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A Comparative Study of Hyperbaric 0.5% Levobupivacaine with Bupivacaine 0.5% for Spinal Anaesthesia in Elective Surgeries

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Abstract

Background: 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**.** Among the popular drugs used for subarachnoid block are bupivacaine and and its enantiomer Levobupivacaine. *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 70 years of age posted for elective lower limb surgeries under subarachnoid block technique were randomly assigned into 2 equal groups. Group L received intrathecal hyperbaric 0.5% levo bupivacaine [total 3.5ml], Isobaric levobupivacaine made hyperbaric by adding 0.5ml of 50% dextrose to 3ml of levobupivacaine, Group B received intrathecal 15mg hyperbaric 0.5% bupivacaine with 0.5ml of normal saline.[total 3.5ml]. *Results:* Group L and Group B had similar onset of sensory blockade. Group L had delayed onset of motor blockade, lesser degree of motor blockade and lesser quality of intraoperative anaesthesia, 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 0.5% bupivacaine remains effective choice than hyperbaric 0.5% levobupivacaine for spinal anaesthesia in elective surgeries, But hyperbaric levobupivacaine is also a better option for shorter procedures and outpatient spinal anaesthesia.

Keywords: Hyperbaric; Bupivacaine; Levobupivacaine; Subarachnoid Blockade.

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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. It reduces surgical stress and attenuates increase in plasma catecholamines and other

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hormones. 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 years 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.

The purpose of this study is to compare the onset, duration of sensory block and motor block, postoperative analgesia and haemodynamic changes occurring with 0.5% hyperbaric bupivacaine and 0.5% hyperbaric levobupivacaine when given intrathecally.

Materials and Methods

Sixty (60) 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 October 2012 to November 2013. The study population was divided by simple random sampling using shuffled sealed opaque envelope method into 2 equal groups (n=35).

Inclusion criteria were patients between 18 to 70 years of age with American Society of Anaesthesiologists Physical Status (ASA) Class 1 & 2.

Exclusion criteria were any contraindications to neuraxial anaesthesia, sensitivity or allergy to any of the study drugs, pregnant patients, patients with obvious spinal deformities and with signs of raised intracranial pressure.

A routine pre-anaesthetic evaluation was conducted on the evening before surgery and relevant investigations done. The patients were pre-medicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally at bed time on the previous night before surgery. They were kept nil orally for 6 hours prior to surgery for solid food and 2 hours for clear liquids. On the day of surgery, patient's basal vital parameters were recorded. Monitoring was done using multiparameter monitor having pulse oximetry, Electrocardiogram (ECG), Non-invasive Blood pressure (NIBP). Intravenous line was obtained with an 18-gauge cannula.

With the patients in left lateral position under aseptic precautions, lumbar subarachnoid block performed with pillow under the head and table flat or in the sitting position when the patient could not be put in lateral position. Lumbar dural tap was done in the L3-L4 interspace, midline approach, using 23 or 25 gauge Quincke's needle, after local infiltration of skin using 2% xylocaine. After obtaining free and clear flow of CSF, drug was administered slowly, making sure of negative aspiration for blood. Patients were made to lie supine immediately after the completion of injection. During surgery all the patients were given intravenous fluids, either normal saline or ringer lactate solution. Patients were grouped into two groups based on the drug given.

Group L: received intrathecal hyperbaric 0.5% levo bupivacaine [total 3.5ml], Isobaric levobupivacaine made hyperbaric by adding 0.5ml of 50% dextrose to 3ml of levobupivacaine.

Group B: received intrathecal 15mg hyperbaric 0.5% bupivacaine with 0.5ml of normal saline [total 3.5ml]

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

1. Assessment of sensory blockade: sensory blockade was assessed by pin prick and time noted for the block to reach different dermatomal level.
   - Onset of sensory block
   - Level of sensory blockade
   - Maximum height reached
   - Duration of analgesia.
2. Assessment of onset of motor blockade.
3. Degree of motor blockade by modified Bromate scale.
4. Quality of intraoperative anaesthesia.
5. Assessment of total duration of motor blockade and total duration of sensory blockade.
6. Duration of analgesia (time between block and first analgesic dose).

7. Time to voluntary mobilization and time to voluntary micturition.
8. Postoperative complications if any. Patients were also monitored for any side effects like nausea, vomiting, sedation, respiratory depression and pruritus. Ramsay sedation scoring was used to assess the sedation

Definitions of the parameters of the study

- Onset of sensory block- This was taken as the time from the deposition of drug to the evidence of analgesia to pinprick at T12 level.
- Upper level of sensory block- the highest dermatome of block was assessed, taken as the interval between the deposition of the drug and the loss of sensation at the highest dermatomal level.
- Onset of motor block was noted. Time taken from onset of paresis to the loss of power i.e. patient was not able to lift the legs.
- Modified Bromage scale 0 = no motor blockade, 1 = hip blockade, 2 = hip and knee blockade, 3= hip, knee and foot blockade.
- Duration for 2 segment regression – time taken for recovery of sensory level to 2 dermatomal segments below the highest level.
- Total duration of analgesia - Time when the patient first complains of pain after spinal block (time for rescue analgesic).

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.

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.

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

Table 1: Age Wise Distribution of Study Subjects

Age in Years	Bupivacaine Group		Levobupivacaine Group	
	No. of patients	%	No. of patients	%
<25	3	10	2	6.67
26-35	3	10	11	36.67
36-45	6	20	4	13.33
46-55	10	33.3	6	20.00
56-65	6	20	4	13.33
66-75	2	6.7	3	10.00
Total	30	100	30	100

Table 2: Comparison of Modified Bromage Scale between the two groups

Modified Bromage scale	Bupivacaine group		Levo Bupivacaine group	
	No. of patients	%	No. 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

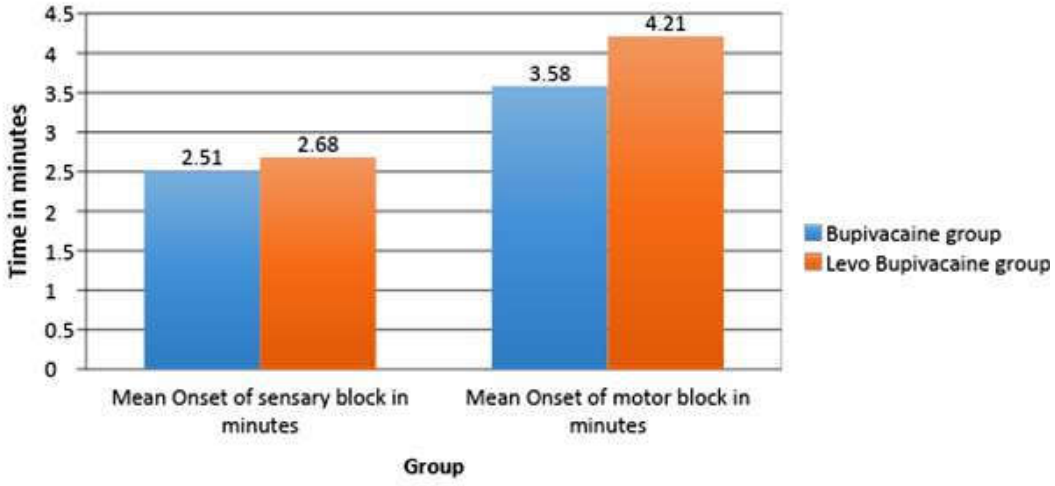
in group L, with a p value of 0.003 which was found to be statistically significant.

Degree of motor blockade is more i.e. 96.7% of the patients in group B belongs to grade 3 when compared to group L i.e. only 63.43% of patients belongs to grade 3 and 36.66% of patients belongs to grade 2 and is statistically significant (p value =0.01).

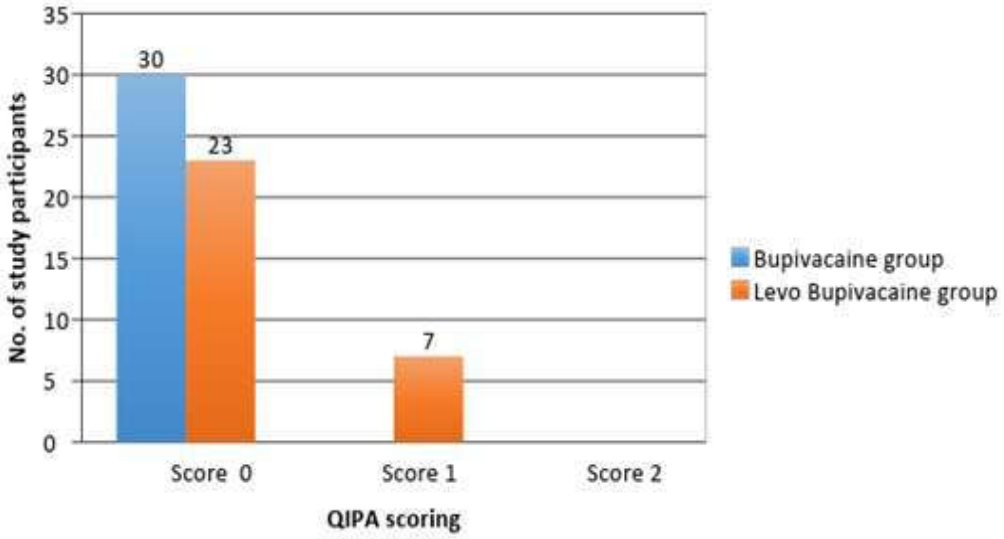
All patients in group B belongs to score 0 of Quality of intraoperative anaesthesia scale i.e. no sensation at the site of surgery. While in group L 76.7% of patients belongs to the score 0 and 23.3% of the patients belongs to score 1, which indicates sensation at the site of surgery but no pain and is statistically significant (p value<0.005).

In group B, 13.3% of patients achieved sensory level of T6, 53.3% of them achieved sensory level upto T8 and 33.3% of them achieved sensory level of T10. Whereas in group L, 10% of patients achieved sensory level of T6, 56% of them upto T8 and 33.3 % of patients achieved sensory level upto T10. However, the difference between two groups was stastically insignificant. (p value 0.9).

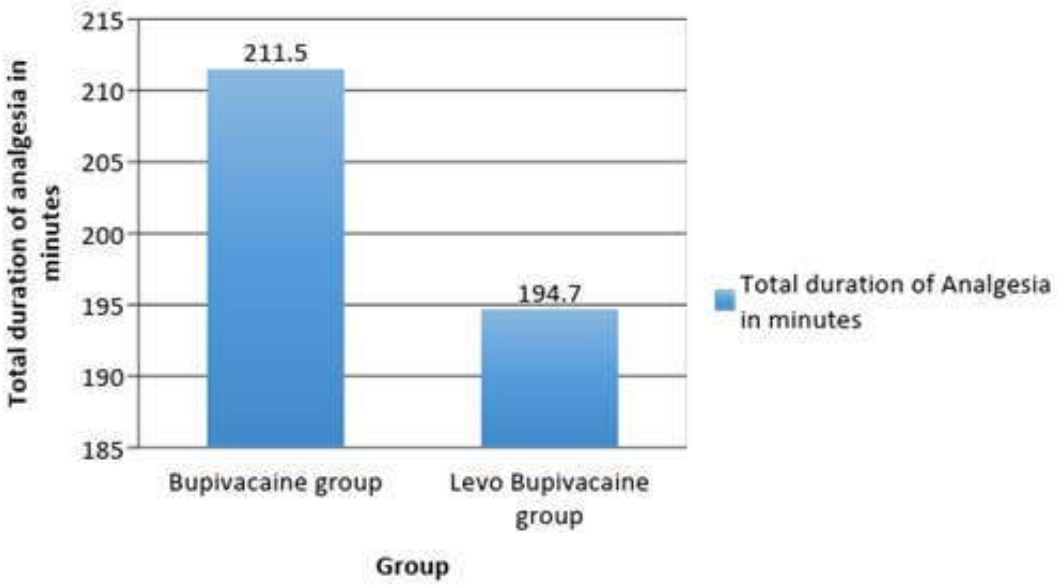
Maximal upper spread of sensory blockade was T6 in 16.7% patients in group B and 20% in group L, T8 in 76.7% patients of group B whereas 24% in group L, T10 in 6.6% patients of group B. Level of maximum upper spread of sensory blockade was similar in both the groups and is statistically insignificant (p value= 0.492).



Graph 1: Mean Onset time of Sensory and Motor Blockade



Graph 2: QIPA Scoring in both the Groups



Graph 3: Duration of Analgesia in both the groups

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

Level of maximum sensory Blockade	Bupivacaine group No. of patients	%	Levo Bupivacaine group No. of patients	%
T6	5	16.7	6	20.0
T8	23	76.7	24	80.0
T10	2	6.6	0	0

Table 4: Duration of Anaesthesia in both the groups

Time in Minutes	Bupivacaine group (17)	Levo Bupivacaine group (14)
Minimum	420	420
Maximum	540	490
Mean + SD	475.8±31.83	452.1±22.1

Table 5: Mean time for voluntary micturition

Time in Minutes	Bupivacaine group	Levo Bupivacaine group
Minimum	460	550
Maximum	620	640
Mean + SD	578.8±42.84	586.4±27.1

Mean two segment regression time in group B was 132.73 mins compared to group L 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 194.7 mins, with p value < 0.01 which is stastically significant.

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

Mean time for patients in group B to mobilize was 475.8 mins and in group L was 452.1 mins which was found to be stastically significant. (p value 0.03).

Table 6: The parameters studied and their significance is depicted in the following table

S. No.		Group B	Group L	P Value
1.	Mean age (yrs.)	46.73	43.27	0.248
2.	Mean onset of sensory block (mins)	2.51	2.68	0.4
3.	Max. sensory level	T6	T6	0.492
4.	Mean onset of motor blockade (mins)	3.58	4.21	0.003
5.	Mean time for two segment regression (mins)	132.73	130.0	0.2
6.	Degree of motor blockade. (modified Bromage scale){%}	III Degree- 96.7	III-Degree 63.4	0.01
7.	Quality of intra operative anaesthesia (%)	Score 0-100	Score 0-76.7 Score 1-23.3	0.005
8.	Mean time of post-operative analgesia (mins)	211.50	194.7	0.001
9.	Mean time for total duration of motor blockade (mins).	188.50	182	0.046
10.	Mean time for total duration of sensory blockade (mins).	207.67	193.1	0.001
11.	Mean time to voluntary mobilization(mins)	475.8	452.1	0.03
12.	Mean time to voluntary micturition(mins)	578.8	586.4	0.9
13.	Complications during surgery			
	Hypotension (%)	40	33.3	
	Bradycardia (%)	6.7	0	
	Hypotension + bradycardia (%)	0	6.7	0.3
	Shivering (%)	3.3	3.3	
	Hypotension+shivering (%)	3.3	0	

Mean time for voluntary micturition in group B was 578.8 mins and in group L was 586.4 mins which is stastically insignificant. (p value 0.9)

There were no post-operative complications in 63.3% of patients in both groups. Hypotension was present in 3.3%, one episode of vomiting was present in 16.7% and PDPH occurred in 3.3% of patients in both the groups. Vomiting second episode was present in 3.3% of patients in group B. Shivering present in 10% of patients in group B and 13.3% of patients in group L.

Discussion

Regional anaesthesia has several advantages over general anaesthesia in terms of reduced bleeding due to hypotension, better intraoperative and postoperative analgesia, awake patient, less requirements of parenteral opioids, decreased incidence of nausea and vomiting, reduction in venous thromboembolism, myocardial infarction, respiratory complications and renal failure

Subarachnoid block is the current wide spread popular anaesthetic technique available today. Subarachnoid block has the definitive advantage that profound nerve block can be produced in a large part of the body by the relatively simple injection of a small amount of local anaesthetic. An ideal anaesthetic agent used in subarachnoid block should have rapid onset of action, intense analgesia, adequate motor blockade, long duration of action, adequate postoperative analgesia and minimal cardiovascular change. 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 18-80 years, posted for various elective surgeries under spinal anaesthesia belonging to ASA physical status [2] and II were selected.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 T12 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 1.5-4 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 Guler 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 – 13.33% in Group B and 10% 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 levobupivacaine when compared to levobupivacaine.

Quality of intraoperative anaesthesia was excellent with bupivacaine group was excellent- score 0 in bupivacaine group in 100% patients indicating that no sensation at the site of surgery and in levobupivacaine group was 76.7% and remaining patients that is 23.3% belongs to score- 1 which indicates sensation at the site of surgery but no pain and no patients belongs to score- 2 which indicates painful sensation at the site of surgery which require supplemental analgesics and it was found to be statistically significant (p value 0.005). Bupivacaine provides excellent analgesia when compared to levobupivacaine.

In bupivacaine group the mean value for total duration of motor blockade was 188.50 ±12.39 mins and in levobupivacaine group 182±12.3mins. For motor blockade P value 0.046 and 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±16.5mins which is comparable to study conducted by Christian Glaser et al. [6].

Post-operative complications were comparable in both groups and postoperatively incidence of vomiting, shivering, post dural puncture headache 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].

Patients were mobilized late in bupivacaine group than in the levobupivacaine group and it was found to be statistically significant (p value 0.03). The same results were found in the study conducted by J.F. Luck et al. [4]. In our study patients micturated late in levobupivacaine group than in bupivacaine group but it was statistically insignificant (p value 0.9). The same results were found in study conducted by Elizabeth A. Alley et al. [11].

Conclusion

The neurological and cardiovascular adverse reactions associated to the accidental intravenous administration are well known, as well as the possible hemodynamic impact of their 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 make levobupivacaine an interesting alternative to racemic bupivacaine.

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