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Comparison of intrathecal fentanyl and sufentanil in low-dose dilute bupivacaine spinal anaesthesia for transurethral prostatectomy

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Background. The administration of low-dose bupivacaine can limit the distribution of spinal block to reduce adverse haemodynamic effects. Intrathecal opioids can enhance analgesia in combination with subtherapeutic doses of local anaesthetics. We aimed at comparing the efficacy of intrathecal fentanyl and sufentanil with low-dose diluted bupivacaine for transurethral prostatectomy (TURP) in elderly patients.

Methods. Seventy patients undergoing TURP were randomly allocated into two groups. Group F (n=35) received fentanyl 25 μg+bupivacaine 0.5% (0.8 ml)+normal saline 0.3 ml and Group S (n=35) received sufentanil 5 μg+bupivacaine 0.5% (0.8 ml)+normal saline 0.7 ml—in total, bupivacaine 0.25% (1.6 ml) intrathecally. Onset and duration of the sensory block, the degree of the motor block, side-effects, and the perioperative analgesic requirements were assessed.

Results. The median peak level of the sensory block was significantly higher in Group S than in Group F (P=0.049). Group S required fewer perioperative analgesics than Group F (P=0.008). The time to the first analgesic request was longer in Group S (P=0.025). There were no differences between the groups for the onset and recovery time of the sensory block, degree of the motor block, quality of anaesthesia, or adverse effects.

Conclusions. Low-dose diluted bupivacaine with fentanyl 25 μg or sufentanil 5 μg can provide adequate anaesthesia without haemodynamic instability for TURP in elderly patients. However, sufentanil was superior to fentanyl in the quality of the spinal block produced.

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Spinal anaesthesia is the most commonly used anaesthetic technique for transurethral resection of the prostate (TURP). Most patients undergoing TURP are elderly and frequently present with cardiac, pulmonary, or other diseases. Therefore, it is important to limit the block level to reduce adverse cardiopulmonary effects in such patients.

Low-dose diluted bupivacaine can limit the distribution of spinal block and yield a comparably rapid recovery,[1] but may not provide an adequate level of sensory block. Intrathecal short-acting lipophilic opioids enhance the analgesia provided by subtherapeutic doses of local anaesthetics due to synergistic effects.[2–4] Several studies have shown that low-dose diluted bupivacaine with fentanyl can provide sufficient anaesthesia with rapid recovery in patients undergoing ambulatory surgery or TURP.[5–7] Sufentanil added to low-dose bupivacaine (7.5 mg) also provides adequate spinal anaesthesia with minimal haemodynamic effects.[8 9] To the best of our knowledge, this is the first comparative study of intrathecal fentanyl or sufentanil combined with low-dose diluted bupivacaine spinal anaesthesia for TURP in elderly patients.

We hypothesized that intrathecal fentanyl and sufentanil may show similar effects on the quality of the spinal block when combined with low-dose diluted bupivacaine in elderly patients undergoing TURP.

Methods

This study was approved by the Institutional Ethics Committee of Yonsei University Medical Center. We obtained written informed consent from 72 ASA I–III patients undergoing elective TURP for benign prostatic hypertrophy. Patients with a history of back surgery, infection at injection sites, coagulopathy, hypersensitivity to local anaesthetics or opioids, mental disturbance, or neurological disease were excluded.

A sample size calculation was performed based on previous study,[10] including the standard deviation of the time to the first request for analgesics. To detect a 30 min difference in the mean duration of the first request for analgesics (two-sided α of 5% and β of 10%), 23 subjects were required per group. We decided to include 35 patients per group to allow for possible dropouts.

This study was conducted in a randomized, double-blind, controlled fashion. One of the investigators prepared the drug solution before anaesthesia. The anaesthetic administrator and the patients were blinded to the type of drug solution and the patient groups. Using a random number sequence, patients were allocated into two groups. Group F (fentanyl group) received bupivacaine 0.5% (0.8 ml) (4 mg) in dextrose 8% solution (Marcaine® Spinal Heavy; Astra, Sodertalje, Sweden)+fentanyl 0.5 ml (25 μg)+normal saline 0.3 ml—in total, bupivacaine 0.25% (1.6 ml) intrathecally and Group S (sufentanil group) received bupivacaine 0.8 ml+sufentanil 0.1 ml (5 μg)+normal saline 0.7 ml—in total, bupivacaine 0.25% (1.6 ml) intrathecally. Patients received no premedication. ECG, non-invasive arterial pressure, and peripheral oxygen saturation were monitored. Before spinal anaesthesia, the patients received sodium chloride 0.9% (300 ml) solution over 20 min. The i.v. infusion was minimally maintained during the surgical procedure to avoid the overloading associated with the absorption of irrigating fluid. Spinal puncture was performed at L_{3-4} or L_{4-5} with a 25 G Quincke needle with the patient in a seated position. After the free flow of clear cerebrospinal fluid (CSF) was observed, the drug mixture was given over 10–15 s with cephalad orientation of the spinal needle bevel. The patients were kept in a seated position for 5 min, and then in a neutral supine position until the sensory block peaked. The level of sensory block, defined as the dermatomal segment with loss of pain sense to pin-prick test with a 22 G hypodermic needle on each side of the midthoracic line, was measured every 2 min, until it reached the peak level with four consecutive tests and then every 10 min during the surgery. We recorded the peak sensory block level, time to peak block level from injection, time to two-segment regression, use of supplemental analgesics perioperatively, and time to the first analgesic request after operation. The degree of motor block at the time of peak sensory block was scored using a modified Bromage scale (1, complete motor block; 2, almost complete motor block: able only to move the feet; 3, partial motor block: is able to move the knees; 4, detectable weakness of hip flexion: able to raise the leg but is unable to keep it raised; 5, no detectable weakness of hip flexion: able to keep the leg raised for 10 s at least; 6, no weakness at all). The quality of anaesthesia was assessed as excellent (no discomfort or pain), good (mild pain or discomfort, no need for additional analgesics), fair (pain that required analgesics), or poor (severe pain that required analgesics) during the operation. Adverse effects such as hypotension, bradycardia, nausea or vomiting, pruritus, shivering, and respiratory depression were recorded during the operation and recovery. Data regarding the volume of intraoperative irrigation fluid and preoperative ultrasound-estimated prostate volume were collected, and systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and heart rate (HR) were recorded every 5 min until the end of surgery. Hypotension was defined by a decrease in SAP of $<$90 mm Hg or $<$75% from the baseline value, and bradycardia was defined as HR $<$45 beats min^{-1}.

Statistical analysis was performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA). Patient characteristics (weight, height, duration of operation, irrigation volume, and preoperative prostate volume) were analysed using Student's *t*-test. Inter-group differences in age, peak block level, and maximum motor block scale were compared using the Mann–Whitney *U*-test. Time to peak block level, time to two-segment regression, and time to the first analgesic requirement were analysed using Student's *t*-test. Categorical data (analgesics and side-effects) were compared using the χ^2 test. A *P*-value of $<$0.05 was considered statistically significant.

Results

Spinal anaesthesia was successfully accomplished in all patients. Forty-nine of 70 patients (70%) had one or more diseases, such as hypertension, diabetes mellitus, coronary disease, arrhythmia, chronic obstructive pulmonary disease, and parkinsonism.

Patient characteristics were similar between the groups (Table 1). The overall quality of spinal anaesthesia was also similar in both groups (Table 2). No significant differences were found in SAP or DAP and HR between the groups.

The peak sensory block level [median (range)] was significantly higher in Group S [T11 (S1–T6)] than in Group F [L1 (S1–T6)] (P=0.049) but no significant differences occurred in the time to peak block level, time to

Table 1 Patient characteristics. Values are expressed as median (range) or mean (SD)

	Group F (n=35)	Group S (n=35)
Age (yr)	69 (58–83)	70 (60–85)
Weight (kg)	66.7 (10.5)	67.0 (9.5)
Height (cm)	167.9 (4.6)	166.6 (6.5)
Duration of operation (min)	40.6 (23.9)	36.9 (21.5)
Irrigation volume (litre)	9.7 (6.3)	8.8 (4.8)
Prostate volume (g)	49.8 (27.7)	49.2 (26.0)

Table 2 Quality of anaesthesia. The data are reported as number of patients. The quality of anaesthesia 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

	Group F (n=35)	Group S (n=35)
Excellent	32	31
Good	2	3
Fair	1	1
Poor	0	0

Table 3 Characteristics of spinal blocks. Values are median (range) or mean (SD). Modified Bromage scale: 1, complete motor block; 2, almost complete motor block, the patient is able only to move the feet; 3, partial motor block, the patient is able to move the knees; 4, detectable weakness of hip flexion, the patient is able to raise the leg but is unable to keep it raised; 5, no detectable weakness of hip flexion, the patient is able to keep the leg raised for 10 s at least; 6, no weakness at all, the patient is able to perform partial knee bend while supine. *Significant difference at P<0.05

	Group F (n=35)	Group S (n=35)
Peak sensory block level	L1 (S1–T6)	T11 (S1–T6)*
Time to peak block (min)	15.4 (9.8)	15.1 (9.8)
Time to two-segment regression (min)	94.9 (28.8)	94.4 (29.8)
Maximum motor block; modified Bromage scale	5 (2–5)	4 (2–5)

two-segment regression, and the degree of motor block. None of the patients had complete motor block (Table 3).

During the postoperative period, 20 patients in Group F (57.1%) *vs* nine patients in Group S (25.7%) required analgesics (P=0.008) and the time to the first analgesics request was longer in Group S (P=0.025). There were no differences in the adverse effects between the two groups (Table 4).

Table 4 Supplemental analgesic use and side-effects. Values are mean (SD) or number of patients (%). *Significant difference at P<0.05

	Group F (n=35)	Group S (n=35)
Supplemental analgesics		
Intraoperative	1 (2.9)	1 (2.9)
Postoperative	20 (57.1)	9 (25.7)*
Time to first analgesic request (h)	7.0 (3.7)	10.6 (3.8)*
Hypotension/bradycardia	0	0
Nausea	2	0
Vomiting	0	0
Pruritus	0	0
Shivering	1	0
Respiratory depression	0	0

Discussion

In this study, we found that the addition of sufentanil 5 μg to a diluted small-dose bupivacaine for spinal anaesthesia effectively increased the sensory block level and postoperative analgesic efficacy without increasing the intensity of the motor block or prolonging the recovery time in elderly patients.

Considering that the prostate gland is mainly supplied by sensory branches from the pelvic plexus, a sacral block may provide sufficient analgesia for TURP, but the block must extend to sensory dermatome T12–L1 in order to avoid the pain or abdominal discomfort from the bladder distention with irrigation fluid.[11 12]

The use of low-dose diluted anaesthetic can shorten recovery time from spinal anaesthesia in addition to limiting the distribution of the block. However, it may not provide an adequate level of sensory block.[1 5] The addition of fentanyl (20–25 μg) to low-dose bupivacaine (4 mg) has been reported to increase the perioperative quality of spinal blocks with fewer cardiovascular changes in elderly patients,[7 13] as has the addition of sufentanil (5 μg) in combination with low-dose bupivacaine (7.5 mg).[8 9] These results are consistent with the results of studies demonstrating that intrathecal opioids enhance analgesia when added to subtherapeutic doses of local anaesthetics.[2 4] This synergism is characterized by enhanced somatic analgesia without any associated effects on the level of local-induced sympathetic or motor block.[3]

We used fentanyl 25 μg and sufentanil 5 μg because there was no benefit to increasing intrathecal dose beyond fentanyl 25 μg or sufentanil 5 μg in regard to duration of analgesia in a previous study.[14] Two independent studies have revealed that the median effective doses (ED_{50}) of intrathecal sufentanil and fentanyl were 2.6 and 14 μg, respectively.[15 16] And relative potency for intrathecal fentanyl to sufentanil in labour analgesia was 1:4.4 at the ED_{50} level.[17] Therefore, intrathecal fentanyl 25 μg and sufentanil 5 μg could be considered as an equipotent dose.

The reasons for the increased block level in the sufentanil group compared with the fentanyl group may be related to the density of drug solution or opioid receptor affinities. There are several factors influencing the spread of local anaesthetic solutions within CSF, such as patient characteristics, physical properties of CSF, injection techniques, and also the dose and properties of the particular drug.[18 19] The density of compounds is believed to be a major determinant in controlling the extent of neural block.[20] Fentanyl and sufentanil have similar densities, and the density of sodium chloride (0.9%) is higher than that of fentanyl or sufentanil.[21] In our study, bupivacaine 0.25% (1.6 ml) consisted of bupivacaine 0.5% (0.8 ml), fentanyl 0.5 ml, and normal saline 0.3 ml (fentanyl group) or bupivacaine 0.5% (0.8 ml), sufentanil 0.1 ml, and normal saline 0.7 ml (sufentanil group). Therefore, the

solution with sufentanil was more dense. Since a density difference as small as 0.0006 g ml^{-1} may influence the movement of local anaesthetics in a spinal canal model,[19] the differences in drug mixture density may be an explanation for the differences we observed in peak block levels for the two groups in this study. The other possible cause may be differing opioid receptor affinity. Sufentanil has a higher affinity for the μ-opioid receptor than fentanyl,[22] so it may increase dermatomal spread. On the other hand, the peak block level was variable in each group (Table 3). This could be due to variability in the cephalic spread of the block among the patients resulting from variability in CSF volume among individuals.[23]

The duration of postoperative analgesia for fentanyl and sufentanil was previously reported to be 1–4 and 2–5 h, respectively, after intrathecal administration as an adjunct to surgical spinal anaesthesia and analgesia.[24] In our study, the incidence of postoperative analgesic requirement was significantly lower in the sufentanil group (P=0.049) and the time to the first analgesic request was longer in the sufentanil group (P=0.008) (Table 4). Although it has been reported that the effects of postoperative analgesia are brief after intrathecal administration of sufentanil because of its rapid clearance from the CSF,[25] intrathecal sufentanil may be superior to fentanyl for postoperative pain relief in elderly patients undergoing TURP. Further research investigating differences in the inherent physiochemical properties of intrathecal fentanyl and sufentanil in elderly patients is warranted.

The incidence of adverse effects was very low in this study (Table 4). Pruritus has previously been reported as the most common adverse effect of intrathecal fentanyl[24 26] and sufentanil,[27 28] which was not the case in our study, but it may not be a problem in elderly patients.

In conclusion, low-dose diluted bupivacaine [bupivacaine 0.25% (4 mg) in dextrose 8%] with fentanyl 25 μg or sufentanil 5 μg provides adequate anaesthesia without haemodynamic instability for TURP in elderly patients. Sufentanil is superior to fentanyl, as it facilitates the spread of the block and offers greater postoperative analgesic efficacy.

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