Original Article

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Comparison of Equivalent Doses of Intrathecal Hyperbaric Levo-bupivacaine and Hyperbaric Bupivacaine for Caesarean Section: A Prospective Randomised Double-blind Study

Anaesthesia Section

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ABSTRACT

Introduction: Subarachnoid Block (SAB) with Hyperbaric Bupivacaine (HB) is the most common anaesthetic technique for Lower Segment Caesarean Section (LSCS). Levo-bupivacaine, an enantiomer of racemic bupivacaine, has been developed to provide anaesthesia with the same effectiveness but with better haemodynamic stability.

Aim: To compare the effectiveness of hyperbaric levo-bupivacaine to HB in achieving sensory and motor blocks in Caesarean Section (CS) using equivalent doses.

Materials and Methods: Eighty parturients aged 18-38 years with no co-morbidities were randomly divided into two groups receiving equivalent doses of HB and hyperbaric levo-bupivacaine for SAB. The effectiveness of the two drugs was compared in terms of the time taken to achieve sensory and motor blocks, as well as the time for block regression for two segments for sensory block and the return of motor block assessed by the ability to flex the ankle joint. Adverse events such as a fall in Systolic Blood Pressure (SBP) and the dose of vasopressor were noted for the two groups.

Results: The time taken to attain a T6 dermatomal block level was 2.43±1.00 and 2.80±1.51 (p-value 0.08) for the bupivacaine and levo-bupivacaine groups, respectively. Complete motor block of the lower limb was achieved in 4.85±1.67 and 5.15±1.82 (p-value 0.53). However, the time to 2-segment regression for sensory block was significantly faster in the levo-bupivacaine group than in the bupivacaine group (125.9±28.56 minutes and 109.13±28.84 minutes, respectively, p-value 0.009). Regression from motor block was also found to be highly statistically significant (158.38±34.92 minutes for bupivacaine and 138.75±25.71 minutes for the levo-bupivacaine group, p-value 0.006). Spinal-induced hypotension was comparable in both groups, but the bupivacaine group needed a much higher repetition of dose of vasopressor than the levo-bupivacaine group.

Conclusion: Levo-bupivacaine is comparable to its racemic isomer bupivacaine in achieving anaesthesia when administered Intrathecally (IT) for CS. However, with equivalent doses, the duration of action is significantly shorter with hyperbaric levo-bupivacaine. Dose adjustment might be required with hyperbaric levo-bupivacaine based on the duration of the surgery. Haemodynamic stability is also similar with both drugs.

Keywords: Caesarean delivery, Intrathecal anaesthesia, Sensory block

INTRODUCTION

The onset of SAB is rapid and effective, providing reliable sensory-motor anaesthesia [1]. It is the most common form of anaesthesia for LSCS, as it is safe and avoids general anaesthesia. Pregnancy is associated with a difficult airway and susceptibility to gastric regurgitation and pulmonary aspiration [2,3].

HB is commonly employed as a Local Anaesthetic (LA) for CS. It is available in a racemic mixture of dextro-bupivacaine and levo-bupivacaine enantiomers [1,3]. Levo-bupivacaine is a relatively new isomer available for SAB compared to racemic bupivacaine. It is a highly potent LA with a slow onset and long duration of action, providing a more avid sensory block than motor block [1,4]. IT Bupivacaine can cause cardiac arrest due to sympathetic block extension [1], while on the other hand, levo-bupivacaine has faster protein binding, which may be associated with reduced cardiac toxicity if inadvertent intravenous administration occurs [4]. In their study, comparing racemic Bupivacaine with levo-bupivacaine and Ropivacaine, Casati A and Baciarello M concluded that levo-bupivacaine has a comparable clinical profile with better cardiac safety [5].

A fall in BP (hypotension) is a common adverse event, occurring in up to 80% of cases of spinal anaesthesia [6], due to sympathetic block and aorto-caval compression from the gravid uterus during CS. There have been multiple studies on isobaric levo-bupivacaine without adjuvants (opioids) [7,8] or with opioid adjuvants [9-11] for safety and clinical effect, but very few studies have been found on hyperbaric levo-bupivacaine [10]. As 0.5% HB is the most commonly used drug to achieve anaesthesia for CS and its hyperbaric S (-) enantiomer, levo-bupivacaine in a dosage of 4-12 mg has the same efficacy in spinal anaesthesia in healthy volunteers [12]. In their comparative study of isobaric and hyperbaric 0.42% levo-bupivacaine for lower abdomen surgery, Sanansilp V et al., found that hyperbaric levo-bupivacaine had a faster and more predictable block than the isobaric counterpart [13]. Therefore, the current study was conducted to compare 0.5% hyperbaric racemic bupivacaine with 0.5% hyperbaric levo-bupivacaine in equivalent doses to determine effectiveness in achieving surgical anaesthesia during elective CS. Hence, this study aimed to compare the effectiveness of hyperbaric levobupivacaine to HB in achieving surgical anaesthesia for CS in equivalent doses.

Primary objective of the study was to compare the time taken for 2-segment regression of sensory block between the two groups and the secondary objective was to compare spinal-induced hypotension of hyperbaric levo-bupivacaine and bupivacaine.

MATERIALS AND METHODS

This was a prospective, randomised, double-blinded clinical trial conducted in the Department of Anaesthesiology, Tomo Riba Institute of Health and Medical Sciences, Arunachal Pradesh India, from January 2023 to November 2023, after approval from the Institutional Scientific Committee and the Institutional Ethics Committee (No. TRIHMS/ETHICS/01/2019-20/57). The current study is registered under the Clinical Trial Registry of India, No: CTRI/2023/09/057768.

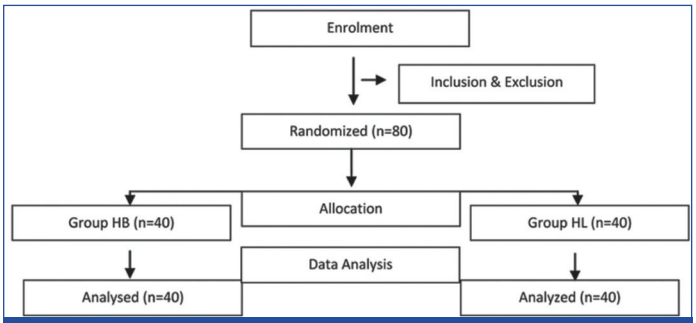
Inclusion criteria: Parturients aged 18 to 40 years with American Society of Anaesthesiology (ASA) I or II physical status who were planned for CS were included in the study.

Exclusion criteria: Those parturients who had some associated systemic illness or emergent surgery and labouring parturient.or those with multiple or twin pregnancy, grand multipara or those with contraindication to neuraxial block or the ones who refused to participate in the study were excluded from the study.

Sample size calculation: The sample size was calculated to be 40 for each group, considering 90% power (Z1-b=1.28) at a 95% confidence interval (Zα/2=1.96), Standard Deviation (SD) from a previous study of 5.795 (mean of pooled SD of 2 groups for 2-dermatomes sensory regression in the study by Duggal R et al., [1]), accuracy to detect a difference (d) of sensory regression by two dermatome levels by five minutes, and an attrition rate of 10%. The calculated sample was 32 for each group, which was adjusted to 40.

Procedure

The mandatory informed consent was obtained from the eligible parturients during the pre-anaesthetic check-up the day before surgery, with vital parameters of HR, BP, and SpO_2 considered as baseline parameters. The consenting participants were allocated into groups by computer-generated randomisation as is depicted in [Table/Fig-1]. Group HB received a dose of 0.5% HB of 10 mg, and the study group HL received 0.5% hyperbaric levo-bupivacaine in an equivalent dose of 10 mg (from the previous study of Duggal R et al., [1]).



[Table/Fig-1]: CONSORT Flowchart Diagram of the stuidy: Total N=80 participants.

Patients were kept nil per orally for at least six hours pre-operatively. Intravenous cannulation with a 20-18 G cannula was done, and preloading with lactated Ringer's solution of 20 mL/kg of the patient's weight was administered. Premedication of Ondansetron 4 mg and Pantoprazole 40 mg was administered intravenously before starting the procedure. Minimal routine monitoring was applied to all cases, including Heart Rate (HR), non-invasive Blood Pressure (BP), Oxygen Saturation (SpO_2%), and electrocardiography after the re-evaluation of the airway and foetal HR. Spinal anaesthesia with 10 mg HB/HL was achieved with a 25-gauge Quincke's spinal Needle at the L3-L4 interspace after confirmation of the Cerebrospinal Fluid (CSF).

Sensory analgesia was tested by pin prick at the mid-axillary line bilaterally every minute after SA, until the desired block level at the T6 dermatome was achieved or 15 minutes of IT LA. The modified Bromage scale was used for the assessment of motor block (0: No motor block, 1: Inability to raise the extended leg; able to move knees and feet, 2: Inability to raise the extended leg and move the knee; able to move feet, and 3: Complete block of motor limb) [14]. The time taken to achieve sensory block level of dermatome level T6 and the time taken to complete motor block were noted down. The 2-segment regression from the previous dermatomal block achieved from SAB was taken as the end-point of sensory anaesthesia, and leg movement of Bromage 2 was taken as the cut-off regression from motor block.

The vitals of the participants were recorded at one minute, three minutes, and thereafter every five minutes of the spinal procedure and until the closure of the skin wound. The patient was shifted to recovery after two consecutive parameters were within the normal limit. The Heart Rate (HR) and non-invasive arterial Blood Pressure (BP) evaluation were conducted whenever the participant complained of discomfort, nausea, or pain. Any episode of hypotension with systolic BP <90 mm Hg or a fall of >20% from the baseline were treated with vasopressors [12].

STATISTICAL ANALYSIS

GraphPad Prism 10.0.2 was used for statistical analysis. An unpaired t-test was used to compare variables for sensory and motor block. A p-value of <0.05 was considered to be statistically significant, and a p-value of <0.001 was considered highly significant. Continuous data are presented as mean±Standard Deviation, and categorical data are presented as proportions or percentages.

RESULTS

In the present study, the authors included 80 participants aged 19 to 38 years, comprising 25 primiparas and 55 multigravidas. The demographic distribution is presented as mean or proportion in [Table/Fig-2]. All the participants included had normal HR and BP before being enrolled in the study.

Parameters		Group HB	Group HL	p-value
Age (years)		30±4.99	28.8±5.34	0.44
Weight (Kg)		69.00±7.65	66.95±9.17	0.48
Height (cm)		152.5±3.86	151.5±4.99	0.21
BMI (Kg/m^2)		29.53	28.98	0.10
Baseline SBP (mm Hg)		123±7.65	122±9.03	0.42
Baseline Heart Rate (HR) (beats per minute)		85±8.13	85.5±8	**0.05**
Gravidae	Primi	11 (27.5 %)	14 (35%)	
	Multi	29 (72.5%)	26 (65%)	

[Table/Fig-2]: Demographic profile.

The mean time (in minutes) to achieve sensory block of T6 was 2.43±1 in the Bupivacaine group and 2.80±1.51 in the levo-bupivacaine group, as shown in [Table/Fig-3], which was not statistically significant. The time to achieve full motor block of the lower limb was 4.85±1.67 minutes and 5.15±1.82 minutes, respectively for groups HB and HL. The regression of the block for sensory as well as motor block was found to be faster in group HL than in group HB, which was shown to be statistically significant. The mean sensory regression of two segments was 109.13±28.84 (range of 45-165) minutes for group L and 125.9±28.56 (range of 65-180) minutes in group B.

Parameters	Group HB (n=40)	Group HL (n=40)	p-value
Sensory Block (min)	2.43±1.00	2.80±1.51	0.08
Motor block (min)	4.85±1.67	5.15±1.82	0.53
Regression of sensory (min)	125.9±28.56	109.13±28.84	**0.009**
Regression of motor (min)	158.38±34.92	138.75±25.71	**0.006**

[Table/Fig-3]: Block parameters.

The maximum sensory block of T3 was observed in one patient in the Bupivacaine group. There were 16 and 14 participants who

achieved the maximum sensory level of T4 in groups HL and HB, respectively, as shown in [Table/Fig-4].

Dermatomal block level	Group HB (n=40)	Group HL (n=40)
T 3	1	-
T 4	14	16
T 6	25	24
Total adequate sensory block	40	40

[Table/Fig-4]: Maximum sensory dermatomal level.

In this study, the authors found hypotension in 37.5% of participants in the HL group, compared to 40% receiving HB, as presented in [Table/Fig-5]. Among the participants experiencing hypotension, 10% in group HL and 22.5% in group HB received repeated doses of the vasopressor (mephentermine). The authors did not encounter any instances of bradycardia or block failure in this study. Nausea and vomiting were observed in 12.5% and 5% of patients in groups HB and HL, respectively. In all study participants, three parturients (1 in HB and 2 in HL) complained of pain, which was treated with Fentanyl 50 µg.

Effects	Group B	Group L
Hypotension	16 (40%)	15 (37.5%)
Dose of vasopressor repeated	9 (22.5%)	4 (5%)
Pain	1 (2.5%)	2 (5%)
Vomiting	5 (12.5%)	2 (5%)
Conversion to GA	-	-
Bradycardia	-	-

[Table/Fig-5]: Adverse effects observe in the groups.

DISCUSSION

The results of the current study indicate that both hyperbaric bupivacaine and levo-bupivacaine in equal doses can achieve adequate sensory and motor blocks when used for spinal anaesthesia. However, the regression from the block in both sensory and motor anaesthesia was found to be much faster with levo-bupivacaine than with bupivacaine when used as the sole anaesthetic.

The mean time required to achieve T6 sensory block was faster in the bupivacaine group than in the levo-bupivacaine group, which is consistent with the findings of Duggal R et al., Rao GD et al., and Guler G et al., [1,2,11]. However, these studies used isobaric levo-bupivacaine with opioids to achieve intrathecal anaesthesia. This finding is contradictory to the finding of Debbarma B et al., who found that the time to achieve mean sensory block was faster with hyperbaric levo-bupivacaine [3]. The onset of motor block was also found to be faster with intrathecal bupivacaine than with levo-bupivacaine, as found in other studies [1,3]. Madhanmohan C et al., in their study of isobaric levo-bupivacaine 12.5 mg and hyperbaric bupivacaine 10 mg, also found a faster onset of sensory and motor block with bupivacaine than with levo-bupivacaine [15]. Goyal A et al., in their study comparing isobaric local anaesthetic and hyperbaric local anaesthetic, found that isobaric levo-bupivacaine and isobaric bupivacaine took a significantly longer time to achieve sensory-motor block than hyperbaric bupivacaine [16]. However, their study did not compare hyperbaric and isobaric levo-bupivacaine, as in the study of Sanasilp V et al., thus, efficacy based on the baricity of the local anaesthetic cannot be determined [13].

The current study shows that 10 mg hyperbaric levo-bupivacaine provides adequate sensory dermatomal and motor blocks for caesarean section. The 2-segment regression from sensory block and motor block was much faster with levo-bupivacaine than with bupivacaine, which is consistent with the findings of Debbarma B et al., and Bremich DH et al., [3,8]. However, Rao GD et al., in their comparative study of hypobaric levo-bupivacaine and hyperbaric bupivacaine with fentanyl, found 2-segment regression to be faster in bupivacaine (114.47±9.28 min) than in levo-bupivacaine (129.17±13.33 min) group, as compared to the present study, where 2-segment regression was faster in hyperbaric levo-bupivacaine (109.13±28.84 min) than in the bupivacaine (125.9±28.56 min) group [2]. The motor regression was found to be faster in the levo-bupivacaine group than in the bupivacaine group, which is similar to the findings of the afore-mentioned studies [1,2,10,17].

However, according to the study by Luck JF et al., who used 15 mg of hyperbaric bupivacaine and hyperbaric levo-bupivacaine for lower abdominal surgeries, they found almost the same duration of sensory and motor block, which contradicts the findings of this study [18].

In the current study, the authors did not encounter block failure, but we had three patients who complained of discomfort and pain during the surgical manipulation, which were managed with fentanyl 50 µg. The dermatomal block levels achieved in the groups in this study have minimal differences.

Spinal-induced hypotension is one of the most common complications in spinal anaesthesia. In the current study, the authors found 40% and 37.5% cases of hypotension in group HL and HB, respectively, which do not align with the findings of Duggal R et al., Rao GD et al., and Guler G et al., who reported much higher cases of hypotension with racemic bupivacaine than its levorotatory isomer in their study [1,2,11]. Metta R et al., found higher cases of hypotension with bupivacaine than levo-bupivacaine in lower abdominal surgery [19].

However, they used isobaric levo-bupivacaine in their studies as compared to hyperbaric levo-bupivacaine used in the current study. Guler G et al., in their study mentioned that the ascription of clinical effect by the baricity of the local anaesthetic has been in question since there are contradictory materials available [11]. The repetition of dosage of vasopressor (vasopressor repeat if Systolic Blood Pressure (SBP) above 100 mm Hg or 20% of baseline) was found to be much higher in the bupivacaine group than in the levo-bupivacaine group in this study. Bajwa SJS and Kaur J in their systemic analysis suggest levo-bupivacaine has lesser cardiovascular and neurological toxicity than bupivacaine [20].

Limitation(s)

The limitations of the study include a small sample size conducted in a single center. This study does not include parturients with emergent surgery, parturients in labour, and those with systemic illness, which may overlook a few factors that could affect the outcome of the study.

CONCLUSION(S)

The authors in this study conclude that hyperbaric levo-bupivacaine has the same efficacy as hyperbaric bupivacaine in achieving sensory and motor block following intrathecal administration during caesarean section. However, the regression from sensory and motor blocks is much faster with levo-bupivacaine than with its racemic isomer bupivacaine. Although the hypotensive effect may be the same for both isomers, bupivacaine necessitates many more repeated doses of vasopressor than its levoisomer.

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