

Original Research

Comparison of Haemodynamic Parameters with Low Dose Intrathecal 0.5% Isobaric Levobupivacaine Versus 0.5% Isobaric Bupivacaine for Inguinal Hernia Repair

Prakash Singh¹ Charuta Gadkari² Shubhada Deshmukh³ Devashree Warnekar⁴

¹Senior Resident, Dept. of Anesthesiology, Narayan Medical College, Jamuhar, Bihar, ²Professor, Dept. of Anesthesiology, NKPSIMS & RC, Nagpur, ³Professor, Dept. of Anesthesiology, NKPSIMS & RC, Nagpur, ⁴Fellow in Regional Anesthesiology at Ganga Hospital, Coimbatore

ABSTRACT

Introduction: Traditionally, local anaesthetic (LA) hyperbaric Bupivacaine (HB) is the most commonly used drug in our clinical practice of spinal anaesthesia. Levobupivacaine has been recently introduced into Indian market and is an interesting alternative to Bupivacaine for spinal anaesthesia. It produces sub arachnoid block with similar sensory and motor characteristics and recovery like Bupivacaine. Intrathecal administrations of 15 mg of Levobupivacaine provide an adequate sensory and motor block lasting for approximately 6.5 hours. Smaller doses (i.e. 5-10mg) have been used in day-case surgeries. The lower cardiac toxicity, along with the equivalent anaesthetic potency, suggests that Levobupivacaine is a safer anaesthetic than the racemic form of Bupivacaine. In this study we propose to compare a combination of low dose Levobupivacaine with Fentanyl to low dose isobaric racemic Bupivacaine with Fentanyl for the characteristics of spinal blockade and hemodynamic parameters. **Material and Methods:** The present study was conducted among 70 patients who were classified as American Society of Anaesthesiologists (ASA) physical status I or II, undergoing elective inguinal hernia repair surgeries under spinal anaesthesia divided into two groups of 35 each. Patients in Group LB were given Levobupivacaine 0.5% isobaric 5 mg (1ml) + Inj. Fentanyl 25 µg (0.5ml) and Group B were given Bupivacaine 0.5% isobaric 5 mg (1ml) + Inj. Fentanyl 25 µg (0.5ml). Pulse rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Peripheral oxygen saturation (SpO₂) and End Tidal CO₂ (etCO₂) were recorded at similar intervals. **Results:** The hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate, EtCo₂ and SpO₂ were stable throughout the surgery and comparable between the two groups. **Conclusion:** Administration of intrathecal 0.5% isobaric Levobupivacaine with Fentanyl resulted in stable and comparable haemodynamic parameters when compared to 0.5% isobaric bupivacaine with Fentanyl. Side effects were comparable between groups. Hence, Levobupivacaine is an attractive alternative to Bupivacaine. Using low doses of local anaesthetic and adding adjuvant results in haemodynamic stability. This can be an advantage for the patients with high cardiac risk presenting for inguinal hernia surgeries.

Keywords: Intrathecal; Levobupivacaine; Spinal anaesthesia

Corresponding author: Dr Charuta Gadkari, Dept. of Anesthesiology, NKPSIMS & RC, Nagpur

This article may be cited as: Singh P, Gadkari C, Deshmukh S, Warnekar D Comparison of Haemodynamic Parameters with Low Dose Intrathecal 0.5% Isobaric Levobupivacaine Versus 0.5% Isobaric Bupivacaine for Inguinal Hernia Repair. HECS Int J Comm Health Med Res 2019; 5(3):24-29

INTRODUCTION

Traditionally, local anaesthetic (LA) hyperbaric Bupivacaine (HB) is the most commonly used drug in our clinical practice of spinal anaesthesia.¹

Bupivacaine hydrochloride (HCL) is an amino acyl LA and there are three forms of commercially available Bupivacaine; isobaric, hypobaric, and hyperbaric Bupivacaine. The difference in densities of the available preparations is believed to affect their diffusion patterns and distribution after injection into the CSF in the

subarachnoid space. The diffusion pattern determines the effectiveness, spread (dermatome height or block height) and side-effect profile of bupivacaine.² The use of low-dose bupivacaine is recommended in order to reduce its cardiovascular side-effects; however, this may not provide an adequate anaesthesia level for surgery.³ Levobupivacaine has been recently introduced into Indian market and is an interesting alternative to Bupivacaine for spinal anaesthesia. It produces sub arachnoid block with similar sensory and motor characteristics and recovery like Bupivacaine. Intrathecal

administrations of 15 mg of Levobupivacaine provide an adequate sensory and motor block lasting for approximately 6.5 hours. Smaller doses (i.e. 5-10mg) have been used in day-case surgeries.⁴ The lower cardiac toxicity, along with the equivalent anaesthetic potency, suggests that Levobupivacaine is a safer anaesthetic than the racemic form of Bupivacaine.^{5,6} The addition of opioids to LA spinal anaesthesia increases anaesthesia quality and ensures effective analgesia during intraoperative and early postoperative periods. For this reason, the strongly lipophilic drugs sufentanil and Fentanyl are preferred. The doses of Fentanyl and sufentanil that would provide effective analgesia and minimum side effects were reported to be 10 to 25mcg and 2.5 to 5 mcg, respectively.⁷ Girgin N K et al⁸ have used dose as low as 5 mg of LA with Fentanyl 25 µg for inguinal hernia repair in ambulatory settings. In this study we propose to compare a combination of low dose Levobupivacaine with Fentanyl to low dose isobaric racemic Bupivacaine with Fentanyl for hemodynamic parameters and the peak sensory level achieved.

MATERIAL AND METHODS

The present double blind randomized trial was conducted among 70 patients (35 in each group) undergoing inguinal hernia repair under subarachnoid block in a tertiary care hospital. The study was approved by the Institutional Ethics Committee (IEC). Subjects were enrolled after obtaining written informed consent for participation in the study. Inclusion criteria consisted of patients 50-70 years aged with 160-180 cm height, 50-70 Kg weight, and American Society of Anesthesiologist (ASA) Physical Status: I, II. Patients with infection at the intended site of spinal needle insertion, history suggestive of hypersensitivity to study drugs, severe cardiac disease, abnormal coagulation status and pre-existing neurological & musculoskeletal disease were excluded from the study. A thorough preanaesthetic examination of the patient was done. Investigations were done as per individual patient assessment and requirement. The study population consisted of seventy patients undergoing elective inguinal hernia repair surgeries under spinal anaesthesia divided into two groups of 35 each. Patients in Group LB were given Levobupivacaine 0.5% isobaric 5 mg (1ml) + Inj. Fentanyl 25 µg (0.5ml) and those in Group B were given Bupivacaine 0.5% isobaric 5 mg (1ml) + Inj. Fentanyl 25 µg (0.5ml). Preparation of patients included standardized protocol of preoperative fasting, premedication and preloading with crystalloid Ringer Lactate. Monitoring included three lead ECG in Standard lead II, Non-invasive blood pressure, respiratory rate, pulse oximetry for peripheral oxygen saturation (SpO₂). The base line heart rate, blood pressure, SpO₂, respiratory rate were recorded. Then after SAB, same were assessed at 1, 3, 5, 10 minutes; then every 10 minutes till next 60 minutes and every 20 minutes thereafter until complete recovery of the block. Under all aseptic precautions, a lumbar puncture was performed with 25 gauge Quincke needle at L2-3 or L3-4 inter space with patient in left lateral position through midline approach. After confirming free flow of clear CSF subarachnoid block was achieved with 1.5 ml of the study solution. Patient was made to lie down supine

immediately on the OT table without any tilt. Surgery was started after confirmation of successful blockade till T8. All patients received oxygen at 2 litres per minute via a binasal prongs throughout the procedure. Arterial oxygen saturation was registered continuously by pulse-oximetry. Fluid administration was continued with Ringer lactate solution at 4-5ml/Kg/H during the intra-operative period. Hypotension (MAP ≤ 30% from baseline or systolic pressure < 90mm of Hg) was treated with administration of 250 ml of Ringer Lactate over 10 min and Injection Ephedrine 6 mg Intravenous, repeated if blood pressure remained low. Bradycardia (HR < 25% from baseline or HR < 50 beats/min) was treated with injection Atropine 0.6 mg Intravenous. The onset of sensory anaesthesia was tested by light pinprick bilaterally in the mid clavicular line. Sensory anaesthesia was defined as the loss of sharp sensation to pinprick test. Peak sensory level was defined as the sensory level which remained same for consecutive three assessments. Peak sensory level achieved was recorded in both the groups. Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Peripheral Oxygen Saturation (SpO₂) and Respiratory Rate were recorded at above defined intervals. After surgery, patients were transferred to recovery room (PACU). Pulse rate, Blood pressure and Peripheral oxygen saturation were recorded every 20 minutes until complete recovery from sensory and motor block.

RESULTS

Table 1 shows demographic details. Group LB had 40.00% of cases in 40 to 50 age group followed by 34.28% in case of 60 to 70 years, 17.14% in 70 to 80 years and about 8.57% of cases in 50 to 60 years of age group. Group B had majority of cases in the age group of 40 to 50 years (48.58%), followed by 17.14% each in 50 to 60 years, 60 to 70 years and 70 to 80 years. The association between the different age groups and the two groups was not significant with a p value of 0.3490

Table 2 shows comparison of maximum sensory levels for two groups. The maximum sensory level was at T5 in Group LB and T4 in case of Group B. This was significant with p value < 0.05 Table 3 provides the descriptive statistics for heart rate according to time points for two groups. In group B, at pre-operative stage, the mean heart rate was (84.11 ± 7.48) /min. The mean heart rate steadily decreased to 73.17 ± 12.20/min at 60 mins. Post operatively it increased to 78.22 ± 9.73/min at 180 minutes. In group LB, at pre-operative stage, the mean heart rate was (83.57 ± 10.54) /min. The mean heart rate steadily decreased to 71.88 ± 10.56/min at 60 mins. Post operatively it increased to 76.67 ± 9.91/min at 180 minutes. After applying independent t test at all different time points, there was no statistical significance between the heart rates of two groups. Table 4 provides the descriptive statistics for Systolic blood pressure according to time points for two groups. In group B, at pre-operative stage, the mean SBP was 121.54 ± 18.81 mm Hg. The mean SBP steadily increased to 124.71 ± 17.69 mm Hg at 60 mins. Post operatively it remained same to 124.65 ± 14.16 mm Hg at 180 minutes. In group LB, at pre-operative stage, the mean SBP was 123.71 ± 17.71 mm Hg. The mean SBP steadily decreased to

122.57 ± 13.86 mm Hg at 60 mins. Post operatively it remained same to 122.17 ± 13.08 mm Hg at 180 minutes. After applying independent t test at all different time points, there was no statistical significance between the SBP of two groups. Table 5 provides the descriptive statistics for Diastolic blood pressure according to time points for two groups. In group B, at pre-operative stage, the mean DBP was 80.62 ± 7.61 mm Hg. The mean DBP steadily increased to 84.4 ± 12.00 mm Hg at 60 mins. Post operatively it increased steadily to 87.42 ± 13.70 mm hg at 180 minutes. In group B, at pre-operative stage, the mean DBP was 82.85 ± 9.61mm Hg. The mean DBP steadily increased to 84.22 ± 12.44 mm Hg at 60 mins. Post operatively it increased steadily to 84.42 ± 12.32 mm Hg at 180 minutes. After applying independent t test at all different time points, there was no statistical significance between the DBP of two groups. Chart 1 provides the descriptive statistics for Mean arterial pressure according to time points for two groups. In group B, at pre-operative stage, the mean MAP was 94.26 ± 9.82 mm Hg. The mean MAP steadily increased to 97.83 ± 10.77 mm Hg at 60 mins. Post operatively it increased steadily to 99.83 ± 12.03 mm Hg at 180 minutes. In group LB, at pre-operative stage, the mean MAP was 96.47 ± 7.49 mm Hg. The mean MAP steadily increased to 97.00 ± 12.27 mm Hg at 60 mins. Post operatively it remained same to 97.00 ± 11.05 mm Hg at 180 minutes. After applying independent t test at all different time points, there was no statistical significance between the MAP of two groups. Chart 2 provides the descriptive statistics for SpO2 according to time points for two groups. Throughout the surgery and post operatively the SpO2 remained hovering around 100 in both the groups and there was no statistical significance between the SpO2 of two groups. Chart 3 provides the descriptive statistics for Respiratory rate according to time points for two groups. Throughout the surgery and post operatively the respiratory rate remained hovering around 16/min in both the groups and there was no statistical difference between the RR of two groups. Table 6 shows the number of patients with adverse effects between the two groups. In Group LB, one patient (2.85%) had nausea and vomiting, two patients (5.71%) had pruritus and four patients (11.42%) developed urinary retention. In both the groups, there were no cases showing post operative respiratory depression. There were four patients (11.42%) experiencing nausea and vomiting, two patients (5.71%) with Pruritus, one patient (2.85%) with urinary retention in Group B. The number of patients with adverse effects were comparable between the groups.

Table 1: Demographic characteristics

Age (yrs)	Groups [No (%)]	
	LB (n=35)	B (n=35)
40-50	14(40.00)	17 (48.58)
50-60	3(8.57)	6(17.14)
60-70	12(34.28)	6(17.14)
70-80	6(17.14)	6(17.14)
TOTAL	35	35
P value*	0.3490	

*P-value estimated using Chi square test

Table 2: Peak Sensory Level Achieved: Comparison of maximum sensory levels for two groups.

Parameters (min)	Groups		P-value*
	LB (n=35)	B (n=35)	
Maximum sensory level (Median)	T5	T4	<0.05

*P-value estimated using Wilcoxon rank sum test

Table 3: Heart Rate and its comparison at each time point between two groups

Heart rate	Group LB N=35		Group B N=35		P value
	Mean	SD	Mean	SD	
pre-op	83.57	10.54	84.11	7.18	0.8020
1 min	82.37	11.87	84.62	8.95	0.3727
3 min	81.74	12.46	82.57	12.14	0.7790
5 min	77.71	12.05	80.6	10.99	0.2990
10 min	78.4	12.40	79.65	11.91	0.6668
20 min	77.25	12.07	78.08	11.66	0.7712
30 min	79.2	13.97	76.48	12.43	0.3938
40 min	76.62	9.08	77.6	8.93	0.6534
50 min	73.74	11.29	74.71	12.35	0.7324
60 min	71.88	10.56	73.17	12.20	0.6389
Post operative					
20 min	73.54	11.08	73.31	11.91	0.9340
40 min	73.34	11.64	74.31	11.77	0.7296
60 min	72.77	11.17	75.28	11.69	0.3610
80 min	73.31	13.35	74.45	10.81	0.6952
100 min	72.8	12.23	76.2	11.69	0.2388
120 min	71.28	11.47	75.22	10.87	0.1446
140 min	75.02	9.94	78.97	10.68	0.1146
160 min	74.62	11.71	78.45	9.94	0.1452
180 min	76.67	9.91	78.22	9.73	0.1634

*P-value estimated using t-test for independent samples

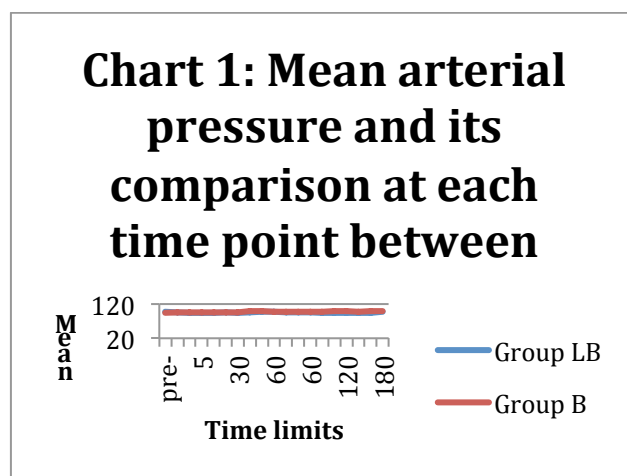


Table 4: SBP and its comparison at each time point between two groups

SBP	Group LB	Group B	P value
-----	----------	---------	---------

	N=35		N=35		DBP	Group LB		Group B		P value	
	Mean	SD	Mean	SD		Mean	SD	Mean	SD		
pre-op	123.71	15.71	121.54	18.81	0.6019	pre-op	82.85	9.61	80.62	7.61	0.2862
1 min	122.11	16.02	121.2	20.29	0.8349	1 min	83.14	9.81	82.14	11.62	0.7656
3 min	120.2	16.67	122.14	17.83	0.6393	3 min	81.48	11.64	81.88	9.88	0.8773
5 min	119.77	15.74	124.22	17.36	0.2644	5 min	81.54	11.91	80.4	9.13	0.6538
10 min	120.05	15.32	124.2	17.28	0.2925	10 min	81.25	11.50	80.71	8.31	0.8217
20 min	120.4	15.17	122.74	16.50	0.5385	20 min	83.11	7.39	80.82	9.54	0.2668
30 min	120.08	15.65	122.34	15.73	0.5493	30 min	81.02	6.62	82.62	10.89	0.4607
40 min	120.6	14.24	121.77	15.39	0.7420	40 min	83.82	12.64	86.94	19.46	0.4305
50 min	121.34	14.24	123.65	17.20	0.5420	50 min	85.14	12.37	87.68	13.84	0.4206
60 min	122.57	13.86	124.71	17.69	0.5747	60 min	84.22	12.44	84.4	12.00	0.9533
Post operative						Post operative					
20 min	121.14	14.06	125.22	16.04	0.2613	20 min	82.2	10.01	83.45	15.63	0.6902
40 min	121.17	13.29	123.14	15.24	0.5662	40 min	82.6	12.30	84.82	16.03	0.5165
60 min	119.74	13.96	122.62	15.42	0.4147	60 min	82.28	12.59	84.77	17.46	0.4971
80 min	118.57	13.23	120.22	15.26	0.6290	80 min	82.25	11.77	85.6	15.71	0.3178
100 min	119.97	13.62	123.68	14.06	0.2657	100 min	81.57	12.32	86.4	15.51	0.1542
120 min	120.28	13.10	123.91	13.63	0.2603	120 min	81.25	12.29	86.28	14.70	0.1254
140 min	120.8	12.93	124.42	13.63	0.2574	140 min	80.91	12.45	84.82	13.97	0.2202
160 min	119.74	13.96	124.77	14.74	0.1475	160 min	81.51	12.18	85.22	13.38	0.2288
180 min	122.17	13.08	124.65	14.16	0.4482	180 min	84.42	12.32	87.42	13.70	0.3390

*P-value estimated using t-test for independent samples

*P-value estimated using t-test for independent samples

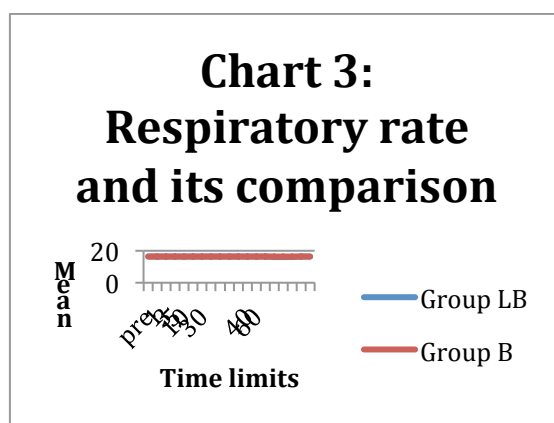
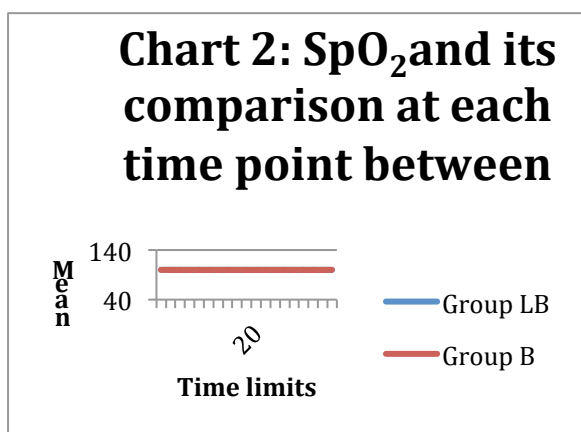


Table 6: Comparison of adverse effects between two groups.

Table 5: DBP and its comparison at each time point between two groups

Adverse events	Group LB(n=35)	Group B(n=35)	P value*
Nausea/vomiting	1(2.85)	4(11.42)	0.3564
Pruritus	2(5.71)	2(5.71)	1.000
Post operative respiratory depression	0(0)	0(0)	
Urinary retention	4(11.42)	1(2.85)	0.3564

*P-value estimated using Fisher's exact test

DISCUSSION

Neuraxial anaesthesia can be undertaken using LA at different doses and baricities. Intrathecal opioids added to LAs produce a well documented synergistic effect without intensifying motor and sympathetic blockades and enable successful anaesthesia with use of a low dose of LA which results in more stable haemodynamics.⁹ 5 mg as a dose of LA in both the groups was selected based on the study by Girgin et al.⁸ A pilot study was conducted to decide feasibility of completing inguinal hernia repair with this dose at our institute. Dose of spinal adjuvant Fentanyl was chosen based on various prior studies carried by Girgin et al,⁸ Ackaboy et al,¹⁰ Misirlioglu et al.¹¹ Since Levobupivacaine is available only in isobaric form for spinal use, isobaric Bupivacaine was used for comparison. Preloading with intravenous fluids offsets the vasodilating effects of sympathetectomy caused by spinal anaesthesia thereby maintaining the venous return and thus the drop in blood pressure is prevented. We have preloaded our patients with Ringer Lactate at 10ml/kg.¹² Patients were comparable with respect to demographic characteristics and duration of surgery was comparable between groups. Peak sensory level is important for patient comfort during surgery and intraoperative maintenance of haemodynamic parameters. Peak sensory level achieved was significantly higher in Bupivacaine group (T4) than Levobupivacaine group (T5). Similar results were reported by Erdil et al, who compared intrathecal (IT) 1.5 ml plain Levobupivacaine + 15 µg Fentanyl and 1.5 plain Bupivacaine + 15 µg fentanyl in TURP procedures, however, Misirlioglu et al who compared Levobupivacaine (7mg) + Fentanyl 25µg and Bupivacaine (7mg) + Fentanyl 25µg for caesarean section reported comparable peak sensory levels. In the present study, there was no statistical significance between the heart rates of two groups. Throughout the operation, HR remained comparable between 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; $p < 0.05$. This result is calculated for comparing with baseline however on comparison between the study groups, the difference was not statistically significant. Changes in heart rate (HR) were within acceptable ranges and number of patients having episodes of

bradycardia were comparable between the groups. These findings are in line with the studies carried by Erdil et al⁷ and Misirlioglu et al¹¹ Decrease in HR can result with extent of sympathetic blockade as well as with the use of Fentanyl. In the present study, systolic blood pressure (SBP) and its comparison was made at each time point between two groups. Values of SBP were comparable and almost stable between the groups during surgery. Number of patients having episodes of hypotension were comparable between the groups. Diastolic blood pressure and its comparison at each time point between two groups showed no statistical difference between the two groups. These findings are consistent with those reported by Misirlioglu et al.¹¹ The difference is that in present study sensory level was higher in Bupivacaine group. There was no statistical difference between the mean arterial pressure values of two groups. Our findings are in line with those by Akcaboy E Y et al¹⁰ however, Erdil et al³ reported significantly lower MAP values in Bupivacaine group than in levobupivacaine group, however, it is important to note that they reported significantly higher peak sensory level in Bupivacaine group. 10% of patients experienced hypotension in LB group, where as 30% of patients experienced hypotension in B group and hypotension appeared early in group B as compared to LB. In the present study, throughout the surgery and post operatively the respiratory rate remained hovering around 16/min in both the groups. Throughout the surgery and post operatively the SpO₂ remained hovering around 100% in both the groups. Studies mentioned so far have not reported on RR and hence there is no comment made in those articles. However, we feel that it was safe to use the drug combinations we used. In present study, patients suffering from side effects were comparable between the groups. However, Goyal A et al¹³ have reported a significant difference between incidence of hypotension and bradycardia in favour of Levobupivacaine. Also incidence of nausea and vomiting was more in Bupivacaine group. Nausea and vomiting can result from IT opiate as well as from repeated episodes of hypotension which were higher in group Bupivacaine. Akcaboy E Y et al,¹⁰ have reported comparable incidence of side effects between the groups. In the present study, adequate sensory and motor blockade was achieved with intrathecal dose of local anaesthetic as low as 5 mg (with adjuvant) so as to complete hernia surgery successfully for both Levobupivacaine and Bupivacaine. No intraoperative sedation was required and though no formal feedback was sought, no surgeon complained regarding quality of block.

CONCLUSION

Administration of intrathecal 0.5% isobaric Levobupivacaine with Fentanyl resulted in stable and comparable haemodynamic parameters when compared to 0.5% isobaric bupivacaine with Fentanyl. Side effects were comparable between groups. Hence, Levobupivacaine is an attractive alternative to Bupivacaine. Using low doses of local anaesthetic and adding adjuvant results in haemodynamic stability. This can be an advantage for the patients with high cardiac risk presenting for inguinal hernia surgeries.

REFERENCES

1. Berde C, GR S. Local Anesthetics. In: Miller R, editor. *Miller's Anaesthesia*. 7th ed. Philadelphia: Elsevier; 2010. p. 913–39.
2. Greene NM. Distribution of local anesthetic solutions within the subarachnoid space. *Anesth Analg*. 1985;64(7):715–30.
3. Erdil F, Bulut S, Demirbilek S, Gedik E, Gulhas N, Ersoy MO. The effects of intrathecal levobupivacaine and bupivacaine in the elderly. *Anaesthesia*. 2009;64(9):942–6.
4. Bajwa SJS, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. *J Anaesthesiol Clin Pharmacol*. 2013;29(4):530–9.
5. Gurbet A, Turker G, Girgin NK, Aksu H, Bahtiyar NH. Combination of ultra-low dose bupivacaine and fentanyl for spinal anaesthesia in out-patient anorectal surgery. *J Int Med Res*. England; 2008;36(5):964–70.
6. Cuvas O, Gulec H, Karaaslan M, Basar H. The use of low dose plain solutions of local anaesthetic agents for spinal anaesthesia in the prone position: bupivacaine compared with levobupivacaine. *Anaesthesia*. England; 2009 Jan;64(1):14–8.
7. Ozyilkan NB, Kocum A, Sener M, Caliskan E, Tarim E, Ergenoglu P, et al. Comparison of intrathecal levobupivacaine combined with sufentanil, fentanyl, or placebo for elective caesarean section: a prospective, randomized, doubleblind, controlled study. *Curr Ther Res*. 2013;75:64–70.
8. Girgin NK, Gurbet A, Turker G, Bulut T, Demir S, Kilic N, et al. The combination of low-dose levobupivacaine and fentanyl for spinal anaesthesia in ambulatory inguinal herniorrhaphy. *J Int Med Res*. 2008;36(6):1287–92.
9. Patil G, Prakruthi C. Comparison of Intrathecal Levobupivacaine and Bupivacaine Combined With Fentanyl, for Infraumbilical Surgeries. *Indian J Res*. 2016;5(2):368–71.
10. Akcaboy EY, Akcaboy ZN, Gogus N. Low dose levobupivacaine 0.5% with fentanyl in spinal anaesthesia for transurethral resection of prostate surgery. *J Res Med Sci*. 2011;16(1):68–73.
1. Misirlioglu K, Sivrikaya GU, Hanci A, Yalcinkaya A. Intrathecal low-dose levobupivacaine and bupivacaine combined with fentanyl in a randomised controlled study for caesarean section: Blockade characteristics, maternal and neonatal effects. *Hippokratia*. 2013;17(3):262–7.
2. Ewaldsson C, Hahn RG. Volume kinetics of Ringer's solution during induction of spinal and general anaesthesia. *Br J Anaesth*. 2001;87(3):406–14.
3. Goyal A, Shankaranarayan P, Ganapathi P. A randomized clinical study comparing spinal anesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective cesarean sections. *Anesth*