

# COMPARISON OF THE ANESTHETIC EFFECTS OF INTRATHECAL LEVOBUPIVACAINE + FENTANYL AND BUPIVACAINE + FENTANYL DURING CAESAREAN SECTION

AYGEN TURKMEN\*, DONDU GENÇ MORALAR\*\*, AHMET ALI\*\* AND AYSEL ALTAN\*

## Abstract

**Background:** Regional *anesthesia* techniques are increasingly preferred for caesarean section. The aim of the present study was to compare the anesthetic effects of levobupivacaine + fentanyl and bupivacaine + fentanyl on the mother and newborn during elective caesarean section under spinal anesthesia.

**Methods:** In this prospective study, 50 gravidas, who were scheduled for cesarean section were enrolled after Ethics Committee approval had been obtained. The patients were randomized into one of the following two groups: bupivacaine + fentanyl group (group B; n = 25), 7.5 mg of 0.5% bupivacaine + 15 µg fentanyl intrathecally; levobupivacaine + fentanyl group (group L; n = 25), 7.5 mg of 0.5% levobupivacaine + 15 µg fentanyl intrathecally. The patients were immediately placed in supine position with 20-30° head up-tilt. The level of sensory and motor blocks were evaluated by pin-prick test and Bromage scale, respectively.

**Results:** The time to sensory block at the T4 dermatome was shorter in group B (group B, 4.8 min; group L, 6.0 min; p <0.05). The time to maximum motor block was also shorter in group B (group B, 3.4 min; group L, 4.7 min; p <0.05). The duration of analgesia was longer in group L compared to group B (group B, 102 min; group L, 118 min; p <0.05).

**Conclusions:** Time to sensory and maximum motor block was shorter in the bupivacaine + fentanyl group. On the other hand, a longer duration of analgesia was achieved in the levobupivacaine + fentanyl group. Although levobupivacaine is a novel drug, it is a good alternative for bupivacaine.

**Key words:** Caesarean section, levobupivacaine, bupivacaine, fentanyl, hemodynamic effects.

\* Assistant Professor, Okmeydani Training and Research Hospital, Anesthesiology and Reanimation Clinic, Istanbul, Turkey.

\*\* Okmeydani Training and Research Hospital, Anesthesiology and Reanimation Clinic, Istanbul, Turkey.

**Corresponding author:** U. Aygen Turkmen, Atakoy Konaklari B2-4 Blok No: 2 Bakirkoy/Istanbul-Turkey, Telephone: +905325175872. E-mail: aygenturkmen@hotmail.com

## Introduction

Regional *anesthesia* techniques are increasingly preferred for caesarean section. With small amounts and various combinations of drugs, systemic and pharmacologic effects are avoided, a deep surgical anesthesia is obtained, and a safer, beneficial, and comfortable anesthesia is provided for the mother and child compared to other techniques. Recently, levobupivacaine, the pure L (-) enantiomer of bupivacaine, is preferred during spinal anesthesia due to its lower cardiovascular side effects and central nervous system toxicity<sup>1-4</sup>. The addition of low doses of opioids to local anesthetics during spinal anesthesia for caesarean section decreases the incidence of local anesthetic (LA)-related side effects, reduces the time to onset of the anesthetic effect, and increases the quality of intra- and post-operative analgesia by reducing the administered dose of the LA<sup>5</sup>. The addition of intrathecal fentanyl to spinal anesthesia is associated with an early time to onset of the *anesthetic effect* and a low incidence of side effects.

There are various factors affecting the spread and duration of block during spinal anesthesia. Factors affecting the spread of the block include volume and dose of the injected local anesthetic agent, rate of injection of the anesthetic solution, position of the patient during and immediately after the injection, age, weight and height of the patient, anatomical structure of the vertebral column, cerebrospinal fluid volume (CSF), level and velocity of the injection, barbotage, location and diameter of the tip of the injection needle, intra-abdominal pressure, pressure of the CSF, and concentration of the local anesthetic. On the other hand, type of the local anesthesia, level of anesthesia and addition of a vasopressor are known to affect the duration of anesthesia<sup>6</sup>.

The aim of the present study was to investigate the effects of low doses of either levobupivacaine or bupivacaine, with intrathecal fentanyl on maternal anesthesia, analgesia, hemodynamics, and the newborn, during elective caesarean section under spinal anesthesia.

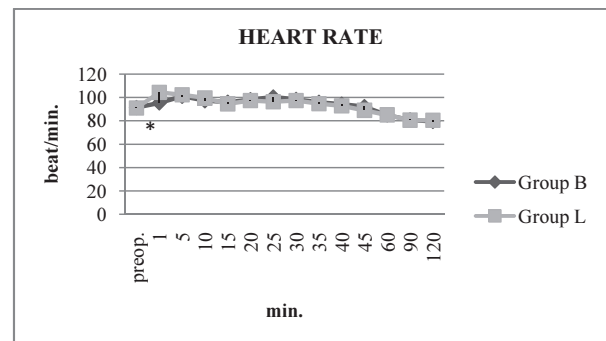
## Materials and Methods

Fifty gravidas (age range, 18-40 years; and

≥37 weeks gestation) who were scheduled for elective caesarean section under spinal anesthesia were enrolled in the study after obtaining Ethics Committee approval and written informed consents from the patients. All procedures performed were in accordance with Declaration of Helsinki. All patients were American Society of Anesthesiologists (ASA) class I-II. The exclusion criteria included allergy to the study medications, contraindication to spinal anesthesia, objection to the use of spinal anesthesia, and morbid obesity.

Injection of 6 % hydroxyethyl starch (HES 130; 7 mL/kg) was administered pre-operatively to all patients within 15-30 minutes, and heart rate (HR), mean arterial pressure (MAP), and peripheral oxygen saturation (SpO<sub>2</sub>) values were monitored. Oxygen therapy was administered to all patients at a rate of 4-6 L/min until delivery.

Fig 1  
Heart Rate



\* p < 0.05

\* HR at the first minute was lower in group B compared to group L. The MAP values of the groups were not significantly different.

Following closed-envelope randomization, patients were divided equally into two groups. The study drugs were prepared in 1.8 mL volumes as 7.5 mg of 0.5% levobupivacaine + 15 µg fentanyl in group L (n = 25) and 7.5 mg of 0.5% bupivacaine + 15 µg fentanyl in group B (n = 25). Dura was reached through the L3-L4 interspace using a 22-gauge Quincke needle while the patient was in a sitting position. The study drugs were injected into the subarachnoid space. The subjects were immediately placed in supine position with 20-30° head up-tilt. The MAP, HR, and SpO<sub>2</sub> values were monitored and recorded during the pre-operative period, from the

1<sup>st</sup> to the 45<sup>th</sup> peri-operative min at 5 min intervals, and then at 45., 60., 90., and 120. Min. intervals. The sensory block was evaluated by pin-prick test. Surgery proceeded when the sensory block at the T4 dermatome was achieved. The time to sensory block at the T4 dermatome and the time to two segment regression were recorded. The level of maximum motor block, the time to maximum motor block, and the duration of motor block were recorded using the Bromage scale (Table 1). The side effects (nausea, vomiting, shivering, headache, sedation, itching, and the need for sedation) were monitored and recorded. A decrease of 20% below the baseline level in MAP or a systolic arterial blood pressure of < 90 mmHg was considered as hypotension. Under these conditions, treatment with repeated doses of ephedrine (5 mg iv) and fluid loading was scheduled to be administered until the blood pressure returned to normal levels. Administration of 0.5 mg of atropine was scheduled when the HR decreased to <50 beats per minute. Respiratory depression was considered to occur at a SpO<sub>2</sub> <92%. Administration of 0.1 mg of naloxone was scheduled for the treatment of respiratory depression. Administration of naloxone (40 µg iv) was scheduled for long-lasting skin conditions marked by itching, while metoclopramide (10 mg iv) was scheduled in the presence of nausea.

Table 1  
Bromage Scale

SCORE	Criteria
0	Free movement of legs and feet
1	Just able to flex knees with free movement of feet
2	Unable to flex knees, but with free movement of feet
3	Unable to move legs or feet

Apgar scores were used to evaluate the health of newborn infants at 1 and 5 minutes after delivery by a pediatrician, who was blinded to the study groups.

All statistical analyses were carried out using SPSS for Windows, version 15.0 (SPSS Inc., Chicago, IL, USA). Results are expressed as the mean ± SD. A t-test and Mann-Whitney U test were used for comparison of quantitative variants. Qualitative variants were compared using a chi-square test. A p <0.05 was considered statistically significant.

## Results

In the present study, the anesthetic effects of levobupivacaine + fentanyl and bupivacaine + fentanyl were compared in patients who were scheduled for caesarean section under spinal anesthesia. There was no statistically significant difference between the two study groups in terms of demographic characteristics (Table 2).

Hypotension was encountered in 13 patients in group B and 9 patients in group L. The MAP values of the groups were not significantly different. HR at the first minute was lower in group B compared to group L (Group B: 95.3 ± 14.03; Group L: 104.3 ± 15.1) (p <0.05) (Fig. 1). The time to sensory block at the T4 dermatome was shorter in group B compared to group L (4.84 ± 1,62; min and 6.07 ± 1.59 min, respectively; p <0.05) and the duration of analgesia was longer in group L compared to group B (118.2 ± 14.9 min and 102,8 ± 18.1 min, respectively; p <0.05) (Table 3). The time to achieve maximum Bromage score was found to be shorter in group B compared to group L (3.44 ± 1.32 min and 4.71 ± 1,89 min, respectively; p <0.05) (Table 4). The number of patients with Bromage grade 3 block was 17 in the levobupivacaine group and 22 in the bupivacaine group. The difference between the

Table 2  
Demographic characteristics

	Group B (n = 25)	Group L (n = 25)	p
Age (years) mean ± SD	26,76 ± 5,6	25,60 ± 5,5	0,408
Weight (kg) mean ± SD	73,32 ± 9,06	74,16 ± 10,5	0,756
Height (cm) mean ± SD	160,9 ± 4,43	158,1 ± 10,1	0,297

There were no statistically significant differences between the two groups.

Table 3  
Sensory block

	Grup B	Grup L	p
Time to sensory block at the T4 dermatom (min.) (mean±SD)	4.84±1,62	6.07±1.59	0,005*
Time to two dermatome regression (min.) (mean±SD)	59,40± 9,38	63,4±12,80	0,303
Duration of analgesia (min.) (mean±SD)	102,80±18.14	118.20±14.92	0,001*

\* Duration of analgesia and the time to sensory block at the T4 dermatome was shorter in group B compared to group L.

time to two dermatome regression (Group B: 59 min.; Group L: 63 min.) and the maximum Bromage score was not statistically significant (Group B: 94.6 min.; Group L: 89.2 min.) ( $p > 0.05$ ).

In group B, nausea was observed in two patients, shivering in one patient, headache in one patient, sedation in three patients, and itching in two patients. In group L, there was nausea in one patient, shivering in one patient, headache in two patients, sedation in two patients, itching in one patient, and the need for sedation in one patient. No significant difference existed between the groups with respect to side effects ( $p > 0.05$ ). The Apgar scores were not significantly different between the groups ( $p > 0.05$ ).

## Discussion

In our study, hypotension was noted in 13 patients in group B and in 9 patients in group L. No statistically significant difference was observed between the groups with respect to MAP.

In the study conducted by Gautier *et al.*<sup>7</sup>,

isobaric bupivacaine (8 mg), ropivacaine (12 mg), and levobupivacaine (8 mg) were administered to the patients ( $n = 90$ ) who were scheduled for caesarean section; however, no significant difference was shown in the incidence of hypotension<sup>7</sup>.

Erdil *et al.*<sup>8</sup> conducted a study involving 80 patients divided into two groups who were scheduled for transurethral resection of the prostate (TURP) and administered 1.5 mL of 0.5% levobupivacaine and bupivacaine, in combination with 15 µg fentanyl. Unlike our study; the MAP that their study was lower in the bupivacaine group between 10 and 30 min after injection.

In the current study, the time to sensory block at the T4 dermatome was shorter in group B. The time to two dermatome regression was 59 min in group B and 63 min in group L; there was no significant difference between the groups ( $p > 0.05$ ).

In the study by Seyhan *et al.*<sup>9</sup>, the time to sensory block at T4 was compared between groups during caesarean section by administration of 9 mg of hyperbaric bupivacaine in group I, 8 mg of hyperbaric

Table 4  
Motor block

	Group B	Group L	P
Max. Bromage Score Mean ± SD	2,88 ± 0,33	2,68 ± 0,47	0,091
Time to achieve Max. Bromage Score (min.) Mean ± SD	3.44 ± 1.32	4.71 ± 1,89	0,020*
Duration of motor block time (min.) Mean ± SD	94,60 ± 19,89	89,20 ± 12,13	0,331

\* The time to achieve maximum Bromage score was found to be shorter in group B compared to group L.

bupivacaine + 10 µg of fentanyl in group II, and 7 mg of hyperbaric bupivacaine + 20 µg of fentanyl in group III. It was demonstrated that the time to sensory block at T4 was minimum in group II ( $260 \pm 58$  sec,  $225 \pm 56$  sec, and  $264 \pm 76$  sec, respectively). The difference between the groups was statistically significant ( $p < 0.01$ ). The time to resolution of motor block was significantly shorter in group III, compared to groups I and II ( $p < 0.01$ ).

In a study by Bremerich *et al.*<sup>10</sup> involving 60 patients who were scheduled for caesarean section and were administered 0.5% levobupivacaine (10 mg) and 0.5% bupivacaine (10 mg) in combination with opioid (10 and 20 µg of fentanyl and 5 µg of sufentanil), the duration of motor block was found to be shorter with levobupivacaine compared to bupivacaine. The number of patients with Bromage score 3 block was 5 in the levobupivacaine group ( $n = 30$ ) and 21 in the bupivacaine group ( $n = 30$ ). In our study, the number of patients with Bromage score 3 block was 17 in the levobupivacaine group ( $n = 25$ ) and 22 in the bupivacaine group ( $n = 25$ ). Gautier *et al.*<sup>7</sup> demonstrated that the time to maximum motor block was 9 min in the bupivacaine group, 14 min in the ropivacaine group, and 13 min in the levobupivacaine group; the duration of motor block was 142 min in the bupivacaine group, 116 min in the ropivacaine group, and 121 min in the levobupivacaine group. In the above-mentioned study, the duration of analgesia and motor block was longer and the time to first analgesic request was longer in the bupivacaine group.

In the current study, the time to maximum motor block was also shorter in group B (group B, 3.4 min; group L, 4.7 min). The duration of analgesia was longer in group L compared to group B (group B, 102 min; group L, 118 min;  $p < 0.05$ ). In a study conducted by Lee *et al.*<sup>11</sup> involving 50 patients who were scheduled for urogenital surgery under spinal anesthesia, the quality of sensory and motor block and the hemodynamic

changes were investigated using levobupivacaine in 24 patients and bupivacaine in 26 patients. Lee *et al.*<sup>11</sup> demonstrated that the time to onset of sensory block was  $10 \pm 6$  min in the levobupivacaine group and  $8 \pm 4$  min in the bupivacaine group, and found that there was no statistically significant difference between the groups. Vanna *et al.*<sup>12</sup> demonstrated that the time to onset of motor block was approximately 7.5 min in the levobupivacaine group and 4.9 min in the bupivacaine group in 70 patients who were scheduled for elective transurethral endoscopic surgery using 2.5 mL of 0.5% intrathecal isobaric levobupivacaine and the same volume of 0.5% hyperbaric bupivacaine. Erdil *et al.*<sup>8</sup> divided 80 patients who were scheduled for TURP into 2 groups and administered 0.5% levobupivacaine and bupivacaine in combination with fentanyl (15 µg). They demonstrated that the time to achieve T10, maximum sensory level, and maximum motor block level was significantly shorter in the bupivacaine group, and that the maximum sensory block level was higher in the bupivacaine group.

Very different onset times of effect and ending times of effect were found during the studies conducted with similar doses. When the factors affecting the onset times of effect are examined characteristics of the patient as well as the dose of local anesthetic and the position of the patient immediately after the technique and injection applied were found important. During this study, we observed that the onset time of effect shortened, the level reached increased and drug dose administered decreased as appropriate techniques and preferred position were applied in a short time.

In our study; time to sensory and maximum motor block was shorter in the bupivacaine + fentanyl group. On the other hand, a longer duration of analgesia was achieved in the levobupivacaine + fentanyl group. Although levobupivacaine is a novel drug, it is a good alternative for bupivacaine.

## References

1. FOSTER RH, MARKHAM A: Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. *Drugs*; 2000, 59(3):551-79.
2. HOWE JB: Local anesthetics: in *Anesthetic Physiology and Pharmacology*. McCaughey W, Clarke RJS, Fee JPH, Wallace WFM (eds) Churchill Livingstone. *New York*; 1997, 83-100.
3. HUANG YF, PRYOR ME, MATHER LE, ET AL: Cardiovascular and central nervous system effects of intravenous levobupivacaine and bupivacaine in sheep. *Anesth Analg*; 1998, 86:797-804.
4. GRISTWOOD RW: Cardiac and CNS toxicity of levobupivacaine: strengths of evidence for advantage over bupivacaine. *Drug Saf*; 2002, 25(3):153-63.
5. Practice Guidelines for Obstetric Anesthesia. An Updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. *Anesthesiology*; 2007, 106:4.
6. LEVINSON G: Spinal anesthesia. In: Benumof J, ed. *Clinical procedures in anesthesia and intensive care*. Lippincott, Philadelphia; 1992, 645-661.
7. GAUTIER P, DE KOCK M, HUBERTY L, DEMIR T, IZYDORCZIC M, VANDERICK B: Comparison of the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Caesarean section. *Br J Anaesth*; 2003, 91:684-9.
8. ERDIL F, BULUT S, DEMIRBILEK S, GEDIK E, GULHAS N, ERSOY MO: The effects of intrathecal levobupivacaine and bupivacaine in the elderly. *Anaesthesia*; 2009, 64:942-6.
9. SEYHAN T, SENTÜRK E, SENBECERIR N, BAŞKAN I, YAVRU A, SENTÜRK M: Spinal anesthesia in cesarean section with different combinations of bupivacaine and fentanyl. *Agri*; 2006, 18:37-43.
10. BREMERICH DH, FETSCH N, ZWISSLER BC, MEININGER D, GOGARTEN W, BYHAHN C: Comparison of intrathecal bupivacaine and levobupivacaine combined with opioids for caesarean section. *Curr Med Res Opin*; 2007, 23:3047-54.
11. LEE YY, MUCHHAL K, CHAN CK: Levobupivacaine versus racemic bupivacaine in spinal anesthesia for urological surgery. *Anaesth Intensive Care*; 2003, 31:637-41.
12. VANNA O, CHUMSANG L, THONGMEE S: Levobupivacaine and bupivacaine in spinal anesthesia for transurethral endoscopic surgery. *J Med Assoc Thai*; 2006, 89:1133-9.