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# Spinal Anesthesia with a Low Dose of Hyperbaric Bupivacaine Plus Fentanyl versus Hyperbaric Bupivacaine for Transurethral Resection of Prostate surgery: Hemodynamic Effects, Duration of Analgesia and Motor Block

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**Abstract**

**Background:** Spinal anesthesia is the most prevalent anesthetic method used for transurethral resection of the prostate (TURP) surgery. Lower motor block and fewer side effects can be achieved by lower doses of anesthesia.

**Aim:** The present study aimed to compare the effects of Spinal anesthesia with a low dose of hyperbaric bupivacaine plus fentanyl with hyperbaric bupivacaine for TURP surgery on hemodynamic effects, duration of analgesia, and Motor block.

**Method:** This randomized-controlled study was conducted on 62 patients undergoing TURP surgery within 2017-18. BF group received 0.5% hyperbaric bupivacaine(1mg) 0.2 ml+fentanyl (20µg) 0.4 ml+5% dextrose 1.4ml, while B group received 0.5% hyperbaric bupivacaine (10mg)2ml. Bromage scale and Visual Analog Scale of pain and Nausea were used. The obtained data were analyzed in SPSS software version (20).

**Results:** Groups were homogenous in terms of demographic characteristics. The time to reach the sensory level of T10 was significantly longer in the BF group, compared to the B group (P<0.001). The motor block score was less in the BF group than the B group. The mean total recovery time of the sensory block to L5 in the BF group was significantly lower than that of the BF group (P<0.001). The mean score of nausea severity during surgery was significantly lower in the BF group, compared to the B group (P=0.02). The hemodynamic stability was higher in the BF group.

**Implications for Practice:** A combination of 1mg bupivacaine with 20µg fentanyl could be used for anesthesia in TURP surgery as an effective method to provide sufficient analgesic effects, as well as lower motor block and side effects.

**Keywords:** Bupivacaine, Fentanyl, Hemodynamic, Nausea, Pain, Spinal anesthesia, Transurethral resection of prostate

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**Introduction**

Benign prostatic hyperplasia (BPH) is one of the most prevalent diseases which affects about 60% of men aged 60 and increases up to 90% in 80- year-old men. BPH is the second common cause of surgery in men over 60 years old(1). More than 60% of these patients are candidates for transurethral resection of the prostate (TURP) surgery that is still the gold standard treatment for BPH (1, 2).

In TURP, two general or spinal anesthetic procedures are used for patients (3). TURP may cause some complications both during and after surgery, as other surgical procedures do. These adverse effects include TURP syndrome, as well as cardiovascular, respiratory, metabolic, and kidney complications (1, 4, 5). One of the rare complications of TURP surgery is bladder rupture (in %7 of cases). The clinical symptoms appear as abdominal pain in the areas surrounding the umbilicus spreading to the shoulders, bradycardia, loss of consciousness, nausea, vomiting, and hypotension (6). Therefore, it is of utmost importance to maintain the level of consciousness and brain function during surgery for the early detection of this problem. Nonetheless, many of these warning signs do not exist in general anesthesia (7-9).

Spinal anesthesia is the most commonly used anesthetic technique for TURP due to its relatively limited impact on myocardial function, blood pressure, and cardiac output (3). In a related study, general anesthesia was found to be associated with decreased cardiac output, mean arterial pressure (MAP), and heart rate (HR). Nevertheless, spinal anesthesia only reduced MAP in TURP surgery (10). The results of the mentioned review study also indicated that spinal anesthesia reduced the mortality rate by one third, compared to general anesthesia. In addition, spinal anesthesia can reduce the risk of deep vein thrombosis (%44), pulmonary embolism (%55), need for analgesic injection (%50), and respiratory depression (Hypoventilation) (%59) (9).

Despite the benefits of spinal anesthesia, injection of spinal anesthesia at a higher level results in some adverse effects, such as systemic hypotension, nausea, restlessness, urinary retention, and bradycardia, especially in the elderly. Moreover, low back pain is usually observed after spinal anesthesia and is associated with repeated needle insertion to find the correct location. If the motor block reaches the upper chest and neck dermatomes, hypoventilation can occur. Therefore, since the bladder and prostate are innervated by the S2-S4 and T11-L1 sensory nerves, T10 sensory blocks are often sufficient to perform TURP surgery under spinal anesthesia (11-13).

Bupivacaine 0.5% is typically used for spinal anesthesia as a safe medicine with low complications around the world (14). Bupivacaine is a long-acting amino-amide anesthetic used to reduce postoperative pain and peripheral nerve block (14). 10-12.5 mg of intrathecal bupivacaine is typically administered to obtain a sensory block up to T10 for TURP. Nonetheless, high doses cause cardiovascular instability and severe motor block in the elderly, and prolonged immobilization after surgery increases the risk of thromboembolism (15-17). Therefore, it is reasonable to use the minimal dose of local anesthetics to create the desired sensory block for surgery with minimal effects on motor status and hemodynamic stability (18).

As evidenced by anesthesia studies, lower motor block, better hemodynamic stability, and fewer side effects can be achieved by lower doses of anesthesia (19, 20). On the other hand, the addition of opiates to bupivacaine increased the duration of analgesia and provided hemodynamic stability with no major complication (18, 21, 22). Fentanyl is a short-acting lipophilic drug used to enhance the quality of spinal anesthesia (18, 23, 24).

Several studies have been performed on the efficacy of bupivacaine alone or in combination with other drugs in short-term surgery; nonetheless, there is no consensus on its composition. In a study conducted by Zohar et al. (2007), spinal block using 3mg bupivacaine and 20µg fentanyl was reported to be effective in TURP surgery (25). In another study, the effects of spinal anesthesia using low-dose bupivacaine plus fentanyl were compared with routine doses of bupivacaine in patients scheduled for TURP. The results were indicative of adequate sensory level in both groups. However, motor block and other side effects were reported to be lower in bupivacaine plus fentanyl group (24). To the best of our knowledge, lower-dose hyperbaric bupivacaine which is desirable for TURP is 1 mg. One study in South Korea on elderly patients demonstrated that using 1 mg bupivacaine plus fentanyl or sufentanil provided appropriate sensory block levels in TURP(6). As illustrated by the related studies, the combination of bupivacaine with opiates has been different. On the other hand, different genetic characteristics can affect the results of the study (For example, spine length is important in drug development, and height is higher in the Iranian population)(6).

Therefore, the present study aimed to compare the effects of 1mg hyperbaric bupivacaine plus 5% dextrose and fentanyl 20µg with the conventional dose of hyperbaric bupivacaine (10mg) on the level of sensory and motor block, pain and nausea severity, hemodynamic status and its side effects in TURP surgery.

**Methods**

This randomized clinical trial was conducted on 62 candidates for TURP surgery in an educational, research, and treatment center in the east of Iran during 2017-2018. This hospital has 300 beds and 7 operating rooms one of which is a urology surgery room. The research setting was the operating room, the recovery room, and the urology department of the hospital. The sample size was estimated based on the results of a study conducted by Kim et al. (2015)(6). Using the sample size formula, the final sample size was calculated to be 31 individuals for each group with a confidence interval of 95%, a test power of %80, and sensory block results ($S_1$=16/9, $S_2$=20/6, $m_1$=52/8, $m_2$=39/6).

The inclusion criteria were as follows: 1) the age range of 60 and above, 2) $ASA_1$ and $ASA_2$ classes (Classification of patients' physical status according to the American Society of Anesthesiologists: $ASA_1$= healthy patients, $ASA_2$= patients with mild or no functional limitations), 3) absence of lumbar disc disease,4) coagulation disorder, 5) allergy to local anesthesia and opioids, 6) mental disorders and neurological diseases, 7) diabetes, uncontrolled blood pressure, and 8) addiction. On the other hand, the patients with a need for sedation, unwanted complications during surgery, surgery duration more than one h, and hypotension greater than 30% from the baseline requiring ephedrine and atropine injection were excluded from the study. The patients were selected using a convenience sampling method. They were assigned to one of two groups of bupivacaine alone (B) or bupivacaine and fentanyl (BF) based on Permuted block randomization (quadruple blocks).

Patient demographic information, height, time of operation, duration of operation, onset time of local anesthesia, time to reach target level (T10), maximal sensory block level, time of sensory block return to L5, and stopping time in recovery were measured and recorded in the demographic and disease information form. Blood pressure before spinal anesthesia was regarded as baseline blood pressure. Blood pressure was recorded immediately and 5, 10, 15, 30, and 45 min after the injection, and the difference with baseline pressure was recorded. The sensory block level was evaluated every 15 min. The time needed for the decrement of the sensory block from T10 to L2 was regarded as the duration of sensory block.

The validity of the demographic and disease information form was confirmed by seven faculty members of the Nursing Department. This questionnaire consisted of 25 items about first name, last name, age, gender, the onset time of operation, duration of operation, onset time of anesthesia, vomiting, mean blood pressure, as well as systolic and diastolic blood pressure after the injection at the intervals of 5, 15, 30, 45 min and one h after the operation. Since the items in this form were objective and had been frequently used in previous studies, its reliability was also verified in this study.

The motor block was evaluated at the time of reaching the sensory block to T10 using the Bromage scale. The most frequently used scale for the assessment of motor block is the Bromage scale and the severity of motor block is assessed by the patient's ability to move their lower extremities. This instrument assesses the patient's strength for flexion of the leg ranging from 1-4: 1= full flexion of knee and feet (none), 2= just able to flex knees (partial), 3= able to flex feet only (almost complete), 4= unable to move feet or knees (complete)(26).

The first author evaluated pain scores by Visual Analog Scale (VAS) criteria immediately after surgery and 15 and 30 min after entering the recovery room,and 2, 6, 12, and 24 hours after leaving. Nausea was also evaluated by VAS criteria using patient self-report and recorded at the same time in BF and B groups. VAS criteria for pain and nausea was scored as follows:0=neither pain nor nausea, 1-3= mild, 4-6= moderate, and 7-10= severe pain and nausea. These scores which ranged between 0-10 and indicated the patient’s amount of pain and nausea were considered and recorded. Moreover, the incidence of vomiting for 24 h was studied. This scale which is a standard tool for the assessment of pain and nausea had been used in several studies and its reliability had been reported as 0.95-0.99% (27-30). In the current study, pain and nausea severity was estimated in 10 patients by two observers (i.e., the first author and nurse). The correlation of VAS used by two observers was calculated by

Pearson's correlation coefficient (r=0.89 and r=0.75, respectively). It is worth noting that the patients in both groups received 100mg Diclofenac rectal suppository after surgical procedure. Any additional analgesic was noted.

The medicines were prepared and provided to the anesthesiologist by the independent researcher in the same 2cc syringes. The syringes in the BF group contained a combination of 0.2 cc of hyperbaric bupivacaine 0.5%, 0.4 cc of fentanyl, and 1.4 cc dextrose solution 5%. On the other hand, the syringes in the B group only contained 2 cc of bupivacaine 0.5%. In the BF group, an insulin syringe was used with a low dose of opioid and bupivacaine to minimize deviation from the amount of medicine before mixing. Before the commencement of the spinal anesthesia procedure, the patients in both groups received 300 ml lactate ringer serum. The patients were positioned in a sitting posture for spinal anesthesia. The spinal anesthesia was performed from L3-L4 or L4-L5 space with spinal needle No. 25. After the examination of the free flow of cerebrospinal fluid, the medicine was slowly injected in 10 sec.

Patients were immediately positioned at the 30-degree angle in Trendelenburg posture, and the sensory block level in the middle of the cervix was controlled using a needle (G22 subcutaneous injection) every 2 min until it reached T10 sensory level. After reaching this level, the patients were returned to the neutral position.

The study protocol was approved by the Ethics Committee of Birjand University of Medical Sciences (IR.BUMS.REC.1396.46). Moreover, after the required permissions were obtained, the research procedures and objectives were explained to the subjects. Thereafter, written informed consent was obtained from all of them and they were assigned to two groups.

The normality of quantitative variables was checked by the Kolmogorov-Smirnov test. The data were analyzed in SPSS software (version 20) using the independent t-test, Mann-Whitney U test, and Friedman test. A p-value less than 0.05 was considered statistically significant.

**Results**

The mean age scores of patients in the BF and B groups were reported as 66.3± 13.2 and 63.4±10.8 years, respectively. The results of Mann-Whitney and independent t-tests revealed that the mean age and height did not differ significantly between the two groups (P>0.05; Table 1).

According to Mann-Whitney test results, the mean time to reach the sensory level of T10 was significantly longer in the BF group than in the B group (P<0.001). Moreover, the motor score after reaching the level of T10 block was significantly higher in patients in the BF group than those in the B group (P<0.001). However, the mean total sensory block recovery time to L5 was significantly higher in patients of the B group, compared to those in the BF group (P<0.001; Table1).

Furthermore, based on Mann-Whitney test results, the mean score of pain immediately after surgery, 15 and 30 min after entering recovery room, as well as 2, 6, 12, and 24 h after leaving recovery, did not differ significantly between the two groups (P>0.05). The intergroup comparison revealed that the mean score of pain severity significantly differed between the BF and B groups (P<0.001). In addition, the result of the independent t-test showed that the number of cases requiring additional analgesics did not differ significantly between two groups (P>0.05; Table1).

The mean score of severity of nausea during surgery in the BF group was significantly lower, compared to the B group (P=0.02). Nevertheless, immediately after the surgery, 15 and 30 min after entering recovery room, as well as 2, 6, 12, and 24 h after leaving recovery, no significant difference was observed between the two groups (P> 0.05). Furthermore, based on the intergroup comparison, no significant difference was detected in the BF and B groups (P=0.06 and P=0.053, respectively) (Table1).

According to Mann-Whitney test results, the two groups were not significantly different (P>0.05) in terms of the mean systolic blood pressure (SBP) before anesthetic injection, compared to immediately after surgery, the mean diastolic blood pressure(DBP) before anesthetic injection, compared to 5 min after surgery, and the mean arterial pressure (MAP) before anesthetics injection, compared to immediately after surgery and 5 min after the surgery. At other times of the study, the independent t-test and Mann-Whitney test results showed that the mean changes in SBP, DBP, and MAP were more significant in the B group, compared to the BF group (p <0.05) (figures 1,2 and 3).

Among 62 included patients, only 1 patient in the B group had vomiting up to 24 h after the surgery.

**Table 1. Comparison of the mean age, height, duration of surgery, time to reach sensory level T10, the total recovery time of sensory block to L5, motor score after reaching the level of T10 sensory block, pain and nausea in patients of both BF and B groups**

| Variable | | BF group Mean ± standard deviation | B group Mean ± standard deviation | Intragroup Comparison (P-value) |
|---|---|---|---|---|
| Surgery duration (min) | | 47.9±7.0 | 47.2±6.7 | 0.65* |
| Age (year) | | 66.3± 13.2 | 63.4±10.8 | 0.35* |
| Height (cm) | | 167.7± 4.7 | 166.7±6.2 | 0.47** |
| Time to reach T10 sensory level (min) | | 9.3± 1.7 | 4.4±1.2 | <0.001* |
| Recovery time of sensory block (min) | | 66.2 ± 9.2 | 77.7 ±8.1 | <0.001** |
| Motor score after reaching T10 sensory block level ( Bromage scale) | | 3.7±0.5 | 1.5±0.7 | <0.001* |
| Pain | Immediately after the surgery | 0.06±0.2 | 0.03±0.1 | 0.56* |
| | 15 min after entering the recovery room | 0.1±0.4 | 0.06±0.2 | 0.62* |
| | 30 min after entering the recovery room | 0.3±0.6 | 0.2±0.5 | 0.60* |
| | 2 h after leaving the recovery room | 1.0±1.7 | 0.6±0.9 | 0.57* |
| | 6 h after leaving the recovery room | 1.1±1.5 | 1.2±1.2 | 0.39* |
| | 12 h after leaving the recovery room | 0.7±1.1 | 1.2±1.3 | 0.06* |
| Intergroup test result (P-value) | | <0.001*** | <0.001*** | |
| Non of cases requiring any additional analgesic | | 3 | 4 | 0.09** |
| Nausea | During surgery | 0.1±0.3 | 0.5±0.8 | 0.02* |
| | Immediately after the surgery | 0.03±0.1 | 0.1±0.5 | 0.16* |
| | 15 min after entering the recovery | 0.1±0.3 | 0.2±0.5 | 0.44* |
| | 30 min after entering the recovery room | 0.1±0.4 | 0.1±0.4 | 0.25* |
| | 2 h after leaving the recovery room | 0.2±0.5 | 0.2±0.8 | 0.50* |
| | 6 h after leaving the recovery room | 0.1±0.4 | 0.06±0.3 | 0.32* |
| | 12 h after leaving the recovery room | 0.0±0.0 | 0.03±0.1 | 0.32* |
| | Immediately after the surgery | 0.0±0.0 | 0.03±0.1 | 0.32* |
| Intergroup test result (P-value) | | 0.06*** | 0.053*** | |

* Mann-Whitney U test
** Independent t-test
*** Friedman test

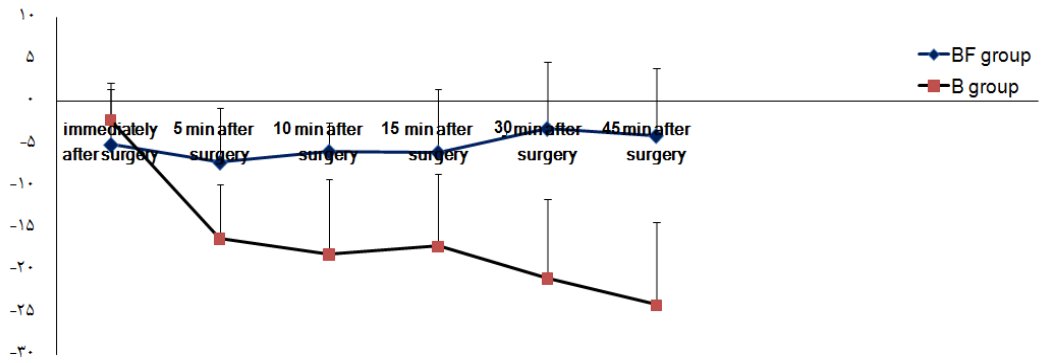


**Figure 1. Comparison of mean changes in systolic blood pressure immediately after surgery, as well as 5, 10, 15, 30, and 45 min after the surgery, compared to before anesthetic injection in the two groups**

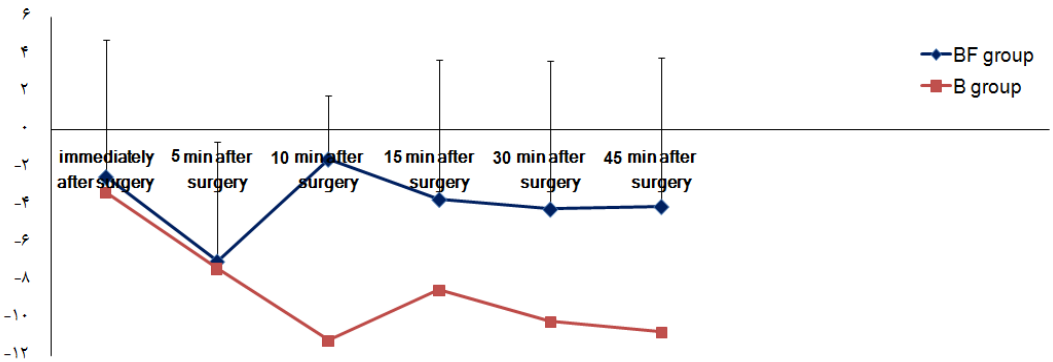


**Figure 2. Comparison of mean diastolic blood pressure changes immediately after surgery, as well as 5, 10, 15, 30, and 45 min after the surgery, compared to before anesthetic injection in the two groups**

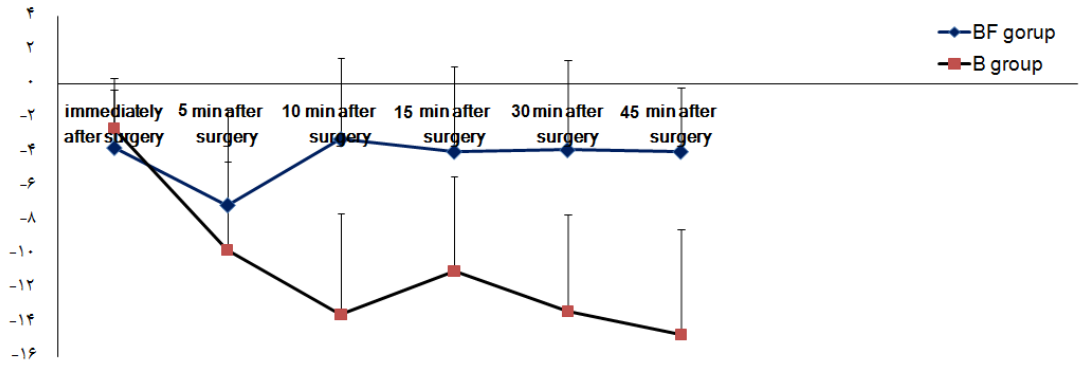


**Figure 3. Comparison of mean arterial pressure changes immediately after the surgery, as well as 5, 10, 15, 30, and 45 min after the surgery, compared to before the injection of anesthetic in patients of BF and B groups**

## Discussion

The current study compared the effects of 1mg hyperbaric bupivacaine plus 5% dextrose and fentanyl 20µg to the conventional dose of hyperbaric bupivacaine (10mg) on the level of sensory and motor block, pain and nausea severity, hemodynamic status and its side effects in 62 candidates of TURP surgery.

In the present study, the time to reach the desired sensory level for TURP (onset of the sensory block) was reported to be longer in the BF group, compared to the B group. The use of opioid seemingly delayed the onset of a sensory block; nonetheless, this hypothesis has not been approved in others studies which have used a combination of opioid with low dose bupivacaine and low dose bupivacaine alone. On the other hand, no difference was observed in the onset of the sensory block in the same doses of bupivacaine in combination with two different opioids, (6). Therefore, in the present study, it seems that the only factor influencing the onset of the sensory block was bupivacaine dosage.

Hypotension is one of the complications of spinal anesthesia that is followed by a reduction in systemic vascular resistance of the sympathetic block which increases with increasing sensory block levels, especially above the T10 level. In our study, blood pressure in both groups was measured at the baseline and then after spinal anesthesia at the intervals of 5, 15, 30, and 45 min. The results of the first 5 min demonstrated no hemodynamic change in the two groups. Nonetheless, in subsequent measurements, the group BF had significantly lower hemodynamic changes than baseline, compared to the group B. Similar to the current study, Kim et al. (2015) used the combination of 1 mg bupivacaine and opioid for patients undergoing resection via the urethra, and no hemodynamic change was observed in any of the study groups (6). Atallah et al. (2015) carried out a study on the use of 7.5mg bupivacaine 0.5% alone or in combination with 10µg fentanyl for spinal anesthesia in patients with percutaneous nephrolithotomy. The result of the mentioned study revealed that using a combination of a low dose of bupivacaine plus fentanyl showed hemodynamic stability (20). Moreover, Arzola et al. (2011) conducted a systematic review study on the efficacy of a low dose of bupivacaine for cesarean section. In this meta-analysis, most studies have indicated that low doses showed hemodynamic stability in patients (31). Furthermore, in their study, Unal et al. (2012) used a low dose of bupivacaine (4mg) alone or in combination with 25µg fentanyl and/or a combination of 3mg bupivacaine with 25µg fentanyl, and hemodynamic symptoms remained stable in all groups (32). It seems that no hemodynamic difference between the two groups in the first 5 min is related to the fact that sensory block did not reach the T10 level in both groups. Nevertheless, after that, the hemodynamic difference observed between the two groups can be attributed to a lower dose of bupivacaine in the group BF, which caused lower sympathetic block effects than that of the group B. The other cause can be the difference between the two groups in terms of spinal expansion. In a spinal model, it was found that spinal extension is affected by the density difference of 0.0006mg /ml (33). Probably due to higher density, spinal extension in the group of 10mg bupivacaine is 5% higher than the group of a lower dose of bupivacaine. Therefore, the level of the sympathetic block will also be higher in these individuals.

In the current study, the severity of nausea in the BF group was significantly lower than that of the B

group. In a study performed by Kim et al. (2009), the incidence of nausea and vomiting in patients receiving low dose bupivacaine was reported to be very low (3). In their study, Kararmaz et al. compared the use of a combination of 4mg bupivacaine 0.5% with 25µg fentanyl c with 7.5mg bupivacaine for prostate resection surgery via the urethra. Similar to our study results, they reported that the incidence of hemodynamic complications, as well as nausea and vomiting, was less in bupivacaine and opioid receiving group, compared to the other group (24). Nausea and vomiting are considered other common complications of spinal anesthesia the main cause of which is the sympathetic block. The severity of nausea depends on the depth of the sympathetic block. Since there is a direct correlation between the depth of sympathetic block and the dose of bupivacaine, the results of the aforementioned studies are reasonable. In the intergroup comparison, the mean score of nausea was not significantly different between the two groups. It can be ascribed due to the fact that the mean score of nausea in two groups at different stages of the study was low (0.03 to 0.5 to 10) and showed minor changes (0.0-0.47).

Furthermore, in the present study, the duration of sensory block was significantly shorter in the BF group, compared to the B group. As evidenced by the obtained data, the duration of sensory block in spinal anesthesia with local anesthetics depends on such factors as bonding protein capacity, fat solubility, local anesthetic dosage, and co-administration of vasoconstrictor (34, 35). A reduced dose of local anesthetics causes a reduction in the duration of the sensory block that does not change with the addition of opioids (36).

In addition, the motor block was significantly lower in the BF group, compared to the B group based on the Bromage scale. These results have also been confirmed in the study conducted by Unal et al. (2012) (32). The level of motor block is often related to the dose of local anesthetics. Therefore, the achievement of this result seems logical.

Moreover, the severity of pain in the first 24 h after TURP was not significantly different between the two groups. This can be due to the addition of opioids to local anesthetic, which increases the duration of analgesia in patients and counteracts the effects of a reduced dose of bupivacaine on decreasing postoperative analgesia. According to the intergroup comparison, the mean score of pain was significantly different between the two groups. It can be ascribed to the effect of time since the effect of drugs disappear and the severity of pain increases.

Every study has some limitations which should be addressed in the paper. One of the limitations of the current study was the impossibility of using the same device to measure vital signs in different sections. Therefore, due to the calibration of the devices, its effects on the results of the study were minimized.

**Implications for Practice**

Spinal anesthesia using 1 mg of hyperbaric bupivacaine combined with 5% dextrose and fentanyl 20 µg for TURP can provide sufficient sensory block, short duration of sensory block, reliable postoperative analgesia. Moreover, it can prevent deep motor block, hemodynamic instability, and nausea which is usually observed using conventional doses of bupivacaine (10mg). Therefore, this method is recommended and it is suggested that further studies be performed on a larger number of patients with the same device and evaluate the rate of intraoperative and postoperative bleeding.

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**Conflicts of Interest**

The authors declare that they have no conflict of interest regarding the publication of the current article.

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