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Research Article

Effect of the Combination of Different Doses of Intrathecal Levobupivacaine and Fentanyl for Caesarean Anesthesia on Motor and Sensory Blocks -

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ABSTRACT

Objective: In our study, we aimed to investigate the effects of different doses of intrathecal levobupivacaine and fentanyl in combined Spinal-Epidural Anesthesia (CSE) on motor and sensory blocks in patients scheduled for elective cesarean section.

Materials and Methods: Our study consisted of pregnant women scheduled for elective cesarean section, who had American Society of Anaesthesiologists (ASA) physical status of class I or II, were between150-180 cm in height, not morbidly obese, and had no contraindications for regional anesthesia. The cases were classified into 3 groups at random. Combined spinal-epidural anesthesia was administered in the sitting position after the pregnant women were informed about the procedure and their approval was obtained. Group 1 received 11 mg of levobupivacaine (2.1 cc), Group 2 received 8 mg of levobupivacaine + 25 µg Fentanyl + isotonic (2.1 cc), and Group 3 received 6 mg of levobupivacaine + 25 µg Fentanyl + isotonic (2.1). The time to reach T4 was assessed by the bilateral pinprick method in the mid-clavicular line with a 25-gauge needle after waiting for at least 10 minutes. Patients were assessed at minute 5 and 10 from the beginning of the operation and at postoperative minute 0, 15, 30, 45 and 60 according to the modified Bromage scale.

Results: In our study, there was no difference in age, weight, height, and parity between the subjects. Comparison of the patients in terms of motor block time revealed a statistically significant difference between the three groups, and motor block time in Group 1 was statistically significantly longer than in Group 3 (p=0.014). Comparison of the patients in terms of the time until sensory block to reach T4 after the administration of spinal anesthesia and the duration of the sensory block revealed no statistically significant difference between the 3 groups. A statistically significant difference was found between the groups in terms of minimum motor block according to the Modified Bromage scale (P=0.0014).A statistically significant difference was found between maximum motor block levels of the groups according to the Modified Bromage scale (P=0.0001).

Conclusion: It was observed that levobupivacaine and levobupivacaine combined with fentanyl provide adequate spinal anesthesia comfort in cesarean operations, the motor block recovery time decreases with a lower dosage of intrathecal levobupivacaine and that the block completely disappears within the first postoperative hour.

Keywords: Sensory block; Motor block; Combined epidural spinal anesthesia; Levobupivacaine; Fentanyl

INTRODUCTION

General and regional anesthesia techniques are used for cesarean delivery. Cesarean section is mostly performed with spinal (intrathecal), epidural or Combined Spinal-Epidural (CSE) technique in developed countries. CSE anesthesia is an alternative preferred in cases where a fast-onset intensive block is desired and the duration of anesthesia can be extended by administering additional anesthetic doses. It can also be used for neuraxial anesthesia in high-risk pregnancies, as it enables low-dose intrathecal local anesthetic and expansion of epidural volume to achieve an adequate level of anesthesia [1].

Levobupivacaine is the S (-) enantiomer of bupivacaine with shorter plasma clearance and elimination half-life. Current pharmacodynamic evidence from animal and human studies suggests that levobupivacaine has a potentially higher margin of safety than bupivacaine as it provides sufficient sensory block in cesarean sections, with lower cardiotoxicity and neurotoxicity and shorter motor block duration in overdose. These properties can make it a good alternative to bupivacaine [2-4].

With the addition of intrathecal opioids, local anesthetic requirements are reduced, whereas low sympathetic blockade and high levels of the sensory blockade can be achieved with the use of low-dose local anesthetics [5-7].

In the postoperative period, prolonged analgesia is the best way to encourage the early mobilization of patients, but prolonged motor blockade caused by neuraxial blockade with long-acting local anesthesia inhibits early mobilization, despite adequate analgesia.

In the present study, we investigated the effect of different doses of intrathecal levobupivacaine and fentanyl on sensory and motor blocks in patients scheduled for elective cesarean section.

MATERIALS AND METHODS

This randomized prospective double-blind study was conducted after obtaining approval from the Department of Anesthesia and Reanimation of Dicle University. Pregnant women with an uncomplicated pregnancy at term (37-41 weeks) and normal fetal heart sounds were included in the study. Exclusion criteria included preterm pregnancy, multiple pregnancies, fetus anomaly, growth retardation, meconium aspiration risk, acid-base pathologies that may affect the balance and antepartum hemorrhage, asthma bronchial, Rh incompatibility, classification of ASA III and above, peripheral neuropathy, neuromuscular or neuropsychiatric disease, alcohol or drug addiction, obesity (body mass index>35), history of hypersensitivity to local anesthetic substances, rejection of spinal anesthesia, scoliosis, low back pain or previous surgery in the lumbar region, blood clotting disorder, infection, frequent analgesic use, and a height below 150 cm and over 180 cm. Participating patients were informed preoperatively and asked to sign the informed consent forms. Subjects were randomly divided into three groups. Vascular access was established from the antecubital vein with a 20-22 gauge venous cannula. Prior to the study, the systolic and Diastolic Arterial Pressures (SAP, DAP), Heart Rate (HR), and Peripheral Oxygen Saturation (SPO2) of the pregnant women were monitored with a bedside monitor.

After the procedure sites were disinfected with an appropriate antiseptic solution, all pregnant women received local anesthetic infiltration on the skin and under the skin at the L3-4 or L4-5 interspace in the sitting position. CSE anesthesia technique was used for all pregnant women. Epidural space was reached using the loss of resistance technique at the midline with an 18 G Tuohy epidural needle (Espocan + Docking System + perifix mSoft Tip - Braun® Combined Spinal Epidural Set). Then, the subarachnoid space was entered using 27 G (Spinocan Braun®) or 26 G (Atraucan 26G 3x1 / 2, Braun®) mm spinal needle, and the following drugs were administered after dripping of CSF.

Group I: 11 mg of levobupivacaine (Chirocaine 50mg / 10ml AbbVie, Takeda Pharmaceuticals Norway) (2.1 cc)

Group II: 8 mg of levobupivacaine (Chirocaine 50mg / 10ml AbbVie, Takeda Pharmaceuticals Norway) + 25 µg Fentanl (fentanyl, Braun, Germany) + isotonic = (2.1cc)

Group III: 6 mg of levobupivacaine (Chirocaine 50mg / 10ml AbbVie, Takeda Pharmaceuticals Norway) + 25 µg Fentanyl (fentanyl, Braun, Germany) + isotonic (2.1cc)

In order to ensure double blindness, the study solution was prepared by another anesthetist. The solution was injected intrathecally within 30 seconds by another practitioner who did not know what the solution contained. The spinal needle was removed immediately afterwards. An 18 G epidural catheter (perifix-Braun®) was passed through the Tuohy needle and directed towards the cephalad. The catheter tip was placed 2-3 cm into the epidural space, the bacterial filter was attached and aspirated, and detection was made after ensuring that no cerebrospinal fluid and blood were in place.

After the administration of CSE, all patients were given the supine position and the operating table was adjusted to a 15º left. Oxygen was provided at a flow rate of 3 liters/min with a mask until the baby was taken out. The time to reach T4 was assessed by the bilateral pinprick method in the mid-clavicular line with a 25-gauge needle after waiting for at least 10 minutes. None of the pregnant women had motor impairment prior to the administration of anesthesia. Motor blockade was measured using a modified Bromage scale [8]. Patients were assessed at minute 5 and 10 from the beginning of the operation and at postoperative minute 0, 15, 30, 45 and 60 according to the modified Bromage scale.

Modified Bromage Scale (MBS):

1: complete motor block,

2: almost complete motor block - only able to move feet.-

3: partial motor block - only able to move the knee,

4: weak leg flexion - able to elevate feet but not hold it-

5: no weakness in leg flexion - able to elevate feet and hold for at least 10 seconds

6: no weakness.

All patients were monitored for 10 minutes after the administration of spinal anesthesia. Sensory block was assessed bilaterally and the time to reach T4 was recorded. If the block did not reach T6 in 10 minutes after the spinal block was performed, 2 ml of 2% lidocaine was administered through the epidural catheter for each non-blocked segment, and the total dose was recorded. The patients' time to T4-T6 regression and the block's time to T10 regression were both recorded. The two-segment sensorial block regression time was recorded by measuring the maximum sensorial block time until regression.

Statistical analysis was performed using SPSS 11.5 for the Windows program. The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. Variables with normal distribution were evaluated by one-way analysis of variance, and the post-hoc Tukey test was used to find out which group caused the difference given that a statistically significant difference was found. Results were expressed as mean ± SD. Chi-square test was used to compare categorical variables and the results were expressed as % (n). The Kruskal-Wallis test was used in the intergroup evaluations of variables that did not conform to a normal distribution, and the Dunn-Bonferroni test was used to determine the source of significance if significance was observed. Statistical significance was considered as $p<0.05$.

FINDINGS

Comparison of the patients in terms of age, height, weight, and gestational week revealed no statistically significant difference between the 3 groups (Table 1).

Comparison of the patients in terms of the time until sensory block to reach T4 after the administration of spinal anesthesia and the duration of the sensory block revealed no statistically significant difference.

Comparison of the patients in terms of motor block time revealed a statistically significant difference between the three groups, and the duration of motor block in Group 1 was statistically significantly longer than in Group 3 ($p=0.014$) (Table 2).

A statistically significant difference was found between the groups in modified Bromage scores at minute 5 ($p=0.001$). Pairwise comparisons with the Dunn-Bonferroni test revealed that the scores in group 3 were higher than the scores in group 1 and group 2 ($p=0.001$, $p=0.031$, respectively) (Table 3).

A statistically significant difference was found between the groups in modified Bromage scores at minute 10 ($p<0.001$). Pairwise comparisons with the Dunn-Bonferroni test revealed that the scores in group 3 were higher than the scores in group 1 and group 2 ($p<0.001$, $p=0.013$, respectively) (Table 3).

A statistically significant difference was found between the groups in modified Bromage scores at postoperative minute 0 ($p<0.001$). Pairwise comparisons with the Dunn-Bonferroni test revealed that

Table 1: Demographic data of patients included in the groups (mean ± SD).

	Group 1	Group 2	Group 3	p
Age (years)	30 ± 7.01	31.5 ± 7.74	31.5 ± 5.28	0.154
Weight (kg)	75.3 ± 13.12	76.7 ± 9.17	81 ± 1.89	0.068
Height (cm)	160.9 ± 3.02	162.50 ± 4.51	161.3 ± 3.45	0.546
Gestational week	37.1 ± 2.25	37.6 ± 2.56	37.8 ± 2.67	0.978

Table 2: Time of sensory block to reach T_4 after the administration of spinal anesthesia, duration of sensory and motor blocks (mean ± SD).

	Group 1	Group 2	Group 3	p
Time of sensory block regression (minutes) to T_4 after the administration of spinal anesthesia	7.2 ± 4.12	8.4 ± 2.98	6.6 ± 4.53	0.265
Sensory block time (Minutes)	65 ± 2.23	68.4 ± 2.67	57 ± 1.12	0.111
Motor block time (Minutes)	136 ± 12.8	12 1± 13.9	98 ± 9.6	*0.03
* Statistically significant				

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the scores in group 3 were higher than the scores in group 1 and group 2 (p<0.001, p=0.002, respectively) (Table 3).

A statistically significant difference was found between the groups in modified Bromage scores at post-operative minute 15 (p<0.001). Pairwise comparisons with the Dunn-Bonferroni test revealed that the scores in group 3 were higher than the scores in group 1 and group 2 (p<0.001, p0.001, respectively) (Table 3).

A statistically significant difference was found between the groups in 30-minute modified Bromage scores (p<0.001). Pairwise comparisons with the Dunn-Bonferroni test revealed that the scores in group 3 were higher than the scores in group 1 and group 2 (p<0.001, p=0.003, respectively) (Table 3).

A statistically significant difference was found between the groups in modified Bromage scores at post-operative minute 45 (p=0.001). Pairwise comparisons with the Dunn-Bonferroni test revealed that the scores in group 3 were higher than the scores in group 1 and group 2 (p=0.003, p=0.004, respectively) (Table 3).

A statistically significant difference was found between the groups in modified Bromage scores at post-operative minute 60 (p=0.001). Pairwise comparisons with the Dunn-Bonferroni test revealed that the scores in group 3 were higher than the scores in group 1 (p=0.005) (Table 3).

A statistically significant difference was found between the groups in terms of the minimum motor block according to the Modified Bromage scale (p=0.0014). While MBS was 6 in 16 of 24 patients in group I, it was 6 in 22 of 24 patients in group II, and 6 in all patients in group 3 (Chart-1).

A statistically significant difference was found between maximum motor block levels of the groups according to the Modified Bromage scale (p=0.0001). Group 1: 10 of 24 patients had MBS 1, Group 2: 1 in 2 of 24 patients had MBS 1, Group 3: None of 24 patients had MBS 1.

DISCUSSION

There is no gold standard for adequate levobupivacaine dose and how much opioid should be used for comfortable CSE anesthesia in cesarean operations, and studies on this subject are ongoing. This study was formulated to evaluate and compare sensory and motor characteristics following spinal anesthesia with different doses of levobupivacaine and fentanyl and their combination.

In applications of spinal anesthesia, adding opioids to local anesthetics helps to benefit from the synergistic effects and decreases the incidence of side effects due to lower doses of local anesthetics.

Table 3: Results at minute 5 and 10 from the beginning of the operation and at postoperative minute 0, 15, 30, 45 and 60 according to the Modified Bromage scale.

	Group 1	Group 2	Group 3	p
	Median (Q1, Q3)	Median (Q1, Q3)	Median (Q1, Q3)	
5th min	2 (2, 3)	3 (2, 3)	3.5 (3, 4.5)	0.001*
10th min	2 (1, 2)	2 (2, 2.5)	3 (2, 3)	<0.001*
Post-op 0th min	3 (1.5, 3)	3 (2, 4)	5 (4, 5)	<0.001*
Post-op 15th min	4 (2.5, 4)	4 (3, 5)	6 (5, 6)	<0.001*
Post-op 30th min	4 (3, 5.5)	5 (4, 5)	6 (6, 6)	<0.001*
Post-op 45th min	5 (4, 6)	5 (5, 6)	6 (6, 6)	0.001*
Post-op 60th min	6 (5, 6)	6 (6, 6)	6 (6, 6)	0.006*

In their study, Roser, et al. [9] performed spinal anesthesia with bupivacaine and levobupivacaine in 58 elderly patients who underwent orthopedic surgery for hip fractures, and no statistically significant difference was observed between the two treatment groups in terms of hemodynamic parameters.

Bidikar, et al. [10] stated that adequate anesthesia was provided with 7.5mg of levobupivacaine (0.5%) + 12.5 mcg fentanyl and 10mg levobupivacaine (0.5%) and that they achieved better hemodynamics with a short-term motor block in the fentanyl group. In their study where the effects of intrathecal bupivacaine combined with sufentanil or morphine were compared, Karaman, et al. [11] found that they exhibited similar motor block times. We combined 25 mcg of fentanyl with 8 mg of levobupivacaine (0.5%) in group II and observed that sufficient anesthesia was achieved in this group and surgical muscle relaxation was significantly better than the other groups. Low-dose local anesthetics are the appropriate option for outpatient, short-term procedures requiring rapid motor function recovery, lower limb surgery, and operations requiring rapid foot function recovery. Low-dose local anesthesia is observed to be sufficient for outpatients since it does not carry a risk of systemic toxicity, however, it is insufficient for major surgical procedures [12].

The prolonged motor block is one of the undesired postoperative side effects in pregnant women. In their study, Liao, et al. [13] compared bupivacaine combined with levobupivacaine and found that motor block onset was longer and motor block regression was shorter in the levobupivacaine group. In their study investigating bupivacaine combined with levobupivacaine, Erbay, et al. [14]. Also found that the motor block regression was shorter in the levobupivacaine group. As in the above study, we added 25mcg of fentanyl into a low dose of 6mg levobupivacaine (0.5%) in group III, and found that it provided adequate anesthesia in 24 patients and that postoperative motor block was cleared in all patients. We recommend this dose in patients who are afraid of becoming paralyzed, have anxiety, and need to be mobilized early.

In their study, Fattorini, et al. [15] reported the onset time for the sensory block of levobupivacaine and bupivacaine as 12 ± 6 min and 9 ± 5 min, maximum sensory block level as T8 in both groups, motor block onset time as 11 ± 6 min and 8 ± 4 min, and block termination time as 256 ± 86 min and 245 ± 86 min, with no statistical difference between the groups. Using the combination of levobupivacaine (8 mg) + sufentanil (2.5 micrograms) in spinal anesthesia for cesarean section, Gautier, et al. [16] reported the mean time to the maximum motor block level as 13 minutes, with the mean time of motor block duration being 121 minutes. The absence of numbness in the legs and preservation of motor functions are key factors that increase maternal satisfaction. Bertini, et al. [17] compared 0.2% bupivacaine and 0.2 % ropivacaine in 73 patients undergoing hip replacement with postoperative patient-controlled analgesia, and obtained higher patient satisfaction in the ropivacaine group due to less motor block, although equally good analgesia was achieved. In our study, Group 1 reached T4 in 7.2 minutes, Group II in 8.4 minutes, and Group III in 6.6 minutes (Table 2). We observed that motor block regression improved with lower doses of local anesthetics. We evaluated the results at minute 5 and 10 after the administration of intrathecal anesthesia, as well as postoperative minute 0, 15, 30, 45, and 60 (Table 3). None of the patients had a complete motor block at minute 5. While the complete motor block was observed in 7 of 24 patients in Group 1 at minute 10, it was observed in 2 of 24 patients

in Group 2, and none of the 24 patients in Group 3. Evaluation of surgical results according to the BMS shows that 6 of 24 patients in Group 1 experienced a complete motor block, while no motor block was observed in Group 2 and Group 3. Evaluation of postoperative minute 60 according to BMS showed that 16 of 24 patients in Group 1 exhibited no weakness, whereas 21 of 24 patients in Group 2 and all 24 patients in Group 3 exhibited no weakness. For all times, a difference was observed between groups. The scores of the patients in Group 3 were higher than the scores of the patients in Group 1 and Group 2 at all times except postoperative minute 60, whereas there was no difference between Groups 1 and 2. At postoperative minute 60, the scores in Group 3 were higher than Group 1, and there was no difference between Group 1 and Group 2, and Group 2 and Group 3 (Table 3).

Kaussenemi, et al. [18] performed a dosage study using 25mcg of fentanyl combined with 10 mg of pure bupivacaine and 5 mg of bupivacaine and reported less motor block development in the fentanyl group while causing little difference in hemodynamics. Pushpavathi, et al. [19] performed a randomized double-blind study, in which they applied spinal anesthesia with 0.5% isobaric racemic bupivacaine and 0.5% isobaric levobupivacaine for lower abdomen and lower extremity surgery in 70 patients between the ages of 18-65, and the sensory and motor blockade characteristics were found to be similar between the 2 groups. Huang, et al. [20] reported that levobupivacaine affected the sensory block rather than the motor block in their in vitro experimental study. These studies indicate that levobupivacaine is similar to bupivacaine in terms of the sensory blockade and that motor blockade lasts shorter in spinal anesthesia combined with fentanyl. In spinal anesthesia, the use of lipophilic opioids combined with local anesthetics increases the quality of anesthesia without extending the duration of motor block, which accelerates the clearance. Low-dose levobupivacaine combined with fentanyl will decrease the duration of the motor block and help early mobilization.

In conclusion, we found that levobupivacaine and fentanyl added to levobupivacaine provided adequate spinal anesthesia comfort in cesarean operations, lower doses of intrathecal levobupivacaine shortened motor block recovery and the block completely disappeared within the first postoperative hour. We have concluded that this is crucially significant in outpatient anesthesia, which is widely used today, in terms of the mother's early mobilization. As previous studies and our study suggest, fentanyl combined with levobupivacaine prolongs postoperative analgesia, therefore, we believe that combination of low-dose levobupivacaine and fentanyl may be useful for providing prolonged sensory blockade and reducing motor block time, which can help patients in early ambulation.

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