 $\pm$ 9.299 min) in two groups were statistically insignificant. The highest level of sensory block attained was comparable in both the groups [Table 2].

Bilateral complete block was observed in all patients. The mean onset of motor block of Group B was shorter than that of Group R (4.83 $\pm$ 0.834 min vs. 5.40 $\pm$ 0.675 min), whereas the mean duration of motor blockade in Group B was longer than that of Group R (154.50 $\pm$ 8.770 min vs. 124.17 $\pm$ 8.915). Both the comparisons were statistically significant ($P = 0.005$ and $P = 0.001$, respectively) [Table 2]. The intensity of postoperative analgesia as per VAS score and time for first requirement of rescue analgesia were comparable and statistically insignificant in both the groups [Figure 4 and Table 3, respectively].

The deleterious effects of SA such as hypotension or bradycardia were not noted in any parturient. Equal number of patients experienced shivering (three each) and vomiting (two each) in both the groups, while only one patient in Group B reported nausea as compared to two patients in Group R ($P = 0.157$ for all these events).

DISCUSSION

Ropivacaine, an S-enantiomer of bupivacaine, as compared to the latter, has lower potential for cardiac and central nervous

systemic toxic effects and shows greater differentiation between sensory and motor blockade with more hemodynamic stability.^[16] Early ambulation, complete recovery with minimum side effects, and adequate fetal safety profile are desirable in parturients undergoing LSCS under SA. Previous studies have demonstrated the safety, efficacy, and tolerability of ropivacaine in SA for cesarean section.^[17]

Khaw *et al.*, in a dose-finding study, assessed the dose response of isobaric spinal ropivacaine for elective cesarean sections and found the ED₅₀ and ED₉₅ of spinal ropivacaine to be 16.7 mg (14.1–18.8) and 26.8 mg (23.6–34.1), respectively.^[18] We used 18.75 mg of isobaric ropivacaine (2.5 ml of 0.75%) and 12.5 mg of isobaric bupivacaine (2.5 ml of 0.5%) in our present study based on the rationale that the duration of action of ropivacaine in SA is approximately 50% to 67% that of bupivacaine.^[19] Moreover, all our patients were term parturient, hence the volume of drug played a major role in the cephalad spread of the drug and the height of the block.^[20] The above dosages were found to be adequate for elective cesarean section and the surgery was completed successfully with no maternal or neonatal adverse effects.

The hemodynamic changes produced in both the groups were comparable, and the findings were consistent with a previous study by Chari *et al.*^[21] Both the groups showed a slight decrease in MAP after subarachnoid block, and the maximum fall of MAP from baseline value was 12.56% in Group B and 11.85% in Group R, therefore none of the patients in this study had hypotension as per the definition. On the contrary, Gunaydin and Tan^[22] found in a similar study that both the isobaric and hyperbaric ropivacaine groups required less ephedrine than the isobaric and hyperbaric bupivacaine groups.

The characteristics of sensory block namely the onset of the block, time to reach the highest level of the block (T3/T4 thoracic segment), time for two-segment regression, and the total duration of block were comparable in both bupivacaine and ropivacaine groups. Our findings seconded those obtained by Kasza *et al.* who in a previous study compared intrathecal hyperbaric bupivacaine and hyperbaric ropivacaine in cesarean section.^[23]

Table 1: Demographic profile of patients and APGAR score of neonates (mean $\pm$ standard deviation)

Demographic parameters	Group B (bupivacaine)	Group R (ropivacaine)	P
Age (years)	25.07 $\pm$ 3.571	24.23 $\pm$ 3.655	0.375
Height (cm)	156.17 $\pm$ 2.878	156.07 $\pm$ 2.912	0.894
Weight (kg)	61.03 $\pm$ 3.296	61.73 $\pm$ 4.266	0.484
ASA status (I/II)	22/8	25/5	0.356
Duration of surgery (min)	46.43 $\pm$ 6.58	45.77 $\pm$ 7.79	0.722
APGAR at 1 min	8.13 $\pm$ 0.507	8.07 $\pm$ 0.450	0.592
APGAR at 5 min	9.10 $\pm$ 0.305	9.10 $\pm$ 0.301	1.000

ASA=American Society of Anesthesiologists

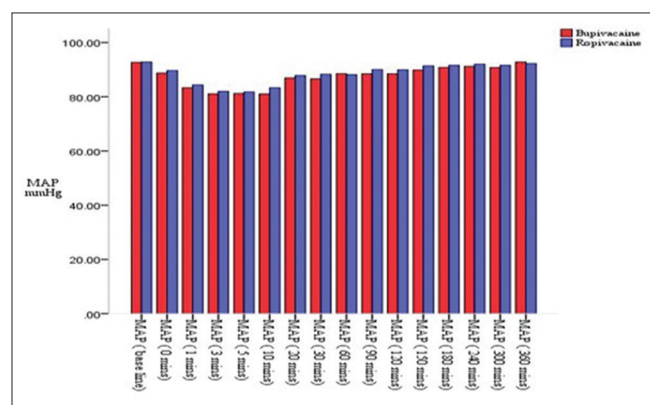


Figure 2: Perioperative variations in mean arterial pressure in the study groups

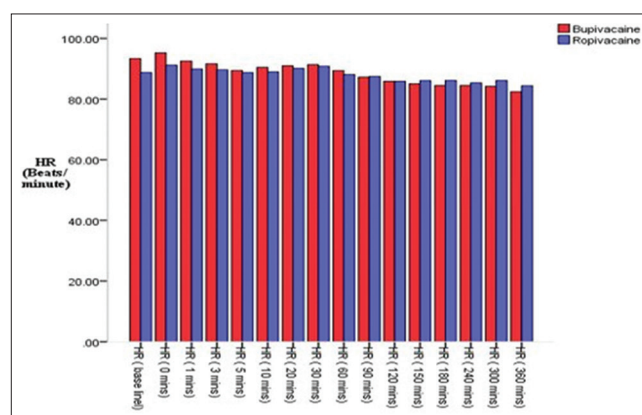


Figure 3: Perioperative variations of heart rate in the study groups

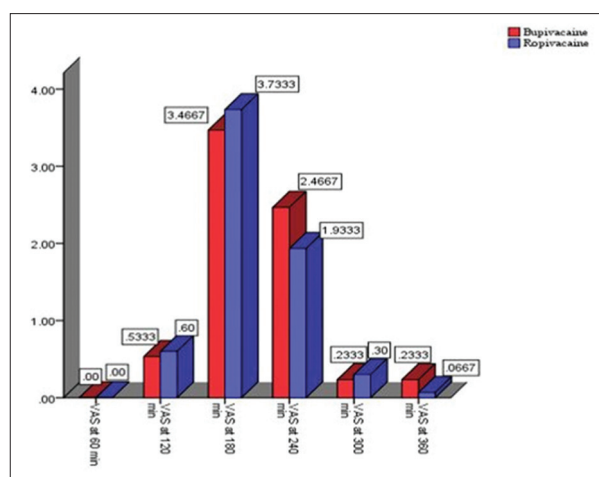
Table 2: Sensory and motor block profile (mean±standard deviation)

Parameters of sensory and motor blockade	Group B (bupivacaine)	Group R (ropivacaine)	P
Onset of sensory block (min)	4.20±0.085	4.33±0.844	0.534
Maximal sensory level reached (T3/T4)	15/15	21/9	0.114
Time taken to reach maximal sensory level (min)	8.60±1.589	9.00±2.034	0.399
Time taken for two-segment regression (min)	79.33±6.915	78.10±6.960	0.494
Total duration of sensory block (min)	176.17±9.255	173.50±9.299	0.270
Onset of motor block (min)	4.83±0.834	5.40±0.675	0.005
Total duration of motor block (min)	154.50±8.770	124.17±8.915	0.001

T=Thoracic vertebral level

Table 3: Rescue analgesia requirement (mean±standard deviation)

Time of requirement of Rescue Analgesia	Group B (bupivacaine)	Group R (ropivacaine)	P
Time of requirement of first dose of rescue analgesia (min)	208±30.445	200±28.765	0.300

**Figure 4:** Postoperative Visual Analog Scale scores at different time intervals in the study groups

In our study, all patients achieved motor blockade of the grade of Bromage Score IV prior to surgery. The mean onset time of motor blockade was quicker in Group B (4.83 ± 0.834 min) than Group R (5.40 ± 0.675 min), and this difference was found to be statistically significant with $P = 0.005$, whereas the mean total duration of motor blockade was shorter in Group R (124.17 ± 8.915 min) compared to Group B (154.50 ± 8.770 min), and the difference between the duration of motor blockade in the two groups was statistically highly significant with $P = 0.001$ [Table 2]. Similar results were obtained by Chari *et al.* who compared isobaric ropivacaine 0.75% and hyperbaric bupivacaine 0.5% in subarachnoid block for lower abdominal surgeries and found significantly delayed onset and shorter duration of motor block in ropivacaine group compared to bupivacaine group.^[21] Contrary to our study, Kasza *et al.*^[23] and Koltka *et al.*^[24] as well found no difference in the onset time of motor block between the bupivacaine and ropivacaine groups in a similar study. Our findings on total duration of motor block in Group B corroborated well with the studies of Layek *et al.*^[5] and Chari *et al.*,^[21] who also found significantly prolonged motor blockade in bupivacaine group

compared to the ropivacaine group. This result can be well explained by the inherent property of differential blockade of ropivacaine (sensory block>>motor block), due to its low lipid solubility and inability to penetrate the large myelinated motor fibers.

In the present study, no significant differences were noted, with respect to the surgical anesthesia in both groups. None of the parturients had any significant adverse effect nor presented with either postdural puncture headache or neurologic symptoms at subsequent postoperative visit. Both the groups remained comparable at all observation time points with respect to the incidences of minor side effects such as nausea, vomiting, and shivering as well as the postoperative analgesia denoted by VAS scores.

The neonatal outcome was satisfactory and comparable in both the study groups. However, the limitation of our study was that we assessed neonatal outcome by Apgar score only and did not include umbilical cord blood gas values and pH neither the uteroplacental blood flow. Hence, we were unable to comment further on the changes of uteroplacental perfusion, if any.

CONCLUSION

Intrathecal isobaric ropivacaine 0.75% (18.75 mg) provided clinically effective anesthesia for elective LSCS with shorter duration of motor blockade, similar duration of sensory blockade, height of blockade, hemodynamics, and adequate postoperative analgesia. This helped in allowing early ambulation and improved patient satisfaction, and therefore this drug can be used as an efficient and safe alternative to the more frequently used bupivacaine, in our daily practice.

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Conflicts of interest

There are no conflicts of interest.

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