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Original Research Article

A Prospective Randomized Study Comparing the Use of Hyperbaric 0.5% Levobupivacaine versus Hyperbaric Bupivacaine 0.5% for Spinal Anaesthesia in Infraumbilical Surgeries

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Abstract:

Background: Subarachnoid block is popular and commonly used worldwide. . Among the popular drugs used for subarachnoid block are bupivacaine, its enantiomer levobupivacaine, and ropivacaine. The experience of intrathecal anaesthesia with levobupivacaine is not well documented. Hence, the purpose of this study is to assess the quality and duration of sensory and motor blockade of levobupivacaine and its side effects, if any, compared to intrathecal bupivacaine during infraumbilical surgeries.

Objectives: A clinical study to compare the effect of spinal anaesthesia with 0.5% hyperbaric levobupivacaine and 0.5% hyperbaric bupivacaine in patients undergoing elective below umbilical surgeries.

Materials and Methods: 60 patients of American Society of Anaesthesiologists physical status class1 and 2 patients with 18 to 60 years of age posted for elective infraumbilical surgeries under subarachnoid block technique were randomly assigned into 2 equal groups. Group L received intrathecal 15mg hyperbaric 0.5% levobupivacaine (3ml), Group B received intrathecal 15mg hyperbaric 0.5% bupivacaine (3ml).

Results: Group L and Group B had similar onset of sensory blockade. Group L had delayed onset of motor blockade and lesser degree of motor blockade, similar level of sensory and maximum upper spread of sensory blockade, time taken for two segment regression time and duration of motor blockade but shorter duration of analgesia when compared to Group B.

Conclusion: Hyperbaric levobupivacaine was found to have similar effects to hyperbaric bupivacaine for anaesthetic effects, hemodynamic parameters, postoperative analgesic necessity time, and the first 24-hour side effects and complications. Levobupivacaine, having a lesser cardiovascular toxicity profile is an alternative to hyperbaric bupivacaine.

Keywords: Hyperbaric; Bupivacaine; Levobupivacaine; Subarachnoid Blockade.

Introduction

Subarachnoid block is popular and commonly used worldwide. The advantage of an awake patient, minimal drug cost and rapid patient turnover has made this the method of choice for many surgical procedures. Subarachnoid block technique enables good cardiovascular stability and makes early discharge to home possible [1].

There is an increased requirement for lower abdominal, lower limb and perineal surgeries. Better understanding of the physiological aspects of subarachnoid block, availability of long-acting local anaesthetic agents and understanding of pharmacokinetics and pharmacodynamics of these agents; have greatly contributed to the reincarnation of subarachnoid block during the last two and a half decades. Regional anaesthesia gives intra and postoperative pain relief with full preservation of mental status and normal reflexes. All local anaesthetics produce a dose dependent delay in the transmission of impulses through the cardiac conduction system by their action on the cardiac sodium and potassium channels. R and S enantiomers have different affinity for the different sodium and potassium ion channels with significant reduction of central nervous system and cardiac toxicity of S enantiomers as compared to R enantiomers.

In recent year's levobupivacaine, the pure S enantiomer of bupivacaine emerged as a safer alternative for regional anaesthesia than its racemic

parent [2]. It demonstrated less affinity and strength of depressant effects onto myocardial and central nervous vital centres in pharmacodynamics studies, and a superior pharmacokinetic profile.

Primary objectives:

- Onset of sensory blockade
- Maximum sensory blockade attained and time taken for the same
- Time taken for two-segment sensory regression
- Onset and duration of motor blockade
- Total duration of analgesia.

Secondary objectives:

- Hemodynamic changes such as hypotension and bradycardia
- Side effects such as hypotension, nausea and vomiting, shivering, urinary retention, and respiratory depression.

Inclusion criteria:

- Adult patients of either sex, aged between 18 and 60 years undergoing infraumbilical surgeries.
- Patients belonging to ASA physical status Class I and Class II
- Patients without any severe comorbid diseases.

Exclusion criteria:

· Patients having any absolute contraindications for spinal anaesthesia such as patient not willing, raised intracranial pressure, severe hypovolemia, bleeding diathesis, local infection and cardiac, respiratory, and CNS diseases

- Pregnant females
- Patients with chronic diseases such as diabetes and hypertension
- Patients with body mass index >30 kg/m2
- Patients shorter than 150 cm.

Materials and Methods

Sixty patients posted for elective below umbilical surgeries were selected for the study after taking an informed written consent. Approval from the ethical committee was obtained. The study was conducted from December 2022 to October 2023. The study population was divided by simple random sampling using shuffled sealed opaque envelope method into 2 equal groups (n=30), Group L and Group B.

All patients were examined and investigated a day before surgery. Patients were kept nil per oral for solids 6 hrs and clear fluids 2 hrs before surgery. They were advised to take tablet alprazolam 0.5mg and tablet ranitidine 150mg night before surgery. On arrival into OT, ECG, Non-Invasive Blood Pressure and Peripheral Oxygen Saturation (as per basic monitoring guidelines) were monitored. An intravenous access was secured using18 Gauge/20 Gauge cannula and patient was preloaded with Ringer lactate solution 15mg/kg. Spinal anaesthesia was performed while placing the patients in the sitting position. Sterilization of patients' back was done with povidone iodine solution 10%. Lumbar puncture was performed using a midline approach at the level of L2–L3 or L3–L4 using 26-G Quincke's spinal needle with the distal port facing laterally, after local infiltration of skin using 2% xylocaine. Once free flow of cerebrospinal fluid was obtained, the study drug was injected into the subarachnoid space at a rate of 0.2 ml/s. The patient was then turned into supine position. The time at which the drug administration was complete, was recorded, and all durations were calculated considering the time of intrathecal injection as time zero. Supplementary oxygen of 4 L was given through Patients were grouped into two groups based on the drug given.

Group L: received 3ml (15mg) intrathecal hyperbaric 0.5% levobupivacaine. Group B: received 3ml (15mg) intrathecal hyperbaric 0.5% bupivacaine. The study drug was prepared by an anaesthesiologist who was involved with randomisation, but was not involved further in the study. The anaesthesiologist who administered the test drug was also the observer of the parameters. Thus, the observer and the patients were blinded for the study drug.

The following parameters were studied:

- Onset of sensory blockade
- Maximum level of sensory blockade attained and the time taken for the same

Quality of intraoperative anaesthesia Includes:

- Time for two-segment sensory regression
- Onset and duration of motor blockade
- Total duration of analgesia.

The spread of sensory block was determined using pin prick test (using a blunt 25G hypodermic needle along the midclavicular line bilaterally) at every minute for first 10 mins, every 10 mins till the end of surgery and thereafter every 30 mins until sensory block was resolved.

Onset, quality, and duration of motor blockade were assessed by Modified Bromage Scale (0-3). Motor blockade was assessed every minute for first 10 mins, every 10 mins till the end of surgery and thereafter every 30 mins until Modified Bromage score of 0 was achieved.

Postoperative pain was assessed by means of visual analogue scale [VAS] (0–10: 0 = no pain and 10 = worst imaginable pain) at 1 h intervals until requirement for supplementary analgesia arose. Heart rate, systolic blood pressure (SBP), diastolic blood pressure, mean arterial pressure (MAP), and

oxygen saturation (SpO2) were recorded at baseline, after intrathecal injection, and then every 2 mins for 20 mins and then every 5 mins until the end of the surgical procedure.

Definitions:

Onset of sensory blockade: The time from intrathecal injection of the study drug to the time to achieve loss of pin prick sensation at the level of T10.

Time taken for maximum sensory blockade: The time taken to achieve the highest level of sensory blockade from the time of injection.

Duration of two-segment sensory regression: The time interval between intrathecal injections of the study drug to regression of sensory block by two segments from the maximum block height.

Onset of motor blockade: The time from the intrathecal injection of study drug to the time to achieve complete motor block i.e. grade 3 by using Modified Bromage scale.

Modified Bromage scale: 0 = no block, 1 = able to flex knees with free movement of feet, 2 = unable to flex knees but able to move feet, 3 = complete block.

Quality of intraoperative anaesthesia Includes:

Score 0: No sensation at the site of surgery.

Score 1: Sensation at the site of surgery but no pain.

Score 2: Painful sensation at the site of surgery with supplemental analgesics

Duration of motor blockade: The time from the intrathecal injection of study drug until the patient recovers to Bromage score 0.

Duration of analgesia: The time interval between block onset and the first analgesic request. Rescue analgesia was provided with intravenous diclofenac 1.5 mg/kg when the Visual analogue Scale (VAS) score was 4 or more.

Hypotension: The reduction of SBP of more than 30% from the baseline value or SBP <90 mmHg, and it was treated with an increased rate of intravenous fluids and vasopressors in the form of Inj. mephentermine 6mg intravenously (was repeated if necessary).

Bradycardia: The reduction in heart rate of more than 30% from the baseline or HR <50 bpm, and was treated with injection atropine 0.3mg increments.

Adverse effects: Patients were monitored for adverse effects such as nausea, vomiting, pruritus, respiratory depression. Ramsay sedation scoring was used to assess the sedation. All the statistical calculations were done using SPSS version 18 for windows. Descriptive statistics were done by calculating mean, standard deviation, range and proportion appropriately. The inferential statistics were done using Chi-square test, Repeated measure ANOVA, One way ANOVA with post hoc test and Kruskal Wallis test. Significant figures $p > 0.05$ is not significant, $p<0.05$ is significant, $p<0.01$ is highly significant.

Results

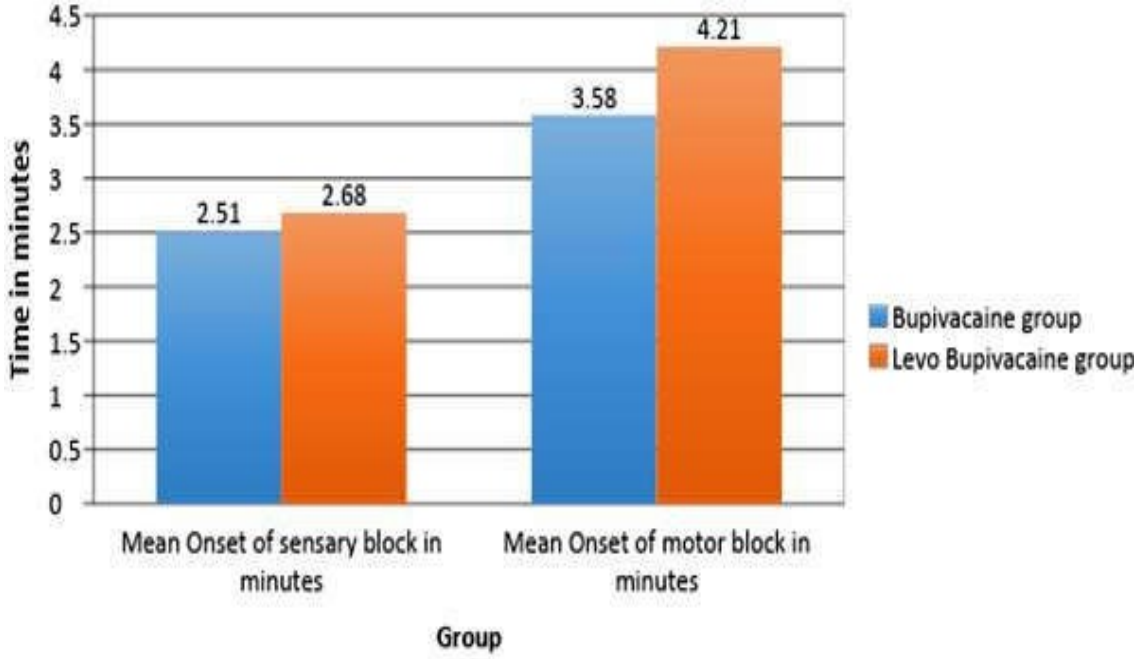
The demographic profile of the patients comparing age, sex, weight, height and also type of surgeries show no statistically significant difference and were comparable in both groups of our study. All base line vital parameters were similar in both groups.

Table 1: Comparison of patient's demographic data between the groups:

Variables	Group B (Mean± SD)	Group L (Mean± SD)	P Value
Age (Years)	44±12.3	39.3±12.2	0.06
Height (cm)	174±7.2	173.3±7.81	0.3
Weight (kg)	65.6±5.9	65.7±5.7	0.9
BMI (KG/M2)	21.73±1.91	21.6±1.75	0.6
Duration of Surgery (min)	43.16±15.11	39±10.11	0.3

Variables	Group B	Group L	P Value
Gender			
Male	22	24	0.7
Female	8	6	
ASA GRADE			
I	20	21	0.3
II	10	9	
Type of Surgery			
Orthopedic	10	6	0.2
General surgery	20	24	

The mean time for the onset of sensory block in group B was observed to be 2.51 mins compared to 2.68 mins in group L, with a p value of 0.4 which was found to be statistically insignificant. The mean time for the onset of motor block in group B was observed to be 3.58 mins compared to 4.21 mins with a p value of 0.003 which was found to be statistically significant.



Graph 1: Mean onset time of Sensory and Motor Blockade

Table 2: Comparison of Modified Bromage Scale between two Groups:

Modified Bromage Scale	Bupivacaine Group		Levobupivacaine group	
	No. of patients	%age of patients	No. of patients	%age of patients
0	0	0	0	0
1	0	0	0	0
2	1	3.3	11	36.6
3	29	96.7	19	63.4

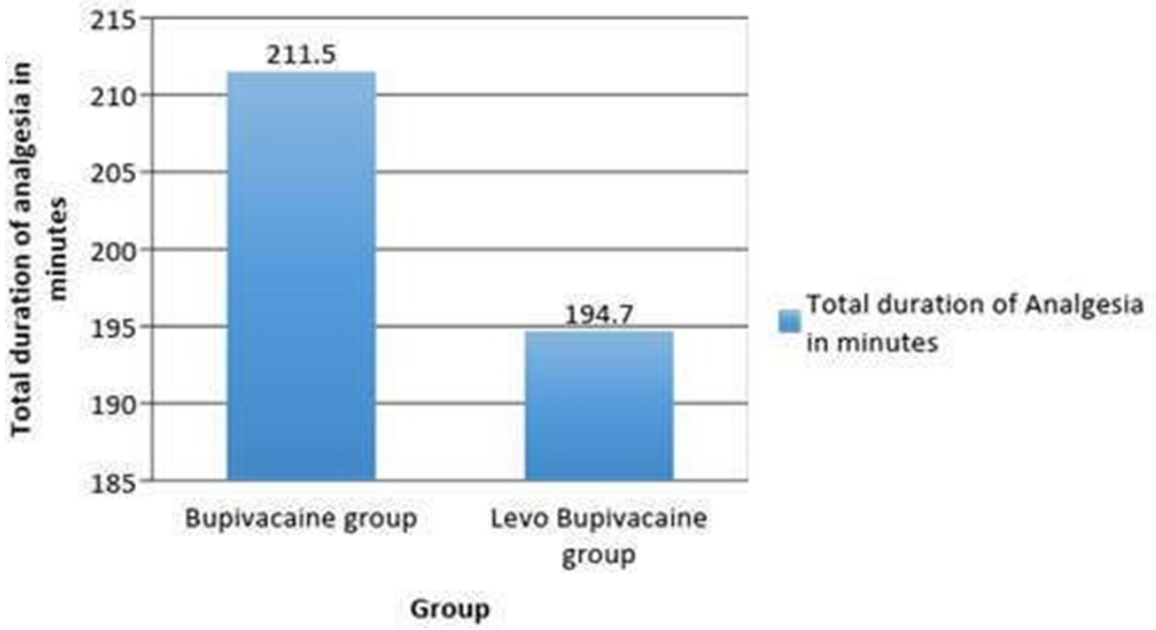
Degree of motor blockade is more i.e 96.7% of the patients in group B belong to grade 3 when compared to group L i.e only 63.43% of patients belong to grade 3 and 36.6%. of patients belong to grade 2 and is statistically significant (p value=0.01). All patients in both groups belong to score 0 of Quality of intraoperative anaesthesia scale i.e. no sensation at the site of surgery.

Table 3: Level of maximum sensory blockade in both the groups:

Level of maximum sensory Blockade	No. of patients in Bupivacaine group	%age of patients in Bupivacaine group	No. of patients in levobupivacaine group	%age of patients in levobupivacaine group
T6	5	16.7	6	20
T8	23	76.7	24	80
T10	2	6.6	0	0

In group B, 13.3% of patients achieved sensory level of T6, 73.3% of them achieved sensory level upto T8 and 13.3% of them achieved sensory level of T10. Whereas in group L, 10% of patients achieved sensory level of T6, 76% of them upto T8 and 13.3 % of patients achieved sensory level upto T10. However, the difference between two groups was statistically insignificant. (p value 0.9). Maximal upper spread of sensory blockade was T6 in 16.7% patients in group B and 20% in group L, T8 in 76.7% patients of group B whereas 80% in group L, T10 in 6.6% patients of group B. Level of maximum upper spread of sensory blockade was similar in both the groups and is statistically insignificant (p value= 0.492). Mean two segment regression time in group B was 132.73 mins compared to group L, which was 130 mins and was statistically insignificant (p value =0.2). Mean and SD of total duration of sensory blockade in Group B were 207.6 and 16.0 mins whereas in group L

were 193.1 and 16.5 respectively. Total duration of motor blockade in Group B was 188.5±12.4 mins whereas in group L was 182±12.3 mins. The mean duration of analgesia in group B was 211.50 mins and in group L was 210.72 mins, with p value 0.5 which is statistically insignificant.



Graph 2: Duration of Analgesia in both the groups

Table 4: Other parameters studied and their significance:

	Group B	Group L	P value
Mean time for total duration of sensory blockade (mins).	207.67	193.1	0.001
Mean time for total duration of motor blockade (mins).	188.50	182	0.046
Mean time for two segment regression (mins).	132.73	130	0.2
Mean time of post-operative analgesia (mins).	211	194.7	0.001

Table 5: Group comparison of Mean Heart Rate in (beats/min)

Time interval in mins	Group B	Group L	P value
0	73.2±6.4	73±4.9	0.2
2	73.5±7.1	72±4.2	0.4
4	72.1±7.4	71±4.5	0.45
6	79.6±6.9	74±5.1	0.54
8	78.2±7.4	73±4.4	0.53
10	76.4±7.3	69±4.2	0,55
12	74.9±6.8	74±5.2	0.62
14	77.2±7.3	73±5.1	0.64
16	78.4±7.5	74±4.0	0.65
18	77.5±6.5	73±4.5	0.63
20	75.2±6.8	71±4.6	0.56
25	73.7±7.1	77±4.5	0.55
30	72.9±7.3	73±5.3	0.57
35	77.1±7.7	74±4.6	0.66
40	76.2±6.9	70±5.4	0.64
45	73.6±6.9	72±5.2	0.67
50	75.2±7.1	72±5.1	0.68
55	77.1±7.2	74±5.3	0.69
60	73.6±7.3	73±5.1	0.70

Table 6: Group comparison of Mean Arterial Pressure (mm of Hg)

Time interval in mins	Group B	Group L	P Value
0	86±8.6	94±8,2	0.059

2	85±8.5	92±8.3	0.052
4	83±8.4	93±8.3	0.059
6	83±8.6	93±8.4	0.046
8	85±7.8	92±8.4	0.053
10	86±7.5	94±8.5	0.049
12	85±6.6	95±8.6	0.056
14	86±6.5	96±8.7	0.057
16	87±6.3	95±8.6	0.048
18	87±6.6	96±8.8	0.049
20	87±6.8	97±8.8	0.047
25	87±6.9	97±8.9	0.048
30	88±5.9	97±8.6	0.049
35	88±5.8	98±8.9	0.056
40	88±5.7	97±9.1	0.057
45	89±5.6	98±9.0	0.055
50	88±5.4	98±9.3	0.058
55	87±5.5	99±9.2	0.057
60	89±5.4	99±9.2	0.058

Table 7: Group comparison of Adverse Effects:

Adverse effects	Group B	Group L	P value
Hypotension	4	3	0.3
Bradycardia	3	2	0.2
Shivering	3	2	0.2
Nausea and Vomitting	0	0	
Pruritis	0	0	

Mean pulse rate changes and blood pressure changes were comparable in both groups and are found to be statistically insignificant. Intraoperative complication between two groups was comparable and is found to be statistically insignificant.

Discussion

Spinal anaesthesia, an age-old technique, used popularly for various infraumbilical surgeries, has traditionally used hyperbaric Bupivacaine as the drug of choice. Bupivacaine introduced by Ekenstam in 1957 seems to fulfil most of the requirements of an ideal local anaesthetic agent. It is a widely used local anaesthetic that has a prolonged action. Bupivacaine may be more cardiotoxic than other local anaesthetics and has been associated with deaths when accidentally injected intravenously. Levobupivacaine is the pure S enantiomer of racemic bupivacaine, developed as an alternative anaesthetic agent to bupivacaine.

Levobupivacaine has similar blocking properties and greater margin of safety due to reduced toxic potential. We started our study with a null hypothesis that hyperbaric levobupivacaine is comparable with hyperbaric bupivacaine in all its characteristics and concluded with the acceptance of null hypothesis.

We started the study with 60 patients in the age group between 18 to 60 years, posted for various elective surgeries under spinal anaesthesia belonging to ASA physical status I and II. There were no statistically significant differences in terms of demographic properties or ASA grading, the mean age, weight, height and gender of patients were comparable in both the groups. The first characteristic studied was the duration of onset of sensory block. The onset of sensory block was taken as the time in minutes from the deposition of drug to the evidence of analgesia to pinprick at T10 level. In the present study, patients who received bupivacaine had a mean onset of sensory block faster than those who received levobupivacaine, but this was statistically insignificant. The onset time of sensory block varied from 1.54 mins in Group B, with a mean of 2.51 mins and 2-5 mins in Group L with a mean of 2.68 mins which was comparable to studies conducted by Gulen Gule. et al. [3] and J.F. Luck et al. [4]

Maximum level of sensory block achieved is comparable in both groups in our study. In majority of the cases the maximum level of sensory block reached was T6 – 16.7% in Group B and 20% in Group L. In F. Fattorni et al. [5] study and Glaser et al. [6] study there was no difference between bupivacaine and levobupivacaine group in the highest level of sensory block achieved in the two groups (T8, T8) or in the time to reach peak level. Time taken for two segment regression of sensory in Group B was 132.73 mins while in Group L was 130 mins and is statistically insignificant with p value 0.2 which is comparable to study conducted by Christian Glaser et al. [6].

The time for onset of motor block in Group B was found to vary between 2 to 5 mins with a mean time of 3.58 mins while in Group L it varied between 3-6 mins with a mean of 4.21 mins which is comparable to the study conducted by J.F. Luck et al. [4]. The difference between the two groups was statistically significant. Degree of motor blockade in bupivacaine group that is number of patients with scale 3 blockade was 96.7% when compared to levobupivacaine group that is number of patients with scale 3 blockade was 63.4% and was found to be statistically significant with p value 0.01. Degree of motor blockade is superior with bupivacaine when compared to levobupivacaine. Quality of intraoperative anaesthesia was excellent in100% patients in both the groups.

In bupivacaine group, the mean value for total duration of motor blockade was 188.50 ±12.39 mins while in levobupivacaine group it was 182±12.3 mins with P value of 0.046 which was statistically significant. This observation is comparable to study conducted by J.F. Luck et al. [4].

In bupivacaine group the mean value for total duration of sensory blockade was 207.67±16.06 mins compared to levobupivacaine group 193.1±16.5 mins which is comparable to study conducted by Christian Glaser et al. [6]. Postoperative complications were comparable in both groups and postoperatively incidence of vomiting, shivering and hypotension were observed and all these incidences were similar in both the groups and statistically not significant. Similar Findings was seen in other studies also [8,9,10].

Conclusion:

The neurological and cardiovascular adverse reactions of bupivacaine associated to the accidental intravenous administration are well known, as well as the possible hemodynamic impact of intrathecal injection.

Since, its introduction into clinical practice, levobupivacaine has been appreciated because of the lower degree of toxicity when compared in particular with the racemic bupivacaine. Investigations have emphasized the association of levobupivacaine to a higher convulsive threshold and to a lower influence on cardiac or stroke indexes and ejection fraction.

Although levobupivacaine has very similar pharmacokinetic properties to those of racemic bupivacaine, several studies support the notion that its faster protein binding rate reflects a decreased degree of toxicity. The decreased cardiovascular and central nervous system toxicity makes levobupivacaine an interesting alternative to racemic bupivacaine.

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