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Intrathecal Hyperbaric Bupivacaine and Isobaric Levobupivacaine for Spinal Anaesthesia: Block Characteristics and Clinical Effects

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Abstract

Introduction: Bupivacaine (0.5% heavy) is used to administer subarachnoid block but carries an increased risk of cardiac and central nervous system toxicity if inadvertently injected intravascularly. Levobupivacaine is S-enantiomer of racemic bupivacaine with lesser systemic toxicity. A study was done to compare isobaric levobupivacaine and hyperbaric bupivacaine for spinal anaesthesia in patients undergoing elective lower abdominal surgeries to study hemodynamic variations, sensory and motor blocking properties of these. *Methods:* A prospective randomized controlled double blind study was conducted in 100 patients of ASA I and II physical status posted for elective lower abdominal surgeries under subarachnoid block, randomized into 2 groups with 50 patients each, received either 3 ml of 0.5% isobaric levobupivacaine (group L) or 3 ml of 0.5% hyperbaric Bupivacaine (group B). Hemodynamic parameters, time for onset of sensory and motor blockade, maximum height of sensory block and total duration of sensory and motor blockade were recorded. Intraoperative or postoperative side effects were noted. *Results:* The incidence of hypotension and bradycardia were comparable between the two groups. Onset of sensory and motor block (L-2.88 ± 1.81, B-2.12 ± 0.47, p value 0.005, L-3.12 ± 1.62, B-2.28 ± 0.81, p value 0.001, respectively) were significantly delayed in levobupivacaine group. The total duration of sensory block (L- 190.04 ± 35.19, B- 204.02 ± 30.06, p value 0.035) and motor block (L-176.65 ± 40.64, B 204.46 ± 29.8, p value<0.001) were higher in bupivacaine group. *Conclusion:* 0.5% isobaric levobupivacaine could be an alternative to 0.5% hyperbaric bupivacaine for spinal anaesthesia with similar hemodynamic changes, side effects and shorter durations of sensory and motor blockade.

Keywords: spinal; anaesthesia; isobaric; levobupivacaine; hyperbaric; bupivacaine.

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Introduction

Subarachnoid anaesthesia (SAB) is the most popular as well as effective technique for infraumbilical surgeries. It provides fast onset and effective sensory and motor blockade. It has an added advantage of preventing complication of General Anaesthesia like polypharmacy, pressor response from intubation, nausea, vomiting, sore throat, excessive sedation etc.

For decades lignocaine had been the local anaesthetic of choice for spinal anaesthesia but limited by its short duration of action and has been implicated in transient neurologic symptoms

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and cauda equina syndrome following intrathecal injection [1]. Bupivacaine is three to four times more potent than lignocaine. Due to its long duration of action, racemic bupivacaine is one of the commonest local anaesthetics used [2]. However, profound myocardial depression and even cardiac arrest can occur after accidental intravascular injection. Resuscitation from bupivacaine induced cardiovascular collapse has been found to be difficult and may be unsuccessful [3]. Levobupivacaine, which is S-enantiomer of bupivacaine, was discovered by Aberg in 1972. He compared the levo-rotatory and dextro-rotatory isomers of mepivacaine and bupivacaine. He showed that cardiac effects of both enantiomers of bupivacaine are different [4].

In common to all local anaesthetics, levobupivacaine reversibly blocks the transmission of action potential in sensory, motor and sympathetic nerve fibres by inhibiting the passage of sodium through voltage-sensitive ion channels in the neuronal membrane. Whereas the inhibitory action is intended to be localized at the site of administration, excessive doses or accidental intravascular injection may lead to activity at the level of other ion channels in excitable tissues followed by unwanted central nervous (CNS) and cardiovascular adverse effects. Levobupivacaine is an interesting alternative to bupivacaine for spinal anaesthesia. The incidence of adverse cardiac and neurological events was significantly higher with bupivacaine as compared to levobupivacaine when used in regional anaesthesia. Similarly, the potential for CNS toxicity is lower with levobupivacaine as compared to bupivacaine [5]. It has been stated that its faster protein binding rate reflects a decreased degree of toxicity and studies done have supported that it has lesser cardiovascular and central nervous system toxicity than bupivacaine [6]. Racemic bupivacaine and levobupivacaine appear to produce a similar pattern of block [7,8]. At low concentrations, levobupivacaine produces a differential neuraxial block with preservation of motor function which may be favorable for ambulatory surgery [9]. Minimum effective local anaesthetic dose of levobupivacaine as recommended by an up- and-down sequential design study is 11.7 mg [10]. Reports using levobupivacaine for epidural or brachial plexus anaesthesia suggested equivalent clinical efficacy to bupivacaine. However, inadequate data for its use in spinal anaesthesia is available. Hence a study was conducted to study and compare the efficacy and safety of intrathecal isobaric levobupivacaine with hyperbaric bupivacaine.

Aims

To study and compare the clinical effects and block characteristics of hyperbaric bupivacaine and isobaric levobupivacaine for spinal anaesthesia in lower abdominal surgeries.

Objectives

The following parameters were studied and compared.

1. The time for onset, level and duration of sensory blockade.
2. The time for onset, degree and duration of motor blockade.
3. Time for 2 segment regression of sensory block.
4. The hemodynamic variations.
5. Adverse effects if any.

Methodology

A prospective randomized controlled, double blind study was conducted in hundred patients undergoing elective lower abdominal surgeries under spinal anaesthesia at Basaveshwara General and Teaching Hospital attached to Mahadevappa Rampure Medical College, Kalaburagi. The study was conducted from November 2015 to January 2017.

By keeping the confidence limits at 95% and power of study at 80%, to detect a minimum of 10% difference in proportion of hypotension between the two groups, the minimum sample size required is 25 in each group. We included 50 patients in each group for better validity of results. 100 patients chosen for the study were divided into 2 groups in a ratio of 1:1, Group L and Group B, of 50 each, by permuted block randomization technique in the ratio 1:1.

Statistical Methods: 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) on metric parameters. Chi-square/ Fisher Exact probability test has been used to find the significance of study parameters on categorical scale between two or more groups.

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used.

Results

It is a clinical randomized controlled double blind study with 100 patients randomly divided into 2 groups of 50 patients each, using permuted block randomisation technique in the ratio 1:1.

Group B – receiving intrathecal bupivacaine. Group L – receiving intrathecal levobupivacaine

They were evaluated for hemodynamic variations, onset and duration of sensory and motor blockade, side effects of the drugs if any.

Demography

The groups are matched with respect to age and gender.

The mean age in Group L is 38.02 ± 11.12 years and in Group B 37.42 ± 10.82 years.

Weight and Height in these samples in the groups were matched.

In our study, Inguinal hernia mesh repair in Levobupivacaine group and open appendicetomy as well inguinal hernia mesh repair were maximum in Bupivacaine group done (Table 1).

Mean duration of surgery is statistically similar in two groups studied p = 0.091.

Bradycarida, shivering and nausea are less with Levobupivacaine group then Bupivacaine but hypotension is more in Levobupivacaine then Bupivacaine group.

Onset of sensory block at L1 and T10 is longer in Levobupivacaine then Bupivacaine, but total duration of sensory block is lesser in Levobupivacaine then Bupivacaine (Table 2).

Onset of Motor block is longer in Levobupivacaine then Bupivacaine, but total duration of motor block is lesser in Levobupivacaine then Bupivacaine (Table 3).

The mean time of request for first analgesic dose was 203.6 minutes in levobupivacaine group and 208.3 minutes in bupivacaine group. (p > 0.05).

Table 1: Procedure

Surgical procedures carried out among the two groups				
Procedure	**Levobupivacaine**		**Bupivacaine**	
	No	%	**No**	%
Anatomical repair hernia	7	14	8	14
Open appendicectomy	9	18	10	20
TURP	2	4	3	6
Post Laparotomy 2^0 suturing	3	6	2	4
Inguinal hernia mesh repair	15	30	10	20
Jabouley's procedure	3	6	7	14
Lumbar sympathectomy	3	6	4	8
Palmo's procedure	4	8	3	6
DJ stenting	4	8	3	6

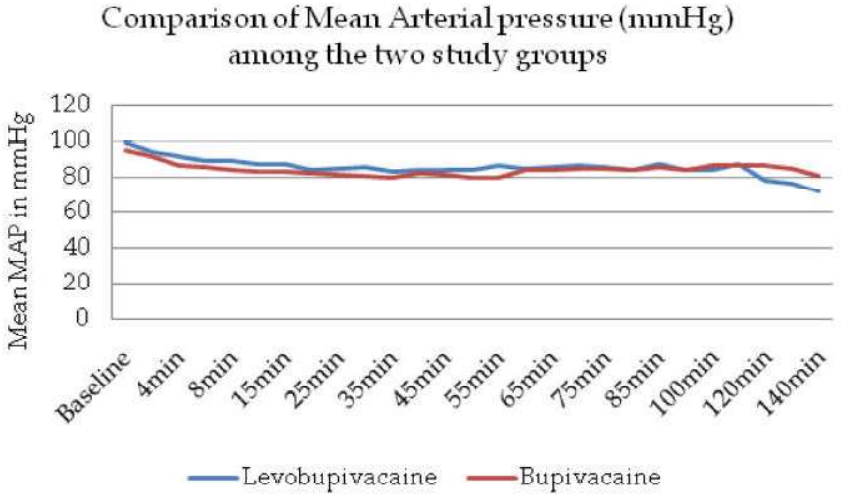

Fig. 1: Comparison of MAP (mm Hg) in two groups studied

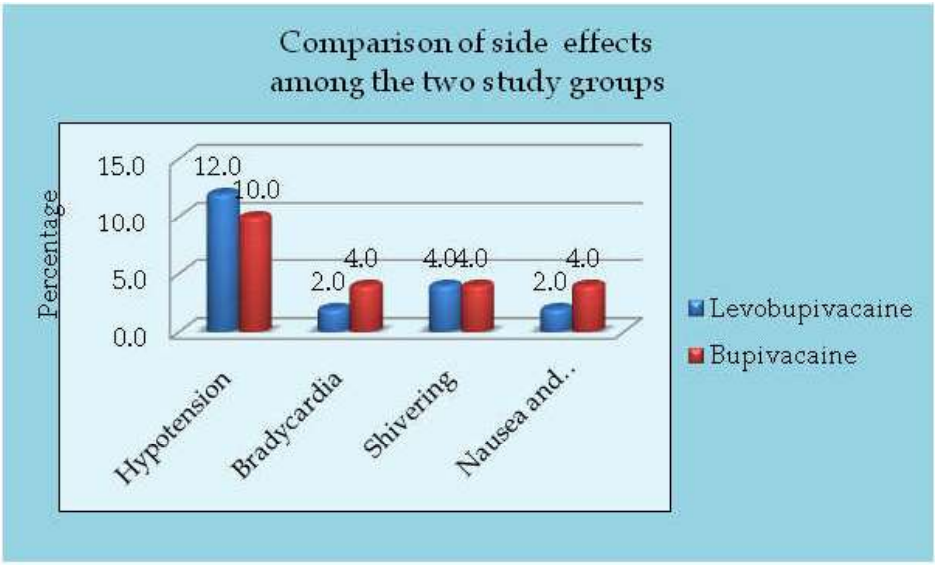

Fig. 2: Comparison of side effects in two groups studied

Table 2: Onset and duration of sensory blockade at L1 and T10.

Parameters	LevoLevobupivacaine group (n=50)	Bupivacaine group (n=50)	p value
Onset of sensory block at L1(min)	2.88 ± 1.81	2.12 ± 0.47	0.005**
Onset of sensory block at T10(min)	5.14 ± 3.76	3.32 ± 1.65	0.002**
Total duration of sensory block(regression to <L1)	190.04 ± 35.19	204.02 ± 30.06	0.035*

Table 3: Onset and total duration of motor blockade:

Parameters	LevoLevobupivacaine group (n=50)	Bupivacaine group (n=50)	p Value
Onset of Motor block B1 (min)	3.12 ± 1.62	2.28 ± 0.81	0.001**
Total duration of motor block (B1-B0) min	176.65 ± 40.64	204.46 ± 29.84	<0.001**

Discussion

"A study for comparing the clinical effects and block characteristics of intrathecal hyperbaric bupivacaine and isobaric levobupivacaine for spinal anaesthesia in lower abdominal surgeries" was undertaken in Basaveshwara General and Teaching Hospital attached to Mahadevappa Rampure Medical College, Kalaburagi to evaluate the hemodynamic variations, sensory and motor blocking properties of isobaric levobupivacaine 0.5% (15 mg) and hyperbaric Bupivacaine 0.5% (15 mg). By keeping the confidence limits at 95% and power of study at 80%, to detect a minimum of 10% difference in proportion of hypotension between the two groups, the minimum sample size required is 25 in each group. We included 50 patients in each group for better validity of results.

Hypothesis made before starting the study

We hypothesized that levobupivacaine administered as spinal anaesthesia for infraumbilical surgeries would provide more stable hemodynamics, similar sensory block and motor block characteristics and fewer side effects as compared to bupivacaine.

Demographic data

Demographic data comparing age, sex, weight, height, ASA grade shows no statistically significant difference among both the groups.

Hemodynamic variations

In our study, intraoperatively hypotension was observed in 6 patients (12.0%) in Group L and

in 5 patients (10.0%) in Group B which was not statistically significant (p value 0.749). Incidence of bradycardia was same in both the groups, 1 patient (2.0%) in each group.

Various studies have shown varying hemodynamic profile of the two drugs. The study of Opas vanna et al. has finding similar to our study and they recorded hypotension in 5.7% in levobupivacaine group and 4% in bupivacaine group, both comparable with p value 0.39 but bradycardia was significantly higher in levobupivacaine group than bupivacaine (25.7% vs 5.7%, p value 0.02) [12].

Luck et al. in their study did not find any statistically significant difference between incidence of hypotension among levobupivacaine and bupivacaine with values being 30% and 25% respectively. Similarly Casati et al. in their study observed that clinically relevant hypotension was reported in 1 patient of bupivacaine group (5%) and 2 patients in both levobupivacaine (10%) and ropivacaine (10%) groups (p value 0.57). Bradycardia was reported in 1 patient of group bupivacaine only (5%) (p value 0.36).

In study conducted by Gulen et al. in pregnant patients hypotension was more in Bupivacaine group than levobupivacaine group (16.6% vs 36.6%). Incidence of bradycardia was 30% in bupivacaine group while in levobupivacaine group was 6.6%, the difference being significant (p value <0.05%). In study by Kazak et al. the number of the patients with hypotension who required intravascular volume expanders was highest in Bupivacaine Group and this result was statistically significant (p< 0.001). Bradycardia necessitating treatment was not observed in any of the patients [16]. Contrary finding was recorded in study done by Sari and his colleagues where they recorded a significantly higher incidence of hypotension in levobupivacaine group than bupivacaine group (36% vs 13%, p value 0.036) [14].

In our study few intraoperative hemodynamic parameters showed statistically significant differences in the two groups, but the differences was not clinically significant. All the patients were hemodynamically stable postoperatively and there was no incidence of hypotension or bradycardia in postoperative period in either group.

Sensory blockade

Onset of sensory blockade

In our study onset of sensory block is considered as loss of cold sensation at L1 dermatome and we also recorded the time taken for onset at T10 dermatome. The mean time for onset of sensory block at L1 was 2.88 ± 1.81 mins in group L and 2.12 ± 0.47 min in group B. This difference is statistically significant (p=0.005). The onset time at T10 was also significantly higher in group L with the time required being 5.14 ± 3.76 min compared to 3.32 ± 1.65 min in group B (p value 0.002). Similar finding was observed in the study conducted by Opas Vanna et al. where they found that time for onset of sensory block at T10 was higher in levobupivacaine group than bupivacaine group (10.0 min vs 7.3 min) but in their study it was not found to be statistically significant (p value 0.22) [12]. Study conducted by Gozaydin and colleagues also found a significantly longer time for onset of sensational block in levobupivacaine group than bupivacaine group (11 min vs 8 mins, p value 0.023) [17].

This finding is not correlating with the values observed by Luck et al. who recorded an average time of 5 min in case of all the three drugs levobupivacaine, bupivacaine, ropivacaine for onset of sensory block at T10 level [21].

Maximum height of sensory block

In our study the maximum sensory level achieved was T4 in Group L in 7 patients and most patients achieved a maximum level of T6 (28 patients) which was similar to Group B where maximum level attained was T4 (3 patients) and most patients achieved a level of T6 (24 patients).

Total duration of sensory block (regression to <L1)

In our study the total duration of sensory block that was defined as the time taken from the onset of sensory blockade at L1 level till the sensory level receded to below L1 dermatome level, was 190.04 ± 35.19 min in levobupivacaine group and 204.02 ± 30.06 min in bupivacaine group (p value 0.035). Hence the total duration of sensory blockade was significantly higher in bupivacaine group.

In study of Glaser and his coworkers the duration of sensory block (min) was 228 ± 77 in levobupivacaine group which was similar to that in bupivacaine group that was 237 ± 88 min [7].

Gozaydin O et al. study found that that the sensational block disappearing time was 244 mins in bupivacaine group which was higher than levobupivacaine group ie. 227 mins but the difference was not statistically significant (p value 0.327) [17]. Kazak and colleagues in their study found that time to L1 regression was 172.4 ± 33.5 min in bupivacaine group, 151.3 ±

25.5 min in levobupivacaine group and 143.5 ± 14.3 min in ropivacaine group. Ropivacaine has significantly shorter duration than bupivacaine or levobupivacaine [16]. The duration was prolonged in bupivacaine group similar to our study.

Onset of motor blockade

In our study the time for onset of motor block at B1 from intra thecal injection was 3.12 ± 1.62 min in levobupivacaine and 2.28 ± 0.80 min in bupivacaine group, a difference that was statistically significant (p value 0.001). Therefore according to our study the onset of motor blockade is significantly delayed in group L.

In the study of *Sari et al.* who observed the onset of motor blockade to Bromage 3 score found that it was achieved faster in bupivacaine group than levobupivacaine group (7.8 ± 4.5 min *vs* 10.9 ± 5.9 min, p=0.02) [14].

In the study carried out by Opas Vanna and colleagues it was observed that the mean time to onset of motor block (Bromage > 0) was 3.9 min in levobupivacaine group and 3.0 min which was not significantly higher (p value 0.52) [12].

M. Mantouvalou et al. in their study found that the onset of motor block (defined as time to achieve a Bromage score of 3 in their study) was significantly faster in the bupivacaine group 8 ± 5 min compared with 12 ± 5 min in the ropivacaine group and 11 ± 7 min in the levobupivacaine group (p < 0.05). However they also observed that the mean time of onset to achieve a Bromage score of 1 was 2 ± 1 min in the bupivacaine group, 3 ± 1 min in the ropivacaine group, and 2 ± 1 min in the levobupivacaine group (p value>0.05) [13]. These differences were not significant.

Total duration of motor blockade

In this study the observed duration of motor blockade was significantly shorter in levobupivacaine group (176.65 ± 40.64 min) than bupivacaine group (204.46 ± 29.84 min), p value <0.001.

Gautier et al. in their study with intrathecal anaesthesia for caesarean section observed that the mean duration of motor blockade was significantly higher in bupivacaine group compared to levobupivacaine and ropivacaine with values being 142 min, 121 min and 116 min respectively with p value being < 0.05, i.e. both levobupivacaine and ropivacaine had significantly shorter duration of motor blockade than bupivacaine [11].

No significant difference was observed in the duration of motor block among bupivacaine and levobupivacaine (278 ± 70 min and 273 ± 80 min, respectively) in the study conducted by M. Mantouvalou et al. Glaser et al. also in their study observed that the duration of motor block was similar in both bupivacaine and levobupivacaine groups (284 ± 80 min, 280 ± 84 min respectively) [13,7].

Time of request for first analgesic dose

In our study the time from onset of sensory blockade to request for first analgesic dose was 203.60 ± 53.64 min in levobupivacaine group and 208.53 ± 52.43 min in bupivacaine group, not statistically significant (p value 0.644)

Gozaydin O et al. in their study recorded the mean first analgesic time to be 188 min in levobupivacaine group and 157 min in bupivacaine group, the difference was not statistically significiant (p value 0.379) [17].

Gautier et al. observed the total duration of analgesia (min) among the three drugs to be 157 in bupivacaine group, 136 in levobupivacaine group and 132 in ropivacaine group (p value < 0.05) [11] ie. Both levobupivacaine and ropivacaine had significantly shorter duration of analgesia than bupivacaine.

Hakan and coworkers found the first analgesic requirement time to be significantly higher in levobupivacaine group than bupivacaine group (389 ± 146 min vs 305 ± 504 min respectively, p value <0.004) [15]. They used fentanyl as adjuvant that is probably a reason why the total durations observed in their study is higher than recorded in our study but the preferential higher duration seen with levobupivacaine with fentanyl could not be explained.

Other Side effects seen after intrathecal administration of the two drugs studied in our study are observed to be similar in both the groups with no statistically significant differences between the two groups. The observed incidence for nausea and vomiting in group L is 0% while in group B is 4%, p value = 1.00 and for shivering the incidence was 4% in both the groups. None of the patients in either group had any other major side effects.

The studies conducted by M. Mantouvalou et al., Hakan and colleagues, also showed similar incidence of side effects between these two drug group patients.

In study of Gulen et al. the incidence of headache,

backache, vomiting was similar in both the groups but nausea was statistically significantly higher in bupivacaine group (3% vs 10%, p value <0.05) [17].

Conclusion

To conclude, our study demonstrates that 3 ml 0.5% isobaric levobupivacaine appears to be an alternative to 3 ml 0.5% racemic hyperbaric bupivacaine for spinal anaesthesia in lower abdominal surgeries, with similar hemodynamic changes, side effects and shorter durations of sensory and motor blockade. With the advantages of shorter durations of sensory and motor blockade, Isobaric levobupivacaine can be preferred in day care surgeries.

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