ISSN 2515-8260 Volume 9, Issue 3, Winter 2022

ORIGINAL RESEARCH

A comparison of intrathecal levobupivacaine with hyperbaric bupivacaine for elective caesarean section: A prospective randomized study

[1] Dr MohdMoazzam Mohiuddin Ansari,[2]Dr.Mamidi Ajay Kumar,[3]Dr.KaramthotRavinayak, [4]Dr. Harish Uppala

[1]Assistant Professor, Department of Anaesthesiology, Sarojini Devi Eye Hospital/ Osmania Medical College, Hyderabad, Telangana, India
[2]Assistant Professor, Department of Anesthesiology& Critical Care, Niloufer Hospital/Osmania Medical College, Hyderabad, Telangana, India
[3]Assistant Professor, Department of Anesthesiology, Gandhi Medical College and Hospital, Secunderabad, Telangana, India
[4]Assistant Professor: Department Of Anaesthesiology & Critical Care: Sultan Bazar Maternity Hospital/ Osmania Medical College

Correspondence:
Dr. Harish Uppala,
Assistant Professor: Department Of Anaesthesiology & Critical Care:
Sultan Bazar Maternity Hospital/ Osmania Medical College

ABSTRACT

Introduction:The subarachnoid block is a safe and time-tested technique for administering anesthesia for cesarean section due to its rapid onset and effective sensory and motor blockade. Bupivacaine is available as a racemic mixture of its enantiomers, dextrobupivacaine and levobupivacaine [1] and is the most frequently used anesthetic agent for cesarean section.

Aims: This study was performed to compare the anaesthetic efficacy and safety of two local anaesthetic agents: Hyperbaric Bupivacaine and Isobaric Levobupivacaine, in patients undergoing elective caesarean section.

Methods and materials: It is prospective study in 100 patients, ASA I-II, were randomized to receive an intrathecal injection of Hyperbaric Bupivacaine or Isobaric Levobupivacaine. Group B (n = 50) received 2 ml of Hyperbaric Bupivacaine 5 mg/ml (10 mg). Group L (n = 50) received 2 ml of Isobaric Levobupivacaine 5 mg/ml (10 mg). The onset and duration of sensory and motor blockade, recovery parameters, hemodynamic changes and side effects for the two agents were compared.

Results: The time of onset of sensory block was faster in Group B (1.80 ± 0.404) when compared with Group L (2.02 ± 0.473). In Group B the time to two segment regression was prolonged (74.68 ± 12.916) when compared with Group L (69.08 ± 3.349) and it is statistically significant. Duration of motor blockade was prolonged in Group B (135.52 ± 4.781) when compared with Group L (100.04 ± 9.165). Hemodynamic variables were more stable in Group L than Group B. Twenty patients in Group B had adverse effects when compared with ten patients in Group L.

Conclusion: 0.5% Isobaric Levobupivacaine 10mg for intrathecal injection of caesarean section produces adequate sensory and motor blockade and stable hemodynamic parameters with minimum adverse effects than 0.5% Hyperbaric Bupivacaine 10mg. We concluded that Isobaric Levobupivacaine is a better alternative for caesarean section.

Keywords: Isobaric Levobupivacaine, Caesarean section,Motor blockade,Hemodynamic parameters.

INTRODUCTION

Spinal anaesthesia was introduced into clinical practice by Karl August Bier in 1898. More than a century has passed and even today, it is one of the most popular techniques for both elective and emergency surgical procedures particularly Caesarean Sections, lower abdominal surgeries, orthopaedic and urological surgeries just to name a few. Spinal anaesthesia is used for providing a fast onset and effective sensory and motor blockade. Bupivacaine is available as a racemic mixture of its enantiomers, (dextrobupivacaine and levobupivacaine). Levobupivacaine is an effective long acting amide local anaesthetic produced as a pure enantiomer. The sensory block is similar to that produced by an equivalent dose of Bupivacaine. However, the motor block provided is of slower onset, lesser intensity and of shorter duration. Levobupivcaine is an L-enantiomer of Bupivacaine. When administered for caesarean section it has been shown to have motor blockade of lesser intensity when compared to Bupivacaine. It is also considered more potent than Ropivacaine due to its greater lipid solubility.

The reduced toxic potential of both the above mentioned drugs is strongly supported by animal and volunteer studies, which report higher plasma concentrations before signs of systemic toxicity appear and also a higher success rate of cardiopulmonary resuscitation in cases of cardiac collapse. In our study we will compare the clinical effects of two drugs Levobupivacaine and Bupivacaine in spinal anaesthesia for elective caesarean section.

MATERIALS AND METHODS

It is prospective study 100 Pregnant women of physical status American society of Anaesthesiologists (ASA) I and II between the age group of 18-35 posted for elective lower segment caesarean section at Osmania Medical College, Sultan Bazar Maternity Hospital, Koti, Hyderabad have been selected for the study. The patients were randomly allocated into two groups comprising of 50 patients in each group. After ethical committee approval and informed consent obtained.

INCLUSION CRITERIA

Age between 18-35 years, ASA physical status I and II, at term elective caesarean Section

EXCLUSION CRITERIA

Pregnant patients having coexisting systemic disorders like neuromuscular diseases, neuronal degenerative disorder, seizure disorder, bleeding and haematological disorders, Cardiac disorders, Diabetes mellitus or gestational diabetes., Pregnant women with hepatic and renal disorders, severe Anaemia, Eclampsia, placenta praevia, abruptio placenta, Parturient in active labour, Twin/complicated pregnancy, Patient refusal, Contraindications to spinal anaesthesia, Allergy to local anaesthetic drugs, Fetal distress and Mentally retarded.

Each patient was reassured, explained the procedure and informed consent taken. All patients were confirmed to be physically fit. Minimal fasting period is 8 hrs, following application of routine monitors (NIBP, ECG, PULSE OXIMETRY), IV line secured with 18G IV cannula. All patients were given aspiration prophylaxis comprising of injection Metoclopramide (10mg) and Ranitidine (50mg) IV 10 min before surgery & preloaded with RL 10 – 12 ml/ kg. Baseline mean arterial BP and pulse rate, Spo2 were noted. Subarachnoid block (SAB) is instituted at L3-L4 or L4-L5 intervertebral space in right lateral position using 25-G Quincke's needle.

Using a sealed envelope technique, patients were equally and randomly divided into two groups.

Group B (n = 50); 10 mg 0.5% (2 ml) Bupivacaine

Group L (n = 50); 10 mg 0.5% (2 ml) Levobupivacaine.
Patients were turned to a 15˚ - 20˚ left lateral supine position. Oxygen 6 L/min was administered via a face mask. Patients were treated with titrated doses of Inj. : Mephentermine 6 mg I.V. if systolic BP <90 mm/Hg or <20% baseline.Inj. : Atropine 0.6 mg I.V. if Heart Rate <50/min. After delivery of baby, Inj. Oxytocin 10 IU in IV drip & 10 IU IM were given.
The sensory level of spinal anaesthesia was assessed by pinprick in axillary line using a 26 G needle, and was recorded at baseline prior to spinal injection, then every 2 minute for the first 15 min after injection, and every five minutes for the next 30 min, and at 45 min. Blood pressure, heart rate, and the extent of motor block were recorded every 2 min for first 15 min ,and 5 min for next 30 min and at 45 min. Once a T4-T6 level has been reached, surgeon was told to start the surgery. Administration of anaesthetic drug and time of analgesic requirement in PACU. The occurrence of adverse events including bradycardia, hypotension, decrease in oxygen saturation SpO2 < 93 %, shivering, nausea and vomiting were also recorded.

STATISTICAL METHODS

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis). Mann Whitney U test has been used to find the significance between two groups for parameters on non-interval scale. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.
* Moderately significant (P value: 0.01<P< 0.05) ** Strongly significant (P value < 0.01) .
The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 and Systat 12.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

All 100 patients in two groups completed the study without any exclusion. We did an inter group analysis and the results were as follows. Of the 100 patients, 50 belonged to Group B (Hyperbaric Bupivacaine) and other 50 categorized as Group L (Isobaric Levobupivacaine). Data were presented as range, mean, standard deviation. The probability value 'P' of less than 0.05 considered statistically significant. Age, weight, height of the patient between both the groups were comparable and were not statistically significant (P > 0.05).

Table – 1 Comparison of demographicdistribution between the two groups

Parameter	Group	Frequency	Mean	Standard Deviation	P Value'T' Test
Age	B	50	24.52	4.001	0.660
	L	50	24.22	2.943	
Weight	B	50	70.78	6.309	0.639
	L	50	71.36	6.049	
Height	B	50	159.56	2.800	0.090
	L	50	160.52	2.815	
Duration of Surgery (in minutes)	B	50	52.02	4.191	0.183
	L	50	53.18	4.466	

The average duration of surgery in both groups was comparable the "P" value of 0.183 which was not significant.

Table-2: Comparison of PR between two groups at various intervals.

Pulse Rate	Group	Frequency	Mean	Standard Deviation	P Value 'T' Test
BASELINE	B	50	83.3	9.632	0.389
	L	50	87.7	8.873	
2 MIN	B	50	84.68	11.372	0.951
	L	50	84.8	7.886	
5 MIN	B	50	82.5	8.364	0.568
	L	50	83.36	6.533	
10 MIN	B	50	82.02	9.951	0.247
	L	50	80.12	5.801	
15 MIN	B	50	87.08	7.286	0.054
	L	50	84.14	7.822	
30 MIN	B	50	86.1	8.154	0.090
	L	50	83.38	7.771	
45 MIN	B	50	90.26	10.301	0.306
	L	50	88.22	9.519	

Table shows distribution of pulse rate at various intervals between two groups and p value is statistically insignificant.

Table –3: Comparison of MAP between two groups at various intervals.

MAP	Group	Frequency	Mean	Standard Deviation	P Value 'T' Test
BASELINE	B	50	90.32	6.504	0.064
	L	50	87.74	7.286	
2 MIN	B	50	88.7	6.427	0.001
	L	50	84.54	5.980	
5 MIN	B	50	70.2	9.162	0.0001
	L	50	85.94	10.363	
10 MIN	B	50	67.94	6.463	0.0001
	L	50	83	6.580	
15 MIN	B	50	68.8	5.503	0.0001
	L	50	83.68	5.984	
30 MIN	B	50	70.66	5.626	0.0001
	L	50	82.56	4.131	
45 MIN	B	50	74.32	4.765	0.0001
	L	50	86.08	3.613	

Table shows the distribution of hemodynamic variables at various interval between the two groups and p value is statistically significant

Table-4: Comparison of SpO2 between two groups at various intervals.

SpO2	Group	Frequency	Mean	Standard Deviation	P Value 'T' Test
BASELINE	B	50	99.16	1.489	0.619
	L	50	99.30	1.313	
2 MIN	B	50	100	0	N/A
	L	50	100	0	
5 MIN	B	50	100	0	N/A

	L	50	100	0	
10 MIN	B	50	99.18	0.940	0.669
	L	50	99.08	1.355	
15 MIN	B	50	99.76	0.517	0.306
	L	50	99.86	0.452	
30 MIN	B	50	99.72	0.453	0.085
	L	50	99.48	0.862	
45 MIN	B	50	99.80	0.494	
	L	50	99.58	0.730	0.081

The distribution of spo2 at various interval between two groups which is statistically insignificant.

Table-5: Comparison of time of sensory and motor block between the two groups

Time of Onset of Sensory block (min)	**Group B**	**Group L**
Range	1-3	1-2
Mean	1.80	2.02
SD	0.404	0.473
P Value	0.014 Significant	
Maximum sensory level (min)		
Range	9-20	8-15
Mean	13.74	11.88
SD	1.482	1.099
P Value	0.0001 Significant	
Time to two segment regression (min)		
Range	65-80	60-75
Mean	74.68	69.08
SD	2.916	3.349
P Value	0.0001 Significant	
onset of motor block (min)		
Range	2-4	3-6
Mean	2.90	4.56
SD	0.505	0.884
P Value	0.0001 Significant	
Time to maximum of motor block (min)		
Range	5-10	6-15
Mean	6.48	11.28
SD	1.199	2.060
P Value	0.0001 Significant	
Duration of motor block level		
Range	125-150	85-120
Mean	135.52	100.04
SD	4.781	9.165
P Value	0.0001 Significant	

In table time to reach maximum sensory block, time to two segment regression,Time of onset of motor block, Time to reach maximum motor block, time to reach maximum motor block, duration of motor block which was statistically significant between two groups.

Table-6: Comparison of peak level of sensory block (T-dermatome) between the two groups

Peak level of Sensory Block	Number of cases in			
	Group B		Group L	
	No.	%	No.	%
T2	11	22%	3	7%
T4	22	44%	14	27%
T6	17	34%	33	66%
Total	50	100%	50	100 %

Median peak level of sensory block was T4 in Group B and T6 in Group F.

Table-7: Comparison of Adverse effects between two groups

Adverse effects	Group B		Group L	
	No	%	No	%
Hypotension	11	22	2	4
Bradycardia	3	6	1	2
Shivering	4	8	5	10
Vomiting	2	4	2	4
Total cases with adverse				
effects	20*	40	10*	20
Total cases without adverse				
effects	30*	60	40*	80
Total	50*	100	50*	100

More than one adverse effect was present in one case in each Group. There was less incidence of Hypotension and Bradycardia in Group L than Group B. But this was statistically insignificant. Shivering, nausea and vomiting in both the groups were comparable.

DISCUSSION

Spinal anaesthesia, providing an effective surgical anaesthesia and postoperative analgesia by ensuring minimal maternal and neonatal side effects, has been reported to be more advantageous than general anaesthesia for caesarean operations. Bupivacaine is a preferred agent in obstetric anaesthesia due to its long lasting action and lower levels of placental transition; most serious side effect is cardiotoxicity, which makes pregnant women, more sensitive to this effect. Levobupivacaine is a more favourable local anaesthetic agent in terms of safety profile with similar pharmacokinetic properties to racemic bupivacaine. However, trials have reported that the cardiovascular and central nervous system-related side effects of levobupivacaine are less than those of bupivacaine, though the onset and duration of action, hemodynamic changes after spinal anaesthesia are the same for levobupivacaine and bupivacaine.

We conducted a randomized, case-control study to evaluate the hemodynamic stability of intrathecal Isobaric Levobupivacaine 10 mg for caesarean, which was based on studies of of Duggal et al[2] 2015 and Gulenguler et al[1] 2012. Gulenguler et al[1] conducted a study to

investigate the clinical efficacy of levobupivacaine and bupivacaine for spinal anaesthesia in caesarean section. Group LF received 10 mg levobupivacaine with fentanyl 15 mcg and Group BF received 10mg bupivacaine with fentanyl 15 mcg.

They observed in group BF motor block was faster and longer, bradycardia, hypotension and nausea less in group LF. Bremerich DH[3] et al carried out a dose finding investigation of levobupivacaine for parturients undergoing elective caesarean delivery in 2007. Parturients received either 7.5, 10 or 12.5 mg intrathecal hyperbaric 0.5% levobupivacaine. They recommended 10 mg levobupivacaine for parturients undergoing elective caesarean section with spinal anaesthesia.

"In our study, sensory block levels required for caesarean section were achieved in both groups, and it was observed that the hemodynamic stability with levobupivacaine was better maintained". Goyal et al[4]conducted a study on 30 parturient for elective caesarean section. They were divided in to Group BF receiving 10 mg bupivacaine and 25 mcg fentanyl, or Group LF receiving 10 mg isobaric levobupivacaine and 25 mcg fentanyl. Haemodynamics like MAP was lower in group BF and in Group LF maximum sensorial block level and postoperative visual analogue scale scores were higher.

“Onset of motor block time, time to max motor block, time to T10 sensorial block, reversal of two dermatome, the first analgesic need were similar in both groups" They concluded that isobaric levobupivacaine is good alternative for cesarean section as it provides less motor block and maintains hemodynamics stability.

In our study we observed that maximum sensory block level in bupivacaine group was higher and development of motor block was faster and lasted longer. “The results of our study are also similar to Gautier et al[17] reported during spinal anaesthesia for caesarean delivery, they compared the same doses of levobupivacaine and bupivacaine, and reported that while adequate anaesthesia was maintained in the 97% of the patients in the bupivacaine group, this rate was 80% in the levobupivacaine group, and duration of motor block and analgesia was shorter in the levobupivacaine".

In a study by Bremerich et al[3] involving 60 patients who were scheduled for caesarean section and were administered 0.5% levobupivacaine (10 mg) and 0.5% bupivacaine (10 mg) in combination with opioid (10 and 20 μg of fentanyl and 5 μg of sufentanyl), the duration of motor block was found to be shorter with levobupivacaine compared to bupivacaine. In a study by Copperjans et al[5] comparing 6.6 mg of bupivacaine supplemented with 3.3 μg of sufentanil, 6.6 mg of levobupivacaine and 10 mg of ropivacaine, they found a better value of systolic blood pressure in the levobupivacaine group. In our study, we used 10mg of 0.5 % hyperbaric bupivacaine for intrathecal injection. We measured the time of onset and duration of sensory block, hemodynamic changes, modified bromage scale, duration of motor block and adverse effects all these were measured from the time of injection of subarachnoid block.

In our study, we found that both Isobaric Levobupivacaine and Hyperbaric bupivacaine produces equal efficacy of motor and sensory blockade. Isobaric levobupivacaine produces effects with minimal adverse effect which is similar to randomized double blind study conducted by Glaser et al[6].Mantouvalou et al[7] performed a study to compare three local anaesthetic agents: racemic bupivacaine and its two isomers: ropivacaine and levobupivacaine, for anaesthetic efficacy and safety in patients undergoing lower abdominal surgery. They found that levobupivacaine required less vasoactive drugs with equal efficacy of motor and sensory blockage.

In our study hypotension is more prevalent in Hyperbaric bupivacaine than isobaric levobupivacaine.In our study we found that the time to two segment regression is earlier in Isobaric levobupivacaine than hyperbaric bupivacaine which is supported by NK Girgin et

al[8] 2012. In our study we found that the potency of two drugs, duration of motor block is higher in hyperbaric bupivacaine (Range 125-150 min,) than Isobaric bupivacaine (Range 85-120 min). A study carried out by Camorcia et al[9] in 2007 compared the relative potencies of intrathecal ropivacaine, levobupivacaine and bupivacaine for motor block. They concluded that potency for motor block when administered via intrathecal route was low for ropivacaine, intermediate for levobupivacaine and high for bupivacaine, which is in keeping with our findings.

Fattorni et al[10] conducted study on eighty patient who has been posted for major orthopaedic surgery . There is no significant characteristic difference in sensory and motor block between the levobupivacaine and bupivacaine. In levobupivacaine group, no incidence of severe hypotension and cardiovascular stability was maintained. Glasser et al[6] compared that in levobupivacaine group causes less incidence of bradycardia and it reduces arterial pressure less compared to bupivacaine.

In my study, we found that occurence of bradycardia is more prevalent in Group B bupivacaine 0.5 % than Group L Isobaric Levobupivacaine 0.5%. This findings has been supported by Mantouvalou et al[11] performed study which said that, compared to both ropivacaine and levobupivacaine , Bupivacaine required more often the use of ephedrine and atropine.

CONCLUSION

0.5% Isobaric Levobupivacaine 10 mg for intrathecal injection of caesarean section produces adequate sensory and motor blockade and stable hemodynamic parameters with minimum adverse effects than 0.5% Hyperbaric Bupivacaine 10 mg. We concluded that Isobaric Levobupivacaine is a better alternative for caesarean section.

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