



# A Comparative Evaluation of Levobupivacaine Hydrochloride and Levobupivacaine Hydrochloride with Dexmedetomidine in Epidural Anesthesia and Postoperative Pain Relief undergoing Infraumbilical Surgeries

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## ABSTRACT

Epidural anesthesia is a versatile technique which is widely used for surgeries for providing intra- and postoperative analgesia. Several adjuvants have been used to prolong the action of the local anesthetic agent used.

**Aims and objectives:** We performed prospective randomized, double blinded controlled study on 90 patients to compare the effects of adding of dexmedetomidine to levobupivacaine in prolonging the analgesia produced by epidural levobupivacaine alone in patients undergoing infraumbilical surgeries and also compared the duration of motor block and sedation scores.

**Materials and methods:** Ninety American Society of Anesthesiologists (ASA) I and II patients (18–60 years), undergoing infraumbilical surgery, were prospectively randomized to one of two groups to receive epidural anesthesia with 17 ml of 0.5% levobupivacaine + 3 ml of normal saline (group L) or epidural anesthesia with 17 ml of 0.5% levobupivacaine with 75 µg (0.75 ml) of dexmedetomidine + 2.25 ml of normal saline (group LD). Various parameters hemodynamic changes, onset time of sensory and motor blockade, highest level of sensory blockade, duration of sensory and motor block, postoperative pain using visual analog scale (VAS) score, and any side-effects were recorded and data were statistical analyzed using student's t-test by statistics calculator SPSS software.

**Results:** The two study groups were similar for mean age, weight and duration of surgery. Mean duration of analgesia was significantly longer in group LD ( $438.33 \pm 38.72$  min) than in group L ( $271.2 \pm 23.77$  min);  $p < 0.05$ . Onset time of sensory and motor blockade was significantly less in group LD as compared to group L;  $p < 0.05$ . Duration of sensory and motor block was significantly higher in group LD when compared to group L ( $p < 0.05$ ). More sedation was observed in group LD.

**Conclusion:** Dexmedetomidine in a dose of 75 µg added as an adjuvant to 0.5% levobupivacaine for epidural anesthesia, during infraumbilical surgeries, prolongs the duration of analgesia of levobupivacaine and increases postoperative sedation, without any other adverse effects.

**Keywords:** Dexmedetomidine, Epidural anesthesia, Postoperative analgesia, Levobupivacaine.

**How to cite this article:** Gupta S, Saluja N, Goyal P, Choudhary B. A Comparative Evaluation of Levobupivacaine Hydrochloride and Levobupivacaine Hydrochloride with Dexmedetomidine in Epidural Anesthesia and Postoperative Pain Relief undergoing Infraumbilical Surgeries. MGM J Med Sci 2015;2(2):78-82.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Epidural anesthesia is one of the most familiar and widely used technique for providing not only perioperative surgical anesthesia but also postoperative analgesia in lower abdominal and limb surgeries.<sup>1</sup> Early postoperative ambulation and rehabilitation with minimally associated pain and discomfort are the most desirable features in modern infraumbilical and lower limb surgeries.<sup>2-4</sup> The intense sensory and motor blockade, along with continuous supine position for a prolonged duration and the inability to move the body during regional anesthesia brings a feeling of discomfort and phobia in many of the patients.<sup>5</sup> The high cephalic spread of local anesthetics may be significant but still its quality sometimes may not correlate with the level of sensory analgesia.<sup>6</sup> At this stage, the impulsive use of large doses of sedation or even general anesthesia with mask defeats the novel purpose of regional anesthesia whereby a continuous verbal contact with the patient is lost. Sedation, stable hemodynamics and an ability to provide smooth and prolonged postoperative analgesia are the main desirable qualities of an adjuvant in neuraxial anesthesia.

Various adjuvants, like epinephrine, fentanyl, dexmedetomidine, clonidine<sup>7-10</sup> when added to levobupivacaine were found to prolong the duration of analgesia dexmedetomidine is a new addition to the class of alpha-2 agonist with varied beneficial effects when administered via epidural route. It acts on both pre- and post-synaptic sympathetic nerve terminal and central nervous system, thereby decreasing the sympathetic outflow and norepinephrine release causing sedative, antianxiety, analgesic, sympatholytic and hemodynamic effects.

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Dexmedetomidine does cause a manageable hypotension and bradycardia which is treatable but the unraveling feature of this drug is the lack of opioid related side-effects like respiratory depression, pruritus, nausea and vomiting.

## AIMS AND OBJECTIVES

To study and compare the effects and efficacy of levobupivacaine and levobupivacaine with dexmedetomidine in epidural anesthesia with reference to the onset and duration of sensory loss, the onset and duration of motor loss, the duration of analgesia and to observe any untoward complications.

## MATERIALS AND METHODS

After approval from the Ethics Committee, a prospective randomized, double blinded controlled study was performed on total of 90 patients of both genders aged 18 to 60 years, with physical status American Society of Anesthesiologist (ASA) I and II, who underwent infraumbilical surgeries, i.e. total knee replacements, total hip replacements, appendectomy, fistulectomy, hernioplasty, etc. lasting not more than 120 minutes. Patients with peripheral or central neurological disease, raised intracranial tension, valvular heart diseases, significant ECG changes, renal disease, endocrinal disease, metabolic diseases, hepatic disease, coagulopathy and bleeding diathesis, body weight of >100 and <45 kg and height of <145 cm were excluded from this study. Patients were divided randomly into two groups: group LD (n = 45): Levobupivacaine with dexmedetomidine and group L (n = 45): Levobupivacaine alone. All patients were premedicated with injection glycopyrrolate 0.2 mg IM. Thirty minutes before surgery, patients were thoroughly counseled during the preoperative evaluation and well informed consent obtained.

In the operation room, a venous access was secured with 18 G cannula, and all the patients were prehydrated with 10 ml/kg of lactated Ringer's solution. Heart rate (HR), electrocardiography (ECG), Noninvasive blood pressure (NIBP), and pulse oximetry (SPO<sub>2</sub>) were monitored and recorded.

Epidural anesthesia was administered via 16 G Touhy needle, with patients in the sitting position at L3 to L4 interspace and epidural space was identified by loss of resistance technique. A test dose of 3 ml of 2% lignocaine with adrenaline was administered into the epidural space. The study solutions were prepared by anesthesia technician who was given written instructions and was unaware of study design to avoid biasing. The following solutions were randomly administered group L (n = 45) 17 ml of levobupivacaine hydrochloride 0.5% with 3 ml

normal saline injected epidurally. Group LD (n = 45) 17 ml of levobupivacaine hydrochloride 0.5 with 75 µg (0.75 ml) of dexmedetomidine and 2.25 ml of normal saline injected epidurally. The pin prick method was used to assess onset time of sensory blockade, whilst Modified Bromage scale (0 = no block, 1 = inability to raise extended leg, 2 = inability to flex knee, and 3 = inability to flex ankle and foot) was used to measure onset time of motor blockade, highest level of sensory and motor blockade were observed immediately after administration of epidural block. Duration of sensory blockade, i.e. time taken for sensory block to regress by two segments below the highest level was noted. Duration of analgesia, i.e. time taken from onset of sensory block to the first request of rescue analgesia was observed. Analgesia was assessed by VAS score at the time of first analgesia request only. Side effects and complications, such as nausea, vomiting, hypotension, bradycardia and shivering due to drugs were notified as well.

Sedation was assessed using 6 points Ramsay Sedation score (1 = Patient anxious and agitated or restless, 2 = patient co-operative, oriented and tranquil, 3 = patient responds to commands only, 4 = patient exhibits brisk response to light glabellar tap or loud auditory stimulus, 5 = patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus, and 6 = patient exhibits no response).

## STATISTICAL METHODS

The data were analyzed using student's t-test by statistics calculator SPSS software. Student's t-test for inter group comparison. All the variables are expressed as mean ± standard deviation. The value of p > 0.05 was taken to be statistically insignificant and p < 0.05 taken as statistically significant. The sample size of 45 in each group was calculated using the prevalence of postoperative pain percentage in infraumbilical surgeries with power of 80% and alpha error of 0.05.

All the data are expressed as mean and standard deviation unless specified.

## RESULTS

The demographic characteristics and duration of surgery in both the groups exhibited marked similarities and did not show any statistical significant variance (p > 0.05) (Table 1).

Onset time of sensory blockade in groups L and LD were 15.96 ± 2.41 and 6.78 ± 1.38 minutes respectively. The mean (±SD) onset time of motor blockade was 19.89 ± 2.26 minutes and 9.73 ± 1.40 minutes in groups L and LD respectively, which was significantly lower in group LD as compared to group L (Table 2).

**Table 1:** Demographic profile and duration of surgery

Variables	Group L (mean ± SD)	Group LD (mean ± SD)	p-value
Age (years)	36.4 ± 11.59	40.02 ± 13.91	0.183
Weight (kg)	64.51 ± 4.69	64.89 ± 5.05	0.714
Height (cm)	166.36 ± 5.03	167.29 ± 4.88	0.374
Duration of surgery (min)	79.84 ± 18.26	86.78 ± 19.72	0.087
Sex ratio (M:F)	36:9	34:11	1.000

\*p &lt; 0.05; statistically significant

**Table 2:** Perioperative characteristics in both the groups

Parameters	Group L	Group LD	p-value
Onset time of sensory blockade (min)	15.96 ± 2.41	6.78 ± 1.38	0.000*
Onset time of motor blockade (min)	19.89 ± 2.26	9.73 ± 1.40	0.000*
Highest dermatome level of sensory block (T4)	55.5%	75.6%	0.000*
Duration of sensory blockade (min)	173.84 ± 12.92	244.78 ± 15.11	0.000*
Duration of motor blockade (min)	199 ± 12.95	279 ± 16.12	0.000*
Duration of analgesia (min)	271.2 ± 23.77	438.33 ± 38.72	0.000*

\*p &lt; 0.05; statistically significant

The maximum sensory level achieved by both the groups is T4, level. The 55.5% of patients in group L and 75.6% of patients in group LD attained the highest sensory level of T4 whereas 37.8% of patients in group L and 24.4% of patients in group LD attained the level of T6. Only 6.7% of patients in group L and none in group LD attained the level of T8, which was significantly higher in group LD as compared to group L (Table 2).

Duration of sensory blockade was 173.84 ± 12.92 minutes, 244.78 ± 15.11 minutes in groups L and LD respectively and the (mean ± SD), duration of motor blockade was 199 ± 12.95 minutes in group L and 279 ± 16.12 minutes in group LD, which was significantly higher in group LD as compared to group L (Table 2).

Duration of analgesia in group L was 271.2 ± 23.77 minutes and in group LD was 438.33 ± 38.72 minutes, which was significantly higher in group LD as compared to group L (Table 2). 82.2% patients in group L and 48.9% patients in group LD had Ramsay Sedation Score of 1, whereas 17.8 and 51.1% patients in group L and LD had Ramsay Sedation Score of 2 respectively. Complications due to drug among both the groups are shown in (Table 3).

## DISCUSSION

Epidural analgesia is now not in the nascent stage. Every anesthesiologist is administering it world widely for post-operative pain relief as it offers better patient outcome.<sup>4</sup>

**Table 3:** Comparison of side effects in patients treated with levobupivacaine with (Group L) or without dexmedetomidine (Group LD)

Complications	Group L		Group LD	
	No.	%	No.	%
Nausea and vomiting	1	2.22	—	—
Hypotension	1	2.22	2	4.44
Bradycardia	—	—	4	8.88
Shivering	4	8.88	—	—
Dyspnea	—	—	—	—
Chest pain	—	—	—	—
Respiratory depression	—	—	—	—

This epidural analgesia offers superior pain relief and early mobilization especially when local anesthetic dose is combined with an adjuvant as compared to local anesthetic used alone.<sup>2</sup> Opioids are most commonly used as adjuvants and are associated with side effects, such as respiratory depression, nausea, urinary retention and pruritis.<sup>7</sup> So various options including alpha-2 agonist are being extensively evaluated as an alternative to benzodiazepines, opioids and ketamine.<sup>11-13</sup> Alpha-2 agonist is clinically used widely as its epidural administration is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis.<sup>9,10</sup>

The synergism between epidural local anesthetics and opioids is well established but evidence regarding combination of local anesthetics with dexmedetomidine through epidural route is scarce in literature.<sup>14,15</sup> Thus, study was conducted to compare the analgesic efficacy, perioperatively, as well as to observe the sedative effect of the dexmedetomidine (alpha-2 agonist) administered epidurally.

The demographic profile in the present study was comparable with respect to age, body weight, sex, height, duration of surgery; throughout the perioperative period patient were calm and comfortable with better sedation score of 2 in 51.1% of patients in group LD and 17.8% of patients in group L. Thus, showing dexmedetomidine produces better sedation when used epidurally.

The mean onset of sensory blockade was significantly (p = 0.000) shorter in group LD (6.78 ± 1.38) minutes as compared to group L (15.96 ± 2.41) minutes. The mean onset of motor blockade was also significantly (p = 0.000) shorter in group LD (9.73 ± 1.40) minutes as compared to group L (19.89 ± 2.26) minutes, further stating that dexmedetomidine promotes faster onset compared to levobupivacaine alone.

The mean duration of sensory blockade was significantly (p = 0.000) longer in group LD (244.78 ± 15.11) as compared to group L (173.84 ± 12.92) minutes. Similarly, the mean duration of motor blockade was significantly (p = 0.000) longer in group LD (279 ± 16.12) minutes as compared to group L (199 ± 12.95) minutes.



The mean duration of analgesia was significantly ( $p = 0.00$ ) longer in group LD ( $438.33 \pm 38.72$ ) minutes as compared to group L ( $271.2 \pm 23.77$ ) minutes showing that dexmedetomidine gives a better perioperative analgesia profile when added to levobupivacaine as compared to levobupivacaine alone. The analgesic effect of dexmedetomidine is caused by the stimulation of dorsal root neuron of spinal cord, where alpha-2 agonists inhibit the release of norepinephrine.<sup>16</sup>

Throughout the surgery, patients were calm and compose among both the groups but sedation scores were significantly better in the LD group as compared to group L. The mean ( $\pm$  SD) VAS score at time of first rescue analgesia request was  $47.91 \pm 10.04$  in group L while it was  $40.04 \pm 5.65$  in group LD.

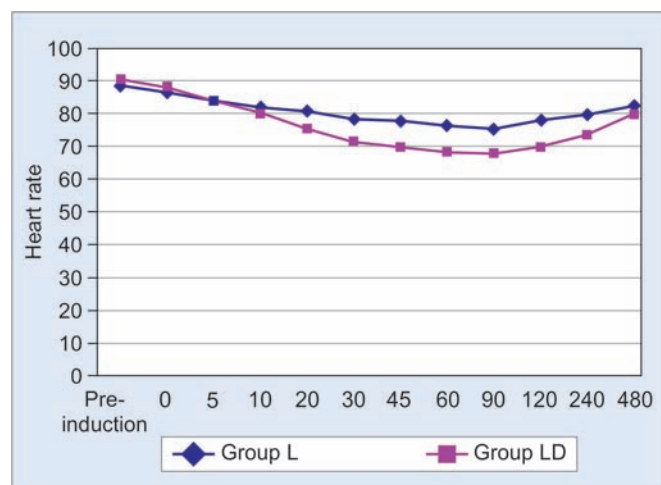
Dexmedetomidine in group LD provided a higher dermatomal level of (T4) in about 75.6% of patients as compared to 55.5% patients in group L.

The cardiorespiratory parameters mean HR (Graph 1), systolic BP (Graph 2), diastolic BP (Graph 3), remained stable throughout the study period which reaffirms the established effects of alpha-2 agonists in providing a hemodynamically stable perioperatively.

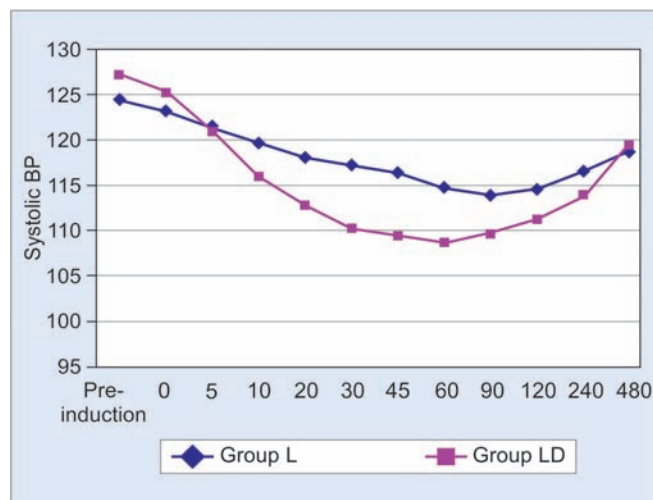
None of the patients had shivering in group LD as compare to 8.8% of patients in group L. Bradycardia was observed in 8.8% of patients of group LD and none in group L (Table 3). Bradycardia in patients having HR of  $< 50$  bpm were treated with injection atropine 0.6 mg intravenously. Bradycardia in group LD can be attributed to dexmedetomidine, an alpha-2 agonist which can again be explained on the basis of its central action, whereby it decreases the sympathetic outflow and norepinephrine release.<sup>16-18</sup>

## CONCLUSION

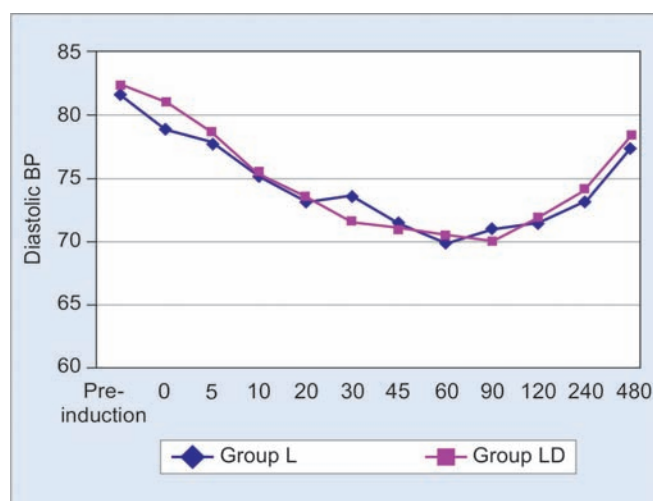
Epidural administration of dexmedetomidine ( $75 \mu\text{g}$ ) with levobupivacaine hydrochloride 0.5% results in faster onset of sensory and motor blockade compared to



Graph 1: Mean heart rate (per minute)



Graph 2: Comparison of mean systolic blood pressure (mm Hg) between two groups at different time intervals



Graph 3: Comparison of mean diastolic blood pressure (mm Hg) at different time intervals in both the groups

levobupivacaine hydrochloride 0.5% alone. Duration of sensory and motor blockade and duration of analgesia were significantly prolonged when dexmedetomidine ( $75 \mu\text{g}$ ) was added as an adjuvant to levobupivacaine hydrochloride 0.5%. Dexmedetomidine ( $75 \mu\text{g}$ ) as an adjuvant to levobupivacaine hydrochloride 0.5% provides superior quality of analgesia (Lower VAS score) without any significant hemodynamic instability.

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