The Effects of Low Dose Levobupivacaine with or without Sufentanil Intrathecally in Transurethral Resection of Prostate

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ABSTRACT

***Aim**: We aimed to compare the clinical efficacy of levobupivacaine alone and levobupivacaine/sufentanil combination in spinal anesthesia for transurethral resection of the prostate (TURP) in elderly patients.*

***Method**: Ninety patients were randomly assigned into two groups to receive either levobupivacaine 10 mg (Group L) or levobupivacaine 7.5 mg combined with 2.5 µg sufentanil (Group LS) for spinal anesthesia. The dermatome level and upper level of sensory blockade, time to develop a sensory block to T10, duration of sensory and motor blockade, Bromage score at the end of surgery, two- segment sensory regression time, and side effects were recorded. The quality of anesthesia was evaluated and rated after the surgery.*

***Result**: There were no significant differences between groups in demographic data or hemodynamic variables in terms of sensory blockade, onset time of sensory blockade to T10 dermatome, and two-segment regression. Bromage score at the end of surgery was significantly higher in Group L ($p<0.05$). The number of patients with maximum motor block was significantly higher in Group L ($p<0.05$). Complete motor block resolution time was longer in Group L ($p<0.05$). There were no significant differences in side effects between groups except for pruritus ($p<0.05$). There were no significant differences between groups in quality of anesthesia.*

***Conclusion**: It was shown that 10 mg levobupivacaine and 7.5 mg levobupivacaine combined with 2.5 µg sufentanil were considered to be convenient for clinical use in TURP surgery with spinal anesthesia; both treatments provided adequate anesthesia with hemodynamic stability in elderly patients.*

***Key words**: Levobupivacaine, sufentanil, spinal anesthesia, elders*

Transütretral Prostat Rezeksiyon Cerrahisinde Sufentanil ile Beraber veya Tek Olarak Düşük Doz Levobupivakainin Etkisi

Amaç: *Bu çalışmada TURP cerrahisi geçirecek yaşlı hastalarda levobupivakain ile levobupivakain ile sufentanil kombinasyonunun klinik etkinliğinin karşılaştırılmasını amaçladık.*

Metod: *90 hasta rastgele 2 gruba ayrılarak spinal anestezi için bir gruba 10 mg levobupivakain (Grup L), diğer gruba 7.5 mg levobupivakain ile 2.5 µg sufentanil (Grup LS) verildi. dermatom seviyesi, maksimum duyusal blok düzeyi, duyusal bloğun T10'a ulaşma zamanı, duyusal ve motor blok süresi, cerrahi sonunda Bromage skoru, 2 segment gerileme zamanı ve yan etkiler kaydedildi.*

Bulgular: *Gruplar arasında demografik ve hemodinamik veriler ile duyusal bloğun T10'a ulaşma ve 2 segment gerileme zamanı açısından anlamlı fark bulunmadı. cerrahi sonunda Bromage skoru ve maksimum motor blok oluşan hasta sayısı Grup L'de yüksekti ($p<0.05$). Komple motor blok çözülme zamanı grup L'de anlamlı olarak uzundu ($p<0.05$). Yan etkiler açısından gruplar arasında kaşıntı dışında anlamlı fark bulunmadı($p<0.05$).anestezi kalitesi açısından gruplar arasında anlamlı fark yoktu.*

Sonuç: *Spinal anestezide 10 mg levobupivakain ve 7.5 mg levobupivakain ile 2.5 µg sufentanil kombinasyonunun uygun olduğu, yaşlı hastalarda kullanımlarının hemodinamik stabiliteyi bozmadan yeterli anestezi sağladığı gösterilmiştir.*

Anahtar kelimeler: *Levobupivacaine, sufentanil, spinal anestezi, yaşlılar*

INTRODUCTION

Subarachnoid block is a widely used technique for transurethral resection of the prostate (TURP) surgery in the elderly, especially in those with respiratory and cardiac problems. This procedure usually lasts less than one hour, and early recovery and discharge are desirable (1,2).

Levobupivacaine, the pure S(-) enantiomer of racemic bupivacaine, has been used routinely in clinical practice because of its significantly decreased cardiovascular and central nervous system toxicity (3,4). For TURP surgery, a dose of 2.3 ml levobupivacaine with fentanyl has been evaluated in a previous study (5); however, no comparative data are as yet available on the use of low-dose levobupivacaine with intrathecal (IT) sufentanil.

Lipophilic opioids added to local anesthetics (LA) can adapt the spinal anesthetic to a specific type and duration of surgery. By using the synergistic analgesic effect of an opioid, it is possible to create adequate spinal anesthesia for surgery with normally subtherapeutic doses of LA. Therefore, IT administration of such a combination improves anesthesia quality, prolongs sensory blockade without prolonged motor block and also reduces LA requirements (6).

The aim of the present study was to identify whether low-dose spinal levobupivacaine alone or in combination with IT sufentanil would provide adequate surgical conditions, clinical efficacy, motor block, and hemodynamic effects in elderly patients undergoing TURP surgery requiring sensory block to at least the tenth thoracic dermatome.

MATERIALS AND METHODS

The study was approved by the institutional ethics committee and performed at Selcuk University Meram Medical Faculty, Anesthesiology Department. We obtained written informed consent from 90 male patients with American Society of Anesthesiologists (ASA) physical status II-III aged 55-75 years who were scheduled to undergo elective TURP surgery with spinal anesthesia. Patients with a history of back surgery, infection at injection sites, coagulopathy, hypersensitivity to local anesthetics or opioids, mental disturbance, or neurological, cardiac or renal diseases were excluded from the study.

The study was conducted in a prospective, randomized, placebo-controlled, and double-blinded manner. One of the investigators prepared the drug solution before anesthesia. The anesthetic administrator and the patients were blinded to the type of drug solution and the patient's group. The patients were randomly assigned into two groups for spinal anesthesia according to a computer-generated randomization table. After routine monitoring and infusion of 7 ml/kg 0.9% sodium chloride solution, patients were premedicated with intravenous (iv) midazolam (0.02 mg/kg) and baseline noninvasive blood pressure (NIBP), heart rate (HR) and peripheral oxygen saturation (SpO2) were recorded. The iv infusion was minimally maintained during the surgery to avoid the overloading associated with the absorption of irrigating fluid. The spinal anesthesia was then performed in sitting position by using a 25- gauge Quincke needle at the L3-4 intervertebral space with midline approach. Group L received 10 mg levobupivacaine 0.5% (Chirocaine®)

***Table 1**. Demographic data of patients.*

	Group L (n:45)	Group LS (n:45)	p value
Age (yr)	*66.1±6.4*	*65.1±6.9*	*0.78*
Height (cm)	*170.4±5.5*	*170.4±4.9*	*0.92*
Weight (kg)	*78.0±10.6*	*75.5±10.3*	*0.57*
ASA II/III	*26/19*	*24/21*	*0.43*
Surgery time (min)	*48.76±7.2*	*46.48±7.3*	*0.64*

Values are mean ± SD or number of patients (n). No statistically significant between-groups differences (p > 0.05).

while Group LS received 7.5 mg levobupivacaine 0.5% combined with 2.5 µg sufentanil (Sufenta®), for a total dose of 2 ml via IT injection. After free flow of cerebrospinal fluid was verified, anesthetic solution was given over 15 s without barbotage or aspiration. Immediately after the injection, patients were placed in the supine position. During the operation, HR, NIBP and SpO2 were recorded every 2 min for 10 min after the spinal anesthesia, every 5 min for 30 min thereafter and every 10 min until the end of the study.

The average of three mean arterial pressure (MAP) measurements obtained at 5-min intervals before spinal anesthesia performed was recorded as baseline MAP. Hypotension was defined as a decrease in MAP of more than 20% from baseline and was treated with incremental iv bolus of 5 mg ephedrine. A heart rate < 45 beats/min was considered as bradycardia and treated with 0.5 mg atropine iv. Supplementary oxygen at 2 lt/min was given via a nasal cannula during the procedure. The sensory blockade was evaluated by pinprick method using a 22 G hypodermic needle, and the motor blockade was assessed according to modified Bromage score (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 flex ankles, knees or hips). Anesthesia was considered adequate for surgery if pain sensation as assessed by the pinprick test was lost at the T10 level; patients were then placed in the lithotomy position and the operation was started. If the sensory block level had not reached T10 dermatome by 20 min, the regimen was switched to general anesthesia. Complete motor recovery was assumed when the modified Bromage score was 0. The dermatome level and upper level of sensory blockade (Tmax) were tested by pinprick stimuli. The time to develop a sensory block to T10, Tmax and the durations of sensory and motor blockade and two-segment regression were recorded. After the surgery, patients were taken to the recovery room where HR, NIBP and SpO2 were monitored. Side effects such as hypotension, bradycardia, pruritus, headache, nausea, vomiting, shivering, and respiratory depression were recorded during the operation and recovery. Nausea and vomiting were treated with iv 10 mg metoclopramide, and 8 mg lornoxicam iv was given when patients complained of pain in the postoperative period. Postoperatively, the quality of anesthesia was rated as: excellent, no discomfort or pain; good, mild pain or discomfort and no need for additional analgesics; fair, pain that required analgesics; or poor, severe pain that required analgesics. Patients were discharged from the recovery room after the motor block was completely resolved.

***Table 2**. Characteristics of sensory level and motor block of spinal anesthesia.*

	Group L	Group LS	p value
Onset time of sensory block to T10, (min)	*4.85±1.8*	*5.31±2.1*	*0.36*
Highest level of sensory block (dermatome)	*T7 (T5-T8)*	*T7 (T5-T9)*	*0.59*
Time of highest level of sensory block (min)	*12.23±5.1*	*13.82±8.0*	*0.22*
Time for two segments regression (min)	*49.47±21*	*52.40±19*	*0.58*
Onset time to Bromage score of 1 (min)	*4.01±1.3*	*4.76±1.6*	*0.6*
Bromage score at the end of surgery	*2.85±0.4*	*2.48±0.5*	*0.002*
Time to complete block resolution (min)	*186.59±21.2*	*119.74±44.8*	*0.001*

Values are median (range) or number (n). p<0.05 compared with group LS.

***Table 3**. Side effects and medications of the patients*

	Group L	Group LS	p value
Hypotension	*0*	*0*	*1.0*
Bradycardia	*0*	*0*	*1.0*
Pruritis	*0*	*7 (15.6%)*	*0.021*
Respiratory depression	*0*	*0*	*1.0*
Headache/dorsal pain	*0/0*	*0*	*1.0*
Nausea/vomiting	*0/0*	*0/0*	*1.0*
Supplemental analgesic	*0*	*0*	*1.0*
Ephedrine/atrophine	*0/0*	*0/0*	*1.0*

Values are number of patients (n) and percentage (%). p<0.05 compared with group L.

Statistical analyses were performed using SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, IL, USA). Presuming an α = 0.05 and β = 0.80, one would need to study 21 patients in each group to detect a mean difference in MAP of 20 mmHg between two groups. Independent sample t-test and Mann-Whitney U test were used for between-group comparisons. For within-group comparisons of hemodynamic data, analysis of variance for repeated measurements was done, which was followed by Bonferroni test. Categorical variables were analyzed using the c2 test. A p value of less than 0.05 was considered statistically significant.

RESULTS

All spinal blocks performed in both groups were successful. Table 1 presents the demographic data of the groups. Patient characteristics (age, weight, height, ASA physical status and mean duration of surgery) were similar between groups. There were also no significant differences between groups in hemodynamic data, including systolic blood pressure (SBP) values, diastolic blood pressure (DBP) values, MAP values (Figure 1) and HR (Figure 2). Patient SpO2 values remained stable throughout the study period. The highest median sensory blockade level achieved was T7 in both groups (range, T5-T8 in Group L; range, T5-T9 in Group LS) (Table 2). Times to highest level of sensory blockade were 12.23±5.1 min in Group L and 13.82±8.0 min in Group LS. There were no significant differences between the two groups in terms of sensory blockade (p>0.05). Onset times of sensory blockade to T10 dermatome were 4.85±1.8 min in Group L and 5.31±2.1 min in Group LS, respectively (p>0.05) (Table 2).

There was no significant difference in two-segment regression time between the groups (49.47±21 min in Group L, 52.40±19 min in Group LS; (p>0.05). Bromage score at the end of surgery was significantly higher in Group L than Group LS (p<0.05) (Table 2). The number

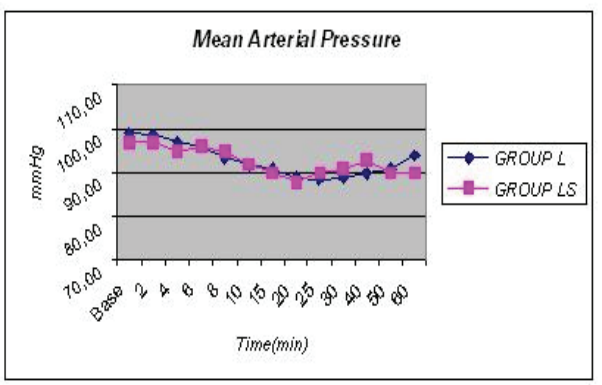

***Figure 1**. Mean arterial pressure of patients. p > 0.05 between groups.*

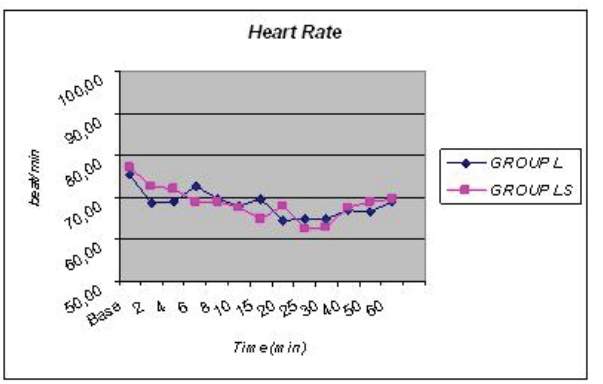

***Figure 2**. Heart Rate of patients. p > 0.05 between groups.*

of patients with maximum motor block with modified Bromage score of 3 was significantly higher in Group L than Group LS ($p<0.05$) (Table 2). Complete motor block resolution times were 186.59±21.2 min in Group L and 119.74±44.8 min in Group LS, respectively, and the difference between the groups was significant ($p<0.05$) (Table 2).

With respect to side effects and complications, no patient in either group suffered from hypotension, bradycardia, headache, dorsal pain, or vomiting ($p>0.05$). There were no significant differences in the incidence of nausea and shivering between the groups ($p>0.05$) (Table 3). Incidence of pruritus was significantly different between groups. Seven patients in Group LS (15.6%) complained of pruritus compared with none of the patients in Group L ($p<0.05$) (Table 3). In addition, no patients required supplemental analgesic medication or ephedrine or atropine during the operation and postoperative period ($p>0.05$) (Table 3).

DISCUSSION

The results of this study indicate that IT administration of 2.5 µg sufentanil combined with low-dose levobupivacaine provided adequate and effective spinal anesthesia for TURP surgery. We thought that this protocol was well suited for this type of surgery because it featured more rapid recovery of full motor power and sensory function than levobupivacaine alone. This suggests a potential synergism between sufentanil and levobupivacaine. Various compounds have been used for IT injection in spinal anesthesia, and the traditionally employed drugs are lidocaine and bupivacaine. However, both of these drugs induce an intense motor blockade, whereas an almost intact motor function of the lower extremities is required in patients undergoing TURP, given that this procedure usually lasts less than one hour and early recovery and discharge are desirable (7,8).

Lee et al. (5) used 2.6 ml 0.5% levobupivacaine alone and 2.3 ml 0.5% levobupivacaine with 15 mg fentanyl for TURP surgery. They found no difference between characteristics of motor and sensorial block. Burke et al. (9) showed that 3 ml 0.5% levobupivacaine achieved satisfactory surgical anesthesia but with an unpredictable spread of sensory blockade. The dosage of levobupivacaine used in our study was low and there was no unpredictable spread of sensory blockade. Small doses of a long-acting LA have been used to provide a short-lasting spinal block. Considering the finding of Carpenter et al. (2) that peak height is the main variable for bradycardia and hypotension during spinal anesthesia, the similar intergroup haemodynamics in our study are consistent with the fact that both of the groups showed a mean peak block height of T7.

Spinal anesthesia is associated with a risk of severe and prolonged hypotension due to the rapid-extension sympathetic block. Hemodynamic consequences are of greater importance in elderly patients with impaired physiological compensatory mechanisms. A spinal block given to a high-risk patient must provide anesthesia of high quality and with adequate duration to avoid the negative effects of any additional anesthesia. A decreased dose of LA reduces the severity and incidence of hypotension after spinal block (6,10). To prevent such failures, an opioid can be used. In this present study, a reduced dose of levobupivacaine combined with sufentanil given as a single shot induced a reliable block with adequate duration and a high quality throughout this surgical procedure. A study of 25 patients showed that combination of 7.5 mg heavy bupivacaine and 5 µg sufentanil provides adequate block for elderly patients undergoing repair of hip fracture (11). In our study, patients in the levobupivacaine group experienced a more profound and long-lasting motor block; however, in the levobupivacaine and sufentanil combination group, the degree of block was adequate for TURP surgery and the surgeon's satisfaction. The shorter recovery from motor block can be explained by the low dose of levobupivacaine and the great variability in cerebrospinal fluid volume in patients (12-14) and the advantages of a brief postoperative pain relief after IT administration of sufentanil due to its rapid clearance from the cerebrospinal fluid (13). In our study, we showed that 7.5 mg levobupivacaine with 2.5 µg sufentanil provides sufficient motor and sensorial blockade for TURP surgery.

It was shown that increasing the dose of sufentanil up to 5 µg significantly increases the incidence of pruritus without any advantage in terms of postoperative analgesia. In addition to pruritus, opioids delivered by the spinal route may produce nausea/vomiting, urinary retention, and respiratory depression mainly due to opioid action at the mu and kappa receptors (15). Consistent with data from the literature (15,16), the pruritus was dose-dependent. It was also the most frequently observed side effect, occurring in 80% of the group receiv-

ing the 7.5 μg dose of sufentanil. In our study, pruritus was higher in Group LS, as it was estimated, after IT sufentanil. The patients complained about the pruritus during recovery from the anesthesia, and reported mild pruritus, with none requiring treatment with naloxone. In addition, none of patients required supplemental analgesia during surgery or the postoperative period.

Respiratory depression after IT sufentanil is a well-known effect (17,18) and may develop within 30 min of spinal injection. None of our patients developed low oxygen saturation or respiratory depression. Should the latter occur after IT injection of sufentanil, the short-term onset might be an advantage compared to the often very late respiratory problems induced by morphine, since the patient is still in the operating room under anesthesiological observation. In this study, none of the patients had respiratory problems because of the lower dosage of the drugs.

In our study, we chose a dose of 2.5 μg sufentanil for two reasons: first, the incidence of adverse effects induced by IT sufentanil is dose-dependent and second, it is important for us to use the lowest effective sufentanil dose for TURP surgery in elderly patients. It was concluded that the 50% effective dose for IT sufentanil was 2.5 μg or less (19). The present study demonstrated that levobupivacaine with co-administered sufentanil 2.5 μg significantly decreased the dose of LA compared with levobupivacaine alone. This means that addition of 2.5 μg sufentanil enhances the potency of spinal anesthesia and produces a significant local anesthetic sparing effect primarily via a spinal site action.

In conclusion, according to the characteristics of sensory and motor blockade and hemodynamic effects, 10 mg levobupivacaine 0.5% and 7.5 mg levobupivacaine 0.5% with the addition of 2.5 μg sufentanil were considered to be convenient for clinical use in TURP surgery with spinal anesthesia and may provide adequate anesthesia with only minimal side effects in elderly patients.

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