

**EFFECT OF INTRATHECAL LEVOBUPIVACAINE AND
BUPIVACAINE WITH FENTANYL ON POSTOPERATIVE
AMBULATION AND ANALGESIA: A RANDOMIZED CONTROLLED
TRIAL.**

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ABSTRACT

Background: This study was conducted with the aim to compare Levobupivacaine and Bupivacaine in terms of ambulation and analgesic efficacy given by intrathecal route in patients undergoing lower abdominal surgery. **Methods:** Seventy patients belonging to ASA PS I & II were included undergoing lower abdominal surgery under subarachnoid block. They were randomly assigned to receive one of the following isobaric Levobupivacaine 10 mg or Bupivacaine 10 mg all combined with Fentanyl 25 µg. Surgery was allowed once the sensory blockade reached T10 level. Sensory changes and motor changes along with hemodynamic parameters were recorded. Time for successful ambulation was also noted. **Results:** Walk of 5 meters in a straight line was taken as the time for ambulation which was shorter in

Levobupivacaine group with mean of 437.14 ± 33.56 min collated with the mean of 460.29 ± 21.75 min in group Bupivacaine which was statistically significant ($p < 0.05$). Hence Levobupivacaine group patients ambulated earlier than bupivacaine. The duration of effective analgesia in Levobupivacaine group was clinically significant with mean of 360.86 ± 42.10 min, hence favouring pain free early ambulation with minimal hemodynamic effects

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compared to Bupivacaine. **Conclusions:** S(-) enantiomer Levobupivacaine has materialized to be a rousing intrathecal local anesthetic agent for day care surgeries.

KEYWORDS: local anesthetics, intrathecal, lower abdominal surgery, subarachnoid, regional techniques.

BACKGROUND

Anesthesiology is a revamping province being introduced by newer and more desirable drugs in its daily practice. This field of practice is also being introduced by various new framework and day-care anesthesia is one such framework. Daycare anesthesiology mandates search for newer drugs that can provide good analgesia and early postoperative ambulation. Hence this study endeavours search of such drug like Levobupivacaine and also attempt to establish its safety for such practices.

Levobupivacaine is a pure Levorotary S enantiomer of already established drug Bupivacaine. Levobupivacaine is showing promising results in past few years due to its more specific action and safer pharmacological profile. Lesser cardiovascular side effects and less motor blockade favours Levobupivacaine for daycare surgeries. Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Myelinated nerves are blocked through exposure at nodes of Ranvier more readily than unmyelinated nerves.

Levobupivacaine exerts similar adverse effects as seen with racemic Bupivacaine but cardiac toxicity, neurological injury and unwanted CNS effects are lower than Bupivacaine. Levobupivacaine has safety-margin of 1.3 and hence toxic effects are not seen until concentration rises by 30%.

This study was conducted with the aim to compare Levobupivacaine and Bupivacaine in terms of ambulation and analgesic efficacy given by intrathecal route in patients undergoing lower abdominal surgery.

METHODS

This prospective randomized double blind study was undertaken in Department of Anesthesiology and Critical care, UCMS & GTB hospital, Delhi after taking approval from the ethical committee.

Sample size of 35 patients per group were taken to detect a difference of 15% change in sensory and motor block of Levobupivacaine from Bupivacaine by taking 80% power of study and 5% level of significance. It was calculated using SPSS version 20 software.

Patients were between the age group of 18-65 years belonging to ASA grade I or II undergoing elective lower abdominal surgery under subarachnoid block. Patients were allocated into two groups randomly. Group L was given Injection Levobupivacaine 10mg + Fentanyl 25ug and Group B was given Injection Bupivacaine 10mg + Fentanyl 25ug.

After proper preanesthetic checkup patients were transferred to operation theater and ASA recommended minimal mandatory monitoring was done. After taking baseline reading intravenous access was taken. Subarachnoid block was given in lateral position with midline approach under all aseptic precautions using 25 G Quincke's needle with designated drug for the particular group.

Parameters such as Heart rate, Blood pressure, SPO2 and respiratory rate were recorded every 5 minutes for first 30 minutes then every 15 minutes for next 90 minutes and then every 30 minutes till the patient felt normal strength in both lower limbs. Sensory block was assessed in terms of maximum level of block achieved, time of onset of block and time to achieve maximum level of block. Motor block was assessed using Modified Bromage scale^[1] (Table 1).

Pain was evaluated by using a 10 cm Visual Analogue scale(VAS)², for 0 represented no pain and 10 represented worst imaginable pain. Duration of effective analgesia was also evaluated and defined as the time to reach a VAS of 3 or more.

STATISTICAL ANALYSIS

Repeated measures were analyzed using ANOVA. Motor and sensory block values were calculated using unpaired student t-test. Qualitative measures were analyzed using Chi-square test. Friedman's test was applied for VAS and MBS separately for each group. Pair wise multiple comparison from baseline were done and p-value were adjusted as per Bonferroni corrections.

RESULTS

Baseline Characteristics

Treatment groups did not differ with respect to patient baseline characteristics. (Table2)

Heart Rate

In intragroup comparison for Heart rate, there was statistically significant difference ($P < 0.001$) between baseline and 180 min in group B, however intergroup comparison yielded no statistically significant difference ($P > 0.05$) between the two groups.

Mean Arterial blood Pressure

During intragroup comparison for Mean arterial blood pressure there was statistically significant difference in group B patients with ($P < 0.001$) baseline and 90, 105, 120, 150, 180, 210, 240. Intergroup comparison also gave statistically significant results. Greenhouse-Geisser adjustment was used for within group interaction because Machuly's Test of Sphericity's significant P value = 0.000 (< 0.001). (Fig. 1).

Time of Onset of Block

The time of onset of block in Group B ranged between 7-12 min with mean of 11.06 ± 1.21 min and in Group L it ranged between 4-11 min with mean of 6.34 ± 1.58 min. Difference between two Groups was statistically significant ($p < 0.001$).

Maximum sensory block

The level of maximum sensory block in Group L ranged between T 6-8 with mean of 6.63 ± 0.94 and in Group B it ranged between T8-9 with mean of 9.09 ± 1.01 . This difference was statistically significant ($p < 0.000$).

Time of two segment regression

Time of two segment regression in Group L ranged between 105-210 min with mean 141.43 ± 29.39 min and in Group B it ranged between 105-210 min with mean of 150.00 ± 30.65 min. This difference was statistically insignificant (Fig. 2).

Duration of effective analgesia

The duration of effective analgesia in Group L showed the mean of 360.86 ± 42.10 min with range of 270-450 min and in Group B the mean was 347.14 ± 39.37 min with range of 270-450 min. This came out to be statistically insignificant but was certainly significant, clinically (Fig. 3).

Time of ambulation

Time of feeling of normal strength by patient in Group L ranged between 240-390 min with a mean of 344.57 ± 33.63 min and in Group B it ranged between 330-390 min with mean of 372.86 ± 22.17 min. This difference came out to be statistically significant ($p < 0.000$).

Time for ambulation was designated when the patient was able to walk 5 meters in a straight line which was shorter in group L with mean of 437.14 ± 33.56 min with range of 330-480 min and in group B the mean was 460.29 ± 21.75 min with range of 420-480 min. this was also statistically significant ($p < 0.05$) (Fig. 4)

Table 1: Modified Bromage scale¹

Parameters		Group B (n=35)	Group L (n=35)	p-value
Age (yrs)	Range	18-65	18-65	0.931
	Mean \pm SD	42.94 \pm 16.87	42.63 \pm 13.22	
Weight (kg)	Range	40-80	50-75	0.714
	Mean \pm SD	65.34 \pm 10.75	66.11 \pm 6.14	
Height (cm)	Range	155-175	157-180	0.540
	Mean \pm SD	167.06 \pm 3.94	167.77 \pm 5.61	

Table 2: Demographic profile

Scale	Clinical sign
1	Complete block (unable to move feet or knee)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knee)
4	Detectable weakness of hip while supine (full flexion of knee)
5	No detectable weakness if hip while supine
6	Able to perform partial knee bend.

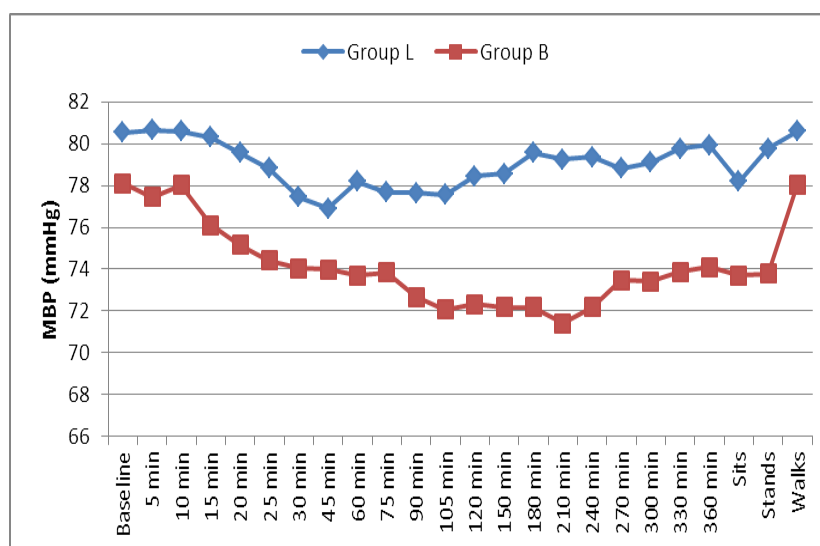
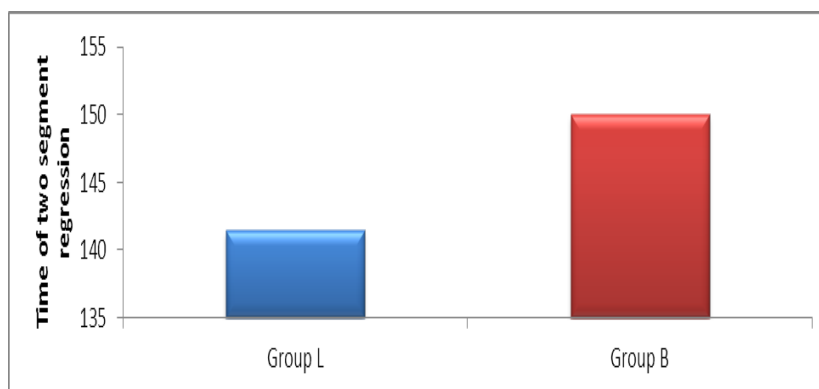
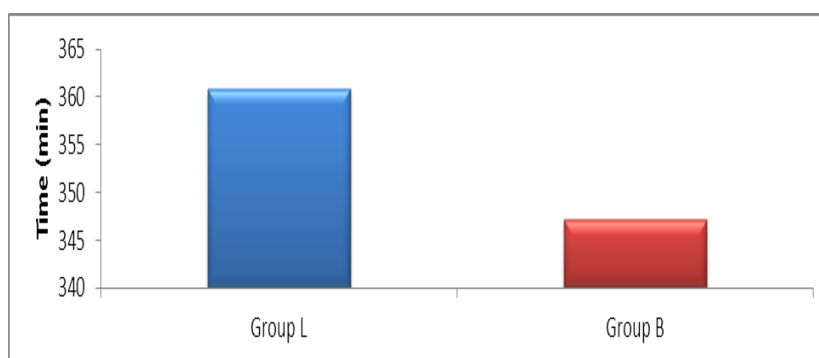
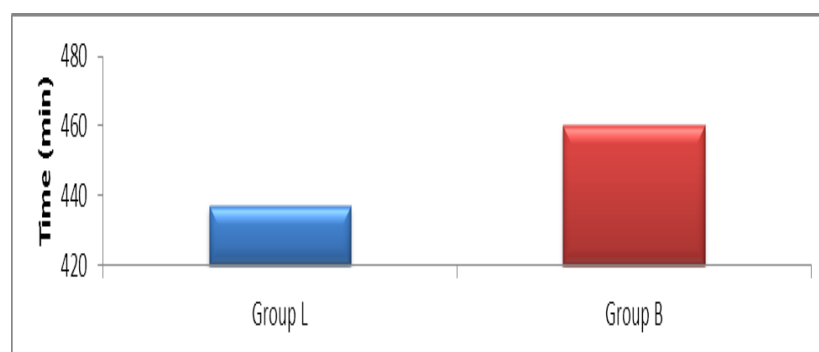


Fig. 1: Mean blood pressure

**Fig. 2: Time of two segment regression****Fig. 3: Duration of effective analgesia****Fig. 4: Time of ambulation**

DISCUSSION

Our results clearly show that Levobupivacaine in low doses of 10 mg along with an adjuvant Fentanyl 25ug is an effective choice for day care ambulatory surgeries providing effectual analgesia for early postoperative ambulation.

Effective ambulation as per our study was defined by the ability of the patient to walk 5 meters in a straight line which was fairly shorter in Levobupivacaine group with mean of 437.14 ± 33.56 compared to mean of 460.29 ± 21.75 min in Bupivacaine group. This is in

accordance with the study conducted by Bremerich et al who compared 10 mg 0.5% hyperbaric intrathecal bupivacaine and with similar dose of levobupivacaine combined with opioids for Caesarean section and found that duration of motor blockade was much shorter with Levobupivacaine.^[3]

Time of feeling of normal strength by patient in Levobupivacaine group was shorter with the mean of 344.57 ± 33.63 min compared to the Bupivacaine group with the mean of 372.86 ± 22.17 min. Our finding is similar to the study conducted by Turkmen et al who compared 7.5 mg of 0.5% bupivacaine with similar dosage of Levobupivacaine with 15 µg of Fentanyl and found that motor blockade was shorter in Levobupivacaine group.^[4]

Bajwa et al showed that Levobupivacaine has got more propensity to block the smaller fibers than the larger one. Hence it may have some sparing effects on motor fibers favouring faster motor blockade recovery.^[5]

Hector et al also discussed while comparing Relative Motor Blocking Potencies that levobupivacaine may demonstrate greater apparent sensory-motor dissociation than racemic bupivacaine, especially if the results are expressed in molar terms.^[6] This translates to approximately 25% reduction in motor block potency due to the difference in the expressed formulation of levobupivacaine. Also in considering the results from representative analgesic and motor block MLAC studies done by Lacassie (2002), Columb (1995), Lyons (1998), it appears that levobupivacaine widens the sensory-motor fibers separation for the piperidoxylidine homologous series of local anaesthetics that have the ability to cause differential sensory and motor neuronal blockade.^[6]

Our study also evince that the duration of effective analgesia in Levobupivacaine group has the mean of 360.86 ± 42.10 min collated with the mean of 347.14 ± 39.37 min in Bupivacaine group which was significant clinically (Fig. 3). The study done by Turkmen et al where 7.5 mg of 0.5% Levobupivacaine was compared with 7.5 mg of 0.5% Bupivacaine with 15 µg of fentanyl also concluded that duration of analgesia was certainly longer in Levobupivacaine group.

Levobupivacaine also exhibited faster onset time for sensory blockade with the mean of 6.34 ± 1.58 min compared to the mean of 11.06 ± 1.21 min for Bupivacaine leading faster dawn of surgery favouring rapid patient turnover being a fruitful bargain for the hospital.

Foster and Macleod found the sensory blockade lasted significantly longer with levobupivacaine than with racemic bupivacaine which might be attributable to a greater intrinsic vasoconstrictor property of levobupivacaine. Also it has been shown that ampoules of levobupivacaine contain 7.5 mg/ml free base (26.0 mmol / litre) whereas corresponding ampoules of bupivacaine contain 6.66 mg / ml free base (23.1 mmol / litre). This suggest that percentage of active bases are more with the Levobupivacaine commercially available preparations thus explaining the difference in terms of sensory blockade compared to Bupivacaine appreciated in our study.^[7]

Also due to more protein binding property of Levobupivacaine it becomes longer acting as sustained release of drug molecules may occur over a greater period of time. These above mentioned aspects are some of the reason due to which duration of effective analgesia is longer with Levobupivacaine seen in our study.

Levobupivacaine also materialized to be a safe local anesthetic for intrathecal use as it has minimal cardiovascular side effects as evidenced by our finding on comparison of hemodynamic parameters. Mean arterial blood pressure (MBP) comparison showed significant difference ($P < 0.05$) between the two groups. Bupivacaine group showed progressive decrease in MBP compared to baseline. Although levobupivacaine has very similar pharmacokinetic properties to those of racemic bupivacaine, several studies involving humans as well as animals 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.^[8]

In conclusion we have shown that S(-) enantiomer Levobupivacaine has proved to be a rousing intrathecal local anesthetic agent for day care surgeries. Both intrathecal Levobupivacaine and Bupivacaine provided adequate sensory-motor blockade for Lower Abdominal surgeries. But time for ambulation was significantly shorter with Levobupivacaine along with adequate clinically significant postoperative analgesia, minimal haemodynamic variation and negligible side effects.

Contributions by Authors

Dr Rishi Kumar Gautam was the prime investigator who carried out this study under the supervision of Dr Rajesh Singh Rautela and co-supervision of Dr Mahendra Kumar. Dr

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