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A Comparative Study of the Anesthetic Potencies and Hemodynamic Changes of 0.5% Isobaric Levobupivacaine and 0.5% Hyperbaric Racemic Bupivacaine for Spinal Anesthesia in Lower Abdominal and Lower Limb Surgeries

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Abstract

Background and Objectives: Spinal anesthesia is widely used, providing a fast onset and effective sensory and motor blockade. Systemic hypotension and bradycardia are the more common side effects seen during the central neuraxial block. Levobupivacaine has been introduced into clinical practice because of its lower toxic effects for the heart and central nervous system. We, therefore, performed this prospective randomized clinical study to compare the clinical efficacy and hemodynamics of 3 ml of 0.5% intrathecal isobaric Levobupivacaine with 3 ml of 0.5% intrathecal racemic Bupivacaine for lower abdomen and lower limb surgeries.

Methodology: 100 patients belonging to ASA physical status I and II scheduled for lower abdomen and lower limb surgeries were randomly selected for the study and were divided into 2 groups of 50 each. Group L (Levobupivacaine group) received 3ml of 0.5% isobaric Levobupivacaine (15mg) intrathecally Group B (Bupivacaine group) received 3ml 0.5% of racemic Bupivacaine (15mg) intrathecally. Onset and duration of sensory block, onset duration and degree of motor block, maximum dermatomal level of sensory block, hemodynamic parameters, and adverse effects if any were studied.

Results: There was a statistically significant difference between both the groups with regards to mean onset of sensory and motor block which was significantly faster in group B when compared to group L. The mean time for peak sensory block was 7.44 mins with Levobupivacaine and 6.84 mins with Bupivacaine (p-value 0.02). The mean onset time for the motor block was 10.99 mins with Levobupivacaine and 10.48 mins with Bupivacaine (p-value 0.05). The maximum sensory height attained ranged between T_4 and T_{10} in both the groups, which was clinically and statistically not significant. The mean time for 2 segment regression was 123.8 mins in group L and 126.5 mins in group B which was statistically not significant (p-value 0.23). The degree of motor block was comparable in both groups. The mean duration of sensory block was 257.4 mins in group L and 259.9 mins in group B which was clinically and statistically not significant (p-value 0.17). The mean duration of motor block was 283.2 mins in group L and the group was 286.3 mins with a p-value of 0.31 which clinically and statistically was not significant. Hypotension and bradycardia were less common in group L than group B which was clinically and statistically significant. 52% of patients in group B and 16% of patients in group L required the use of vasopressor with a statistically significant p-value of <0.001. 30% of patients in group B had bradycardia compared to 8% in group L with a p-value of 0.002. The incidences of other side effects were comparable in both the groups.

Conclusion: Levobupivacaine 15 mg (3ml of 0.5% Isobaric) has significantly a late onset of sensory and motor block but had a similar duration of sensory and motor block compared to Bupivacaine 15 mg (3ml). However, Bupivacaine required more often the use of a vasopressor and sympathomimetic drug compared to Levobupivacaine. So Levobupivacaine could be advisable inpatient whose clinical history demandsthe cardiovascular impact of spinal anesthesia to be minimized.

Keywords: Levobupivacaine; Bupivacaine; Intrathecal; Isobaric.

Introduction

Spinal anesthesia is widely used, providing a fast onset and effective sensory and motor blockade. It has many advantages like simplicity, easy to perform, rapid onset of action, and good muscle relaxation. It has an added advantage of preventing complications of General Anaesthesia like airway manipulation, Polypharmacy, the pressor response from intubation, nausea, vomiting, sore throat, excessive sedation, etc. Systemic hypotension and bradycardia are the most common side-effects seen during the central neural block. Marked hypotension may be harmful, particularly in elderly patients with limited cardiac reserve. Age and a high level of the block are the two main factors known to play a role in the development of hypotension after spinal anesthesia.[1] Bupivacaine (1-butyl-2', 6'-pipercoloxylidine), is an amino amide local anaesthetic.[2] Racemic bupivacaine is the most frequently used long-acting agent for spinal anesthesia. The use of low dose racemic bupivacaine is recommended to reduce its cardiovascular side-effects[3,4] Levobupivacaine (S-1-buty l-2 piperidylformo-2', 6'-xylazine hydrochloride) is a pure S(-)-enantiomer of racemic bupivacaine. It is a new long-acting local anesthetic.[5] Owing to the lower affinity of the S (-) isomer to cardiac sodium channels compared to the R isomer, it is associated with fewer cardiac side effects.[6,7] The objective of the present study is to investigate the clinical efficacy and safety of isobaric solution of levobupivacaine compared with racemic bupivacaine in spinal anesthesia for lower abdominal and lower limb surgery.

Methodology

This clinical study was conducted on 100 adult patients of ASA physical status I and II in the age group of 20 to 60 years of either sex, posted for elective lower limb, lower abdominal, gynecological, and urological surgeries under spinal anesthesia after taking informed consent at Vinayaka Mission's Kirupananda Variyar Medical College Hospital, Salem over 24 months. After approval from the hospital ethical committee, a comparative study was carried out on 100 adult patients 100 patients belonging to ASA physical status I and II scheduled for lower abdomen and lower limb surgeries were randomly selected for the study and were divided into 2 groups of 50 each. Group L (Levobupivacaine group) received 3ml of 0.5% isobaric Levobupivacaine (15mg) intrathecally Group B (Bupivacaine group) received 3ml 0.5% of racemic Bupivacaine (15mg) intrathecally. Onset and duration of sensory block, onset duration and degree of motor block, maximum dermatomal level of sensory block, hemodynamic parameters, and adverse effects if any were studied.

Methods for Collection of Data

100 patients undergoing surgical procedures will be randomly selected. Informed, written consent will be taken from patients. Result values will be recorded using a preset proforma. Patients who will be selected for the study will be randomly allocated to 2 groups of 50 each on an alternate basis, namely: a) Group B: Received 3ml of 0.5% intrathecal hyperbaric Bupivacaine (15 mg) b) Group L: Received 3ml of 0.5% intrathecal Isobaric Levobupivacaine (15 mg).

Inclusion criteria: Age - 20 to 60 years of both sex,◦ American Society of Anaesthesiologists (ASA) grade I and II,◦ Patients giving valid informed consent,◦ Patients undergoing elective general surgical/urological/gynecological/plastic and orthopedic lower limb operations.

Exclusion Criteria: Patients' refusal to spinal anesthesia,◦ ASA grade III and IV,◦ Age < 20, and > 60 years. Patients with a history of allergy/ hypersensitivity to the study drugs or any local anesthetic General contraindications for spinal anesthesia. A pre-anesthetic checkup was carried out with a detailed history, general physical examination, and systemic examination. Airway assessment and spinal column examination were done.

Procedure: The patient was shifted on the OT Table, IV access was obtained on the forearm with 18G IV cannula and the patient was preloaded with 500 ml Ringers Lactate solution before the spinal block. The monitors connected included non-invasive BP, Oxygen saturation using a pulse oximeter, and ECG. Baseline Pulse rate, BP, and SpO_2 were recorded. Under strict aseptic precautions, a lumbar puncture was performed in the left lateral position by midline approach by using a disposable 25 G Quincke Babcock spinal needle at L_2-L_3 or L_3-L_4 intervertebral space. After confirmation of the free flow of CSF, the study drug was administered at 0.1 ml/sec. The patient was turned supine immediately after the injection with a pillow under their head and was put in a neutral position. After the spinal block, Pulse rate, NIBP and SpO_2 were measured at 0, 1, 3, 5, 10, 15, 30, 60, 90, 120 and 180 mins. Hypotension was defined as a 20% decrease in blood pressure from baseline values and was treated with incremental IV boluses of ephedrine 6mg. Bradycardia was defined as a pulse rate of less

than 60bpm and treated with IV atropine 0.3mg. Patients were monitored continuously using NIBP, SpO_2, and ECG. After giving spinal anesthesia, oxygen was given by facemask at 4 lts/min and the fluid therapy was with lactated Ringers solution and DNS.

Statistical Methods

Descriptive and inferential 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 a 5 % level of significance. The following assumptions on data are made assumptions: 1. Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, Cases of the samples should be independent. Student t-test (two-tailed, independent) has been used to find the significance of study parameters on a continuous scale between two groups (Intergroup analysis) on metric parameters. Chi-square/Fisher Exact probability test has been used to find the significance of study parameters on a categorical scale between two or more groups. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1,Med Calc 9.0.1,Systat 12.0, and R environment ver. 2.11.1 were used for the analysis of the data, and Microsoft Word and Excel have been used to generate Graphs, Tables, etc.

Observation and Results

A total of 100 ASA I and ASA II patients who underwent lower abdominal and lower limb surgeries under subarachnoid block were randomly selected and were divided into 2 groups of 50 each. Group L (Levobupivacaine group) received 3ml of 0.5% isobaric Levobupivacaine 15mg intrathecally. Group B (Bupivacaine group) received 3ml of 0.5% hyperbaric Bupivacaine 15mg intrathecally.

Table 1: Demographic Profile.

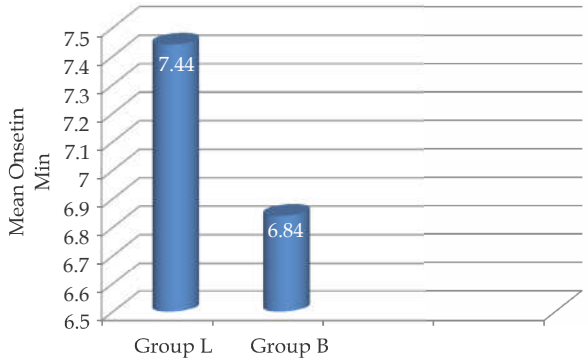
Parameter	Group L		Group B		t value	P-value
	Mean	SD	Mean	SD		
Age (yrs)	39.0	10.5	37.5	7.9	0.82	0.42,ns
Height (cm)	163.6	5.8	161.5	5.0	1.94	0.06,ns
Sex (M:F)	31:19		29:21		-	0.68,ns

Table 1 The mean age in group L was 39 years and the mean age in group B was 37.5 years. In group L 31 were males and 19 were females and in group B 29 were males and 21 were females. Unpaired t-test, *P < 0.05, Significant

Table 2: Onset of Sensory and Motor Block.

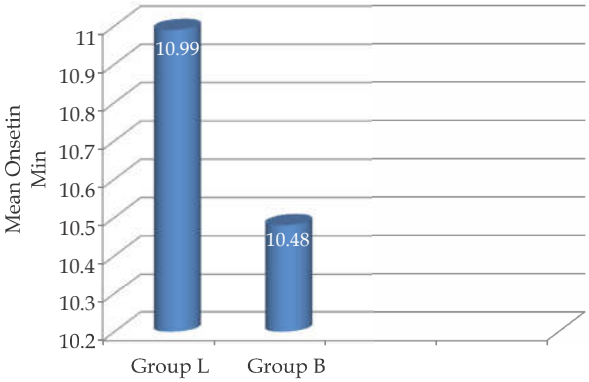
Parameter	Group L		Group B		t value	p-value
	Mean	SD	Mean	SD		
Sensory block(min)	7.44	0.97	6.84	1.61	2.26	0.02,ns
Motor block(min)	10.99	1.19	10.48	1.37	1.99	0.05,ns

Table 2, Graph 1 The mean time for onset of sensory block in group L was 7.44mins and in the group, B was 6.84 mins with a p-value of 0.02 which was statistically and clinically significant. Unpaired t-test, *P < 0.05, Significant.

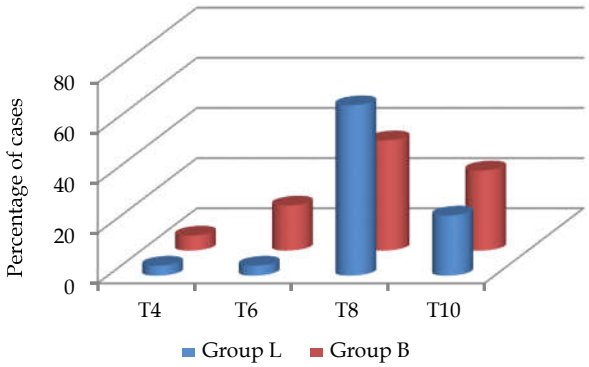


Graph 1: Onset of Sensory Block.

Graph 2 The mean time for onset of motor blockade (Bromage 3) was 10.99 mins for group L and 10.48 mins for group B with a p-value of 0.05 which was clinically and statistically significant.

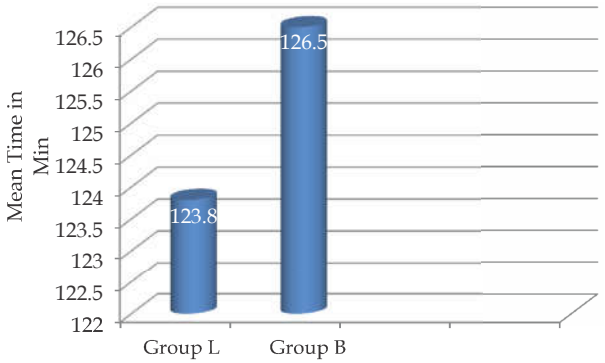


Graph 2: Onset of Motor Block.



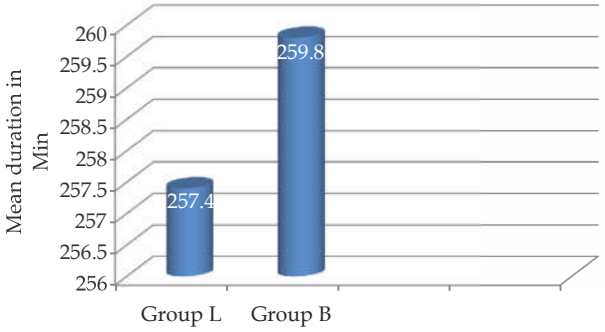
Graph 3: Highest Level Of Sensory Block.

Graph 3 The highest level of block achieved in group L was T_4 with 2 (4%) patients achieving it and in group B was also T_4 with 3 (6%) patients achieving it. 68% of patients in group L and 44% of patients in group B achieved a maximum sensory blockade of up to T_8 dermatomal level. These findings were clinically and statistically not significant.



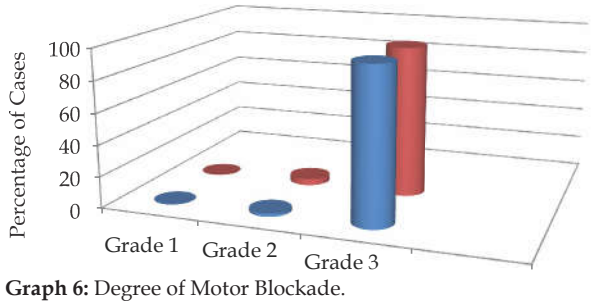
Graph 4: Time For 2 Segment Regression.

Graph 4 The mean time taken for 2 segment regression of sensory block was 123.8 mins in group L and 126.5 mins in group B with a p-value of 0.40 which is clinically and statistically not significant.



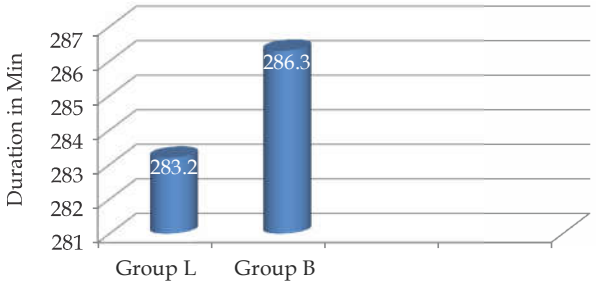
Graph 5: Duration Of Sensory Block.

Graph 5 The mean value for the duration of sensory block was 257.4 mins in group L and for group B the mean duration was 259.8 mins. This was not significant clinically or statistically with a p-value of 0.17.



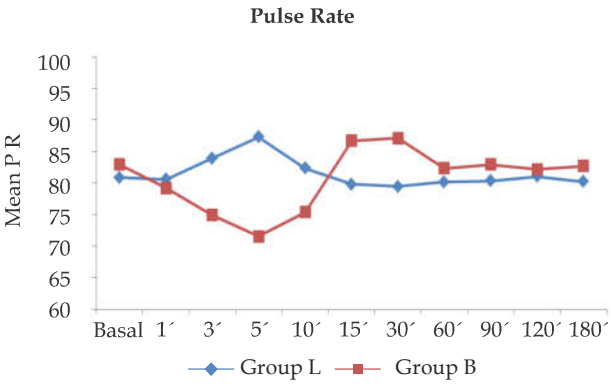
Graph 6: Degree of Motor Blockade.

Graph 6 98 % of patients in group L and 96% of patients in group B had grade 3 or complete motor block. This was clinically and statistically not significant.



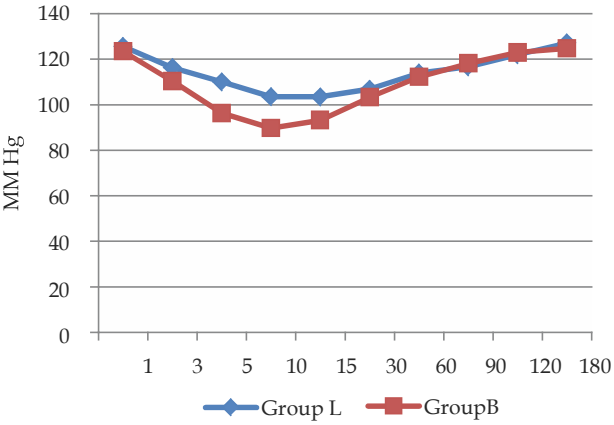
Graph 7: Duration of Motor Block.

Graph 7 The mean duration of motor block (time to recovery of complete motor block i.e, grade 0) was 283.2 mins for group L and 286.3 mins for group B. This was clinically and statistically not significant (p 0.31).



Graph 8: Comparison of Pulse Rate Between Two Groups.

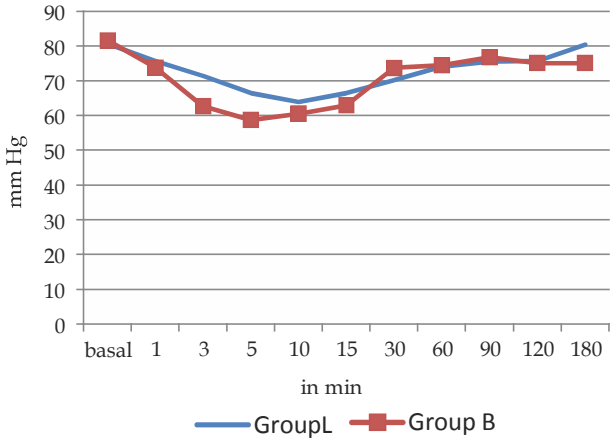
Graph 8 The baseline heart rate was comparable in both groups. In group B there was a significant fall in pulse rate compared to baseline starting from 1 min to 10 mins and there was the statistically significant intergroup difference with a p-value of < 0.05 when compared with group L. This was both clinically and statistically significant.



Graph 9: Comparison of Systolic Blood Pressure Between Two Groups.

Graph 9 Baseline systolic blood pressures were

comparable in both groups. There was a slight reduction in systolic blood pressure after spinal anesthesia in both groups. The magnitude of fall however was significant only in group B (p-value < 0.05) with the intergroup comparison. This fall in blood pressure was more pronounced from 1st minute up to 10 minutes after spinal injection.



Graph 10: Comparison of Diastolic Blood Pressure between two groups.

Graph 10 The baseline diastolic blood pressure values were comparable. Both groups showed a reduction in diastolic blood pressure after spinal anesthesia. Intergroup comparisons showed a more significant fall of diastolic blood pressure in group B (p <0.05) and this was from 3rd minute up to 10 minutes after spinal injection.

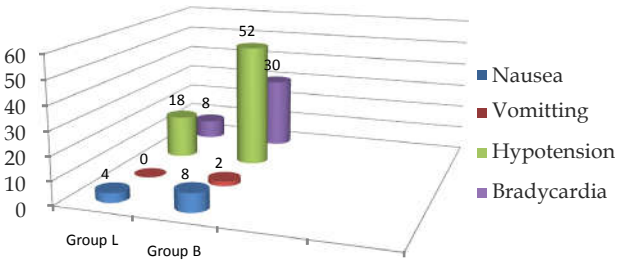
Table 3: Oxygen Saturation.

Time Interval (min)	Group L		Group B	
	Mean	SD	Mean	SD
Basal	98.5	0.5	98.3	0.6
1'	98.2	0.8	98.4	0.7
3'	98.3	0.8	98.5	0.6
5'	98.6	1.0	98.4	0.7
10'	98.8	0.9	98.3	0.7
15'	98.7	1.0	98.2	0.9
30'	98.6	0.9	98.4	0.5
60'	98.5	0.9	98.4	0.5
90'	98.7	0.7	98.4	0.5
120'	98.4	0.6	98.40	0.6
180'	98.7	0.8	98.5	0.6

Table 3 There was no significant change in oxygen saturation (SpO_2) following subarachnoid block in both the groups. The SpO_2 values were comparable in both groups.

Unpaired t-test

* P < 0.05, Significant



Graph 11: Side Effects.

Graph 11 Nausea was seen in 2 patients of group L (4%) and 4 patients of group B (8%). Vomiting was seen only in 1 patient of group B. 52% of patients had hypotension and 30 % of patients had bradycardia in group B, whereas in group L 16% had hypotension and 8% had bradycardia. Incidence of hypotension (p-value <0.001) and bradycardia (p-value 0.002) was higher in group B than group L which was clinically and statistically significant. No case of allergy, respiratory depression, shivering and other side effects were reported.

Discussion

A subarachnoid block is a commonly employed anesthetic technique for performing surgeries of the lower abdomen and lower limb. It is a safe, economical, and easy to administer a technique which also offers a high level of post-anesthesia satisfaction for the patient. The technique is simple, has a rapid onset, and is reliable. The risk of general anesthesia including mishaps due to airway management is avoided by this technique. Systemic hypotension and bradycardia are the most common side-effects seen during the central neural block. Marked hypotension may be harmful, particularly in elderly patients with limited cardiac reserve. Bupivacaine is a local Anaesthetic used routinely for spinal anesthesia because of its high potency and minimal neurologic symptoms. Racemic bupivacaine is the most frequently used long-acting agent for spinal anesthesia. The use of low dose racemic bupivacaine is recommended to reduce its cardiovascular side-effects.[3,4] Levobupivacaine (S-1-butyl-2piperidylformo-2′,6′-xylazine hydrochloride) is a pure S(-)- enantiomer of racemic bupivacaine. It is a new long-acting local anesthetic.[8] Owing to the lower affinity of the S (-) isomer to cardiac sodium channels compared to the R isomer, it is associated with fewer cardiac side effects.[9,10] Hence this study was conducted to assess the anesthetic potency and hemodynamic effects of intrathecally administered Levobupivacaine compared with intrathecal administered racemic Bupivacaine in patients coming for surgeries of

lower abdomen and lower limb. The equipotent ratio between Levobupivacaine and Bupivacaine is considered to be 0.97 (Ying Y Lee et al).[24] Since hyperbaric Levobupivacaine is not available in the market, we chose isobaric 0.5% Levobaupivacine 15 mg and isobaric 0.5% Bupivacaine 15 mg as an equipotent dose for this study. In our study, the majority were middle-aged in both groups. In group L (Levobupivacaine group) there were 31 males and 19 females and in group B (Bupivacaine group) there were 29 males and 21 females.[11] The mean heights in the group were also identical. These parameters were kept identical in both the groups to avoid variations in the intraoperative and postoperative outcomes of the patients.[13] The mean time for onset of peak sensory block in Group L was 7.44 mins and in Group B was 6.84 mins with a p-value of 0.02 which was statistically significant. This observation was comparable to the study done by Ashton D'Souza et al, who compared the anesthetic efficacy and safety of Hyperbaric 0.5% Bupivacaine, Isobaric 0.75% Ropivacaine and Isobaric 0.5% Levobupivacaine. The mean sensory onset time for Bupivacaine was 5.25 mins and Levobupivacaine was 6 mins. It was found that hyperbaric bupivacaine produces a spinal block which has a sensory block with an earlier onset of clinically significant sensory and motor block as compared to isobaric levobupivacaine. In another study done by F. Erdil et al[23] in their study of 80 patients posted for TURP, Time to reach T_{10} and peak sensory block was significantly shorter in group Bupivacaine compared to group Levobupivacaine ($p < 0.05$) which was 6.4 ± 2 mins for Bupivacaine and 7.8 ± 1.9 mins for Levobupivacaine which is similar to the observation in our study. So Bupivacaine produced a clinically earlier onset of peak sensory block compared to Levobupivacaine. A study of one hundred-twenty ASA I-III patients, conducted by M Mantouvalou et al[20] noted a similar trend for maximum cephalad spread variation of the sensory block between the isobaric bupivacaine group and isobaric levobupivacaine. In our study, the highest level of sensory blockade was similar in both groups. The highest level of block achieved in group B was T4 with 3 (6%) patients achieving it and in group L highest level achieved was also T_4 with 2 (4%) patients achieving it. 68 % of patients in group L achieved a level of T_8 and in group B 44 % of patients achieved a sensory block upto T8. Glasser et al[12] in their study noted the time for 2 segment regression was similar in between the 2 groups and was 152±48 mins for the Levobupivacaine group and was 155±50 mins for the Bupivacaine group. This correlates with the finding in our study. In our study, the time for 2 segment regression of sensory block was 123.8±10.4 mins for group L and in the group, B was 126.5±12.1 mins with a p-value of 0.40 which was statistically not significant. In our study, there was no difference with the duration of sensory block among the 2 groups. Ashton D'Souza et a[l27] found that the onset of motor block was quicker with the Bupivacaine group which was a mean time of 4.5 mins and for the Levobupivacaine group the meantime was 5.25 mins. Our study showed the mean duration for the onset of motor block in group B was 10.48 mins and group L was 10.99 mins with a p-value of 0.05 which was statistically significant. The mean onset time-correlated with the study conducted by F. Fattorini et al[17] showed the mean onset time for the motor block in the Bupivacaine group was 9 ± 5 mins and in the group,Levobupivacaine was 12 ± 6 mins. Glaser et al[12] noted that the duration of the motor block in the levobupivacaine group was 280±84 mins and in the bupivacaine group was 284±80 mins. This correlated with our study which showed the mean duration of the motor block for group L was 283.2 mins and in the group, B was 286.3 mins with a p-value of 0.31 which was statistically not significant. There was a reduction in both systolic blood pressure and diastolic blood pressure in both the groups but the magnitude of fall was more in group B than in group L. The pronounced fall in blood pressure was more from 1st minute after spinal injection up to 15 minutes after the injection in group B.[18,19] The incidence of hypotension was more in group B (52% patients) which required more often the use of vasopressor drug inj ephedrine IV bolus compared to group L (16% patients) with a p-value of <0.001 which was clinically and statistically significant. This correlated in a study of one hundred-twenty ASA I-III patients, conducted by M Mantouvalou, et al[20] who observed that 42.5% of patients of the Bupivacaine group had hypotension compared to 17.5% patients of the Levobupivacaine group. In our study, we noted that the incidence of hypotension and bradycardia was significantly higher with the Bupivacaine group than with the Levobupivacaine group.[21] Levobupivacaine was found to be more cardio stable amongst the two after spinal injection. This may be attributed to the lower affinity of the S (-) isomer to cardiac sodium channels compared to the R isomer and thus is associated with fewer cardiac side effects.[14,15] The incidence of nausea and vomiting were comparable between both groups in our study. Nausea was seen in 2 patients of group L (4%) and in 4 patients of group B (8%) with a p-value of 1.0 which was clinically not significant. Vomiting was seen only in 1 patient of group B

(p-value 0.31). No other side effects were noted in the study.[22,24]

Conclusion

Our study reveals that 15 mg of isobaric Levobupivacaine (3ml of 0.5%) when administered intrathecally provides adequate anesthesia for lower abdomen and lower limb surgeries and is an alternative to 15 mg of hyperbaric Bupivacaine. (3ml of 0.5%). There is however a delayed onset of action of peak sensory and motor blockade with Levobupivacaine compared to Bupivacaine. Levobupivacaine is similar to Bupivacaine in two segments sensory block regression time, duration of sensory and motor block, and degree of motor block. Bupivacaine required more often the use of vasoactive drug ephedrine and sympathomimetic drug atropine compared to Levobupivacaine. So Levobupivacaine could be advisable in patients whose clinical history demands the cardiovascular impact of spinal anesthesia to be minimized.

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