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Original Research Article

# Comparative Study between Intrathecal Hyperbaric Ropivacaine (0.75%) And Hyperbaric Bupivacaine (0.05%) with Fentanyl as an Adjuvant in Patients under Going Elective Caesarean Section: Randomized Double-Blind Clinical Trial

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**Conflict of interest: Nil**

**Abstract:**

**Aim:** To compare hyperbaric spinal Ropivacaine to hyperbaricspinal Bupivacaine with Fentanyl as an adjuvant for elective caesarean delivery in a prospective, randomized, double blinded study.

**Materials and Methodology:** A total of 66 parturients for elective caesarean deliveries received either 15 mg of hyperbaric Ropivacaine (0.75%) (N = 33) or 10 mg of hyperbaric Bupivacaine (0.05%) (N= 33) with 10µg of Fentanyl. Thesensory and motor blockades were assessed and compared between the groups. Surgeons and patients' satisfaction were also noted.

**Result:** The two groups had similar demographics, and similar timefor onset sensory block to T6 and peak level but duration of sensory block was less in Group R compared to Group B (P<0.001). Total duration of motor blockade was also less in Ropivacaine group (P<0.001) leading to early ambulation and increase the patients and surgeons' satisfaction score.

**Conclusion:** In this prospective, double-blind study, 15 mg of hyperbaric Ropivacaine (0.75%) proved as effective as 10 mg of hyperbaric Bupivacaine (0.05%) for spinal anaesthesia during caesarean sections. Patients who received Ropivacaine reported higher satisfaction levels, especially regarding early ambulation, as rated by both surgeons and patients.

**Keywords:** Hyperbaric Ropivacaine (0.75%), Ambulation, Caesarean section, spinal anaesthesia.



## Introduction

Spinal Anaesthesia (Sub-Arachnoid Block - SAB) represents a well-established and secure approach for administering anaesthesia during caesarean sections (CS). This method is distinguished by its capacity to induce effective sensory and motor blockade, rapid onset of action, minimal adverse effects on neonatal well-being, and superior regulation of cardiovascular and stress responses [1]. The prevalent practice for spinal anaesthesia in caesarean sections involves utilizing a racemic mixture of hyperbaric Bupivacaine, primarily due to its controlled diffusion facilitated by gravitational forces, resulting in a swifter onset of anaesthesia [2]. Bupivacaine is a commonly employed agent for spinal anaesthesia during caesarean deliveries. Recently, Ropivacaine has gained prominence due to its enhanced selectivity in blocking sensory nerve fibres over motor fibres, as well as its reduced propensity for cardiac toxicity in overdose situations [3]. Both Ropivacaine and Bupivacaine are categorized within the amino-amide class of local anaesthetic compounds. While they share a common mechanism of action with other local anaesthetics, they exhibit distinct disparities in their structural, physiochemical, pharmacokinetic, and pharmacodynamic attributes [4-6]. Ropivacaine is characterized by its enantiomerically pure composition, specifically the S-enantiomer, whereas Bupivacaine comprises a racemic mixture of two enantiomers (R and S) within the same class.

Although structurally akin to Bupivacaine, Ropivacaine is associated with reduced neurotoxicity and cardiac toxicity [7,8].

Ropivacaine is a local anaesthetic characterized by structural and pharmacodynamic attributes akin to those of Bupivacaine [9,10]. Numerous investigations have been undertaken for a comparative analysis of Ropivacaine and Bupivacaine concerning their utilization in spinal anaesthesia among obstetric patients undergoing caesarean deliveries [11-13]. Although there were variations in the administered doses of Ropivacaine, Bupivacaine, and Morphine across the three studies, all consistently reported favorable intraoperative anaesthetic conditions. Notably, Danelli et al. [11] noted a shorter duration of sensory blockade with Ropivacaine, whereas Ogun et al. [12] did not discern any disparity in the regression time of sensory blockade when comparing isobaric solutions of Ropivacaine and Bupivacaine.

When intrathecal administration of Bupivacaine and Ropivacaine, in conjunction with 10 µg Fentanyl and 200 µg Morphine, was employed for caesarean sections, the median effective dose of 50% (ED50) and ED95 values for 0.5% isobaric Bupivacaine were calculated at 7.25 mg and 13 mg, respectively. In contrast, for isobaric Ropivacaine, the corresponding ED50 and ED95 values were 16.7 mg and 26.8 mg, respectively [14]. However, it is important to note that the determination of equipotent doses of intrathecal Ropivacaine and Bupivacaine remains a topic of ongoing debate within the scientific community [11,15]Therefore, the aim of this study was to conduct a comparative analysis of the efficacy of intrathecal hyperbaric Ropivacaine (0.75%)and hyperbaric Bupivacaine(0.05%), in conjunction with Fentanyl (10 µg) as an adjuvant, in elective caesarean sections. Our assessment encompassed an evaluation of the intraoperative anaesthetic quality, effectiveness, and duration of both sensory and motor blockades. Furthermore, we sought to gather feedback from both surgical practitioners and patients to comprehensively gauge the outcomes.

**Materials and Methodology**

This prospective, double-blind, randomized trial was conducted at the GMERS Medical College and Hospital,a tertiary care teaching hospital in Gotri, Vadodara, Gujarat, India, for a six-months duration. The study protocol received approval from the institute's Ethics Committee (IHEC/23/OUT/FR0014).

A total of 66 term parturients with uncomplicated pregnancies, scheduled for elective caesarean delivery, were recruited after obtaining their written informed consent. The inclusion criteria comprised parturients with ASA status II, aged 18-40 years. Those with hypersensitivity to local anaesthetics, short stature (<140 cm), contraindications to neuraxial block, twin pregnancies, or obstetric complications such as pre-eclampsia, antepartum haemorrhage, Placenta previa/ Placental abruption, or foetal compromise were excluded. A principal investigator conducted the enrolment after a comprehensive pre-anaesthetic assessment. Subsequently, participants were randomly assigned to either Group Bor Group R, employing a computer-generated list of random numbers, followed by concealed group allocation using sealed opaque envelopes.

After a fasting period of 12 hours for solids and 2 hours for clear liquids, an 18G intravenous (i.v.) cannula was secured then Inj.Ondansetron 0.08mg/kg was given to the parturient 1 hour prior to surgery. In the operating theatre, the sealed envelope was handed over to the junior resident who attached all the monitors to the parturient (electrocardiogram, pulse oximetry, and non-invasive blood pressure). The parturient baseline heart rate (HR), systolic, diastolic, and mean blood pressure (SBP, DBP, and MBP) were recorded and co-loaded with 10 mL/kg of Ringer's lactate solution within 20 minutes. The drug syringes for the spinal block were prepared by the junior resident as per the group allotted in the sealed envelope, following which the resident was not further involved in the study.

Under all aseptic and antiseptic precautions, the patient was placed in the left lateral decubitus position, and a subarachnoid block was attempted with a 25G Quincke spinal needle in the L2-L3 or L3-L4 interspace using a midline approach. A total of 2.2 ml of the drug was injected at a rate of 0.2 ml/sec after ensuring the free flow of cerebrospinal fluid from the needle, as per their randomization.

Subsequently, the patient was immediately turned supine, and a wedge was placed below the right flank to achieve left uterine displacement, creating a 15-degree uterine tilt. All patients received supplemental oxygen through a transparent face mask at a flow rate of 5L/min. At the time '0,' which was considered the end of the intrathecal injection, an assessment of the sensory and motor characteristics of the subarachnoid block, along with vital signs, was conducted at 1-minute intervals initially, followed by 2-minute intervals. This assessment continued until surgical anaesthesia was achieved by the anaesthesiologist who performed the block.The segmental level of sensory block, determined by response to pinprick, was assessed bilaterally along the midclavicular line. The time to the onset of sensory block at level L1 and the maximum level attained was recorded.The degree of motor blockade was evaluated using the Modified Bromage scale. Induction of anaesthesia was considered achieved when at least the T6 dermatome was anesthetized.

At the conclusion of the surgery, the duration of the surgical procedure and surgeons satisfaction score (in terms of bleeding, muscle relaxation) were recorded. The patient was transferred to the Post Anaesthesia Care Unit (PACU). In the PACU, patients underwent monitoring at 15-minute intervals until regression of sensory and motor blockade was observed. Patients were instructed to indicate the intensity of pain on the Numerical Rating Scale (NRS), as explained preoperatively. Complete analgesia was defined as the time duration from 'time 0' to the first complaint of pain, while effective analgesia was defined as the time duration from 'time 0' to an NRS score of ≥4, at which point rescue analgesia with Inj. Tramadol 2 mg/kg was administered. Subsequently, this rescue analgesic was repeated every 8 hours within the first 24 hours. In cases where patients demanded analgesia and their NRS score was ≥4 within half an hour of receiving the rescue dose, Inj. Diclofenac Sodium 75mg i.v. was administered. Postoperatively, patients were continuously monitored for complications and adverse events for up to 24 hours. In instances where patients experienced nausea and vomiting, Inj. Ondansetron 0.08 mg/kg was administered. Patients with failed blocks or those with inadequate or incomplete blocks, were excluded from the study.

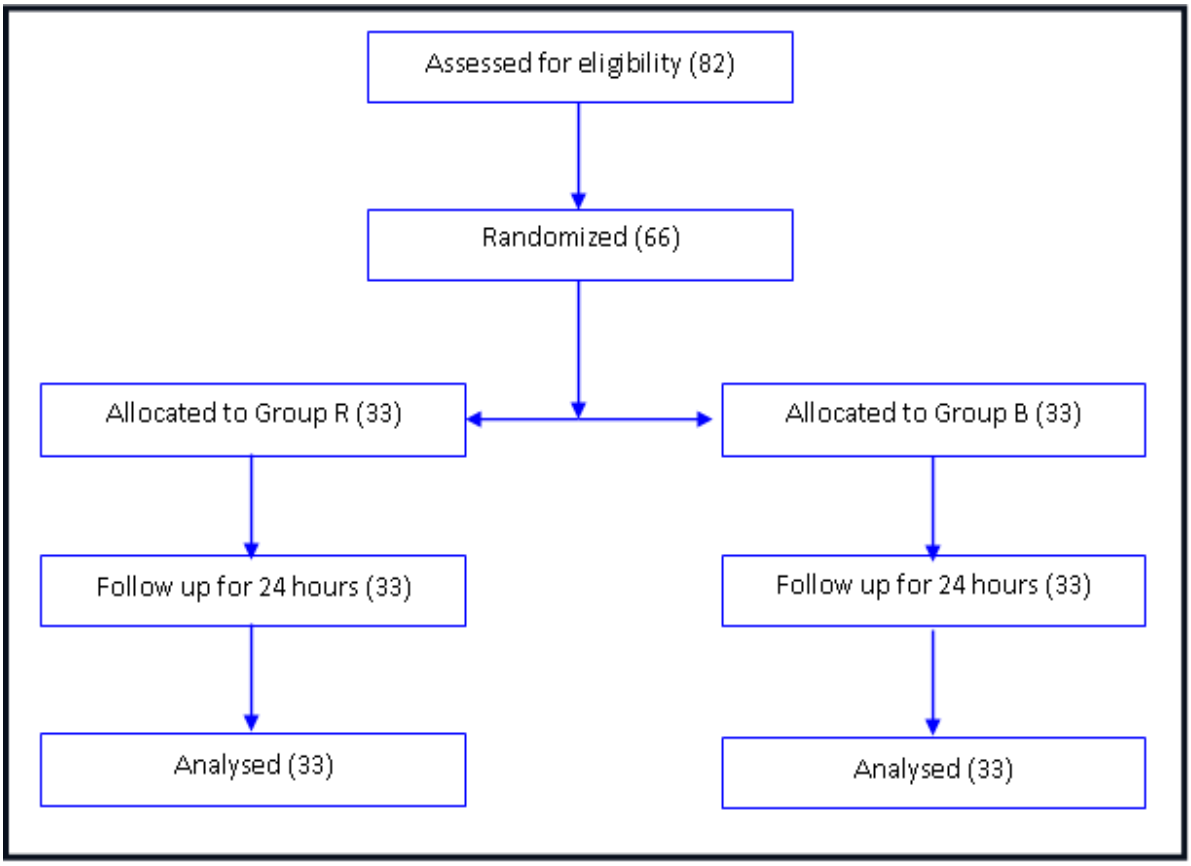


**Figure 1: CONSORT chart of the study**

**Statistical Analysis**

Based on a pilot study involving 10 cases (5 in each group), a sample size of 60 participants was determined through power analysis using Statulator. This calculation aimed to achieve a statistical power of 80% with a significance level of 5% for the detection of a true difference of 1.5 minutes in the mean onset time between the two groups.

Consequently, a total of 66 patients were enrolled in the study, with 33 allocated to each group, accounting for potential dropouts or cases lost to follow-up. Statistical analysis was done using SPSS software16.0.Data obtained was tabulated in the form of Mean± Standard deviation and analysed with Chi-square test for proportion and unpaired t-test for Quantitative data and non-parametric data were compared using Mann –Whitney U test.

**Result**

All 66 enrolled patients successfully concluded the study. Notably, no significant disparities were observed in terms of age, weight, height, gestational age, the interval from the initiation of spinal anaesthesia to surgery, or the duration of the surgical procedure when comparing the two groups, as summarized in Table 1.

**Table 1: Demographic data of Study groups**

| Variables | Group R | Group B | P value |
|---|---|---|---|
| Age (Years) | 25.6 ± 3.51 | 26.4 ± 5.07 | 0.61 |
| Weight (Kg) | 70.6 ± 10.2 | 71.9 ± 9.81 | 0.46 |
| Height (cm) | 162.71 ± 3.52 | 163.04 ± 2.83 | 0.81 |
| ASA Status II | 33 | 33 | 0.99 |
| Duration of Surgery | 54.71 ± 8.34 | 53.20 ± 9.11 | 0.18 |
| Gestational age Weeks | 37.7 ± 1.6 | 38.1 ± 1.2 | 0.12 |

The characteristics of the block in both groups were detailed in Table 2. The onset of sensory blocks exhibited comparable profiles in both groups. However, a statistically significant difference was observed in the onset of motor block when the Bupivacaine and Ropivacaine groups were compared, as illustrated in Table 2.

Furthermore, it is noteworthy that the regression of both sensory and motor blocks occurred at a swifter rate in the Ropivacaine group ($p<0.001$). Surgeon and patients' satisfaction score were described in the table 2. Both have more satisfaction with the Ropivacaine as compare to Bupivacaine but only patient satisfaction reached to statistically significant level.

Effective analgesia in terms of 1st Rescue analgesia time was prolonged in Group B as compared to Group R ($p<0.05$) as shown in table 2. The incidence of bradycardia, and hypotension were not different intraoperativeor post-operative in both the groups. (Table 3) Intraoperative Heart rate, MAP, NRS score were describe in the figure 2,3 and 4 respectively which were comparable at all the times and statistically non-significant.

**Table 2: Sensory and Motor parameters with surgeon and patients' satisfaction score**

| | Variables | Group R | Group B | P value |
|---|---|---|---|---|
| Sensory | Onset (L1) | 1.37 ± 0.28 | 1.49 ± 0.41 | 0.38 |
| | T10 | 1.78 ± 0.15 | 1.93 ± 0.23 | 0.32 |
| | Peak | 4.41 ± 0.69 | 4.76 ± 0.71 | 0.17 |
| | Duration (min) | 156.25 ± 9.8 | 206.25 ± 13.68 | <0.001 |
| Motor | Onset (Bromage - I) | 1.65 ± 0.49 | 1.51 ± 0.38 | 0.05 |
| | Bromage - II | 2.84 ± 0.55 | 2.51 ± 0.41 | 0.01 |
| | Peak (Bromage -III) | 5.92 ± 0.69 | 5.21 ± 0.71 | 0.0003 |
| | Duration (min) | 140.12 ± 12.95 | 175.31 ± 18.66 | <0.001 |
| Analgesia | Duration of Analgesia(min) | 138.25 ± 27.44 | 146.75 ± 24.20 | 0.19 |
| | 1st rescue analgesia time(min) | 188.57 ± 9.33 | 250.14 ± 12.62 | <0.05 |
| Surgeon Satisfaction score | Excellent | 33 | 32 | 0.99 |
| | Satisfactory | 0 | 1 | |
| | Unsatisfactory | 0 | 0 | |
| Patient's satisfaction score | Excellent | 32 | 23 | <0.05 |
| | Very Good | 1 | 8 | |
| | Good | 0 | 2 | |
| | Fair | 0 | 0 | |
| | Poor | 0 | 0 | |

**Table 3: Complications and rescue analgesia**

| Side Effects | Group R | Group B |
|---|---|---|
| Bradycardia | 00 | 01 |
| Hypotension | 01 | 01 |
| Shivering | 00 | 00 |
| Vomiting | 00 | 00 |

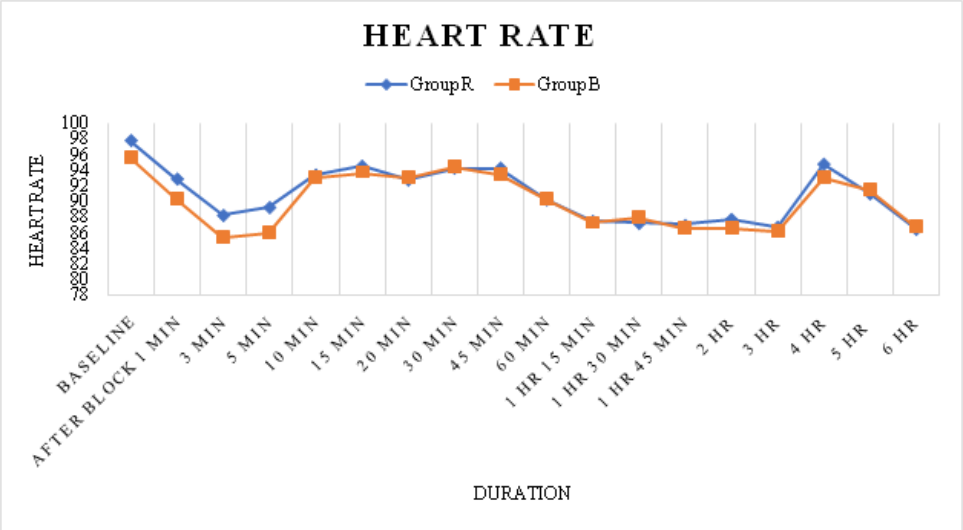


**Figure 2: Comparison of Heart Rate between Group R and Group B**

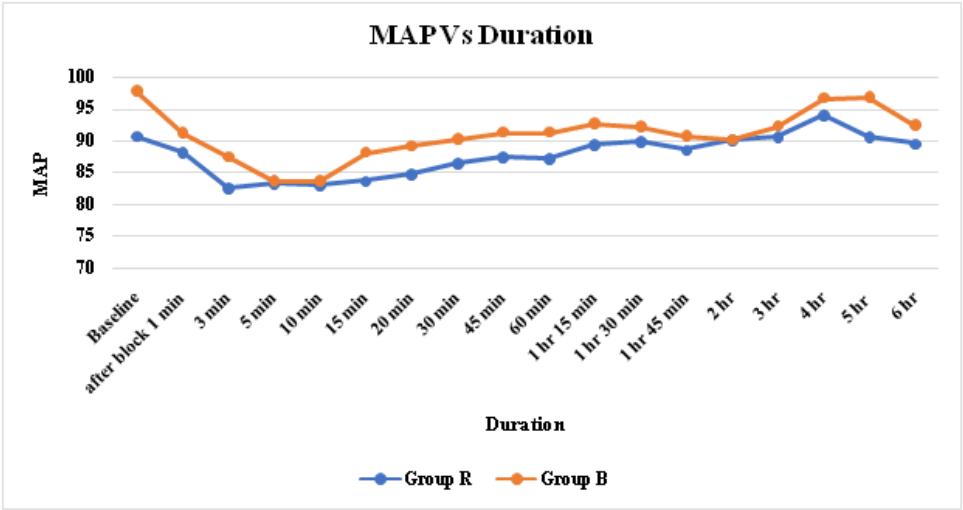


**Figure 3: Comparison of Mean Arterial Pressure between Group R and Group B**

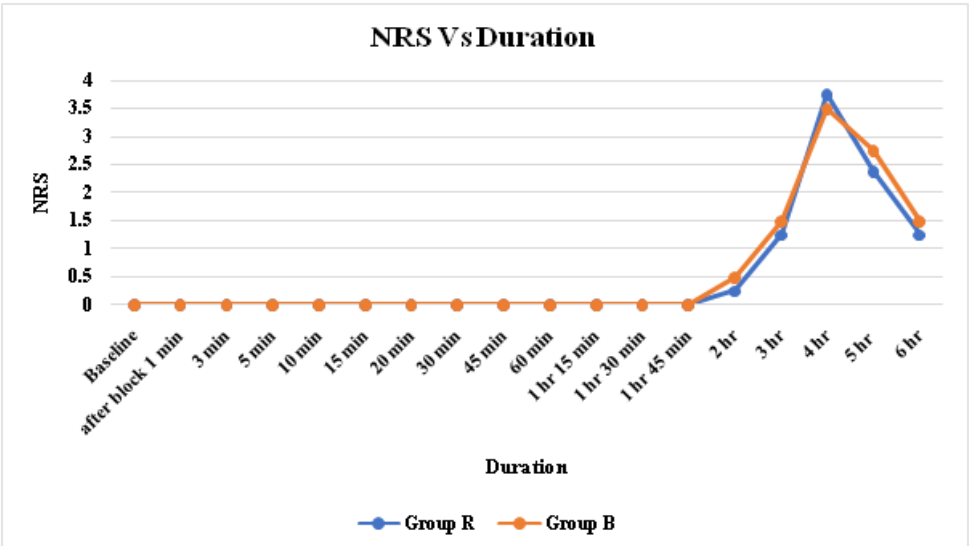


**Figure 4: Comparison of Mean NRS Score between Group R and Group B**

## Discussion

In this prospective, double-blind, randomized study, our findings indicated that the administration of 15 mg of hyperbaric spinal Ropivacaine (0.75%) in combination with 10 µg of Fentanyl resulted in the attainment of effective clinical anaesthesia characterized by a shorter duration of sensory and motor block. This outcome was in comparison to the administration of 10 mg of hyperbaric Bupivacaine (0.05%) with an equivalent opioid dosage, in the context of elective caesarean delivery. Notably, the patients who received Ropivacaine exhibited significantly higher levels of satisfaction, a facet previously unreported in the literature. Furthermore, the quality of intraoperative muscle relaxation, as rated by obstetricians, was consistently deemed excellent in all patients who received spinal Ropivacaine.

In the current investigation, the time required to achieve sensory onset up to the T10 level in Group R (1.78 ± 0.15 min) exhibited a degree of similarity with that observed in Group B (1.93 ± 0.23 min), with a resulting insignificant P value of 0.32.These findings align with the results of a study conducted by Al-Abdulhadi O et al., which involved a comparative evaluation of intrathecal hyperbaric Bupivacaine and hyperbaric Ropivacaine for caesarean sections. In that study, the time taken to achieve sensory onset up to the T10 level was reported as 1.88 ± 0.89 min for Bupivacaine and 1.96 ± 1.18 min for Ropivacaine, with no significant differences noted [16]. Similarly, Malinovsky et al. and Erturk et al. investigated the use of intrathecal Ropivacaine and Bupivacaine in dose ratios of 3:2 for urological and orthopedic surgeries, respectively. Their findings indicated that these agents provided comparable anaesthesia levels [3,17] In our institutional practice, the duration of a caesarean section typically averages 58 minutes. The administration of spinal Ropivacaine has demonstrated the production of a sufficiently prolonged block. The inclusion of an opioid, in this case, Fentanyl alongside hyperbaric Ropivacaine has shown potential for enhancing the quality of anaesthesia, mirroring the effects seen when adding an opioid to hyperbaric Bupivacaine [18]. The effectiveness of clinical anaesthesia achieved in our study aligns with the findings of prior investigations conducted by Danelli et al. and Chung et al. [11,13]. It is worth noting that the dose of spinal Ropivacaine employed in our study, which was 15 mg, differs from that used in previous studies, where dosages of 20 mg and 18 mg were administered [11,13]. Furthermore, it is important to highlight that, unlike previous investigators who solely incorporated Morphine, our study incorporated Fentanyl into the spinal solution.

The onset of motor block in the hyperbaric Bupivacaine group was notably swifter when compared to the hyperbaric Ropivacaine group. Conversely, the regression of both sensory and motor blocks occurred at a quicker pace in the Ropivacaine group in contrast to the Bupivacaine group. Additionally, within the Bupivacaine group, the regression of sensory block was observed to outpace that of motor block, while in the Ropivacaine group, motor block regressed faster than sensory block. Notably, the duration of analgesia was slightly prolonged in the Bupivacaine group.

These findings affirm that spinal Bupivacaine exhibits greater potency than Ropivacaine in terms of motor block onset, sensory and motor block regression, as well as the duration of analgesia. This difference may be attributed to the lower lipid solubility of Ropivacaine, resulting in a more gradual penetration of the drug into the large myelinated A fibres compared to the more lipid-soluble Bupivacaine [19]. Comparable outcomes were reported in studies conducted by Singh et al. [20], Chung et al. [13], Danelli et al. [11], Eryilmaz et al. [14], Bhat et al. [21], Chari et al. [22], Al-Abdulhadi O et al. [16], and Ingale et al. [23].That longduration of action delays recovery of motor function and prolongspostanaesthetic care unit stay after delivery while Ropivacaine provided early ambulation [16].Intraoperative complications as hypotension, bradycardia, shivering and others as nausea, vomiting and headache were found in few patients in both groups but with no significant difference and treated accordingly. Similar findings were in the study done byAl-Abdulhadi O et al. [16].

## Conclusion

This prospective, randomized, double-blind study has recognized that the administration of 15 mg of hyperbaric Ropivacaine (0.75%) yields spinal anaesthesia of comparable effectiveness to that achieved with 10 mg of hyperbaric Bupivacaine (0.05%) during caesarean section procedures. Notably, patients who received Ropivacaine reported significantly greater satisfaction levels in surgeons and patients both, particularly in patients with regard to early ambulation.

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