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Original Research Article

A comparative study of intrathecal bupivacaine and levobupivacaine for patients undergoing caesarean section

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ABSTRACT

Background: The present study was conducted to compare the effects of 0.5% isobaric levobupivacaine and 0.5% hyperbaric bupivacaine in pregnant females undergoing caesarean section.
Methods: Study was conducted on 100 pregnant females undergoing caesarean section. They were randomly divided into two groups B and L receiving 2 ml of 0.5% hyperbaric bupivacaine and 0.5% levobupivacaine respectively. Two groups were compared with regard to sensory block, motor block, haemodynamic stability and complications if any.
Results: Time to achieve sensory blockade till T6 dermatome was prolonged in group B (162.52±80.55 sec) as compared to group L (139.40±49.79 seconds) (p value= 0.087). Prolonged duration of motor blockade was observed in group B (160.76±6.56 minutes) as compared to group L (131.48±14.42 minutes) (p<0.001). Less haemodynamic stability was seen in patients of group B with more incidence of hypotension and bradycardia.as compared to group L.
Conclusions: Levobupivacaine is nearly equally effective to bupivacaine to produce sensory and motor blockade with comparable onset time and better haemodynamic stability with lesser side effects.

Keywords: Bupivacaine, Caesarean section, Levobupivacaine, Local anaesthetics, Spinal anaesthesia

INTRODUCTION

Spinal Anaesthesia (SA) is the most common anaesthesia technique used for the lower segment Caesarean Section (CS).[1,2] Due to the various physiological changes affecting the airway, and increased chances of aspiration in pregnancy, administration of General Anaesthesia (GA) to the obstetric patient is a challenging job. Regional anaesthesia is relatively safe, easy, reliable and economical technique for CS as compared to GA. It reduces the risk of airway manipulation and placental transfer of anaesthetic drugs to the fetus.[2,3]

Hyperbaric bupivacaine is commonly used Local Anaesthetic (LA) for SA. It is known to have prolonged motor blockade and is associated with side effects like hypotension, bradycardia, nausea and vomiting due to extension of sympathetic block. Accidental intravenous administration, may result in lethal cardiac and CNS toxicity.[4,5]

Levobupivacaine is newer LA that had been approved for intrathecal administration in recent years. Levobupivacaine is pure S (-) enantiomer of bupivacaine.[6] The levobupivacaine is a high potency, long acting LA with a relatively slow onset of action. It has a lower propensity to block inactivated cardiac sodium and potassium channels along with faster rate of dissociation compared to bupivacaine.[7] Due to its faster protein binding rate it has reduced cardiac toxicity on

overdose/ intravenous administration. Plain levobupivacaine is isobaric to CSF. It has an advantage of a more predictable spread.[8-10] It has more specific effects on motor fibres as compared to sensory fibres. It has intermediate motor effects as compared to bupivacaine. Advantage of prolonged sensory blockade and faster recovery from motor blockade with less hypotension by levobupivacaine makes it suitable for obstetric surgery.[11] Some of the studies have shown decreased incidence of various side effects like hypotension, bradycardia, nausea and vomiting as compared to bupivacaine when used for spinal anaesthesia for caesarean section.

In the current study author compared the effect of hyperbaric bupivacaine and isobaric Levobupivacaine in patients undergoing lower segment CS under SA.

METHODS

This prospective randomized and double-blind study was conducted from February 2018 to April 2019 after approval by hospital ethical committee. Informed consent from all the participants was obtained.

Inclusion criteria

A total of 100 pregnant females, having the physical status of Grade-II according to American Society of Anesthesiologists, scheduled for CS under SA were selected for participation in the study.

Exclusion criteria

Patients with history of pre-eclampsia and eclampsia, uncontrolled diabetes mellitus, heart disease, morbid obesity, vertebral deformities, coagulation abnormalities and pregnant females with height <150 cm and >170 cm were excluded from the study.

Patients were examined pre-operatively and detailed clinical history, general physical examination were recorded. All routine investigations were carried out. The patients were kept fasting for 6 hours prior to the scheduled time of surgery. They were premedicated with tablet ranitidine 150 mg orally a night before and tablet ranitidine 150 mg and metoclopramide 10 mg orally 2 hours prior to surgery.

In the operating room, monitoring comprising of electrocardiography (ECG), pulse oximetry (Spo2) and Non-Invasive Blood Pressure (NIBP) were established. Baseline readings of vital parameters were recorded. Intravenous line was secured with appropriate size intravenous cannula. Patients were randomly allocated using sealed envelope containing code numbers to either of the two groups B and L. Patients in group B (n=50) received 10 mg of bupivacaine (hyperbaric) and patients in group L (n=50) received 10 mg of levobupivacaine (Isobaric).The study drug was loaded and administered by fellow anaesthesiologist not involved in the study. The anaesthesiologist involved in data collection and analysis was blinded to the group allocation.

Under all aseptic and universal precautions, SA was administered in sitting position at the L3-L4 interspace using 25G Quincke spinal needle and the study drug injected. The patient was then turned supine. Sensory block was assessed using a cotton ball soaked in ethyl alcohol everyone minute till 5 minutes and reassessed every 5 minutes for 30 minutes and every 15 minutes post operatively until sensory block was back to L2 dermatome level. Loss of cold sensation till T6 dermatome level was considered adequate for commencement of surgery. Time to achieve sensory blockade till T6 dermatome level was recorded (interval between intrathecal administration of drug and spread of sensory block till T6 level). Maximum height of sensory block achieved, time to attain maximum height of the block and duration of sensory block (interval from intrathecal drug administration to the point of L2 regression) was recorded. Degree of motor block was assessed using modified Bromage Score (MBS).[12]

Motor block was assessed at the same interval as sensory block. Onset time of motor blockade was recorded and taken as interval between intrathecal administration of drug till Bromage score of 3 was achieved. Duration of block was noted (interval from intrathecal drug administration to the point at which Bromage score was back to zero).

Haemodynamic parameters of the patient before the block (basal), everyone minute till 5 minutes then after every 5 minutes till the end of surgery were recorded. Any episode of hypotension, bradycardia, nausea and vomiting were recorded. Hypotension was defined as a 20% reduction in systolic blood pressure from the baseline value. Ephedrine 5 mg IV stat was administered to treat hypotension and, whenever needed, atropine 0.3 mg IV was administered when the HR dropped to 50 beats/min or <20% of the basal value. Episode of nausea and vomiting was treated by injection ondansetron 4mg IV.

The comparison of normally distributed continuous variables between the groups was performed using Student's t test. Nominal categorical data between the groups were compared using Chi-square test or Fisher's exact test as appropriate, $p<0.05$ was considered statistically significant.

RESULTS

Data of all 100 patients enrolled in the study were included in the analysis. The age, weight, height, and duration of surgery of the patients were comparable in both the groups (Table 1). Mean time to achieve sensory blockade till T6 Level was higher in Group B (162.52±80.55 sec) as compared to group L (139.40±49.79 sec) and time to achieve maximum height

of sensory block was also higher in group B (252.02±111.65) as compared to group L (215.02±89.34). Time of regression of sensory block till L2 Level was faster in group L. Maximum height of sensory blockade achieved in both the groups was T4. Forty-seven patients in group B and 41 patients group L achieved maximum height till T4. The significant difference (p<0.01) was found in time to achieve motor blockade till Bromagen score 3 [group B (305.18±110.74 sec) vs group L (419.31±174.68 sec)] and time to regression of motor blockade [group B (160.76±6.56 min) vs group L (131.48±14.42 min)] (Table 2).

Table 1: Patient characteristics.

Patient parameters	Group B (n=50) Mean±SD	Group L (n=50) Mean±SD	p value
Age (Yrs)	24.44±3.37	24.14 ± 3.17	0.648
Height (in cm)	157.54±4.46	157.40±4.88	0.881
Weight (in Kg)	62.02±7.13	61.28±8.31	0.634
Duration of Surgery (min)	57.50±10.04	54.90±9.50	0.186

Table 2: Characteristics of sensory and motor block.

Sensory and motor block evaluation	Group B Mean±SD	Group L Mean±SD	p value
Time to achieve sensory blockade till T6 Level (Sec)	162.52±80.55	139.40±49.79	0.087
Time to achieve maximum height of sensory block (Sec)	252.02±111.65	215.02±89.34	0.07
Time of regression of sensory block till L2 Level (Min)	193.22±10.61	171.52±17.27	<0.001*
Maximum height of sensory blockade	T4(47) T6(3)	T4 (41) T6 (7) T2 (2)	0.26
Time to achieve motor blockade till Bromage score 3 (Sec)	305.18±110.74	419.31±174.68	<0.001*
Time to regression of motor blockade (min)	160.76±6.56	131.48 ± 14.42	<0.001*

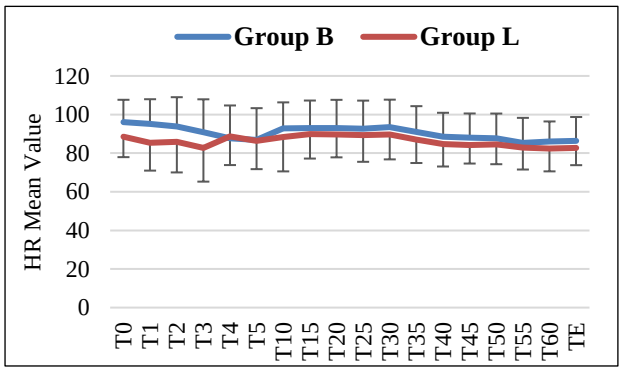

Figure 1: Comparison of HR at between the two groups.

Haemodynamic parameters recorded showed no variation in mean HR in both the groups. However slight fall in MAP was found in group B when compared to group L but this fall was not statistically significant (Figure 1 and 2).

Though incidence of hypotension and bradycardia was frequent in group B than group L but was statistical non-significant. Incidence of nausea was significantly more with group B (Table 3).

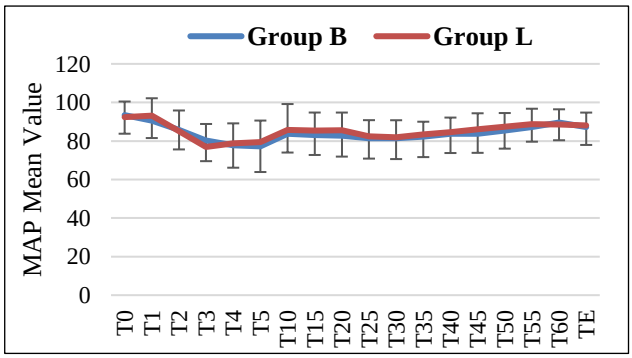

Figure 2: Comparison of MAP at between the two groups.

Table 3: Complications.

Complications	Group B (n=50)		Group L (n=50)		p value
	Present	Absent	Present	Absent	
Bradycardia	17	33	6	44	0.002*
Hypotension	33	17	19	31	0.002*
Nausea	13	37	4	46	<0.001*
Vomiting	5	45	1	49	0.226

DISCUSSION

Levobupivacaine being enantiomer of bupivacaine with high potency has been approved for intrathecal use.[6] At low concentration, levobupivacaine is favourable for ambulatory surgery as it produces a differential neuraxial block with preservation of motor function.[8]

In this study, both the groups were comparable in terms of demographic variables like age, weight, height, and were statistically non-significant. In present study, sensory block level required for CS was achieved adequately in both groups. The time to reach T6 sensory height, was less in group L as compared to group B (group L-139.40±49.79 sec, group B-162.52±80.55 sec,) indicating early onset with Levobupivacaine. Babu et al, and Debbarma et al, showed similar duration in their studies.[3,13] Duggal et al, recorded onset time 3.6±0.08 minutes in bupivacaine group and 3.87±0.73 minutes in levobupivacaine group. This time was significantly higher than recorded in this study despite the equal dose used in both studies.[14] Contrary to our results Babu et al, Duggal et al, and Madanmohan et al, recorded onset time of bupivacaine faster than levobupivacaine.[3,14,15] However all the studies concluded that characteristic of sensory block in both bupivacaine and levobupivacaine are nearly comparable. Time to reach the maximum height of sensory block was more in group B than group L in the present study and was similar to studies of Debbarma et al, and Madanmohan et al, Kumar et al, and Duggal et al, recorded extremely high duration to reach maximum height in contrast to this study, which may be attributed to difference in weight and height of study subjects.[2,13-15] Majority studies and present study observed that bupivacaine took longer time to achieve the maximum height as compared to levobupivacaine except Kumar et al, and Madanmohan et al, who found this time to be longer in levobupivacaine.[2,15] Maximum height of sensory blockade in the present study was T4 in the majority of the cases in both the groups which was similar to that observed by Debbarma et al, (T4 in both groups).[13] Babu et al, Duggal et al, and Madanmohan et al, reported this height to be T6 with levobupivacaine and T4 with bupivacaine.[3,14,15] It was observed height of sensory block with bupivacaine was T4 and between T4-T6 with levobupivacaine using an approximate dose of 10 mg. Time to regression to L2 dermatome was less with levobupivacaine (171.52±17.27 minute) as compared to bupivacaine (193.22±10.61 minute) in the present study. Though variation in duration was observed, but majority studies observed shorter regression time with Levobupivacaine than bupivacaine.[3,13,14,16] In contrast, Kumar et al, observed longer time to regression with Levobupivacaine.[2] Bupivacaine still proven to provide larger duration analgesia as compared to levobupivacaine. Factors that influence these action can be position of patient, spread of injection and baricity of solution.[13] Some authors suggested that isobaric levobupivacaine in CSF acts indifferently to gravitational forces. Therefore, level of the sensory block after intrathecal isobaric levobupivacaine are unaffected by the patient position following the injection. This might be an advantage over bupivacaine which result in a high level of block due to the tendency to spread unexpectedly higher even after adequate fixation time.[14]

Present study illustrated that, time to achieve motor blockade till MBS-3 was faster and its duration was longer, in parturients in Group B as compared to those in group L. This faster onset can be due to hyperbaricity of bupivacaine. In the present study time of the motor block recovery was more variable in levobupivacaine group. In ranged from 60 minutes to 200 minutes in few patients. Our results were nearly comparable with results of Babu et al, and Gori et al, but shorter regression time was reported by Duggal et al, and Debbarma et al.[3,13,14,16] Studies documented that duration of motor block for levobupivacaine was shorter as compared to bupivacaine. Pharmacokinetics of levobupivacaine shows that, it is metabolised by CYP2A2 in liver and has higher clearance rate (28-37 mgkg-1min-1).[13] Difference in potency ratio of levobupivacaine/ bupivacaine as reported by various authors range from 0.75 to 0.87. ED95 dose of levobupivacaine for CS in SA is reported to be 12.56 mg.[15] We administered 10 mg of levobupivacaine which was less than ED95 for CS. Levobupivacaine is known to have lower affinity towards Aα fibers (somatic motor fibers) than bupivacaine, which may result in lesser motor block.[2] All these factors can result in short duration of motor block as well as sensory block in patients receiving levobupivacaine.

No significant difference in haemodynamic parameters in any of the groups was observed. Fall in HR was observed a few intervals, but no significant change were found throughout the study period. Fall in MAP was observed at 3-5 minutes after administering of SA in both the groups. This fall in MAP was more in group B as compared to group L though not statistically significant. Comparable observation was noted by Kumar et al, and Madanmohan et al.[2,15]

Though hypotension is one of the most common complications following SA but it is of great importance in CS as besides problem to mother, it can hamper placental perfusion which can be harmful to the fetus also. Hypotension and a further decrease in cerebral blood flow is the most common cause of nausea and vomiting after SA for cesarean section. Hypotension, bradycardia, nausea and vomiting was more pronounced in group B as compared to group L.[14,17,18] Hypotension and bradycardia observed following SA can be due to sympathetic blockade produced by anaesthetic which is more with hyperbaric drug as compared to isobaric drug. Less hypotension with levobupivacaine explain the lower incidence of nausea and vomiting found in group L, in the present study although not significant statistically.

A similar trend was observed by previous authors that incidence of above complications was relatively less in

levobupivacaine group. Levobupivacaine bears an additional property of reducing cardiac and neurotoxicity. It has reduced potential of myocardial depression and arrhythmogenicity and hence greater safety margin than bupivacaine.[15,19,20] Isobaric levobupivacaine is less sensitive to patient position following injection, which might be an advantage over bupivacaine, which has the tendency to migrate unexpectedly high even after an adequate time of fixation, resulting in high spinal and thus causing late complications like hypotension, bradycardia and nausea.[13]

CONCLUSION

Authors conclude that bupivacaine and levobupivacaine, both were found to be effective drugs in producing desired anaesthesia and analgesia. Levobupivacaine had an early onset of sensory block but, delayed onset of motor blockade. It also showed significantly shorter and less pronounced sensory and motor block when compared to bupivacaine, which may help in early ambulation. Levobupivacaine is nearly equally effective to bupivacaine to produce sensory and motor blockade with comparable onset time and better haemodynamic stability.

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