ORIGINAL ARTICLE

A retrospective comparison of intrathecal levobupivacaine with bupivacaine for elective lower segment cesarean section

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ABSTRACT

Aims: The aim of our study was to compare the onset and duration of sensory and motor block, hemodynamic effects, neonatal outcome and adverse effects of isobaric levobupivacaine and hyperbaric bupivacaine in parturients undergoing elective lower segment cesarean section.

Methodology: Clinical records of parturients, who had undergone elective cesarean section and who had received either isobaric levobupivacaine 2 ml or hyperbaric bupivacaine 2 ml, and fulfilled inclusion and exclusion criteria were reviewed retrospectively and sorted out in two groups of 30 each. Variables investigated included demographic profile, ASA grading, block characteristics, hemodynamic parameters, neonatal apgar score and any anesthesia related complications.

Results: One hundred and forty medical records were evaluated. Demographic profile, block characteristics and anesthesia related complications were similar in both of the groups and statistically insignificant. There was more drop in systolic blood pressure in bupivacaine group at second (p=0.001) and fourth minute (p=0.006), when compared to levobupivacaine group.

Conclusion: Isobaric levobupivacaine is a good alternative to hyperbaric bupivacaine for subarachnoid block due to its better hemodynamic stability in cesarean sections.

Key words: Apgar score; Bupivacaine; Cesarean section; Levobupivacaine; Retrospective Study; Anesthesia, Spinal

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INTRODUCTION

Spinal anesthesia offers many advantages for cesarean delivery.[1] A faster onset, good muscle relaxation, dense neural block and the use of minimal drugs are some of its favorable points over general anesthesia. The main disadvantages include nausea & vomiting, hemodynamic instability and limited duration of anestheisa.[2] Bupivacaine, because of its long action, high potency and minimal transfer to the placenta was widely used in obstetric anesthesia. However, it is cardiotoxic and deaths have been reported due to its toxicity.[3,4,5] The R-isomer of bupivacaine is mainly responsible for this unwanted cardiotoxicity because of its avid and prolonged binding to inactivated cardiac sodium (Na^+) channels.[6,7,8] This led to introduction of levobupivacaine (S isomer of bupivacaine) for regional anesthesia, which has a lower risk of cardiotoxicity and neurotoxicity due to its decreased potency at the sodium channels and faster protein binding rate.[9] The symptoms are usually self-limiting and easily treatable.

Although use of levobupivacaine for spinal and epidural anaesthesia has been well described in literature, very few studies have examined the effects of levobupivacaine in obstetric anaesthesia.[10-13] Therefore, we undertook this study in patients undergoing elective cesarean section to compare the block characteristics, hemodynamic stability, adverse effects and neonatal outcome of intrathecal isobaric levobupivacaine with hyperbaric bupivacaine.

METHODOLOGY

The study protocol was approved by institutional ethical

committee at Mandya Institute of Medical Sciences, Mandya, Karnataka, (India) and patient anonymity was ensured during data collection. Anesthesia records of 140 parturients undergoing elective cesarean section from January to April 2015 were retrieved. Inclusion criteria were parturients of ASA 1 and 2, ages 18-35 yrs, weighing between 50-80 kg and height between 150-180 cm. Parturients posted for emergency surgery, and who had preeclampsia, eclampsia, antepartum hemorrhage, gestational diabetes, precious pregnancy, gravida greater than three, known cardiovascular or cerebrovascular disease, and with prostaglandin use were excluded from the study. Parturients received either 2 ml of 0.5% isobaric levobupivacaine or 2 ml of 0.5% hyperbaric bupivacaine. They were divided into two groups of 30 each; levobupivacaine group (L) and bupivacaine (B) group.

Standard protocols of pre-anesthetic check-up, investigations, and preoperative orders were followed. Informed consent was taken prior to surgery. On the night of surgery parturients were premedicated with oral ranitidine 150 mg. Metoclopramide 10 mg and ranitidine 50 mg were given IV one hour prior to surgery. Basic monitoring consisted of electrocardiogram (ECG), non-invasive blood pressure (NIBP) and pulse oximetry (SpO_2). All patients were preloaded with 10 ml/kg of ringer's lactate solution. Spinal anesthesia was performed in left lateral position at L2-3 or L3-4 space using 25 G Quincke spinal needle. The patients were placed supine with a left lateral tilt following the subarachnoid block. Oxygen was administered through face mask. Oxytocin 10 IU in infusion and methylergonovine maleate 200 mg IM were given to all parturients after clamping of umbilical cord.

Sensory level was assessed by pinprick sensation using a blunt 25 G needle along the mid-clavicular line bilaterally. The time to reach T10 dermatome (onset time), the maximum sensory level achieved, time for two segment (the duration of sensory block) were recorded. The motor block was assessed according to the modified Bromage scale (0 = No paralysis, able to flex hips/knees/ankles; 1 = Able to move knees, unable to raise extended legs; 2 = Able to flex ankles, unable to flex knees; 3 = Unable to move any part of the lower limb). For motor blockade, onset time was considered as time from spinal injection to achievement of Bromage 3, whereas duration was considered as time between Bromage 3 to Bromage 0. In the intraoperative period, vital parameters (HR, SBP and Spo_2) were recorded immediately after the block, every 2 min for first 10 min and every 5 min till the end of surgery.

Any complication, e.g. hypotension, bradycardia, nausea, vomiting, shivering or headache were noted and treated accordingly. A drop in SBP, of > 20% from the baseline or < 90 mmHg, was considered as hypotension and was treated with bolus of mephentermine sulphate 6 mg. A drop of heart rate (HR) > 20% or less than 50 per min was considered as bradycardia and treated with atropine 0.6 mg IV. Neonatal outcome was assessed by the Apgar score at 1 and 5 min.

The sample size was based on the duration of analgesia (mean and standard deviation) in both groups from previous studies. This was obtained after accepting an alfa error of 5% (95% confidence interval) and beta error of 20%. From this we calculated the sample size to be 30.

Data from all case records were transferred into Microsoft Excel™ for statistical analysis.

Statistical analysis: Statistical evaluation was performed by using SPSS 11.5 (SPSS Inc., Chicago, IL). Normally distributed continuous variables are expressed as mean (SD) and non-normally distributed data variables as median (range). Differences between groups were analyzed by Student's unpaired 't' test for normally distributed data. Chi-square test was used for categorical variables. The value of $P < 0.05$ was considered significant.

RESULTS

Demographic data in both the groups were comparable as shown in Table 1. There was no significant differences in baseline SBP and HRs, time of surgical incision or

Table 1: Comparison of demographic profile of the 2 groups (Data presented as Mean ± SD)

Parameter	Group L (N = 30)	Group B (N = 30)	P value
Age	23.57 ± 2.24	23.90 ±1.75	0.523
Weight	63.40 ± 6.44	62.80 ± 6.84	0.728
Height (cm)	155.90 ± 3.60	155.97 ± 3.96	0.946
Baseline HR (beats per min)	101.03 ± 18.87	96.73 ± 11.57	0.292
Baseline SBP (mmHg)	123.80 ± 13.01	126.83 ± 10.04	0.316
Time of surgical incision*	5.37 ± 0.99	5.43 ± 1.22	0.818
Duration of surgery (min)	49.63 ± 5.57	51.23 ±5.69	0.276
Apgar score	7.33 ± 0.71	7.62 ± 0.76	0.143

* Time in min (from spinal injection to surgical incision)

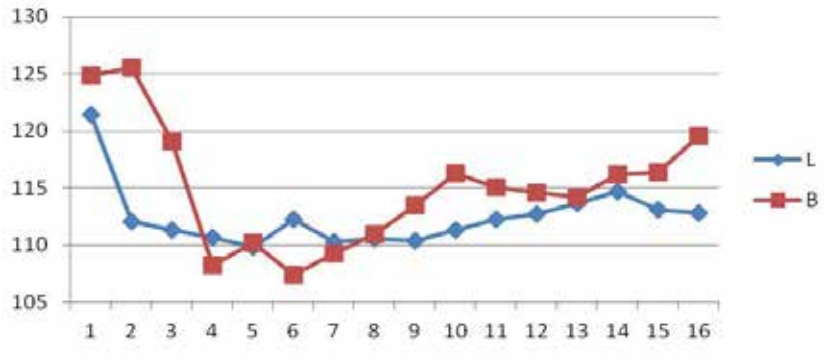

Figure 1: Comparison of systolic blood pressure

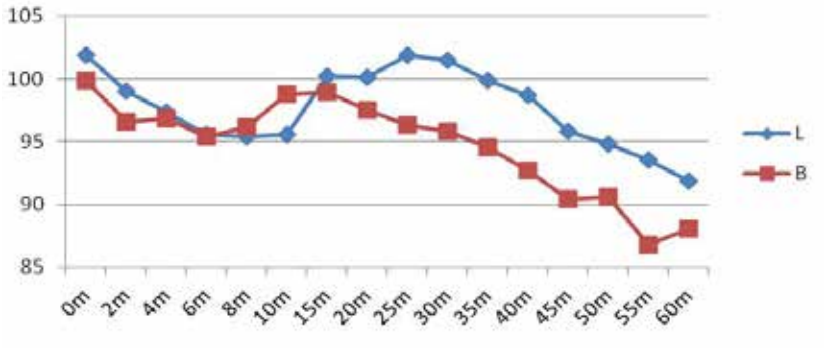

Figure 2: Comparison of heart rate

duration of surgery.

No significant difference was found in newborn apgar scores at 1 and 5 min.

With regard to block characteristics, no significant difference was found in time to achieve T10 sensory block between groups. The highest dermatomal level recorded in majority of parturients in both groups was T4, with the exception of one in Group L and three parturients in Group B who showed block level upto T2.

The time taken to attain T10 and T6 sensory levels and time to 2-segment regression of sensory block are mentioned in Table 2. No significant differences were found between the groups regarding onset of motor block, duration of maximum motor block and regression of motor block. (Table 2).

The frequency of hypotension was significantly higher in Group B, compared to Group L [15 vs. 7 ($p < 0.05$)] (Table 5). There was a drop in SBP at second ($P = 0.001$) and fourth minutes ($P = 0.016$) in Group B compared to Group L, which was statistically significant. Co-efficient of variation in SBP was more in Group B at 4, 10, 45 and 60 min. Difference was also found in the rest of values except in 0, 8 and 40th minute (Table 3; Figure 1). Baseline HR was comparable in both the groups (Table 4; Figure 2).

Only one patient experienced bradycardia in Group L compared to 4 patients in Group B. Nausea, vomiting and shivering were more frequent in Group B than in Group L (Table 5).

DISCUSSION

Spinal anesthesia offers better quality of anesthesia for parturients undergoing elective cesarean section. Simplicity, rapid onset, dense neural block are its main advantages when compared to general anesthesia,[1,2] however the rapid onset of sympathetic blockade may result in abrupt, severe hypotension.[14] Many methods have been used to reduce hypotension, including dose reduction, use of prophylactic vasopressors, preloading with fluids and recently, use of cardiostable drugs like levobupivacaine and ropivacaine.[15,16]

Table 2: Characteristics of intrathecal blocks in two groups (Mean ± SD)

Parameters	Group L	Group B	P value
Time to sensory block to T10 (min)	1.73 ± 0.69	1.57 ± 0.57	0.312
Time to sensory block to T6 (min)	3.23 ± 0.73	3.03 ± 0.81	0.078
Time to 2-Segment regression (min)	61.97 ± 7.32	61.57 ± 7.70	0.453
Regression to T10 (min)	125.50 ± 7.35	126.50 ± 8.11	0.619
Onset of Motor Block (B2) (min)	3.33 ± 1.10	3.20 ± 0.85	0.599
Max. motor block (B4) (min)	4.30 ± 1.58	3.40 ± 1.07	0.781
Time to regression of motor block (B0) (min)	118.83 ± 12.26	128.33 ± 10.93	0.663
Total duration of analgesia (min)	129.00 ± 10.70	143.83 ± 10.72	0.453

**P value < 0.05 considered significant*

Table 3: Comparison of systolic blood pressure

Time (min)	Group L (Mean ± SD)	Group B (Mean ± SD)	P value
0	121.43 ± 10.42	124.87 ± 10.65	0.212
2	112.10 ± 14.30	125.50 ± 14.60	0.001
4	111.37 ± 13.84	119.10 ± 9.86	0.016
6	110.63 ± 14.64	108.27 ± 12.70	0.507
8	109.80 ± 14.75	110.20 ± 14.55	0.916
10	112.27 ± 10.39	107.43 ± 14.65	0.146
15	110.27 ± 12.00	109.30 ± 12.02	0.756
20	110.57 ± 10.95	110.97 ± 12.11	0.894
25	110.40 ± 9.88	113.47 ± 11.29	0.268
30	111.37 ± 9.97	116.30 ± 11.30	0.078
35	112.27 ± 9.04	115.10 ± 10.92	0.278
40	112.73 ± 9.26	114.60 ± 9.24	0.438
45	113.70 ± 7.26	114.23 ± 11.36	0.829
50	114.72 ± 6.85	116.20 ± 8.94	0.481
55	113.13 ± 6.63	116.41 ± 8.16	0.215
60	112.78 ± 6.70	119.57 ± 11.51	0.125

Table 4: Comparison of heart rate (beats / min)

Time (min)	Group L (Mean ± SD)	Group B (Mean ± SD)	P value
0	101.87 ± 21.34	99.87 ± 13.64	0.667
2	99.03 ± 17.54	96.57 ± 14.02	0.550
4	97.30 ± 18.25	96.83 ± 18.91	0.923
6	95.53 ± 19.75	95.40 ± 19.48	0.979
8	95.43 ± 20.06	96.17 ± 16.28	0.877
10	95.57 ± 17.93	98.77 ± 15.31	0.460
15	100.17 ± 16.43	98.93 ± 14.38	0.758
20	100.13 ± 16.67	97.50 ± 14.54	0.517
25	101.90 ± 15.69	96.33 ± 13.97	0.152
30	101.43 ± 16.37	95.80 ± 11.66	0.130
35	99.87 ± 15.16	94.53 ± 10.72	0.121
40	98.70 ± 16.06	92.67 ± 11.08	0.096
45	95.83 ± 15.16	90.43 ± 12.54	0.138
50	94.79 ± 15.39	90.57 ± 14.53	0.283
55	93.56 ± 17.38	86.76 ± 14.13	0.226
60	91.89 ± 19.56	88.07 ± 13.97	0.590

Table 5: Side effects

Side effects	Group L (n = 30)		Group B (n = 30)	
	Number	Percentage	Number	Percentage
Hypotension	7	26.6	15	50.0
Bradycardia	1	3.3	4	13.3
Nausea /Vomiting	5	16.6	8	26.6
Shivering	3	10.0	5	16.6

The dose is decreased slightly for very short and obese patients, and it is increased slightly if the block is performed in the sitting position. A dosage between 7.5 - 15 mg of levobupivacaine has been used for cesarean section. Bremerich DH et al[17] and Parpaglioni et al[18] reported minimum effective intrathecal levobupivacaine dose to be 10 and 10.58 mg respectively in cesarean section which was similar to our observation. In our study we chose a dose of 10 mg of isobaric levobupivacaine and 10 mg of hyperbaric bupivacaine.

In our study, we did not find any significant differences in onset time, time to maximum sensory and motor block as well as duration of sensory and motor block between two groups. Similar results have been reported in earlier studies comprising of non-obstetric surgeries.[19,20] Glaser et al[21] compared 3.5 ml of isobaric levobupivacaine to 3.5 ml of isobaric bupivacaine in patients scheduled for elective hip replacement and found equal potency and hemodynamic stability between the two drugs. Similarly, Bay-Nielsen et al[22] observed similar analgesic effects of 0.25% levobupivacaine and bupivacaine for infiltration analgesia in inguinal hernia repair. The apparent equipotency of bupivacaine and levobupivacaine reported in these studies may be explained by the large dose of local anesthetics used, which may have masked the differences in potencies.[23]

In contrast to our study, Guler et al[24] and Gautier et al[23] observed differences in motor and sensory block between two drugs in cesarean section. Their results showed shorter duration of sensorty and motor block with isobaric levobupivacaine. Paradoxically, a study by Turkemen et al observed a longer sensory and motor block, and a longer duration of analgesia with levobupivacaine compared to bupivacaine.[25]

A potency hierarchy of intrathecal bupivacaine > levobupivacaine > ropivacaine in cesarean section patients has been confirmed in clinical studies.[26,27] However, further studies regarding the efficacy and potency of local anesthetics are needed to confirm this in obstetric patients.

Our study has shown that levobupivacaine has better pharmacodynamic profile when compared to bupivacaine. There was a higher incidence of hypotension in bupivacaine group compared to levobupivacaine group. Some studies have attributed the cause of hypotension to hyperbaricity of the drug effecting the peak block height when compared to isobaric drugs.[28] In our study peak block height was comparable in both the groups. Hypotension may be attributed to other variables like lumbar puncture at higher level like L2-L3, which was done in most of our patients. Glaser et al[21] reported that levobupivacaine, as compared with bupivacaine, causes less bradycardia, which may reduce the fall in arterial pressure as shown by our study. Intragroup variation of SBP and HR was more frequent in bupivacaine compared to levobupivacaine group. Similar results were reported by Coppejans et al.[26] The study reported spinal levobupivacaine for cesarean section causes hypotension than racemic bupivacaine.

Besides hypotension, other common side effects like bradycardia, nausea, vomiting, shivering were more frequent in bupivacaine group compared to levobupivacaine group in our study.

LIMITATIONS

It was a retrospective study and we could not eliminate bias. Moreover, the sample size was small.

CONCLUSION

Isobaric levobupivacaine produces more hemodynamic stability when compared to hyperbaric bupivacaine, which makes it a preferable choice for spinal analgesia in cesarean sections. However, large, multi-center, prospective randomized studies are needed to establish its equipotency to confirm the differences or superiority of one drug over the other.

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Authors' Contribution:

ABN: Concept and design of the study, retrieval and analysing the data, drafting the article, final approval of the manuscript

SG: Concept and design of the study, general supervision of the study

UNP: Retrieval and analysis of the data, drafting the manuscript

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