SPINAL ANESTHESIA FOR TRANSURETHRAL RESECTION OPERATIONS: LEVOBUPIVACAINE WITH OR WITHOUT FENTANYL

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Abstract

Background: The objective of the present study was double fold; to compare the characteristics of spinal blocks produced by 0.5% levobupivacaine with and without fentanyl in transurethral resection and to test the hypothesis that, fentanyl added to levobupivacaine, may be used as an alternative to pure levobupivacaine solution, in spinal anesthesia.

Methods: Forty males, aged >60 years, ASA I-III patients scheduled for elective transurethral resection were included in a prospective, randomized, double-blinded study. Following a spinal tap, intrathecal injection in Group L (n = 20), 2.5 mL of 0.5% levobupivacaine and in Group LF (n = 20), 2.2 mL of 0.5% levobupivacaine with fentanyl 15 μg (0.3 mL) was performed. The characteristics of sensory and motor block, hemodynamic data, side effects, patient and surgeon satisfaction were recorded. Patients were observed until the level of sensory block was S_1 and the Bromage score was 0.

Results: There were no significant differences between the two groups for patient demographic, intraoperative, hemodynamic parameters, side effects and satisfaction. The highest level of sensory block was T_9 in the Group L, and T_6 in the Group LF ($p = 0.001$). Duration of motor block was shorter in Group LF than in Group L (291.00 ± 81.08 min in Group L; 213.75 ± 59.49 min in Group LF) ($p = 0.001$).

Conclusion: Both regimes are effective, and the addition of fentanyl to levobupivacaine may offers the advantage of shorter duration of motor block and may be used as an alternative to pure levobupivacaine solution in spinal anesthesia, for transurethral resections.

Key Words: Anesthetic technique, anesthesia, spinal; Anesthetics, local, levobupivacaine; Analgesics, opioid, fentanyl.

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Introduction

Spinal anesthesia is widely used for transurethral resections because it allows early recognition of symptoms caused by overhydration, transurethral resection of prostate (TURP) syndrome, and bladder perforation.

Many patients undergoing TURP or TURBT (transurethral resection of bladder tumour) have coexisting pulmonary or cardiac disease[1]. By reducing the dose of local anesthetic used, side effects can be decreased. However, a low dose of local anesthetic cannot provide an adequate level of sensory block.

Levobupivacaine is the S(-)- enantiomer of racemic bupivacaine. Levobupivacaine has similar efficacy but an enhanced safety profile when compared to bupivacaine, a major advantage in regional anesthesia[2,3]. Intrathecal opioids added to local anesthetics enhance analgesia without intensifying motor and sympathetic block, and make it possible to achieve successful anesthesia in spite of the use of a low dose local anesthetic[4-6].

Levobupivacaine may be a proper alternative local anesthetic for spinal anesthesia in elderly patients with coexisting systemic disease for TUR operations. By adding fentanyl to levobupivacaine, side effects can be reduced. In this study we aimed to investigate the characteristics and side effects of spinal blocks achieved by levobupivacaine with or without fentanyl, for TURP-BT operations.

Methods and Materials

After obtaining the approval of the Ethics Committee of our Institution and patients' informed consent, 40 males, aged >60 years, ASA I-III patients scheduled for elective TURP or TURBT operations were included in a prospective, randomized, double-blind study. Patients with uncontrolled hypertension, infection at the injection site, disorders of coagulation, history of headache, reluctance to the procedure, neurologic disease or hypersensitivity to amide local anesthetics or fentanyl, were excluded.

No premedication was given. Patients were randomly assigned into two equal groups for spinal anesthesia according to numbers inserted in sealed envelopes. After routine monitoring and infusion of 8 $mL.kg^{-1}$ of sodium chloride 0.9% solution, baseline hemodynamic values were recorded and then spinal anesthesia was performed with the patient in the left lateral position, using a 25 G Quincke needle at the L3-4 interspace and a midline approach. In Group L (n = 20), 2.5 mL of 0.5% levobupivacaine (Abbott Laboratories, Elverum, Norway) and in Group LF (n = 20), 2.2 mL of 0.5% levobupivacaine with fentanyl citrate 15 μg (0.3 mL) (Abbott Laboratories, North Chicago, USA) were administered via intrathecal injection.

Solutions were prepared by another anesthesiologist so that the anesthesiologist performing the block was unaware of which drug was injected.

Densities of the solutions were measured at 37°C by refractometry (T2-NE, Atago Co. Ltd, Japan). The densities of the pure levobupivacaine and levobupivacaine plus fentanyl solutions were 1.008 and 1.007, respectively.

The direction of the needle aperture was cranial during the injection. After free flow of cerebrospinal fluid was verified, anesthetic solution was given in 15 s without barbotage or aspiration. Immediately after the injection, the patients were placed in the supine position.

Heart rate (HR), non-invasive systolic, diastolic and mean arterial blood pressures (SAP, DAP, MAP) and oxygen saturation (SpO_2) were recorded every 2.5 min for 15 min after intrathecal injection and every 5 min thereafter. A 30% decrease from baseline SAP or SAP <90 mmHg was treated with incremental iv boluses of ephedrine 5 mg and bradycardia (HR <45) was treated with iv atropine 0.5 mg. Supplementary oxygen 2 L min^{-1} was given via a nasal cannulae if SpO_2 was less than 93% with the patient breathing ambient air.

Sensory and motor block were assessed every 2.5 min for 15 min after intrathecal injection and every 5 min thereafter until the sensory block regressed to S_1. Anesthesia was considered adequate for surgery if pain sensation as assessed by the pinprick test, was lost at the T_{10} level. Patients were then placed in the lithotomy position and operation started.

The time to achieve sensory block of T_{10}, highest level of sensory block, the time to two-segment

regression of sensory block and the time to regression of sensory block to S_1, were recorded.

Motor block was assessed using the Modified Bromage Scale (0 = no motor block, 1 = inability to raise extended legs, 2 = inability to flex knees, and 3 = inability to flex ankle joints). Onset time of motor block, maximum motor block (Bromage score), duration of motor block (the time from intrathecal injection to the regression of motor block to Bromage score = 0) and duration of complete motor block (the time from intrathecal injection to the regression of the block to a Bromage score of <3) were recorded also. Complete motor block was defined as a Bromage score of 3.

Pain was assessed every 5 min from the beginning of surgery using the 10 score Visual Analog Pain Scale (VAS). In the event a patient complaned of a pain score over three, 1.5 μ. kg^{-1} iv fentanyl would be administered, and in case of failed spinal block, general anesthesia would be performed. Midazolam would be given intravenously in 0.5 mg increments as indicated for anxiolysis.

Volume of glycine used, duration of surgery and patient and surgeon satisfaction were recorded at the end of the operation. Patients were interviewed regarding their opinion of the anesthetic procedure. Likewise, the surgeon was asked to estimate the operating conditions on a scale of excellent, good, fair and poor. Patients were observed until the level of sensory block was S_1 and the Bromage score was 0.

Adverse effects such as hypotension, bradycardia, nausea, vomiting, shivering, sedation, respiratory depression and pruritus, were recorded. Nausea and vomiting were treated with metoclopramide 10 mg iv. Paracetamol 1 gr iv (Bristol Myers Squibb, Renaudin Laboratories, Itxassou, France) was given during infusion lasting 15 min when the patient complained of pain in the postoperative period. The patients were discharged from the recovery room after the motor block was completely resolved, had stable vital signs, minimal nausea or vomiting and no severe pain or bleeding.

Our primary endpoint was the difference in the duration of motor block between the two groups. Other endpoints included were the difference, between the two groups, in the characteristics of sensory block, operating conditions, hemodynamic and side effects.

A sample size of 19 patients per group was required to detect a 30 minute difference according to the duration of motor block between two groups with a power of 80% and $\alpha = 0.05$, based on a pilot study. Twenty patients were included in each group. All of the data were analysed with SPSS 12 (SPSS Inc., Chicago, IL., USA) software. Descriptives were quoted as mean ± SD, median (range), number (incidence) as appropriate. Statistical analyses were performed using Student's t test (for parametric data) and Mann-Whitney U test (for non-parametric data). The incidences of side effects and satisfactions were analysed using Fisher's exact test and Chi-Square test. The paired t-test was used to investigate hemodynamic changes over time in each group. Statistical significance was set at the $p<0.05$ level.

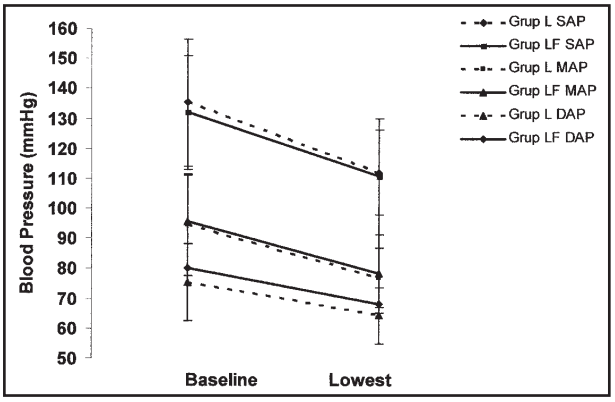
Results

There were no significant differences between the two groups in demographic data, ASA classification, type and duration of operation or volume of glycine used ($p>0.05$) (Table 1).

Hemodynamic parameters were similar in both groups before and during operation ($p>0.05$) (Figure 1).

Fig. 1

Baseline and lowest blood pressures after spinal anesthesia



L = Levobupivacaine; LF = Levobupivacaine plus fentanyl. SAP = Systolic arterial pressure, MAP = Mean arterial pressure, DAP = Diastolic arterial pressure. There were no significant differences between two groups ($p>0.05$)

The highest level of sensory block was T_9 (T_4-T_{10}) in Group Lو and T_6 (T_3-T_{10}) in Group LF, respectively ($p = 0.001$). The time to achieve sensory block of T_{10}, time to two-segment regression of sensory block, time

Table 1
Demographic and Perioperative Data

	Group L (n = 20)	Group LF (n = 20)	p
Age (yr)	70.20 ± 7.33	68.80 ± 5.80	0.674
Weight (kg)	71.15 ± 10.31	71.85 ± 7.23	0.902
Height (cm)	170.20 ± 6.04	171.55 ± 4.23	0.369
ASA Grade (I/II/III)	2/13/5	3/13/4	0.856
Type of operation			
TUR-Prostate/Bladder tumour	12/8	13/7	0.744
Duration of operation (min)	68.00 ± 26.82	74.75 ± 32.50	0.478
Volume of glycine (L)	15.65 ± 10.60	17.00 ± 13.36	0.755

Data are means ± standard deviation or number of patients.
L = Levobupivacaine; LF = Levobupivacaine plus fentanyl.

to regression of sensory block to S_1, onset time of motor block, maximum motor block and duration of complete motor block, were similar in both groups (p>0.05). On the other hand, duration of motor block was shorter in Group LF than Group L (p = 0.001) (Table 2).

No patient required supplemental oxygen, analgesia or anxiolysis intraoperatively. There were no significant differences between the two groups with respect to side effects (Table 3) or patient or surgeon satisfaction (p>0.05).

The surgeon satisfaction was 35% excellent, 65% good in Group L, 50% excellent, 50% good in Group LF and the patient satisfaction was 35% excellent, 55% good, 10% fair in Group L, 65% excellent, 30% good, 5% fair in Group LF, respectively (p = 0.337 for surgeon satisfaction and p = 0.165 for patient satisfaction).

Table 3
Side Effects in Groups L and LF

	Group L (n = 20)	Group LF (n = 20)	p
Hypotension	3 (15)	3 (15)	1.0
Bradycardia	3 (15)	4 (20)	1.0
Nausea	2 (10)	1 (5)	1.0
Vomiting	0	0	-
Shivering	0	0	-
Sedation	0	4 (20)	0.106
Respiratory	0	0	-
depression	0	0	-
Pruritus			

Data are number of occurrences and incidences (%).
L = Levobupivacaine; LF = Levobupivacaine plus fentanyl.

Table 2
Characteristics of Spinal Anesthesia in Two Groups

	Group L (n = 20)	Group LF (n = 20)	p
Sensory block			
Time to T_{10} (min)	6.50 ± 2.62	6.32 ± 3.50	0.525
Highest level (dermatome)	T9 (T4-T10)	T6 (T3-T10)	0.001*
Time to two segment regression (min)	107.00 ± 52.35	106.00 ± 48.62	0.950
Time to regression to S_1 (min)	376.75 ± 80.03	337.25 ± 61.29	0.088
Motor block			
Onset time of Bromage 1 (min)	4.00 ± 1.49	3.60 ± 1.07	0.931
Maximum motor block (n)			
(Bromage Score 3/2)	19/1	18/2	0.553
Duration of motor block (min)	291.00 ± 81.08	213.75 ± 59.49	0.001*
Duration of complete motor block (min)	167.00 ± 58.47	145.75 ± 51.79	0.231

Data are means ± standard deviation, median (range) or number of patients.
L = Levobupivacaine; LF = Levobupivacaine plus fentanyl.
* p<0.05: A significant differences between the two groups.

Discussion

This study demonstrates that 15 μg fentanyl added to 2.2 mL of 0.5% levobupivacaine provides adequate anesthesia which is similar to that obtained from 2.5 mL of 0.5% levobupivacaine for TURP-BT operations, and the lower-dose of local anesthetic used with fentanyl may offer the advantage of shorter duration of motor block.

It has been well documented that a combination of opioids and local anesthetics administered intratechally has a synergistic analgesic effect[7-8]. The use of racemic bupivacaine with fentanyl in spinal anesthesia for urologic surgery is effective. Kuusniemi et al found that the addition of fentanyl 25 μg to 5 mg of bupivacaine for spinal anesthesia resulted in effective anesthesia with motor block of short duration[5]. Kararmaz et al compared the intrathecal injection of bupivacaine 4 mg with fentanyl 25 μg and bupivacaine 7.5 mg and found that the sensory block was adequate for surgery in both groups, but the density and duration of motor block were more in the bupivacaine group[9].

Ben-David et al found that a small dose of fentanyl (10 μg) added to dilute bupivacaine(3 mL of 0.17% solution) in ambulatory patients undergoing knee arthroscopies intensified and increased the sensory block without increasing the intensity of motor block or prolonging recovery[4]. Goel et al showed that intrathecal fentanyl 12.5 μg added to bupivacaine 0.17% 5 mg in a total volume of 3 mL produced optimal surgical conditions for minor urological procedures[10]. Reuben et al suggested that a combination of low dose fentanyl (<20 μg) and bupivacaine produced satisfactory analgesia in elderly patients undergoing lower extremity revascularization procedures, in their study[11].

Beers et al reported that although a subarachnoid block $\geq L_1$ provided adequate analgesia during TURP operations, the level of sensory block at T_{10} was necessary to provide adequate analgesia because bladder distension elicited pain under the block levels $<T_{10}$[12].

At the time of designing our study there was only one published trial that compared plain solutions of 0.5% levobupivacaine with or without fentanyl, in spinal anesthesia[13]. Lee et al[13] compared the 2.6 mL of 0.5% levobupivacaine and 2.3 mL of 0.5% levobupivacaine with fentanyl 15 μg in spinal anesthesia, but there were no data regarding time to two segment regression, time to S_1 regression of sensory block and onset time, duration of motor block or complete motor block. In addition, there was no data about the densities of solutions and rate of injection. Our study was therefore designed to give more details.

Although Lee et al found that highest level of sensory block was similar between the two groups, in our study, however the combination of levobupivacaine with fentanyl reached a higher level of sensory block. The resolution of motor block was faster in this combination group than in the levobupivacaine group. Low dose local anesthetic used in levobupivacaine with fentanyl group, offered the advantage of shorter duration of motor block. This result was consistent with the resulting from the other studies which investigated the effects of bupivacaine with or without fentanyl in spinal anesthesia[5,9]. The clinical significance of a reduced duration of motor block resuting from lower-dose levobupivacaine plus fentanyl would be early ambulation. The duration of sensory block to S_1 level, however, was not different between the groups, so the overall block resolution was not different. Our results may be used as a building stone for further dose-response studies.

The duration of injection and baricity of injected solutions may be reasonable factors explaining the differences in the highest level of sensory block between two our study that of Lee's. We injected the local anesthetic solution in 15 s where as Lee did not suggested this time.

In considering our measurements, levobupivacaine plus fentanyl solution is more hypobaric than the pure levobupivacaine solution. No data is given about the densities of solutions in the study of Lee[13]. Opioids such as fentanyl are hypobaric and when added to a local anesthetic will render the subsequent mixture even more hypobaric[14]. Parlow et al stated that the addition of opioids to isobaric local anesthetics alters the density of the resulting solutions, as well as the direction and extent of spread in a spinal model[15].

In Lee et al study, three patients (12%) in levobupivacaine group developed shivering. Hypotension occured in four patients (16%) (one

in group levobupivacaine and three in group levobupivacaine with fentanyl). No patient had nausea, vomiting or pruritis. In our study, side effects related to the spinal fentanyl (pruritus and vomiting) did not occur similar to the results of Lee et al.

Patient satisfaction was good in all cases in the study of Lee et al[13]. In our study, there were no significant differences between the two groups with respect to side effects or patient and surgeon satisfaction.

In conclusion, both regimes are effective, and fentanyl added to levobupivacaine, in the dosage used in the present study, may offer an advantage of decreased duration of motor block and could be an alternative to the use of pure levobupivacaine solution in spinal anesthesia for transurethral resections.

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