



Anaesthesiology

COMPARATIVE EVALUATION OF INTRATHECAL ANAESTHETIC EFFICACY OF COMBINATION OF HYPERBARIC LEVOBUPIVACAINE WITH MORPHINE VERSUS HYPERBARIC BUPIVACAINE WITH MORPHINE IN CAESAREAN SECTION - A DOUBLE BLINDED RANDOMIZED CONTROL TRIAL

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ABSTRACT **Background And Aim:** Bupivacaine and Levobupivacaine are stereoisomers, with Bupivacaine containing adextro isomer, which is more likely to cause fatal dysrhythmias. In contrast, Levobupivacaine is the pure L (-) enantiomer of Bupivacaine and does not contain dextro isomers, resulting in significantly reduced arrhythmogenic potential compared to the racemic mixture. Notably, both Levobupivacaine and Bupivacaine are now available in Hyperbaric formulations. The aim of our study was to compare the efficacy of Hyperbaric Bupivacaine 0.5% with morphine and Hyperbaric Levobupivacaine 0.5% with morphine for spinal anaesthesia in elective caesarean sections. The comparison focused on intraoperative efficacy, including the quality of anaesthesia, postoperative analgesia, and associated adverse effects. **Methods:** 90 parturients posted for elective caesarean section belonging to ASA-II were randomly grouped using SNOSE technique into Group L- who received 2ml of 0.5 % Hyperbaric Levobupivacaine with Morphine 100mcg and Group B received 2ml of 0.5 % Hyperbaric Bupivacaine with Morphine 100mcg administered intrathecally in sitting posture. The parturient was made to lie down in supine posture with 10 cm wedge underneath the right buttock. The study assessed the onset time and duration of sensory and motor blockade, time required to reach height of sensory blockade at T4, postoperative analgesia, and any associated adverse effects. **Result:** There was no significant difference between the groups in terms of age, height, weight, or BMI. The mean time for the onset of Bromage III was 2.68 ± 0.54 minutes in the Bupivacaine group, whereas in the Levobupivacaine group, it was 3.19 ± 0.40 minutes ($p < 0.05$). The mean time for achieving analgesia to pinprick at T10 was 3.10 ± 0.55 minutes in the Bupivacaine group, compared to 3.76 ± 3.39 minutes in the Levobupivacaine group ($p < 0.05$). The mean time to reach the maximum height of analgesia at T4 was 5.10 ± 0.45 minutes in the Bupivacaine group, while in the Levobupivacaine group, it was 5.75 ± 0.40 minutes ($p < 0.05$). The mean time for recovery to Bromage 0 was significantly longer in the Bupivacaine group (200.4 ± 41.6 minutes) compared to the Levobupivacaine group (155.5 ± 35.2 minutes) ($p < 0.05$). The total duration of postoperative analgesia without the need for rescue analgesia was also longer in the Bupivacaine group (560.3 ± 68.6 minutes) than in the Levobupivacaine group (458.1 ± 58.5 minutes). The Visual Analog Scale (VAS) scores for pain intensity were 2.2 ± 0.7 for Bupivacaine and 2.0 ± 0.8 for Levobupivacaine, with a p-value of 0.104, indicating a clinically notable but not statistically significant difference. Furthermore, the frequency of rescue analgesia use was 11 patients (24.4%) in the Bupivacaine group and 8 patients (17.8%) in the Levobupivacaine group. Perioperative hemodynamic stability was more pronounced in the Levobupivacaine group, with a significant p-value of < 0.05 , and was associated with fewer adverse effects compared to the Bupivacaine group. **Conclusion:** Our study demonstrated that hyperbaric levobupivacaine with intrathecal morphine offers better hemodynamic stability compared to racemic bupivacaine with intrathecal morphine, with a significantly lower incidence of hypotension. While it had a slightly slower onset and shorter analgesic duration, postoperative pain scores remained comparable. The levobupivacaine group required less rescue analgesia, indicating a favorable pharmacodynamic profile. These findings support its use in patients needing stable hemodynamics and early recovery. Further studies should explore dose optimization for enhanced outcomes in fast-track surgical care.

KEYWORDS : Cesarean Section; Spinal Anesthesia; Bupivacaine; Levobupivacaine; Morphine.

INTRODUCTION

The American Society of Anesthesiologists Task Force on Obstetric Anaesthesia recommends neuraxial techniques over general anaesthesia (GA) for most lower-segment caesarean sections (LSCS). Spinal anaesthesia (SA) is the preferred neuraxial approach because it provides reliable surgical conditions, avoids airway manipulation in parturients who frequently present with a difficult airway and a 'full stomach,' and reduces exposure to systemic anaesthetics. Compared with GA, SA facilitates effective analgesia and muscle relaxation while the mother remains awake, thereby minimizing fetal exposure to maternal anaesthetic drugs, improving early postoperative analgesia, and enabling immediate mother and infant bonding. A single-shot spinal is also fast and technically straightforward, yields a dense block with a low failure rate ($< 1\%$), and is cost-effective.

Bupivacaine, introduced in 1963, has been the most widely used intrathecal local anaesthetic for LSCS. Conventional bupivacaine is a racemic mixture; its dextro isomer exhibits higher affinity for cardiac sodium channels and has been implicated in serious cardiotoxicity. Levobupivacaine, the pure S(-) enantiomer, demonstrates a more favourable safety profile in animal and clinical studies, with lower rates of seizures and cardiovascular collapse. However, it is modestly less potent, with a shorter sensory block and a less intense motor block compared with racemic bupivacaine. Baricity influences intrathecal drug spread and block characteristics. Hyperbaric solutions generally

provide more predictable cephalad spread, longer duration of clinically useful anaesthesia, and faster regression with earlier motor recovery than plain solutions.

In India, hyperbaric bupivacaine has long been available for spinal anaesthesia, whereas hyperbaric levobupivacaine 0.5% entered the market only recently. Consequently, most prior comparisons between bupivacaine and levobupivacaine in LSCS examined isobaric preparations. Evidence on hyperbaric levobupivacaine in obstetric spinal anaesthesia, particularly in combination with intrathecal opioids, remains limited in the Indian population. Intrathecal adjuvants, especially opioids, are routinely added to enhance block quality and extend postoperative analgesia while preserving autonomic and motor functions. Morphine, in low intrathecal doses, provides prolonged postoperative analgesia after caesarean delivery and is commonly paired with long-acting local anaesthetics. Nevertheless, hyperbaric bupivacaine alone may not sustain analgesia into the early postoperative period, necessitating supplemental analgesics; combining an opioid addresses this limitation.

Despite the clinical advantages of levobupivacaine and the introduction of its hyperbaric formulation, there is a paucity of evidence evaluating its use with intrathecal morphine in Indian obstetric practice. We hypothesize that hyperbaric levobupivacaine (0.5%) combined with morphine (100 μ g) will provide intraoperative

anaesthesia and postoperative analgesia that are at least comparable to, if not superior to, the conventional combination of hyperbaric bupivacaine (0.5%) with morphine (100 µg). The present study aimed to compare the efficacy of intrathecal hyperbaric bupivacaine 0.5% with morphine 100 µg and intrathecal hyperbaric levobupivacaine 0.5% with morphine 100 µg in parturients undergoing elective caesarean section. The primary objective was to assess intraoperative quality of anaesthesia, including onset, maximum sensory level, and duration of sensory and motor blockade. The secondary objectives were to evaluate hemodynamic stability (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure), postoperative pain, and the incidence of adverse effects.

MATERIALS AND METHODS

Study Design and Duration

This was a prospective, double-blind, randomized controlled trial conducted between July 2023 and February 2025 conducted at JSS hospital, Mysuru after getting approval from the institutional ethical committee.

Sample Size

Sample size was estimated based on previous literature, considering a standard deviation of 18.3 for Group 1 and 13.6 for Group 2, with a mean difference of 10. The calculated effect size was 0.6269. At a 5% alpha error and 80% power, the required sample size was 41 per group. Allowing for dropouts, 45 participants were included in each group, yielding a total of 90 parturients.

Study Population

Parturients aged 18-40 years with singleton pregnancies at 37-42 weeks of gestation, belonging to ASA physical status II, and scheduled for elective caesarean section under spinal anaesthesia at JSS Hospital, Mysore were included in the study. Women were excluded if they refused to participate, had multiple pregnancies, a body mass index (BMI) >30 kg/m², pregnancy-induced hypertension, gestational diabetes mellitus, spinal deformities, bleeding disorders, acute cardiovascular or respiratory illness, allergy to amide local anaesthetics, or any diagnosed psychiatric illness.

Randomization and Blinding

Participants were randomized into two groups using the shuffled sealed opaque envelope (SNOSE) technique. The anaesthesiologist performing the spinal anaesthesia was not involved in subsequent data collection. An independent observer, blinded to group allocation, recorded perioperative parameters. Parturients were also blinded to their group assignment:

- Group B (n=45): 10 mg (2 mL) of 0.5% hyperbaric bupivacaine with 100 µg morphine.
- Group L (n=45): 10 mg (2 mL) of 0.5% hyperbaric levobupivacaine with 100 µg morphine.

Morphine (10 mg/mL) was diluted with normal saline to 1 mg/mL and 0.1 mL (100 µg) was drawn for administration.

Conduct of Anaesthesia

All patients underwent standard pre-anaesthetic assessment 24 hours prior to surgery. Fasting guidelines were followed (6 hours solids, 2 hours clear fluids). IV access was secured before surgery. Standard monitoring included ECG, non-invasive blood pressure (NIBP), heart rate (HR), and pulse oximetry (SpO₂). Baseline SBP, DBP, MAP, HR, and SpO₂ were recorded. Spinal anaesthesia was performed with a 25G Quincke needle at the L2-L3 or L3-L4 interspace in the sitting position. Patients were immediately placed supine with a 10 cm wedge under the right buttock. Sensory block was assessed with pinprick, every minute for 10 minutes, then every 5 minutes until completion, and motor block was assessed using the Modified Bromage Scale (0-3). Surgery commenced once a sensory block to T4 was achieved.

Monitoring and Management

Heart Rate and Blood Pressure were recorded every 2 minutes for 15 minutes, every 5 minutes for the next 30 minutes, then every 30 minutes up to 2 hours. Hypotension (>20% fall in SBP) was treated with IV ephedrine 6 mg and bradycardia (HR <60 bpm) was treated with IV atropine 0.6 mg. Patients were monitored until complete recovery of motor and sensory function. All patients received IV paracetamol 1 g every 6 hours. Pain was assessed with the Visual Analog Scale (VAS) and IV diclofenac (1-1.5 mg/kg/day) was given if VAS score was ≥3. The primary outcomes were the time to onset of sensory block, time to maximum sensory block, duration of sensory

block and motor blockade assessed using the Modified Bromage Scale. Secondary outcomes included haemodynamic parameters, postoperative pain scores, and adverse effects.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using SPSS version 22 (IBM, Somers, NY, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed data were expressed as mean ± standard deviation and compared between groups using the independent samples t-test. Non-normally distributed data were presented as median (interquartile range) and compared using the Mann-Whitney U test. Categorical variables were expressed as frequencies and percentages, with intergroup comparisons performed using the chi-square test or Fisher's exact test as appropriate. Repeated haemodynamic measurements were analysed using repeated-measures ANOVA. A two-sided p-value <0.05 was considered statistically significant. The study was conducted and reported in accordance with the CONSORT checklist.

RESULTS

Table 1 shows the demographic and anthropometric characteristics of the study population. The mean age of participants was comparable between Group B (27.1 ± 4.3 years) and Group L (26.9 ± 4.1 years). Similarly, the mean height (154.6 ± 3.8 cm vs. 152.4 ± 4.8 cm), weight (63.3 ± 7.5 kg vs. 62.0 ± 7.3 kg), and BMI (26.2 ± 3.1 kg/m² vs. 25.8 ± 3.3 kg/m²) did not differ significantly between the two groups, indicating that baseline characteristics were well matched.

Table 1: Demographic and anthropometric profile of participants in Group B and Group L (N=90)

Variable	Group B (n=45) Mean (SD)	Group L (n=45) Mean (SD)
Age (in years)	27.1 (4.3)	26.9 (4.1)
Height (in cm)	154.64 (3.8)	152.4 (4.8)
Weight (kg)	63.33 (7.5)	62.02 (7.3)
BMI (kg/m ²)	26.2 (3.1)	25.8 (3.3)

In Table 2, Group B demonstrated a faster onset of analgesia, with a shorter time to achieve sensory block at T10 (3.10 ± 0.55 vs. 3.76 ± 3.39 min, p<0.01), motor block to Bromage III (2.68 ± 0.54 vs. 3.19 ± 0.40 min, p<0.01), and maximum sensory level at T4 (5.1 ± 0.45 vs. 5.75 ± 0.45 min, p<0.01) compared to Group L. However, Group B also showed a longer duration of block, as indicated by delayed return to Bromage 0 (200.4 ± 41.6 vs. 155.5 ± 35.2 min, p<0.01) and prolonged time to first pain sensation at the incision site (560.3 ± 68.6 vs. 458.1 ± 58.5 min, p<0.01). Postoperative VAS scores were slightly higher in Group B compared to Group L (2.2 ± 0.7 vs. 2.0 ± 0.8), but this difference was not statistically significant (p=0.104).

Table 2: Intraoperative characteristics and duration of analgesic effect in Group B and Group L (N=90)

Parameter assessed	Group B (n=45) Mean (SD) / n (%)	Group L (n=45) Mean (SD) / n (%)	p-value
Commencement of analgesia			
Time taken for analgesia to pin prick at T10 (min)	3.10 ± 0.55	3.76 ± 3.39	<0.01
Time taken for onset of BROMAGE III (min)	2.68 ± 0.54	3.19 ± 0.40	<0.01
Time taken for maximum height of analgesia at T4 (min)	5.1 ± 0.45	5.75 ± 0.45	<0.01
Termination of analgesic effect			
Time taken to return to Bromage 0 (min)	200.4 ± 41.6	155.5 ± 35.2	<0.01
Time taken for pain sensation at the incision site (min)	560.3 ± 68.6	458.1 ± 58.5	<0.01
VAS Score	2.2 ± 0.7	2.0 ± 0.8	0.104
Frequency of rescue analgesia used	11 (24.4%)	8 (17.8%)	0.606

Bupivacaine achieved a faster onset of sensory block at T10, motor block to Bromage III, and maximum sensory level at T4 compared with levobupivacaine. It also produced a longer motor block (200.4 min vs. 155.5 min) and delayed onset of pain at the incision site (560.3 min vs. 458.1 min). However, levobupivacaine allowed earlier motor recovery,

reflecting its advantage for faster postoperative mobilization. Rescue analgesia was required more frequently in the bupivacaine group (24.4%) than in the levobupivacaine group (17.8%), while more than half of the participants (57.8%) did not require any rescue analgesia.

Regarding hemodynamic parameters, baseline values of heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were comparable between the two groups. Heart rate did not differ significantly at any time point ($p > 0.05$). However, SBP was consistently higher in the levobupivacaine group at several intervals, reaching statistical significance at 1, 11, 13, 15, 30, 60, and 90 minutes ($p < 0.05$). For instance, at 30 minutes, mean SBP was 119.8 ± 8.6 mmHg in Group L versus 112.5 ± 7.9 mmHg in Group B ($p < 0.01$). Similarly, DBP and MAP values showed significantly higher readings with levobupivacaine at later stages of the intraoperative period (30-90 minutes). At 60 minutes, the mean DBP was 77.6 ± 6.2 mmHg in Group L compared with 71.3 ± 5.9 mmHg in Group B ($p < 0.01$), while MAP at the same time point was 91.4 ± 6.5 mmHg in Group L versus 85.1 ± 6.1 mmHg in Group B ($p < 0.01$). The incidence of hypotension was significantly lower in the levobupivacaine group (8.9%) compared with the bupivacaine group (28.9%) ($p < 0.05$). No cases of bradycardia, nausea, vomiting, pruritus, postoperative urinary retention, or respiratory depression were observed in either group.

Discussion

In this randomized controlled trial, we compared hyperbaric bupivacaine 0.5% with morphine 100 µg and hyperbaric levobupivacaine 0.5% with morphine 100 µg for spinal anaesthesia in parturients undergoing elective caesarean section. Both groups were similar in terms of demographic and anthropometric characteristics, ensuring comparability of outcomes.

Our study showed that the onset of sensory and motor blockade was significantly faster with bupivacaine compared to levobupivacaine. The mean time to reach T10 sensory level, maximum sensory level at T4, and Bromage III motor block were all shorter in the bupivacaine group ($p < 0.01$). These findings are in line with those of Guler et al. (2005), who also reported a faster onset and prolonged duration of motor block with bupivacaine compared to levobupivacaine. Similarly, Thakore et al. (2012) observed that levobupivacaine had a relatively slower onset of action, though their protocol with fentanyl as an adjuvant showed a marginal advantage for levobupivacaine. Kala et al. (2017), however, found levobupivacaine to reach T4 sensory level faster than bupivacaine, which contrasts with our findings and may be attributed to their methodological difference of administering a 20° lateral tilt during injection, possibly affecting cephalad spread.

With respect to motor block characteristics, our results showed that bupivacaine produced a denser and longer-lasting motor block, whereas levobupivacaine allowed earlier recovery, with the time to return to Bromage 0 being significantly shorter in Group L (155.5 minutes vs. 200.4 minutes, $p < 0.01$). This aligns with the findings of Sinchana et al. (2019), Deepa and Chandran (2018), and Guler et al., all of whom demonstrated that levobupivacaine provides a shorter motor block duration, thereby facilitating early ambulation. Clinically, this property is advantageous in obstetric patients, where enhanced recovery protocols emphasize early mobilization to reduce thromboembolic risk and promote mother-infant interaction.

In terms of duration of analgesia, we observed that bupivacaine provided longer-lasting postoperative analgesia, with delayed onset of pain at the incision site compared to levobupivacaine. This is consistent with other studies reporting shorter sensory block and earlier pain onset with levobupivacaine. By contrast, Thakore et al. and Kala et al. noted a longer sensory block with levobupivacaine, again reflecting variability in study designs, adjuvant use, and dosing regimens. Nevertheless, our study found that despite shorter block duration, levobupivacaine was associated with reduced rescue analgesic requirement, suggesting a pharmacodynamic profile that may preferentially spare motor fibers while preserving adequate sensory analgesia.

Regarding hemodynamic stability, heart rate and SpO₂ remained comparable across both groups. However, systolic blood pressure was significantly higher in the levobupivacaine group at several time points (1, 11, 13, 15, 30, 60, and 90 minutes), while diastolic blood pressure and MAP were also higher in Group L at later intervals (30-90 minutes). This greater stability with levobupivacaine concurs with earlier studies which demonstrated reduced incidence of hypotension

and cardiovascular adverse events. In our study, the incidence of hypotension was significantly lower with levobupivacaine (8.9%) compared to bupivacaine (28.9%), an observation of particular clinical significance given the high prevalence of maternal hypotension during spinal anaesthesia.

In terms of safety profile, both groups were free from serious adverse effects such as bradycardia, nausea, vomiting, pruritus, urinary retention, or respiratory depression. The absence of pruritus in our study, despite the use of intrathecal morphine, may be attributed to the administration of intravenous ondansetron post-blockade, which is known to reduce opioid-induced pruritus through 5-HT₃ antagonism. This supports the safety of low-dose intrathecal morphine in combination with both local anaesthetic agents.

Our findings add to the growing evidence that while bupivacaine provides faster onset and prolonged duration of block, levobupivacaine offers significant advantages in terms of hemodynamic stability, reduced incidence of hypotension, and earlier motor recovery—features that make it especially attractive in obstetric anaesthesia where early mobilization and maternal safety are prioritized. The clinical implication is that levobupivacaine may be considered a safer alternative in high-risk parturients and in enhanced recovery after caesarean (ERAC) protocols.

LIMITATIONS & FUTURE DIRECTIONS

Although this study provides important insights, it has limitations. It was a single-center trial with a modest sample size and excluded high-risk parturients such as those with preeclampsia or obesity, limiting generalizability. Hemodynamic outcomes were restricted to intraoperative and early postoperative phases, and long-term maternal or neonatal outcomes were not assessed. Despite these limitations, the study is strengthened by its randomized, double-blind design and strict adherence to the CONSORT guidelines. Future research should focus on larger multicenter studies including high-risk obstetric populations, evaluate different adjuvants and dosing strategies, and explore maternal satisfaction and neonatal outcomes. Further evaluation of intrathecal morphine at incremental doses of 50 µg, 75 µg, and 150 µg is warranted to comprehensively assess its efficacy and adverse effect profile.

CONCLUSION

This study demonstrated that hyperbaric bupivacaine with intrathecal morphine is associated with a faster onset of sensory and motor blockade and longer duration of analgesia compared to hyperbaric levobupivacaine with morphine. However, levobupivacaine provided superior hemodynamic stability, with a significantly lower incidence of hypotension, and allowed earlier motor recovery, facilitating early postoperative mobilization. Both agents offered comparable postoperative pain scores and had an excellent safety profile without major adverse effects. These findings suggest that levobupivacaine, despite its slightly slower onset and shorter block duration, represents a safer alternative in parturients where cardiovascular stability and enhanced recovery are prioritized. Future multicenter studies, including high-risk obstetric populations and varied dosing regimens, are recommended to optimize its role in obstetric anaesthesia.

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