## **Original** Article

# Low dose levobupivacame 0.5% with fentanyl in spinal anaesthesia for transurethral resection of prostate surgery

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## Abstract

**BACKGROUND:** Levobupivacaine 0.5% and bupivacaine 0.5% were shown to be equally effective in spinal anaesthesia. In previous studies, low dose bupivacaine with an intrathecal opioid was used successfully in urological surgery. The aim of this study was to evaluate the clinical effectiveness and block quality of low dose levobupivacaine, and compare it with low dose bupivacaine when they are combined with fentanyl in transurethral resection of prostate surgery.

**METHODS:** Forty nine patients undergoing transurethral prostate surgery were enrolled in this prospective, randomized and double blind study. Patients in levobupivacaine group received 5 mg levobupivacaine + 25  $\mu$ g fentanyl and bupivacaine group received 5 mg bupivacaine + 25  $\mu$ g fentanyl. Demographic data, surgery times, hemodynamic parameters, block qualities and patient and surgeon satisfactions were recorded.

**RESULTS:** Demographic data, surgery times and patient and surgeon satisfactions were similar in both groups. Hemodynamic parameters were comparable and stable during the procedure in both groups. Sensory block characteristics were comparable and clinically effective in both groups. While 3 patients in bupivacaine group had Bromage score of 3 at the beginning of the surgery, no patient in levobupivacaine group had this score and this difference was significant (p = 0.042). Bromage scores at the end of the surgery were comparable in both groups.

**CONCLUSIONS:** In conclusion, for transurethral prostate surgery 5 mg levobupivacaine with 25  $\mu$ g fentanyl can provide stable hemodynamic profile, patient and surgeon satisfaction and effective sensorial blockade with less motor blockade in spinal anaesthesia; so it could be used at low doses as a good alternative to bupivacaine.

KEYWORDS: Levobupivacaine, Bupivacaine, Fentanyl, Anaesthesia, Spinal, Transurethral Resection of Prostate.

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Spinal anaesthesia for transurethral resection of prostate (TURP) operations has been frequently used, because symptoms of over hydration, TURP syndrome and bladder perforation can be recognized earlier. At the same time, short acting spinal anaesthesia with minimum motor block can be useful in preventing the patient from the complications related with delayed immobilization. It can be assumed that recovery and mobilization of the patient could be faster, if the motor block was less intense. For this purpose, short acting or low doses of local anaesthetics can be used.<sup>1,2</sup>

Levobupivacaine 0.5% and bupivacaine 0.5% were shown to be equally effective in spi-

nal anesthesia. In literatures, no studies could be detected in which levobupivacaine was reported to be used in low doses intrathecally for TURP surgery. The aim of this study is to evaluate the clinical effectiveness, block quality and hemodynamic effects of low dose levobupivacaine and also compare it with low dose bupivacaine when they are combined with fentanyl in spinal anaesthesia for TURP surgery.

## **Methods**

This study was performed in Ankara Numune Training and Research Hospital, Ankara, Turkey. After obtaining approval from Institutional Ethics Committee and written informed

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consent from all patients, 50 ASA I-III patients who were scheduled for elective TURP surgery were enrolled in this prospective, randomized and double blind study. Patients having known hypersensitivity to amide local anesthetics, abnormal coagulation profile, with spinal anomalies or skin infections and unwilling to accept regional anaesthesia were excluded.

Patients were not premedicated before surgery. Before lumbar puncture, an intravenous (IV) cannula was inserted and an infusion of NaCl 0.9% was started. All spinal anaesthesias were performed at the level of L3-L4 with a 25 G Whitacre needle, in sitting position by the same anesthesiologist. Patients were randomized into two groups via sealed envelope technique. Patients in levobupivacaine group (L) received intrathecal 5 mg 0.5% levobupivacaine + 25 µg fentanyl, and in bupivacaine group (B) received intrathecal 5 mg 0.5% bupivacaine + 25 µg fentanyl at an injection rate of 120 sec. The anesthesiologist who performed spinal anaesthesia was blinded to the group of study solution. The study solutions were prepared by another anesthesiologist.

Electrocardiogram, non invasive blood pressure and oxygen (O<sub>2</sub>) saturation of all patients were monitored with PETAS KMA-175 monitor (PETAS Corp., Ankara, Turkey) and recorded as before spinal anaesthesia, every 2 minute for 20 minute after spinal anaesthesia, every 5 minute thereafter for 30 minute and at the end of the surgery. Supplementary 2 mL.min<sup>-1</sup> O<sub>2</sub> was given to all patients via a face mask.

Quality of anaesthesia was assessed by testing for sensory and motor blockade. Sensory blockade was monitored with the pinprick test at every 2 minute for 20 minute, at the end of the surgery and in recovery room until S2 segment regression. Time to achieve sensory block of T10, max spread of sensory block, time to two segment regression and time to S2 regression were recorded. Motor blockade was assessed based on a modified Bromage scale (as 0 no paralysis, able to = flex hips/knees/ankles; 1 = able to move knees,

unable to raise extended legs; 2 = able to flex ankles, unable to flex knees; 3 = unable to move any part of the lower limbs) every 2 minute for 20 minute, at the end of the surgery and in recovery room. Bromage scores at the beginning and at the end of surgery were noted.

Fifteen minutes after the initiation of spinal anaesthesia, if the sensory block had reached to T10, permission was given to start the operation. If the sensory blockade was inadequate, general anaesthesia via a laringeal mask was induced.

A decrease more than 25% from baseline level or to < 60 mmHg in mean arterial pressure was defined as hypotension and treated with IV 5 mg ephedrine bolus. Heart rate  $\leq$  50 beats/min was defined as bradycardia and treated with IV 0.5 mg atropine bolus and these were all noted. Other adverse effects like pruritis, nausea, vomiting, shivering and respiratory depression were also recorded.

In the case of anxiety, IV 1 mg midazolam was given for sedation. At the end of the surgery, patient and surgeon satisfaction were assessed as good, fair or poor.

Statistical analysis was performed using SPSS 11.5 version (SPSS Inc; Chicago, IL, USA). Sample size was calculated to provide 80% power to detect 25% reduction in the incidence of complete motor block in L group compared with B group. Independent samples t test for parametric data, Mann Whitney U test for non parametric data and Chi square test for frequency data were performed for statistical analysis. A p value < 0.05 was considered as statistically significant. Data were expressed as mean ± standard deviation (SD) or median (range) or number of patients (n).

#### Results

One patient in L group declined to go on with regional anaesthesia after receiving the study medication because of serious anxiety and excluded from the study. Demographic data and mean duration of the surgery were similar in both groups (Table 1). Levobupivacaine in transurethral prostatectomy

	<b>Group L</b> ( <b>n</b> = 24)	<b>Group B</b> (n = 25)
Age (year)	63.81 ± 7.42	$65.24 \pm 5.93$
Height (cm)	$163.12\pm6.9$	$162.6\pm7.14$
Weight (kg)	$71.61 \pm 7.45$	$69.82 \pm 9.12$
ASA (I/II/III)	5/15/4	6/16/3
Duration of surgery (minute)	$62.31 \pm 17.32$	$64.4 \pm 18.42$

Table 1. Demographic data and duration of surgery in groups

Mean arterial pressures and heart rates were comparable and stable during the surgery in both groups (Figure 1, Figure 2).

Sensory and motor block qualities are shown in table 2. Sensory block qualities were similar and clinically effective in both groups. At the beginning of the operation, 3 patients in B group had Bromage score of 3, but none of the patients had Bromage score of 3 in L group. This difference was found statistically significant (p = 0.042). Bromage scores at the end of the surgery were comparable in groups.

Hypotension, bradycardia and respiratory depression requiring treatment were not seen

in any of the patients during the operation. Five patients in L group (20.8%) and 6 patients in B group (24%) had pruritis; 2 patients in L group (8.3%) and 1 patient in B group (4%) had nausea. No one vomited in either group. Shivering was not seen in any patient. Incidences of side effects were comparable in groups.

Three patients in B group and 2 patients in L group required supplementary sedation with IV midazolam. Patient and surgeon satisfaction were similar in both groups. Only for 1 patient in B group the surgeon satisfaction was fair. All the other patient and surgeon satisfactions were good in both groups.



Figure 1. Mean Arterial Pressures (MAP) in groups



Figure 2. Heart Rates (HR) in groups

	Group L $(n = 24)$	<b>Group B</b> (n = 25)	
Time to achieve sensory block of T10 (minute)	$11.27 \pm 1.42$	$10.98 \pm 1.66$	
Max spread of sensory block	T7 (T6-T10)	T8 (T6-T10)	
Time to two segment regression (minute)	$67.41 \pm 8.13$	$64.16\pm7.17$	
Time to S2 regression (minute)	$121.25 \pm 15.96$	$116.4 \pm 15.51$	
Bromage scores at the beginning of the surgery $(0-1/2/3)$	17/7/0	11/11/3*	
Bromage scores at the end of the surgery $(0-1/2/3)$	20/4/0	16/9/0	

**Table 2**. Sensory and motor block qualities in groups

\* p < 0.05 group B vs. group L

## Discussion

For TURP surgery a sensory block extending to T10 dermatome is necessary to provide adequate analgesia, since monitoring intravesical pressure is not available always.<sup>3</sup> This study suggests that, 5 mg 0.5% levobupivacaine with 25  $\mu$ g fentanyl usage in spinal anaesthesia can provide adequate sensorial blockade without motor block, stable hemodynamic profile and good patient and surgeon satisfaction for TURP surgery.

Levobupivacaine, the S-(-)-enantiomer of bupivacaine was shown to be equally effective,

in spinal and epidural anaesthesia.<sup>4-8</sup> Levobupivacaine was shown to have sensory-motor dissociation in epidural <sup>9</sup> and probably in spinal route.<sup>10</sup> Lee et al firstly evaluated the effectiveness of 2.6 mL 0.5% levobupivacaine in spinal route in urological surgery and found that, onset time, degree of sensory and motor block and hemodynamic changes were similar to those for 2.6 ml 0.5% racemic bupivacaine.<sup>8</sup> In the study of Vanna et al 2.5 mL of 0.5% isobaric 1 and 0.5% hyperbaric b showed to have equally effective on onset time and duration of sensory blockades.<sup>11</sup> By using small doses of local anaesthetics, one can limit the distribution of spinal block. But low doses of local anaesthetics could not provide an adequate level of sensory block.<sup>1</sup> Adjuvant agents like opioids can be used to enhance analgesia and successful spinal anesthesia. Fentanyl has been widely used as an adjunct to local anesthetics for enhancement of analgesia without intensifying motor and sympathetic block in spinal anaesthesia.<sup>12,13</sup>

In previous studies 1,2,14 dose sparing effect and augmentation block of bupivacaine with intrathecal fentanyl usage were confirmed in urological surgery. By this combination of bupivacaine and fentanyl, dose reduction of bupivacaine can be provided and this will cause less sympathetic blockade, also resulting in lower incidence of hypotension, early recovery and mobilization. Since the usage of low dose levobupivacaine in spinal anaesthesia for urological surgery has not been reported yet, we tried to compare the effectiveness of the low doses of levobupivacaine and bupivacaine when they are combined with fentanyl, which were showed to be effective in spinal anaesthesia for TURP surgery when used in higher doses. By using 5 mg levobupivacaine + 25 µg fentanyl, an effective sensorial blockade was provided with less motor blockade than usage of 5 mg bupivacaine + 25 µg fentanyl.

Vercauteren et al reported that, slight motor impairment seems to occur more often with the use of racemic bupivacaine and they suggested to perform further studies to confirm that levobupivacaine causes less or short lasting motor impairment.<sup>15</sup> Also in the study of Camorcia et al, the potencies for motor block of intrathecal ropivacaine, levobupivacaine and bupivacaine were compared and bupivacaine was found to have more potency for motor block when compared with bupivacaine and ropivacaine.<sup>10</sup> The present findings about less motor block in levobupivacaine group was also consistent with these studies.

As known, spinal opioids carry the risk of respiratory depression especially in elderly patients.<sup>16,17</sup> In the previous study,  $O_2$  supplementation was continuously administered via a face mask. Only small doses of IV midazolam were used in a few patients for sedation. No respiratory depression or transient hypoxia was observed in either group. It can be suggested that, 25 µg intrathecal fentanyl in combination of small doses of midazolam can be safely administered when  $O_2$  supplementation was continued during the procedure.

As also shown in other studies that bupivacaine was used in low doses,<sup>1,13,14</sup> no hypotensive period was observed in either groups in the present study. Pruritis is the common adverse effect of intrathecal fentanyl usage which was also reported by other investigators.<sup>18,19</sup> In the present study, 20.8% of patients in L group and 24% of patients in B group had pruritis; however none of the patients needed treatment. No shivering was observed in any of the current patients, which was also consistent with the studies of Chow et al <sup>20</sup> and Kang et al.<sup>21</sup>

#### Conclusions

In conclusion, for TURP surgery, that is requiring a sensory block to at least T10 dermatome, using low dose 5 mg levobupivacaine with 25  $\mu$ g fentanyl can provide similar stable hemodynamic profile, good patient and surgeon satisfaction and effective sensorial blockade as 5 mg bupivacaine with 25  $\mu$ g fentanyl in spinal anaesthesia. These findings and at the same time the less motor blockade seen in levobupivacaine usage can suggest the usage of low dose of levobupivacaine with fentanyl as a good alternative to bupivacaine in spinal anaesthesia for TURP surgery.

#### **Conflict of Interest**

Authors have no conflict of interests.

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### **Authors' Contributions**

EYA carried out the design and coordinated the study, participated in most of the study and prepared the manuscript. ZNA provided assistance in the design of the study, coordinated and carried out the study and participated in manuscript preparation. NG provided assistance in all the study. All authors have read and approved the content of the manuscript.

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