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# Outcome of Low-Dose 0.5% Levobupivacaine (Plain) And Low-Dose 0.5% Bupivacaine (Heavy) Combined with Fentanyl in Spinal Anaesthesia For Transurethral Resection of Prostate: A Comparative Study

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**Key words:**
Levobupivacaine, TURP, Spinal Anaesthesia.

**Abstract:**

***Background:*** *Spinal anaesthesia is widely used for transurethral resections of prostate (TURP) because it allows early recognition of symptoms caused by over hydration, TURP syndrome, and bladder perforation. Patients undergoing TURP surgery have coexisting pulmonary or cardiac disease.*

***Objective:*** *To evaluate the outcome of the two anaesthetic agents – levobupivacaine and bupivacaine in TURP surgery when they are combined with fentanyl.*

***Method:*** *Total eighty patients were selected by inclusion and exclusion criteria, and then the selected patients were randomly divided into 2 groups (40 in each). levobupivacaine group (1) was received intrathecal 0.5% levobupivacaine 5mg (1 ml) + 25 micro gram fentanyl (0.5ml) and in bupivacaine group (2) was received intrathecal 0.5% bupivacaine heavy 5 mg(1ml) +25 micro gram fentanyl(0.5ml) slowly @1ml/10sec. Heart rate, non-invasive systolic, diastolic and mean arterial blood pressures and oxygen saturation (SpO2) were recorded immediately before intrathecal injection and every 3 min for 15 min after intrathecal injection and there after every 5 minutes upto 40 minutes and at the end of surgery.*

***Results:*** *All the haemodynamic variables except heart rate were almost statistically matched. Half of levobupivacaine group and 30% of the bupivacaine group achieved a sensory block up to the level of T10. Sixty percent of the levobupivacaine and 15% of the bupivacaine group at the beginning of the surgery had modified Bromage score '1'. None of the levobuppivacaine and 15% of the bupivacaine groups had a Bromage score '3'. The recovery from motor block was significantly earlier in the levobupivacaine group compared to that in the bupivacaine group. Over half (55%) of the former group exhibited complete recovery at the end of surgery as opposed to only 20% of the latter group.*

***Conclusion:*** *For TURP surgery, a low dose of levobupivacaine with fentanyl can provide an adequate sensory blockade and can be used as a good alternative to bupivacaine.*

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**Introduction:**

Despite advances in surgical and anaesthetic techniques, major surgery can still be associated with significant postoperative undue events. The objective of anaesthesia is to facilitate surgery at minimal risk to the patient and to ensure optimal recovery following the procedure[1]. The excellent recovery profile of any anaesthetic agents represents an important clinical benefit. Both anaesthesia and pre-anaesthetic agents can affect the recovery time of patients as well as recovery from sensory and motor blockade. Drugs that are not accumulated in the body are usually beneficial for early recovery and do not cause any delayed or recurrent adverse effects even after prolonged administration[2].

For transurethral resection of prostate (TURP) surgery a sensory block extending to T10 dermatome is necessary to provide adequate analgesia. 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. Meanwhile, short acting spinal anaesthesia with minimum motor block can be useful in preventing the patients from the complications related to delayed immobilization. It can be assumed that recovery and mobilization of the patients could be faster, if the motor block was less intense. For this purpose, short acting or low doses of local anaesthetics are preferred[3,4].

Levobupivacaine has similar efficacy but an enhanced safety profile when compared to bupivacaine, a major advantage in regional anesthesia[5,6]. However, very few literatures have so far reported the use of levobupivacaine in low doses intrathecally for TURP surgery. Lee et al[7] (2003) was the first evaluate 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. Akcaboy et al[8] (2011) demonstrated that 5 mg 0.5% levobupivacaine with 25 micro gram fentanyl usage in spinal anaesthesia could provide adequate sensorial blockade without motor block, stable haemodynamic profile and good patient and surgeon satisfaction for TURP surgery.

The purpose of this study is to evaluate the outcome (clinical efficacy, block quality and haemodynamic effects) of low-dose levobupivacaine and also to compare it with low dose bupivacaine when they are combined with fentanyl in spinal anaesthesia for TURP surgery.

**Methods and Materials:**

This prospective randomized clinical trial was carried out in the Department of Anaesthesiology, Sir Salimullah Medical College Mitford Hospital (SSMCMH), Dhaka over a period of six months between march 2013 to august 2013. The study was performed after obtaining the approval of the Ethics Committee of our Institution. Patients were selected who were aged between 50-70 years with ASA class I & II and scheduled for TURP under spinal anesthesia.Patients were excluededd as they were having a history of significant cardiac, pulmonary hepatic or renal diseases,ASA class>III , Chronic drug or alcohol abuse, contraindications of spinal anaesthesia and hypersensitivity to local anaesthetics/ fentanyl. Patients' informed consent was taken from each the patients or their legal attendant. The sample size at the 5 % level of significance and 80% power was calculated 80.The selected patients were randomly divided into 2 groups (40 in each) by card drawn method.

Patients were not premediated before surgery. Before lumbar puncture, an intravenous (IV) cannula 18G was inserted and an infusion of NaCl 0.9%(Normal Saline) /Hartmann's solution was started @ 10ml/kg body weight within 20 minutes of induction. All spinal anesthesia was performed at the level of L3-L4/L4-L5 with a 25 G Quincke type needle under aseptic condition and local anaesthetic skin infiltration (2% Lidocaine 1 ml), in sitting position by the same anesthesiologist. The patients were immediately turned supine. Patients in the levobupivacaine group( group I) received intrathecal 0.5% levobupivacaine 5 mg (1 ml) + 25 μg fentanyl (0.5 ml) (total volume 1.5 ml), and in the bupivacaine group (group II)received intrathecal 0.5% bupivacaine heavy 5 mg (1 ml) +25 micro gram fentanyl (0.5 ml) (total volume 1.5 ml) slowly @ 1 ml/10sec. The drug was prepared by an independent anesthesiologist. The anesthesiologist who performed the spinal anaesthesia was blinded to the study groups.

Heart rate (HR), non-invasive systolic, diastolic and mean arterial blood pressures (SAP, DAP, MAP) and oxygen saturation (SpO2) was recorded immediately before intrathecal injection and every

3 min for 15 min after intrathecal injection and thereafter every 5 minutes up to 40 minutes and at the end of surgery. Quality of anaesthesia was assessed by testing for sensory and motor blockade. Sensory blockade was monitored with the pinprick test at every 3 minutes for15 minutes, at the end of the surgery and in the recovery room until S2 segment regression. Time to achieve sensory block of T10, maximum spread of sensory block, time to two segment regression and time to S2 regression was recorded. Motor blockade was assessed based on a Modified Bromage Scale (BMS) (as 0 = no paralysis, able to flex hips/knees/ankles; 1 = able to move knees, but 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 3 minutes for 15 minutes, at the end of the surgery and in the recovery room. Modified Bromage Scores at the beginning and at the end of surgery was noted. Fifteen minutes after the initiation of spinal anaesthesia, if the sensory block reaches to T10, permission was given to start the operation. If the sensory blockade is inadequate, general anaesthesia was induced.

A decrease in mean arterial pressure > 25% from baseline level was defined as hypotension and was treated with IV 5 mg ephedrine bolus. Heart rate equal or less than 45 beats/min was defined as bradycardia and treated with IV 0.6 mg atropine bolus and these were noted. Other adverse effects like pruritis, nausea, vomiting shivering and respiratory depression also were recorded. In case of anxiety, 2 mg midazolam was given an IV for sedation. If the patient complained of pain during operation, 25 micro gram fentanyl was administered IV.

**Data processing statistical analysis:**The data were processed and analysed using SPSS Version 17 (Statistical Package for Social Sciences). The test statistics used to analyse the data were descriptive statistics, Chi-square ($\chi^2$) Probability Test, Student's t-Test and Repeated Measures ANOVA. For all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ was considered significant. The summarized data were presented in the form of tables and charts.

**Results:**

A total of 80 patients scheduled for transurethral resection of prostate (TURP) under spinal anesthesia were randomly divided into two groups – Levobupivacaine (group I) and Bupivacaine (heavy) (group II). It was observed which of the two anesthetic agents provides better outcomes in terms of extent and duration of motor and sensory blockade and haemodynamic stability. The findings derived from the data analysis are presented below.

**Table I:** *Comparison of baseline characteristics between groups*

| Baseline Characteristics | Group I(n = 40) | Group II (n = 40) | p-value |
|---|---|---|---|
| Age (years)# | 60.1 ± 6.4 | 60.7 ± 5.8 | 0.778 |
| Weight (kg) # | 65.6 ± 6.6 | 66.7 ± 6.4 | 0.961 |
| ASA grade* | | | |
| Grade I | 5 (25%) | 7 (35%) | 0.659 |
| Grade II | 10 (50%) | 10 (50%) | |
| Grade III | 5 (25%) | 3 (15%) | |
| Pulse (b/min)# | 78.9 ± 8.2 | 88.1 ± 10.1 | 0.001$^{ss}$ |
| SBP (mmHg) # | 130.8 1.6 | 137.3± 3.4 | 0.110 |
| DBP (mmHg) # | 79.3 ± 4.9 | 82.5 ± 7.3 | 0.109 |
| Mean BP (mmHg)# | 62.1 ± 5.0 | 64.1 ± 6.5 | 0.243 |
| $SpO_2$ (%)# | 97.8 ± 0.89 | 98.7 ± 0.6 | 0.501 |

Figures in the parentheses indicate corresponding %; * Chi-squared Test ($\chi^2$) was done to analyzed the data. # Data were analyzed using Unpaired t-Test and were presented as mean ± SD.

Table I shows that the study subjects of both levopbupivacaine and bupivacaine groups were almost similar in terms of age, weight and ASA grade ($p = 0.778$, $p = 0.961$ and $p = 0.659$). All the haemodynamic variables (systolic, diastolic and mean blood pressures and oxygen saturation) except pulse were almost homogeneously distributed between groups ($p= 0.110$, $p = 0.109$, $p=0.243$ and $p = 0.501$ respectively). The pulse rate, although, was significantly lower in the former group than the latter group, they were within normal physiological range.

**Table II:** *Comparison of heart rate at different time intervals between groups*

| Pulse# (beats/minute) | Group I(n = 40) | Group II(n = 40) | P value |
|---|---|---|---|
| At baseline | 77.9 8.2 | 88.1 ± 10.1 | 0.001 |
| At 3 minutes | 76.9 ± 7.9 | 88.3 ± 10.3 | < 0.001 |
| At 6 minutes | 76.0 8.5 | 87.2 ± 10.9 | 0.001 |
| At 9 minutes | 74.4 ± 8.4 | 84.5 ± 10.9 | 0.002 |
| At 12 minutes | 73.6 9.1 | 83.7 ± 9.9 | 0.002 |
| At 15 minutes | 72.2 ± 8.3 | 82.7 ± 9.9 | 0.001 |
| At 20 minutes | 71.6 8.8 | 81.1± 9.8 | 0.003 |
| At 25 minutes | 71.8 ± 8.7 | 81.1 ± 8.8 | 0.002 |
| At 30 minutes | 72.6 7.9 | 80.7 ± 8.1 | 0.003 |
| At 35 minutes | 72.5 ± 7.1 | 80.2 ± 8.1 | 0.003 |
| At 40 minutes | 73.0 6.4 | 79.6 ± 7.9 | 0.006 |
| At the end of surgery | 73.9 ± 6.6 | 80.4 ± 7.2 | 0.005 |

# Data were analysed using Student's t-Test and were presented as mean ± SD.

The heart rate of the levobupivacaine group was somewhat lower than that of bupivacaine group at entry, although both were within normal range. This difference was maintained up to the end of surgery (Table II). However, there was no significant difference between the groups in terms of changes in heart rate that occurred from baseline to endpoint of the study.

Fig. 1 depicts the changes in SBP at different time interval following intervention. The differences in systolic blood pressures between two groups at any point of observation were not significant ($p > 0.05$). Fig.2 showed that mean diastolic blood pressures at baseline and at 3 minutes interval were somewhat lower in the levobupivacaine group than those in the bupivacaine group, although the differences were not statistically significant ($p > 0.05$).

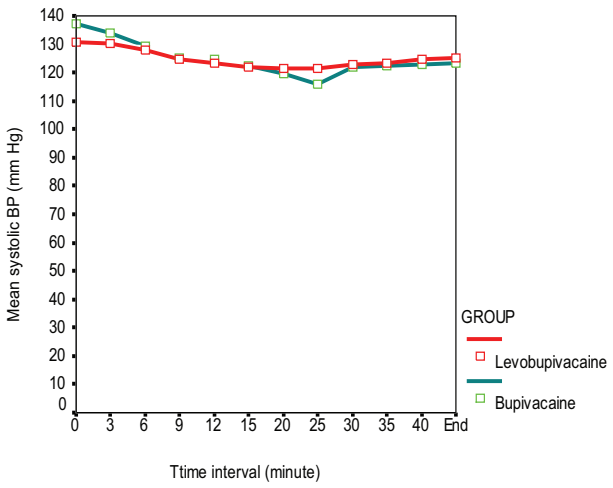


**Fig.-1:** *Monitoring of SBP at different time interval*

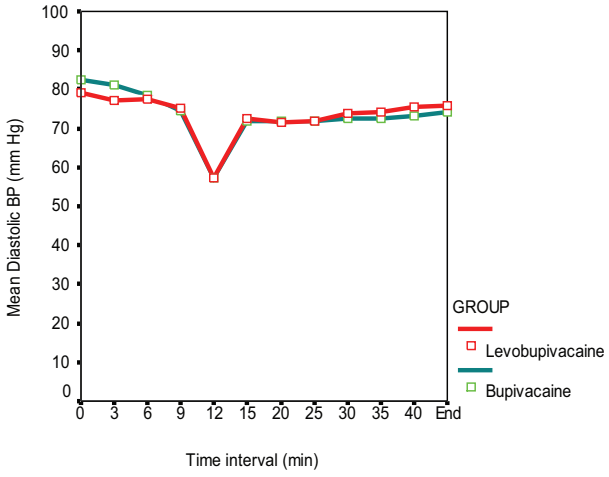


**Fig-2:** *Monitoring of DBP at different time interval*

Like diastolic blood pressures, the mean blood pressures of levobupivacaine group at baseline and at 3 minutes interval were somewhat lower than those in the bupivacaine group, although the differences were not statistically significant p > 0.05). At 6 minutes the mean blood pressure of the two groups almost equalizes and dropped to around 35 mmHg in either group at 12 minutes of observation and no significant change was noted thereafter at any level of evaluation up to the end of observation (Fig.3).

Oxygen saturation of the bupivacaine group was significantly better (varied between 98.5 – 99%) compared to that of levobupivacaine group which varied from 97.5 – 98%. The difference between the two groups at all levels of evaluation was statistically significant (p < 0.05) (Fig. 4).

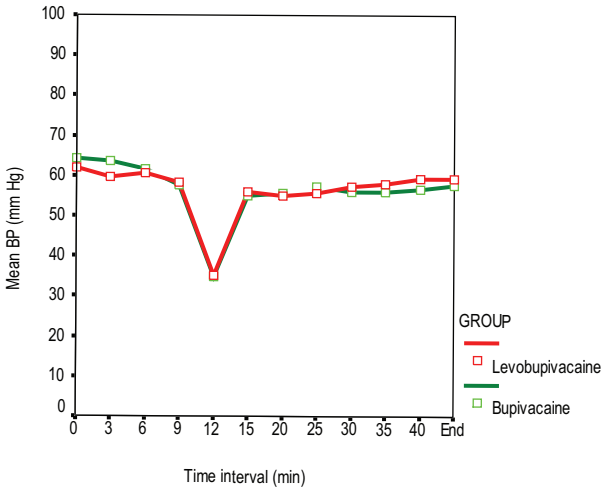


**Fig.-3.** *Monitoring of mean BP at different time interval*

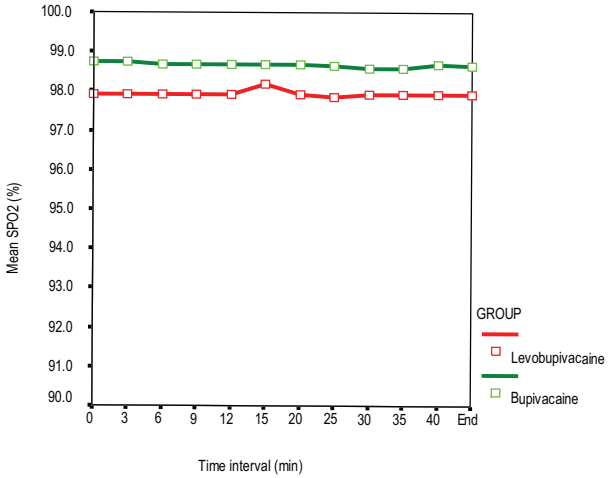


**Fig.-4:** *Monitoring of SpO2 at different time interval*

There was no significant difference between the groups in terms of outcome variables (shown in table III), except time to recovery from motor block. The time to recovery from motor block was significantly earlier in plain levobupivacaine group than that in bupivacaine heavy group (p < 0.001). Extension of sensory block up to T10 was achieved in 50% of the levobupivacaine and 30% of bupivacaine groups.

At the beginning of surgery 60% of the levobupivacaine group had Bromage score 1 while 70% of the bupivacaine group had Bromage score 2. The difference between the two groups in terms of Bromage score at the beginning of surgery was significant (p = 0.007). At the end of surgery, 55% of the former group and 20% latter group exhibited a Bromage score of '0' (p = 0.053) (Table IV).

**Table III:** *Different sensory and motor block parameters between groups*

| Sensory and motor block parameters | Group-I(n = 40) | Group-II(n= 40) | P value |
|---|---|---|---|
| Time to sensory block (min)# | 10.2 ± 1.4 | 9.4 ± 1.8 | 0.099 |
| Extension of sensory block* | | | |
| T7 | 2(10%) | 0(0.0 ) | 0.086 |
| T8 | 3(15%) | 4(20%) | |
| T9 | 5(25%) | 10(50%) | |
| T10 | 10(50%) | 6(30%) | |
| Time to motor block (min)# | 4.3 ± 1.1 | 3.9 ± 1.0 | 0.167 |
| Time to recovery from motor block (min)# | 102.9 ± 9.1 | 118.2 ± 7.3 | < 0.001$^{SS}$ |
| Time to segment regression# | 63.2 ± 3.9 | 65.6 ± 3.9 | 0.074 |
| Time to S2 regression# | 113.4 ± 9.0 | 108.2 ± 14.7 | 0.190 |

Figures in the parentheses indicate corresponding %; *Chi-squared Test **($c^2$)** was done to analyzed the data.# Data were analyzed using Unpaired t-Test and were presented as mean ± SD. ss=statistically significant.

**Tab IV:** *Bromage score at the beginning and end of surgery between groups*

| Bromage scores (0-3) | Group I (n = 40) | Group II (n = 40) | P value |
|---|---|---|---|
| At the beginning of surgery* | | | |
| 1 | 12(60.0) | 3(15.0) | 0.007 |
| 2 | 8(40.0) | 14(70.0) | |
| 3 | 0(0.0) | 3(15.0) | |
| At the end of surgery* | | | |
| 0 | 11(55.0) | 4(20.0) | 0.053 |
| 1 | 8(40.0) | 12(60.0) | |
| 2 | 1(5.0) | 4(20.0) | |

Figures in the parentheses indicate corresponding %; *Chi-squared Test ($\chi^2$) was done to analyzed the data

**Table V:** Comparison of side effects between groups

| Side-effects | Group I (n = 40) | Group II (n = 40) | P value |
|---|---|---|---|
| Pruritus* | 2(10.0) | 7(35.0) | 0.127 |
| Total amount of ephedrine required (mg) | 0.0 ± 0.0 | 5 ± 0.3 | ——- |

Figures in the parentheses indicate corresponding %; * **Chi-squared Test ($\chi^2$)** was done to analyzed the data

Pruritus was the only side-effect encountered. The incidence of pruritus was considerably higher in the bupivacaine group than that in the levobupivacaine group (p = 0.127).

While none of the levobupivacaine group required any ephedrine, 2 patients in the bupivacaine required it. The mean requirement of ephedrine in the bupivacaine group was 5 mg (Table V).

**Discussion:**

In the present study demographic characteristics (age and weight) and ASA grade were almost identically distributed between the two study groups. All the haemodynamic variables except heart rate were almost statistically matched. Half of the levobupivacaine group achieved a sensory block up to the level of T10 which in the bupivacaine group was achieved in 30% of the patients. The modified Bromage score '1' at the beginning of the surgery was observed in 60% of the levobupivacaine and in 15% of the bupivacaine group. None of the levobupivacaine and 15% of the bupivacaine groups had a Bromage score '3'. Thus the findings of the present study demonstrate that 5 mg of 0.5% levobupivacaine with 25 μg fentanyl usage in spinal anaesthesia can provide an adequate sensorial blockade without adequate motor block (low modified Bromage score) and more or less stable hemodynamic profile for TURP surgery. For TURP surgery a sensory block extending to T10 dermatome is necessary to provide adequate analgesia, since monitoring intravesical pressure is not available always[9]. The recovery from motor block was also on an average 17 minutes earlier in the levobupivacaine group compared to the bupivacaine group. Over half (55%) of the former group exhibited complete recovery at the end of surgery as opposed to only 20% of the latter group.

Consistent with the findings of the present study several studies showed Levobupivacaine and bupivacaine to be equally effective, in spinal and epidural anaesthesia[7.10.11..12]. Levobupivacaine was shown to have sensory-motor dissociation in epidural[13] and probably in spinal route[14]. Lee et al[15] (2005) firstly evaluated the effectiveness of 2.6 mL of 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. Vanna and associates[16] showed that both isobaric solution of levobupivacaine and hyperbaric solution of racemic bupivacaine in spinal anesthesia were similar in terms of time to block suitable for surgery, duration

of sensory block, time to two segments regression, time to T12 regression, time to onset and offset of motor block, verbal numeric pain scores at the start of the operation and adverse events.

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 duration of sensory block[3]. Adjuvant agents like opioids can, therefore, be used to enhance analgesia and successful spinal anaesthesia. Fentanyl has been widely used as an adjunct to local anaesthetics for enhancement of analgesia without intensifying motor and sympathetic block in spinal anaesthesia[17.18].

In previous studies[3.4.19] 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 data regarding the usage of low dose levobupivacaine in spinal anaesthesia for urological surgery are limited, we tried to compare the effectiveness of the low doses of levobupivacaine and bupivacaine when they are combined with fentanyl, which have already been shown 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[20] 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. The present finding about less motor block in levobupivacaine group is going in favour of this study.

The present study did not show any significant side-effects in either group except pruritus (10% in the levobupivacaine group and 35% in the bupivacaine group). Pruritis is the common adverse effect of intrathecal fentanyl usage which was also reported by other investigators[21.22]. As known, spinal opioids carry the risk of respiratory depression especially in elderly patients[23], no respiratory depression or transient hypoxia was observed in either group in the present study. However, sharply contrasting with other studies that bupivacaine used in low doses[3.17.19] do not produce hypotensive period, the present study showed a sharp fall of diastolic and mean blood pressures at 12 minutes of observation and 2 patients in the bupivacaine group needed treatment with ephidrine.

Levobupivacaine is increasingly popular in replacing bupivacaine because of its equipotency with lower cardiovascular and central nervous system side effects. It has very similar pharmacokinetic properties to those of racemic bupivacaine, several studies supported the notion that its faster protein binding rate reflects a decreased degree of toxicity. The lethal dose for levobupivacaine was significantly smaller than for bupivacaine.

**Conclusion:**

From the findings of the study it can be concluded that, for TURP surgery that requires a sensory block to at least T10 dermatome, a low dose of 5 mg levobupivacaine with 25 μg fentanyl can provide adequate sensorial blockade without adequate motor block and maintains a more or less stable hemodynamic profile. These findings suggest the usage of low dose of levobupivacaine with fentanyl as a good alternative to bupivacaine in spinal anaesthesia for TURP surgery.However, as the present study was conducted in a single center, multicenter study with a further larger sample is recommended to put forward a general recommendation.

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**Conflict of interest:** None declared

**Ethical approval:** *The study was approved by the Institutional Ethics Committee of SSMC.*

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