

**A COMPARISON OF EPIDURAL LEVOBUPIVACAINE 0.5% WITH RACEMIC BUPIVACAINE 0.5% FOR LOWER ABDOMINAL SURGERY**Shilpashri A. M<sup>1</sup>, Anand Srivastava<sup>2</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT:** Epidural anaesthesia is one of the regional techniques for lower abdominal, lower limb, pelvic and vascular surgeries where complications are very less compared to spinal anaesthesia. Several central nervous system and cardiovascular adverse reactions have been linked to the R (+) isomer of bupivacaine, one of the most widely used local anesthetics in clinical practice. Its levorotatory isomer, levobupivacaine was shown to have a safer pharmacological profile with less cardiotoxic and neurotoxic effects. Hence this study was undertaken in our institute, to compare the effectiveness of the recently introduced epidural Levobupivacaine with epidural Bupivacaine for anesthesia in lower abdominal surgeries. This prospective, single center parallel group, double blind study conducted over a span of 1 year with 30 patients in each group, was effective in proving that levobupivacaine can be used as a safe alternative to Bupivacaine for epidural anesthesia in lower abdominal surgeries since it provided prolonged sensory block with lesser side effects.

**KEYWORDS:** Bupivacaine, Epidural, Levobupivacaine, Lower abdominal surgery.

**INTRODUCTION:** Bupivacaine, the widely used local anaesthetic in regional anaesthesia is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, levobupivacaine, S (-) isomer and dextrobupivacaine, R (+) isomer. Several central nervous system and cardiovascular adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anaesthesia have been linked to the R (+) isomer of bupivacaine. The levorotatory isomers were shown to have a safer pharmacological profile with less cardiotoxic and neurotoxic effects and it is attributed to its faster protein binding rate.

The pure S (-) enantiomers of bupivacaine, i.e., ropivacaine and levobupivacaine were thus introduced into clinical anaesthesia practice. Levobupivacaine has been recently introduced into Indian market and is being widely used in various health set-ups.<sup>1</sup>

Hence this study was undertaken to compare the effectiveness of epidural Levobupivacaine with epidural Bupivacaine for anaesthesia in lower abdominal surgeries. 0.5% Levobupivacaine (Isobaric) and 0.5% Bupivacaine (Isobaric) used for epidural anesthesia were compared with respect to the onset & highest level of sensory block, degree & duration of motor blockade, duration of sensory analgesia, hemodynamic changes like heart rate, blood pressure and respiratory rate at various time intervals. Intra operative and postoperative complications such as nausea, vomiting, hypotension, bradycardia, respiratory depression.

**MATERIALS AND METHODS:** After institutional committee approval and written informed consent, patient with ASA grade I or II, aged 18-60 years scheduled to undergo elective lower abdominal surgery with epidural anesthesia were enrolled in this prospective, single centre parallel group, double blind study. This study was conducted in JJMMC DAVANAGERE over a span of 1yr from October 2013 to September 2014 involving 60 patients.

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The study population was randomly divided into two groups with 30 patients in each group. Study group L received 17ml of 0.5% Levobupivacaine (Isobaric) by epidural route and study group R received 17ml of 0.5% bupivacaine (Isobaric) by epidural route. All the patients were pre-medicated before the operation with 2mg of midazolam.

Patients were preloaded with 8-10ml/kg of ringer's lactate before the epidural analgesia. With electrocardiography and pulseoximetry basal systolic, diastolic, mean blood pressure, heart rate, peripheral oxygen saturation and ECG readings were performed.

**PROCEDURE:** Drug and equipments necessary for resuscitation and general anaesthesia was kept ready. An epidural kit was used. IV line was secured using 18G cannula and the patient was preloaded with 500 ml Ringers lactate. Base line blood pressure, heart rate and respiratory rate were noted.

The patient was placed in left lateral position or sitting position. With all aseptic precautions a skin wheal was raised in L3-L4 interspace with 1ml of 2% Lignocaine. An 18 G Tuohy needle was passed through this space for about 2cm. The stylet was removed and a 10ml dry glass syringe with an air column of 5ml was firmly attached to the hub of the Tuohy needle. The epidural space was identified by the loss of resistance to air. Once the epidural space was confirmed, the glass syringe was disconnected. Absence of blood or CSF was verified. An 18G epidural catheter was passed through epidural space in cephalad direction until 3cm is in the space. 3ml of 2% Lignocaine with adrenaline 1:200000 was given as test dose. This is to exclude the presence of needle in epidural vein or subarachnoid space. 4 minutes later, 17ml of the study drug was injected through the epidural catheter intermittently over 3 minutes. All the patients were monitored for cardio respiratory problems, side effects if any and were given supplemental oxygen. Fluid management was done according to requirements including fluid deficit, maintenance, blood loss etc.

The onset of sensory block was tested by pin-prick method using a 27 gauge hypodermic needle. Absence of pain from a pin prick at the T10 level was recorded as the onset time of sensory block and duration was noted from the onset of sensory block to complete return of sensation of pain.

The time interval between the administration of drug into epidural space and the patient's inability to lift the straight extended leg (Modified Bromage scale) was recorded as onset time for motor block. And the degree of motor block was assessed by Modified Bromage scale.

### **Modified Bromage Scale<sup>2</sup>:**

- 0-Able to raise leg straight, full flexion of knees and feet.
- 1-Inability to raise leg, just able to flex knees, full flexion of feet.
- 2-Unable to flex knees, but some flexion of feet possible.
- 3-Unable to move legs or feet.

The duration of motor block was taken from time of injection to complete regression of motor block. (Ability to lift the extended leg i.e. modified Bromage scale-0).

Patients were monitored for heart rate, blood pressure and respiratory rate at 0, 2, 5, 15, 30, 60, 90, 120 and 180 minutes after administration of epidural block.

Side effects such as nausea, vomiting, backache, retention of urine, respiratory depression were observed for, recorded and treated accordingly.

Datas obtained were expressed as Arithmetic mean, Standard deviation, Student's unpaired t test, Fisher's exact test.

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**RESULTS: Onset of Sensory Block:** The mean time for onset of sensory block in Levobupivacaine group (group L) was 11.6±1.4 minutes and 12.4±1.9 minutes in Bupivacaine group (Group R). The onset of sensory block in group R was delayed by only few seconds than group L (p= 0.07), so the difference was not statistically significant.

**Onset of motor Block:** The mean time for onset of motor block in Levobupivacaine group (group L) was 19.8±1.9 minutes and in Bupivacaine group (group R) it was 15.8±1.3 minutes. There is highly significant statistical difference between the two groups (p<0.001).

**Highest level of sensory block:** In patients of Levobupivacaine group (group L), 63.3% attained T6 level, 30% attained T7 level and 6.7% attained T10 levels. In Bupivacaine group (group R) 60% attained T6 levels, followed by 30% attaining T7 level and 10% attaining T10 level. This implied that there was no difference in the highest level of sensory block achieved in both groups. (p=0.89)

**Degree of Motor Block:** The degree of motor block was tested by modified Bromage scale. On comparison it was found that, in Levobupivacaine group (group L) there were 6 patients (20%) who had grade 2 block and 24 patients (80%) who had grade 3 block. In Bupivacaine group (group R), 4 patients (13.3%) had grade 2 block and 26 patients (86.7%) had grade 3 block. The percentage distribution of patients who had grade 2 and grade 3 block was similar in both the groups. (p=0.49)

**Duration of Motor Block:** The mean duration of motor block in Levobupivacaine group (group L) was 286.6±12.5 minutes, whereas in Bupivacaine group (group R) it was 231.6±7.9 minutes. The p value was 0.07, indicating that the difference was not significant. This implied that the duration of motor blockade was similar in both the groups.

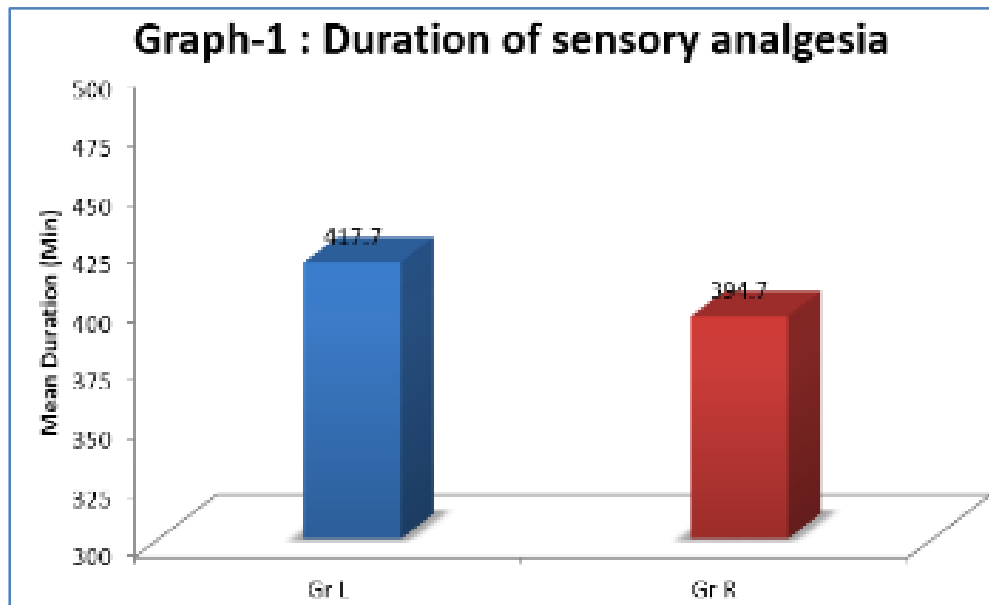
### Duration of Sensory Analgesia:

Duration of Sensory Analgesia (min)	Gr L		Gr R	
	Mean	SD	Mean	SD
	417.7	8.6	394.7	9.3
Mean Diff	23.1			
t value	9.99			
P value	< 0.001, HS			

**Table 1: Duration of Sensory Analgesia**

Student's unpaired test.

The mean duration of sensory analgesia in Levobupivacaine group (group L) was 417.7±8.6 minutes. In Bupivacaine group (group R) the mean duration was 394.7±9.3 minutes. The p-value was <0.001, indicating the difference was highly significant. This implied that duration of sensory analgesia in Levobupivacaine group was significantly longer than Bupivacaine group.



Haemodynamic parameters.

**Pulse Rate:**

PR	Gr L		Gr R		Mean Diff	P value
	Mean	SD	Mean	SD		
0'	74.6	4.8	75.6	5.1	0.97	0.46
2'	86.8	5.5	87.9	5.2	1.03	0.46
5'	89.9	4.0	92.4	4.2	2.43	0.03
15'	90.1	4.1	91.6	5.0	1.57	0.19
30'	77.8	3.6	78.9	4.9	1.07	0.34
45'	77.5	3.3	78.5	4.4	1.00	0.32
60'	76.7	1.9	77.0	2.5	0.30	0.60
90'	76.0	1.7	76.1	2.3	0.13	0.80
120'	75.3	1.7	75.6	2.3	0.33	0.53
180'	74.5	2.1	75.3	2.5	0.83	0.17

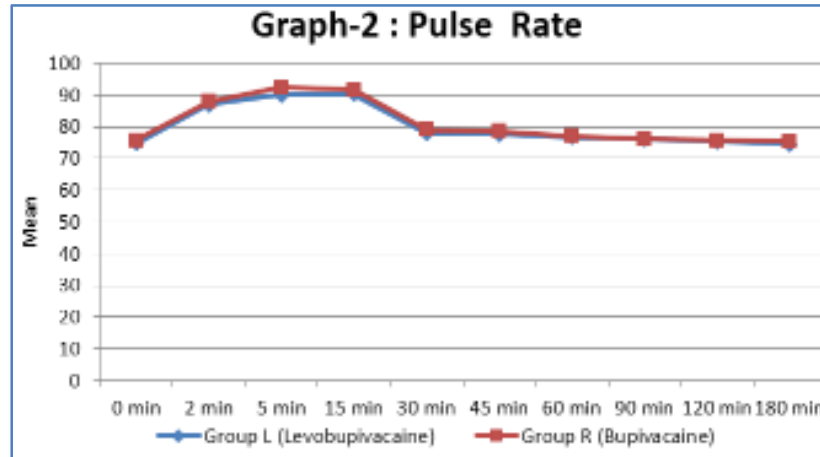
Table 2: Pulse Rate Comparison

Student's unpaired t test,

\* P < 0.05, S, P > 0.05, not sig. (ns).

The mean pulse rate was compared between the two groups at 0, 2, 5, 15, 30, 45, 60, 90, 120 and 180 minutes. There was no significant difference between the Levobupivacaine and Bupivacaine group with respect to pulse rate when recorded at these time intervals.

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**Systolic Blood Pressure:** The mean systolic blood pressure changes over the time intervals between the Levobupivacaine (group L) and Bupivacaine group (group R) was compared. It was found that the systolic blood pressure did not differ between the two groups.

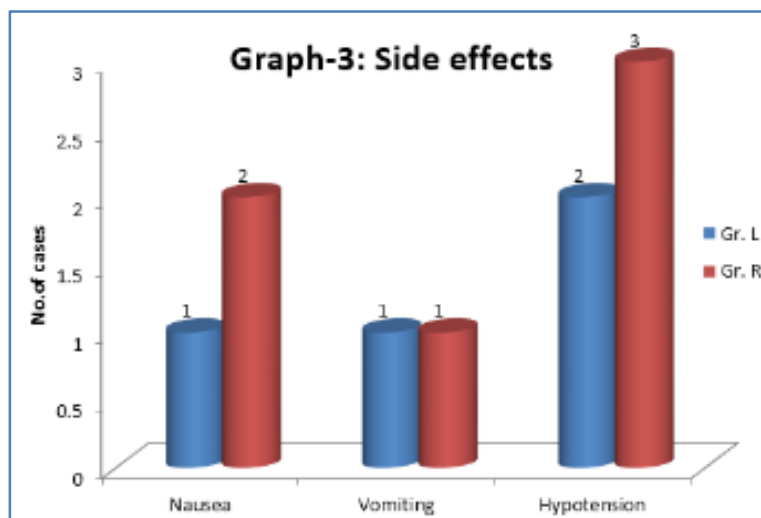
Diastolic blood pressure:

As with the systolic blood pressure, the mean diastolic blood pressure changes over the time intervals between Levobupivacaine (group L) and Bupivacaine (group R) groups were similar. The difference was not statistically significant.

Respiratory rate:

The mean respiratory rate at 0, 2, 5, 15, 30, 45, 60, 90, 120 and 180 minutes in Levobupivacaine group was compared to that of Bupivacaine group. The difference was not statistically significant at any of the time intervals with respect to respiratory rate.

**Side Effects:** In Levobupivacaine group (group L), 7% patients had hypotension, 3% had nausea and 3% had vomiting. In Bupivacaine group (group R), 10% patients had hypotension, 7% had nausea and 3% had vomiting. There was no significant difference between the two groups with regard to these side effects.



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**DISCUSSION:** Epidural anaesthesia is widely practiced regional anaesthesia technique for many lower abdominal and lower limb surgeries. Beneficial effects of epidural anaesthesia over spinal anaesthesia are decreased frequency of hypotension, extended duration of surgery and effective postoperative analgesia.

The local anaesthetic drugs currently available for epidural anaesthesia offer a varied degree of efficacy, from drugs of low potency such as Procaine to drugs eight to ten times potent such as Etidocaine and Bupivacaine. Unfortunately, as the potency of local anaesthetics increases so does their toxicity. Bupivacaine, one of the most widely utilized local anaesthetics, has been the subject of intense investigation because of sudden cardiovascular collapse in some patients.<sup>3,4,5</sup>

Levobupivacaine is a new amino-amide local anaesthetic agent similar in structure to Bupivacaine. Levobupivacaine is prepared as the *s*-isomer rather than a racemic mixture such as Bupivacaine. Previous studies involving the isomers of local anaesthetics suggest that the systemic toxicity of the *S*-isomer of various compounds may be less than that of racemic preparations.

Levobupivacaine-The isolated *S* (-) isomer of bupivacaine, has been shown to be less cardiotoxic than bupivacaine in preclinical studies.<sup>6</sup>

The aim of this study was to compare the effects of 0.5% Levobupivacaine (isobaric) with that of 0.5% Bupivacaine (isobaric) for epidural anaesthesia in elective lower abdominal surgeries.

In the present study the patients studied in both the groups did not vary much with respect to age, sex or weight.

**ONSET OF SENSORY AND MOTOR BLOCKADE:** In our study, there was no statistically significant difference with regard to onset of sensory block. However statistically significant difference was found with regard to onset of motor block between two groups.

Cox CR et. al who conducted a study comparing Levobupivacaine with Bupivacaine found no significant differences in the onset time of sensory block.<sup>7</sup>

Casati A et. al concluded that Levobupivacaine 0.5% produces an epidural sensory block of similar onset as that produced by the same volume of 0.5% Bupivacaine.<sup>8</sup>

Kopacz et al, found a significant slower onset of lower extremity motor block.

These results are similar to our study.<sup>9</sup>

**HIGHEST LEVEL OF SENSORY BLOCK:** Kopacz et al conducted a study comparing epidural levobupivacaine 0.75% with Racemic Bupivacaine of lower abdominal surgery. They found that Levobupivacaine and Bupivacaine showed equivalent efficacy for the time taken to reach sensory block adequate for surgery. Sensory block at T10 was achieved within 15 minutes of administering the epidural injection and both groups and the maximum spread of sensory block was observed within 30 minutes.<sup>9</sup>

From the above study we conclude that the highest level of sensory block is similar between Levobupivacaine and Bupivacaine. These findings were similar to our study.

**DEGREE OF MOTOR BLOCKADE:** Kopacz et al, found that the degree of motor blockade was similar in both Levobupivacaine and Bupivacaine group.<sup>9</sup>

Cox CR et. al found no difference in the intensity of motor block between the levobupicaine and bupivacaine group.<sup>7</sup>

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Casati A et. al concluded that the degree of motor block was similar for both Levobupivacaine and Bupivacaine group.<sup>8</sup>

These findings are similar to our study.

**DURATION OF MOTOR BLOCK:** This difference was statistically non-significant.

Kopacz et al, compared 0.75% Levobupivacaine 20 ml with 0.75% Bupivacaine 20 ml in 56 patients and found no significant difference in the duration of motor block.<sup>9</sup>

Casati A et. al concluded that the duration of motor block with 0.5% Levobupivacaine and 0.5% Bupivacaine was similar.<sup>8</sup>

Cox CR et. al found no significant difference in the duration of motor block between the two groups.<sup>7</sup>

From the above studies we conclude that the duration of motor block was similar between the 2 groups, much like our studies.

**DURATION OF SENSORY ANALGESIA:** In our study, the mean duration of sensory analgesia in Levobupivacaine was 417.7±8.6 min. In Bupivacaine group, the mean duration was 394.7±9.3 min, indicating that there is significant difference in the duration of sensory analgesia among the two groups.

Kopacz et al 2000 also found that sensory block is substantially longer than motor block.<sup>9</sup>

Cox CR et. al concluded that increasing concentration of Levobupivacaine (i.e. 15 ml 0.75% Vs 0.5%) prolongs the duration of sensory and motor block without increasing the incidence of adverse side effects.<sup>7</sup>

These findings were similar to our study.

### **HAEMODYNAMIC CHANGER:**

**Heart Rate and Blood Pressure:** In our study, the two groups did not differ significantly with respect to heart rate at any time individual. There were no episodes of bradycardia in either group. The changes in mean systolic blood pressure and diastolic blood pressure at any time interval were statistically and clinically insignificant.

Cox et al,<sup>7</sup> Bader et al,<sup>10</sup> Kopacz et al<sup>9</sup> evaluated SAP, DAP, MAP, HR and SPO<sub>2</sub> in their studies and did not find a significant difference between 2 groups.

From the above discussion we conclude that epidural administration of Levobupivacaine produces similar changes in the hemodynamic parameters as that of Bupivacaine. These findings are similar to our study.

**Respiratory Rate:** None of our patient's experienced respiratory depression and the mean respiratory rate between both the groups was statistically insignificant.

Our study found no changes in the respiratory rates between the 2 groups which corroborated with the other studies conducted by Kopacz et al,<sup>9</sup> Cox et al.<sup>7</sup>

**Side Effects:** In Levobupivacaine group, 7% patients had hypotension, 3% had nausea and 3% had vomiting. In Bupivacaine group, 10% had patients had hypotension, 7% had nausea and 3% had vomiting, indicating no significant difference between the two groups with regard to these side effects.

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Bhatt et al, reported that side effects of levobupivacaine with bupivacaine and other local anaesthetics of amide group were the same. The most common side effects are – nausea, vomiting, hypotension, headache, postoperative pain.<sup>11</sup>

Kopacz et al, reported that hypotension was the most common side effect and was experienced by a similar proportion of patients in both treatment groups at the start of surgery (21% levobupivacaine, 18% bupivacaine) and during surgery (32% in both treatment groups).<sup>9</sup>

The reported side effects in the above studies were similar in both groups as was noticed in our study.

**CONCLUSION:** Based on the present clinical comparative study, we conclude that isobaric 0.5% Levobupivacaine, when administered through epidural route, provides adequate anaesthesia for lower abdominal surgeries.

### **Levobupivacaine Provided:**

- Adequate sensory block.
- Equivalent efficacy for the time taken to reach sensory block.
- The sensory block is substantially longer than motor block.

In our study, Levobupivacaine and Bupivacaine both showed excellent sensory/motor separation.

As expected decrease in systolic blood pressure, diastolic blood pressure is attributable to sympathetic block accompanying epidural anaesthesia.

Hence Levobupivacaine can be used as a safe alternative to Bupivacaine for epidural anaesthesia in lower abdominal surgeries.

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**COMPETING INTERESTS:** None

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