Original Research Article

A Comparative Study of Efficacy of Intrathecal Levobupicaine and Bupivacaine for Caesarean Section

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Abstract

Introduction: Spinal Anaesthesia (SA) is the most common anaesthesia technique used for the lower segment Caesarean Section (CS).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.**Materials and Methods:** This prospective randomised, double-blinded study was conducted in the Department of Obstetrics and Gynaecology, Sheikh Bhikari Medical College, HazaribagKolghati Jharkhand. After getting institutional ethics committee approval and written informed consent from all the parturients, a total of 180 parturients who met the inclusion criteria undergoing caesarean section under spinal anaesthesia, were enrolled for study. **Results:** All the 180 patients who were enrolled in this double-blinded, randomised comparative study, completed the study. There was no dropout and the study results are shown below. Table 1 shows distribution of demographic profile in two study groups. There was no statistically significant difference in age, weight or height distribution among the study groups as 'p' value >0.05 and hence the groups were comparable to each other in terms of age, weight and height. Table 2 shows distribution of onset of sensory block, onset of motor block, duration of surgery and duration of analgesia in two study groups. There was statistically significant difference in onset of sensory block and motor block and duration of analgesia and no statistically significant difference in duration of surgery.
Conclusion: Thus, in conclusion, levobupivacaine seems to be an effective alternative to intrathecal bupivacaine in infra-umbilical surgeries like caesarean section with reduced toxic potential and excellent quality of analgesia.

Keywords: Spinal Anaesthesia, levobupivacaine, bupivacaine, General 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.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 bupivacaine and Levobupivacaine in patients undergoing lower segment CS under SA.

Materials and Methods

This prospective randomised, double-blinded study was conducted in the Department of Obstetrics and Gynaecology, Sheikh Bhikari Medical College, Hazaribag Kolghati Jharkhand. After getting institutional ethics committee approval and written informed consent from all the parturients, a total of 180 parturients who met the inclusion criteria undergoing caesarean section under spinal anaesthesia, were enrolled for study. To estimate sample size, thorough review of literature of related text books were done before estimating sample size for the study. Searches included standard text books and internet indexing services such as PubMed, Medline and Index Medicus. Based on literature data and using the Power and sample size calculation software (version 2.1.30, DuPont & Plummer, February 2003) with α-error of 0.05, β-error of 0.9,

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acceptable mean difference of 5.85 unit (min), expected standard deviation of 10 and non-inferiority margin 5 units, a minimum sample size of 67 subjects was required per group for a two-tailed hypothesis. We decided to recruit 90 patients to each group to make up 10% dropouts from the study groups.

Inclusion criteria being ASA physical status I & II patients selected for elective caesarean section.

Exclusion criteria being patient's refusal, known cardiac diseases (like ischaemic heart disease, heart failure, valvular heart diseases and conduction disorder); known renal, hepatic, coagulation disorder; any neurological disorder; patients using beta blocker, antipsychotic drugs, sedatives; spinal deformities; trauma and local infection; allergy to aminoamide local anaesthetic; pre-eclampsia; eclampsia; twin pregnancy. Onset of sensory block was assessed by pinprick with 23 G needle using Hollmen scale [0=ability to appreciate a pinprick as sharp, 1=ability to appreciate a pinprick as less sharp, 2=inability to appreciate a pinprick as sharp (analgesia), 3=inability to appreciate a pin touching]. Onset and degree of motor block by Modified Bromage Scale (0= able to flex whole lower limb at hip, 1=able to flex knee but unable to flex at hip, 2=able to flex ankle but unable to flex knee, 3=no movement of lower limb). Duration of analgesia by the end point when the first rescue analgesic required, was assessed by using 0-10 linear Visual Analogue Scale and haemodynamic variables (SBP, DBP, MAP, HR) monitored using multichannel monitors. Study tools: Hollmen Scale, VAS, Modified Bromage Scale, Pulse Oximeter, NIBP monitor. Complete pre-anaesthetic evaluation was performed in each parturient including detailed history taking, thorough physical check-up (weight, height of all the patients) and assessment of spine, airway examination and assessment and routine preoperative investigations. All parturients received ranitidine 150 mg orally the night before and on the morning of surgery and parturients were kept fasting from midnight before surgery. Using table of random number, 180 patients were allocated into two groups (90 in each group). In this prospective, double-blinded study, 180 parturients belonging to ASA physical status I and II were randomly allocated into two groups, Group L (n=90) received 0.5% isobaric levobupivacaine 2.5 mL (12.5 mg) and Group B (n=90) received 0.5% hyperbaric bupivacaine 2.5 mL (12.5 mg). The study drugs were prepared by an anesthesiologist who was not otherwise involved in the study. The anaesthesiologist performing the block and observing the effects were also blinded to the treatment group.

Following arrival in the anaesthetic room, IV access was established with 18 G cannula in a large vein on the dorsum of hand and prehydration was done with 10 mL per kg lactated Ringer's solution. Anaesthesia machine, airway equipment, difficult airway cart, drugs for resuscitation and general anaesthesia were kept ready in hand before starting the procedure. ASA standard monitors were connected for HR, O_2 saturation, NIBP and ECG monitoring. Patients were placed in the sitting position. The overlying skin was prepared with povidone-iodine spirit, followed by antiseptic draping. After proper identification of the space, subarachnoid block was given at the level of L3-4 interspace using a 25 G Quincke point needle. The correct needle placement was identified with the free flow of cerebrospinal fluid (CSF) and 2.5 mL of study drug was injected over 0.2 mL/sec. After removal of the spinal needle, patients were turned to a 15-20 degree left lateral supine position. Oxygen 5 L/min. was administered via a facial mask.

Haemodynamic monitoring was started immediately. The level of sensory block was determined bilaterally by response to pinprick using Hollmen Scale in the anterior axillary line. Sensory block was assessed at 2 min. post injection and at 1 min. intervals thereafter and permission to perform operations was given once a T4-T6 level had been achieved. The onset time of sensory block was recorded. The motor block was determined by modified Bromage Scale at 2 min. post injection and at 1 min. intervals thereafter. The onset time and highest scale of motor block was recorded. Heart rate and blood pressure was recorded using standard non-invasive monitors before intrathecal injection and then every 5 min. interval till the end of surgery. Operation duration was recorded as time until end of operation after administration of local anaesthetics. After the completion of surgery, patients were shifted to PACU (post anaesthesia care unit). Assessments of sensory regression was continued at 30-min. intervals following the completion of surgery until it regressed up to T10 dermatome and duration of analgesia was monitored by VAS when the patient required the first rescue analgesic. Rescue analgesic was administered when patient had a VAS Score >3 in the form of Injection Diclofenac sodium 75 mg intramuscularly. Side effects such as nausea, vomiting, headache, hypotension, bradycardia and shivering were recorded. Hypotension (defined as systolic blood pressure <90 mmHg or a decrease of 20% below the baseline level in MAP) was treated with intravenous mephentermine 3-9 mg or intravenous phenylephrine 50 µg and additional lactated Ringer's solution. Bradycardia defined as heart rate <50 bpm was treated with intravenous atropine 0.3-0.6 mg. Patients were followed up daily for any adverse events during their hospital stay.

Results

All the 180 patients who were enrolled in this double-blinded, randomised comparative study, completed the study. There was no dropout and the study results are shown below. Table 1 shows distribution of demographic profile in two study groups. There was no statistically significant difference in age, weight or height distribution among the study groups as 'p' value >0.05 and hence the groups were comparable to each other in terms of age, weight and height. Table 2 shows distribution of onset of sensory block, onset of motor block, duration of surgery and duration of analgesia in two study groups. There was statistically significant difference in onset of sensory block and motor block and duration of analgesia and no statistically significant difference in duration of surgery.

Onset of sensory block is faster in B group (5.13 ± 0.87) than group L (5.72 ± 1.10). Onset of motor block is faster in B group (5.47 ± 0.75) than L (7.00 ± 0.95). There was no significant difference in duration of surgery in both the groups. The duration of analgesia (min.) was significantly more in L group than in B group, as 'p' value was <0.05.

Table 3 shows statistically significant difference between the patients of Group L and Group B as p value was <0.05 (student's independent t-test), found in pulse rates (Table 3) in any time of measurement except baseline and at 30 min. The statistically significant difference in p value (p value < 0.05) by student's independent t-test was found in mean arterial pressure (Table 3) at any time of measurement except baseline and 20 minutes. Side effects- nausea, vomiting, hypotension, bradycardia were more in B group (Table 4).

Table 1: Demographic Features of the Patients

Variables	Group L (N=90)	Group B (N=90)	P Value
Age (years)	23.43±2.5	23.10±2.2	0.83
Weight (kg)	62.75±2.73	63.18±3.46	0.51
Height (cm)	153.65±3.67	153.46±3.56	0.84

Table 2: Onset of Sensory Block, Onset of Motor Block, Duration of Surgery, Duration of Analgesia

Variables	Group L (N=90)	Group B (N=90)	P Value
onset of sensory block (min.)	5.72±1.08	5.12±0.85	0.001
onset of motor block (min.)	7.00±0.86	5.47±0.70	0.001
duration of surgery (min.)	44.46±2.41	44.18±2.67	0.60
Duration of analgesia (min.)	124.42±2.61	120.56±2.42	0.001

Table 3:Comparison of Pulse Rate and Mean Arterial Pressure (MAP) between Two Groups

	Pulse rate bpm			MAP (mm Hg)		
Time min	Group L	Group B	P Value	Group L	Group B	P Value
Baseline	106.32±7.56	105.10±6.3	0.43	89.12±5.78	89.81±6.56	0.59
5	78.93±11.45	106.32±.52	0.001	80.09±4.86	92.10±4.14	0.001
10	71.71±9.21	97.16±5.24	0.001	74.14±6.32	89.30±6.50	0.001
15	72.40±7.42	93.70±5.02	0.001	78.65±4.06	84.78±6.40	0.001
20	84.16±7.65	91.50±5.03	0.001	75.35±54.17	76.79±7.56	0.24
25	73.71±7.90	85.89±9.86	0.001	68.32±4.86	79.50±8.04	0.001
30	80.31±14.27	82.56±10.97	0.40	75.03±6.25	85.37±9.58	0.07
45	73.98±6.72	81.61±6.12	0.001	74.76±5.42	85.37±9.62	0.001
60	75.02±6.43	80.04±3.44	0.001	75.42±6.12	90.01±2.68	0.001

Table 4: Comparison of Side Effects between the Two Groups

Side effects	Group L	Group B	Total
Nausea and vomiting	4 (8.7%)	5 (11%)	9 (10%)
Shivering	3 (6.66%)	4 (8.88%)	7 (7.77%)
Hypotension	6 (13.3%)	8 (17.7%)	14 (15.55%)
Bradycardia	2 (4.44%)	4 (8.88%)	6 (6.6%)

Discussion

The present study was undertaken to compare the onset and duration of effective anaesthesia and analgesia. The comparison of clinical efficacy of group-L and group-B, in terms of onset and duration of analgesia, was assessed along with pulse rate, blood pressure (SBP, DBP, MAP) at regular intervals throughout the perioperative period in elective caesarean delivery.

In our study, the demographic profiles were comparable for age, weight and height in both the groups (Table 1). Table 2 shows the duration of surgery performed in two groups. Applying appropriate statistical test, it was concluded that the two groups were comparable (p=0.60) in terms of duration of surgery.

Table 2 shows the time for onset of sensory block and motor block in the two groups. The mean onset of sensory block to reach T6 in Group L was 5.72 ± 1.10 minutes and in Group B was 5.13 ± 0.87 minutes. Appropriate statistical test shows significant difference (p=0.00) in the onset of sensory block between the two groups. The mean onset time of motor block to maximum level in Group L were 7.00 ± 0.95 minutes and in Group B were 5.47 ± 0.75 minutes. With appropriate statistical test, p value became 0.00. Hence, it shows that there was statistical significant difference as p is <0.05 in the time of onset of motor block between the patients in Group L and Group B.

In 2012, Turkmen A, Moralar DG, Ali A, Altan in a prospective study on 50 pregnant mothers undergoing caesarean section who received either bupivacaine (0.5%) 7.5 mg + fentanyl 15 mcg or levobupivacaine (0.5%) 7.5 mg intrathecally concluded that time to sensory and maximum motor block was shorter in the bupivacaine + fentanyl group but longer duration of analgesia in the levobupivacaine + fentanyl group. Our observation is similar to the results of Bajwa SS et al, who in their study of Clinical profile of levobupivacaine in regional anaesthesia found that the time to onset of sensory and maximum motor block as well as the duration of analgesia is slightly longer with intrathecallevobupivacaine as compared to bupivacaine in caesarean section. In 2014, Del-Rio Vellosilo et al. did a study using 12.5 mg of isobaric bupivacaine and levobupivacaine in two different groups for knee arthroscopy under subarachnoid block. They found that onset of sensory (p = 0.018) and motor (p = 0.003) block was faster in bupivacaine group compared to levobupivacaine group. In 2002, Alley et al conducted a double blind study on 18 healthy volunteers to receive two spinal anaesthetics, one with bupivacaine (0.5%) and other with levobupivacaine (0.5%) of equal milligram dose (4, 8, 12 mg), determined that equal dosage of hyperbaric levobupivacaine and bupivacaine provided a similar sensory and motor response without any specific advantages. Glaser C et al in 2002 conducted a study for elective orthopaedic hip replacement with spinal anaesthesia receiving 3.5 mL isobaric levobupivacaine (0.5%) or 3.5 mL isobaric bupivacaine (0.5%) and found both the drugs had equal effective potencies with regards to onset and duration of sensory and motor blockade. They found that levobupivacaine showed a more sustained sensory and motor blockade. In 2006, Fattorini F et al conducted a prospective study on 60 patients, scheduled for hip or knee replacement surgery under spinal anaesthesia to receive either 3 mL levobupivacaine 0.5% or bupivacaine 0.5% bupivacaine and found similar onset time both of sensory and motor block between levobupivacaine and bupivacaine and time for regression of motor blockade was also same. In 2008, Mehta A et al compared intrathecal administration of newer local anaesthetic agents ropivacaine and levobupivacaine with bupivacaine in patients undergoing lower limb surgery. Seventy five patients were randomly assigned to receive isobaric intrathecal bupivacaine 15 mg, levobupivacaine 15 mg, or ropivacaine 15 mg. They concluded bupivacaine provided longer duration of analgesia and motor block vs. levobupivacaine and ropivacaine. The levobupivacaine and ropivacaine are an interesting alternative to racemic bupivacaine. In a study on comparison of intrathecal 3.0 mL isobaric levobupivacaine with 3.0 mL hyperbaric bupivacaine in elderly patients undergoing TURP or TUR of urinary bladder, Gulec D et al showed that levobupivacaine has statistically significant (p = 0.0001) longer onset of maximum motor block time (9.84±3.10 minutes) as compared to bupivacaine (6.49± 2.2 minutes). Erdil F et al in their study on the effects of intrathecal levobupivacaine and bupivacaine in 80 elderly patients, came to the conclusion that although the degree of motor block was similar in both the groups, the time to maximum motor block was 19.1 ± 5.4 minutes in levobupivacaine group while it was

9.5 ± 4.2 minutes in bupivacaine group proving statistically significant longer onset of maximum motor block with levobupivacaine. Our finding is also supported by the findings of Del-Rio Vellosilo et al.who noticed faster onset of maximum motor block in the bupivacaine group compared to levobupivacaine group. Mantouvalou M et al suggested that onset of maximum motor block was faster in bupivacaine group (8 ± 5 min.) compared to levobupivacaine group (11 ± 7 min.) using 3 mL of 0.5 isobaric solution in each group[8-10].

Conclusion

The present study showed that intrathecal isobaric levobupivacaine 12.5 mg provided late onset of sensory and motor block and longer duration of analgesia compared to hyperbaric bupivacaine 12.5 mg in patients of elective caesarean section. All the patients were Haemodynamically stable in both groups. Thus, in conclusion, levobupivacaine seems to be an effective alternative to intrathecal bupivacaine in infra-umbilical surgeries like caesarean section with reduced toxic potential and excellent quality of analgesia.

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