Original Research Article

A Prospective Study of Efficacy of Intrathecal Isobaric Levobupivacaine 12.5 Mg and Hyperbaric Bupivacaine 10 Mg for Caesarean Section

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Abstract

Introduction: Neuraxial anaesthesia in caesarean sections has become an established technique. The various local anaesthetics and opioids have been used, either alone or in combination. Smaller doses of opioids with local anaesthetics supplemented by intrathecal route have been recommended for spinal anaesthesia in parturients undergoing caesarean sections. Spinal anaesthesia is preferred over epidural anaesthesia due to its rapid onset, the greater degree of muscle relaxation and lower dose requirement of local anaesthetics in caesarean cases. It ensures reliable and good quality of block.**Materials and Methods:** This prospective randomised, double-blinded study was conducted in the Department of Anaesthesia, Government Medical College, Ananthapuramu. Written informed consent from all the parturients, a total of 90 parturients who met the inclusion criteria undergoing elective caesarean sections under spinal anaesthesia, were enrolled for study. **Results:** All the 90 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. Table1 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 elective caesarean section with reduced toxic potential and excellent quality of analgesia.

Keywords: Intrathecal anaesthesia, sensory block, motor block, caesarean section.

Introduction

Neuraxial anaesthesia in caesarean sections has become an established technique. Various local anaesthetics and opioids have been used, either alone or in combination[1]. Smaller doses of opioids with local anaesthetics supplemented by intrathecal route have been recommended for spinal anaesthesia in parturients undergoing elective caesarean section[2]. Spinal anaesthesia is preferred over epidural anaesthesia due to its rapid onset, the greater degree of muscle relaxation and lower dose requirement of local anaesthetics in caesarean cases. It also ensures reliable and good quality of block[3].Central neuraxial techniques are an indispensable part of modern anaesthetic practice, providing alternatives to general anaesthesia whenever appropriate. Subarachnoid block is the most commonly administered neuraxial anaesthesia for caesarean delivery because it is easy to perform[4].Bupivacaine is a well-established long-acting local anaesthetic which like all amide anaesthetics has been associated with cardiac toxicity when used in high concentration or when accidentally administered intravascularly. Levobupivacaine is the S (-) isomer of bupivacaine, developed as an alternative to bupivacaine, after the evidence of its less cardiotoxicity and neurotoxicity[5].

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Bupivacaine, the widely used local anaesthetic in regional anaesthesia is available in a commercial preparation as a racemic mixture (50:50) of its enantiomers namely levobupivacaine, S (-) isomer and dextrobupivacaine, R (+) isomer. Severe central nervous system and cardiovascular system perturbances occur on inadvertent intra vascular injection. This has been linked to R-isomer of bupivacaine. The levo rotatory isomer seems to have a safer pharmacological profile with less cardiac and neurotoxic effects [3,4].This safety profile is attributed to its faster protein binding rate[3].Levobupivacaine ((2s)-1-Butyl-N-26-dimethyl phenyl)) piperidone-2-carboxamide is an amino amide local anaesthestic drug belonging to family of n-alkyl substitute pipecoloxylidide. Its chemical formula is $C_{18}H_{28}N_2O$.Alpha 1-Glycoprotein is the main binding site for levobupivacaine. Protein binding of levobupivacaine is more (97%) than that of racemic bupivacaine (95%). Levobupivacaine produces sub arachnoid block with similar sensory, motor block and recovery profile like bupivacaine at low concentration levobupivacaine produces a differential neurological block with minimal effect on motor block[9-15]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[6]. In the current study authors compared the effect of bupivacaine and Levobupivacaine in patients undergoing lower segment caesarean section under spinal anaesthesia.

Materials and Methods

This prospective randomised, double-blinded study was conducted in the Department of Anaesthesia, Government Medical College, Ananthapuramu. Written informed consent from all the parturients, a total of 90 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, acceptable mean difference of 5.85 unit (min), expected standard deviation of 10 and non-inferiority margin 5 units, a minimum sample size of 37 subjects was required per group for a two-tailed hypothesis. We decided to recruit 45 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 blockers, antipsychotic drugs, sedatives; spinal deformities; trauma and local infection; allergy to amino amide local anaesthetic; pre-eclampsia; eclampsia; twin pregnancy.

Onset of sensory block was assessed by pinprick with 23 G hypodermic needle using Hollmen scale[7] [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[8] (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 enquiry in to history through 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, 90 patients were allocated into two groups (45 in each group).

In this prospective, double-blinded study, 90 parturients belonging to ASA physical status I and II were randomly allocated into two groups, Group L (n=45) received 0.5% isobaric levobupivacaine 2.5 mL (12.5 mg) and Group B (n=45) received 0.5% hyperbaric bupivacaine 2 mL (10 mg). The study drugs were prepared by an anaesthesiologist 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 pre loading 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, O2 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 the 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 face mask.

Haemodynamic monitoring was continued. 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 sensory 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 0.6 mg. Patients were followed up daily for any adverse events during their hospital stay.

All raw data were entered into a predesigned excel spreadsheet and analysed using standard statistical software (IBM SPSS version 20). Numerical data was expressed as means, medians and standard deviation of mean. Categorical data was expressed as percentages. Numerical data between two groups which was normally distributed was analysed using Student's independent two tailed t-test. A p value of less than 0.05 was considered statistically significant.

Results

All the 90 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

S. No	Parameters	Group L, (n=45)	Group B, (n=45)	P value
1	Age in years	23.22 ± 2.6	23.11 ± 2.4	0.83
2	Weight (Kg)	62.82 ± 2.97	63.29 ± 3.77	0.51
3	Height cm)	153.69 ± 3.88	153.84 ± 3.82	0.84

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

S. No	Variables	Group L, (n=45)	Group B, (n=45)	P value
1	onset of sensory block (min)	5.72 ± 1.10	5.13 ± 0.87	0.001
2	onset of motor block (min)	7.00 ± 0.95	5.47 ± 0.75	0.001
3	duration of surgery (min)	44.47 ± 2.42	44.18 ± 2.76	0.60
4	Duration of analgesia (min)	124.49 ± 2.64	120.58 ± 2.51	0.001

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

	Pulse Rate bpm			MAP (mmHg)		
Time min)	Group L	Group B	P value	Group L	Group B	p value
Baseline	106.33 ± 7.58	105.20 ± 6.5	0.43	89.11 ± 5.76	89.80 ± 6.58	0.59
5	78.93 ± 11.47	106.40 ± .57	0.001	80.09 ± 4.94	92.13 ± 4.13	0.001
10	71.71 ± 9.21	97.18 ± 5.35	0.001	74.05 ± 6.72	89.31 ± 6.54	0.001
15	72.40 ± 7.43	93.71 ± 5.02	0.001	78.78 ± 4.05	84.91 ± 6.41	0.001
20	84.18 ± 7.65	91.51 ± 5.05	0.001	75.36 ± 4.16	76.89 ± 7.68	0.24
25	73.73 ± 7.93	85.91 ± 9.98	0.001	68.40 ± 4.92	79.51 ± 8.01	0.001
30	80.31 ± 14.27	82.58 ± 10.97	0.40	75.00 ± 6.60	78.11 ± 9.40	0.07
45	73.98 ± 6.75	81.62 ± 6.11	0.001	74.80 ± 5.48	85.36 ± 9.60	0.001
60	75.04 ± 6.46	80.07 ± 3.55	0.001	75.44 ± 6.02	90.02 ± 2.98	0.001

Table 4: Comparison of Side Effects between the Two Groups

S. No	Side Effects	Group- L	Group- B	Total
1	Nausea and vomiting	4 (8.8%)	5 (11.11%)	9(10%)
2	Shivering	3 (6.66%)	4 (8.88%)	7 (7.77%)
3	Hypotension	6 (13.33%)	8 (17.77%)	14 (15.55%)
4	Bradycardia	2 (4.44%)	4 (8.88%)	6 (6.66%)

Discussion

The present study was undertaken to evaluate the onset and duration of effective anaesthesia and analgesia by comparing levobupivacaine with bupivacaine. 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[7,8].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=0.001) 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.Mantouvalou M et al[11] in their study suggested that there was a slight reduction in mean arterial blood pressures after the spinal injection in all groups, which however was significant only in the bupivacaine group. In addition, the decrease in heart rates after local anaesthetic agent's injection was significant in all groups. Erdil F et al[12] in their study demonstrated that in group bupivacaine, MAP values were significantly lower than in group levobupivacaine, starting from 10 min[9] until 30 min. after injection; p <0.05. In group levobupivacaine, MAP was significantly lower at 25, 35, 55 and 60 min., compared to baseline; p < 0.05. In group bupivacaine, MAP was significantly lower at 5 min. and thereafter, compared to baseline; p <0.05. Throughout the operation, pulse rate was similar in the two groups. However, it was lower in both groups compared to baseline, starting from 25 min. in group levobupivacaine and 15 min. in group bupivacaine; p <0.05[10].Table 4 shows the incidence of side effects in the study groups. Four patients (9%) in Group L and five patients (11%) in Group B had incidence of nausea and vomiting compare with other group. Three patients (7%) in Group L complained of shivering, whereas the number in Group B was four (9%).Minimum effective local anaesthetic dose of levobupivacaine as recommended by up and down sequential design study is 11.7 mg. Traditionally the levobupivacaine dose used for spinal anaesthesia has been 15 mg[13].Onset of sensory block in few studies was slower when compared to our study. Because the study population in our study are parturients, hence faster on set of action.Our study correlates with study done by Turkmen A et al[14] where they have found the duration of analgesia was comparable in both the groups.

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 10 mg in patients of elective caesarean section. All the patients were haemodynamically stable in both groups. The adverse effects in both the groups were comparable.

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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