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ORIGINAL ARTICLE

A randomized comparison of different doses of intrathecal levobupivacaine combined with fentanyl for elective cesarean section: prospective, double-blinded study

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Abstract
Purpose Levobupivacaine may produce a sensory and motor block different from that produced by bupivacaine, which is the most popular local anesthetic in parturients undergoing cesarean section. The aim of this study was to investigate the block characteristics, the clinical efficacy, surgeon and patient satisfaction, and hemodynamic effects of using different doses of intrathecal plain levobupivacaine combined with fentanyl.
Methods One hundred twenty women undergoing elective cesarean section with a combined spinal–epidural technique were enrolled. The parturients were randomly assigned to receive one of the following: levobupivacaine 5 mg (group 5), 7.5 mg (group 7.5) or 10 mg (group 10), all combined with fentanyl 25, 15 or 10 μg, respectively.
Results Anesthesia was effective in 60, 82.5 and 100% of the patients in the levobupivacaine 5, 7.5 and 10 mg groups, respectively. Levobupivacaine 10 mg provided longer durations of analgesia and motor block and greater patient and surgeon satisfaction, although the incidence of hypotension was lower in groups 5 and 7.5 than in group 10 (12.5, 17.5 and 42.5%, respectively). Intraoperative epidural supplementation was higher in group 5 than in group 7.5 (40 and 17.5%, respectively), whereas no patients in group 10 were given an epidural bolus dose.
Conclusions The incidence of hypotension was higher in the levobupivacaine 10 mg group, even though this group presented more effective anesthesia and greater patient and surgeon satisfaction compared with the levobupivacaine 5 and 7.5 mg groups. As a result, we believe that levobupivacaine 7.5 mg combined with fentanyl 15 μg is suitable for combined spinal–epidural anesthesia in elective cesarean section.

Keywords Levobupivacaine · Fentanyl · Combined spinal–epidural anesthesia · Cesarean section

Introduction

Spinal anesthesia is the most commonly used regional technique for cesarean section, due to its simplicity of execution, fast onset and predictable effects [1]. However, in high doses, intrathecal local anesthetics may produce high levels of sensory and motor block and hypotension. It is particularly important for parturients undergoing cesarean section, as maternal hypotension causes decreasing maternal cardiac output and uteroplacental blood flow. The addition of various doses of opioids may allow the dose of local anesthetic to be reduced, producing a synergistic effect that enhances analgesia and prolongs the duration of the sensory block without intensifying motor block [2–5]. Fentanyl, which is the ideal opioid in obstetrics, is much more lipid soluble than morphine and hence does not tend to spread intrathecally to the fourth ventricle in sufficient concentrations to cause respiratory depression [1, 6].

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Levobupivacaine, the *S*-(−)-enantiomer of racemic bupivacaine, has recently been used for obstetric spinal anesthesia and appears to be a valid, safe and interesting alternative to bupivacaine [7]. Although it exhibits less toxicity towards the central nervous system and the heart than equivalent concentrations of bupivacaine, the risk of systemic toxicity it presents is related to either overdosing or unwanted intravascular injection during epidural or peripheral nerve blocks. The potential advantages of levobupivacaine compared with bupivacaine are less motor block and less profound hypotension [8–11]. It has more specific effects on sensory rather than motor nerve fibers [10]. Gautier and colleagues [8] suggested that intrathecal levobupivacaine had reduced motor blocking properties compared to racemic bupivacaine at equivalent doses. A study reported that there was a tendency for better systolic blood pressures and a lower incidence of severe hypotension with levobupivacaine compared to ropivacaine and bupivacaine [11]. The longer-lasting sensory block and the rapid mobilization of patients due to the faster recovery from motor block and reduced hypotension associated with levobupivacaine may be particularly advantageous in obstetric patients [1, 3].

There are few studies in which the use of levobupivacaine with fentanyl is compared to its use without fentanyl in spinal anesthesia for cesarean section [5, 12, 13]. In this study, we tested the hypothesis that there would be differences in block height, sensory level, side effects and patient comfort among groups upon increasing the dose of opioid and decreasing the dose of local anesthetic.

The principal aim of this study was to determine the optimal combination of levobupivacaine and fentanyl by comparing their motor and sensory block characteristics and their side effects for spinal anesthesia in parturients for cesarean section. However, a combined spinal–epidural approach was required in our study, as low doses of spinal anesthetic were used.

Methods

After ethics committee approval, and having obtained written informed consent, 120 women between 18 and 40 years old who were scheduled for elective cesarean section under combined spinal–epidural anesthesia, were at term with a singleton pregnancy, had an American Society of Anaesthesiologists (ASA) physical status of class I or II, and were 156–170 cm in height were enrolled into this prospective, randomized, double-blind study. Exclusion criteria were a known hypersensitivity to amide local anesthetics, general contraindications against spinal anesthesia, obesity (women weighing >100 kg), cardiac and endocrine diseases, hypertension, and a height of less than 155 cm.

Before the study, patients were instructed on the methods used for sensory and motor assessments. Prior to transfer to the operation room, baseline blood pressure and heart rate were calculated as the mean of three recordings made in the ward. All parturients received Ringer's lactate solution 15–20 mL/kg 15–20 min before the block, and antacid prophylaxis consisted of ranitidine 50 mg and metoclopramide 10 mg intravenously. On arrival in the operating room, routine physiological monitoring was applied, including electrocardiogram (ECG), noninvasive blood pressure, heart rate (HR), and pulse oximetry (Datex-Ohmeda AS/3, Helsinki, Finland). The parturients were randomly allocated to three groups; 5 mg of levobupivacaine with 25 μg fentanyl (group 5), 7.5 mg of levobupivacaine with 15 μg fentanyl (group 7.5), and 10 mg of levobupivacaine with 10 μg fentanyl (group 10), according to a computer-generated randomization table. Each woman received 2.3 or 2.5 mL (depending on the patient's height: 2.5 mL if >160 cm; 2.3 mL if <160 cm) from a freshly prepared and sterile syringe containing isobaric levobupivacaine 0.5% (Chirocaine, Abbott Laboratories, Istanbul, Turkey) plus fentanyl. The study drugs were diluted with normal saline to achieve the desired volume in our protocol. To facilitate blinding, all central blocks were performed by one anesthetist, and syringes containing the study solution were prepared immediately before injection by another anesthetist who played no further role in the study. Neither the anesthetist performing the block nor the parturient herself was aware of the drug combination.

The combined spinal–epidural (CSE) catheterization (Espocan, B. Braun, Melsungen, Germany) was performed with the patients in the left lateral position. An 18-gauge (G) Tuohy needle was inserted into the L3–4 or L4–5 interspace using the loss of resistance to saline technique to identify the epidural space. A 27-gauge Whitacre spinal needle was then placed through the Tuohy needle until the dura mater was punctured. After checking for free flow of the cerebrospinal fluid, the spinal solution was administered into the subarachnoid space with the spinal needle orifice facing cephalad over a 15–20 s period without barbotage. An epidural catheter was inserted 4 cm into the epidural space and aspirated; no test dose was given. Patients were immediately positioned supine with a 15° left lateral tilt. All parturients received oxygen (4 L/min) via a facemask.

An independent observer, who was blinded to group allocation, recorded the following variables: HR, systolic blood pressure (SBP), time to maximum level of sensory block, time to two-segment regression from the maximum block height, onset time motor block, degree of motor block, duration of sensory and motor block, and the need for epidural supplementation. Sensory levels were checked bilaterally along the midclavicular line by pinprick using a 25-gauge Whitacre needle, motor block was assessed based

on a modified Bromage scale (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 move any part of the lower limb) [7]. The onset time of motor block was defined as the interval between intrathecal administration and a Bromage score of 1. The duration of sensory or motor block was defined as the interval from intrathecal administration to the T10 regression time or to the point at which the Bromage score returned to zero. These tests were performed every 1 min until delivery, then at 5-min intervals until the end of surgery, and finally at 15-min intervals until the sensory variables receded to T10 and motor variables were back to normal. SBP and HR were recorded at 2-min intervals until delivery, and then every 5 min. Surgery was allowed to proceed if the upper dermatome level of the loss of discrimination to pinprick was at or above T5. After delivery, 5U or 10U oxytocin was administered by slow intravenous injection. The following side effects were considered: hypotension (a 20% fall in SBP below pre-anesthesia levels or SBP $<$ 100 mmHg), which was treated immediately with 5 mg of intravenous ephedrine; bradycardia (defined as a HR $<$ 60 beats/min), which was treated by 0.5 mg of intravenous atropine; and nausea or vomiting (treated with ondansetron 4 mg i.v.) [1]. The incidence of side effects such as nausea, vomiting, itching and hypotension was noted. The presence of nausea and vomiting was measured on a three-point scale of 1, 2 or 3, indicating no nausea and no vomiting, nausea only, or both nausea and vomiting, respectively. Systolic blood pressure was chosen to define hypotension because many investigators believe that spinal sympathectomy primarily affects systolic blood pressure [14].

For pain, a 100-mm visual analog scale (VAS, 0 mm: no pain, 100 mm: worst imaginable pain) was used intraoperatively. Before anesthesia, parturients were instructed that fetal extraction might be associated with some degree of discomfort. In the case of unbearable discomfort (VAS $\geq$ 40 of 100-mm scale or maternal request for rescue), 10–15 mL of lidocaine 2% plus epinephrine 1:200,000 were injected epidurally. If the women failed to respond to rescue and still experienced some discomfort (VAS $\geq$ 40) they were excluded from the study, as we may have had some problems with the CSE. During the procedure, the surgeons evaluated muscle relaxation according to a four-point scale (1, excellent; 2, good; 3, fair; 4, poor) [8]. Also, immediately after surgery, patient satisfaction was evaluated using the following scoring system: 0, not satisfied; 1, moderate; 2, good; 3, very good [15].

Statistical analysis

The study was designed to test three hypotheses: that different doses of the three anesthetic solutions may result in different maximum cephalad sensory block heights, intraoperative VAS scores, or incidences of hypotension. As no information was available regarding the expected differences in these parameters among groups, the required sample size was calculated according to our pilot study. The primary endpoint was a difference among groups in the maximum cephalad sensory block height. Prospective power analysis based on data from the previous pilot study in our department showed that assigning 34 patients to each group would lead to a detection power of 80% ($\alpha = 0.05$, $\beta = 0.20$) when attempting to find the maximum cephalad sensory block height; 37 patients per group would yield a detection power of 80% when searching for a 30% difference in the incidence of hypotension and a 20% difference in the VAS scores between levobupivacaine 10 and the other two groups.

Statistical analysis was performed with the SPSS (SPSS for Windows, release 13.0) statistical package. The results are presented as mean $\pm$ standard deviation, median (range) or n (%), as appropriate. Patient and surgical characteristics among the groups were compared using one-way analysis of variance followed by the Bonferroni correction. For hemodynamic changes within the groups, repeated-measures analysis of variance followed by a post-hoc Bonferroni test were performed. Block characteristics were compared using the Kruskal–Wallis and two-tailed Mann–Whitney U tests. The incidences of adverse effects and epidural supplementation were analyzed using the χ^2 test and Fisher's exact test. A p value of <0.05 was considered statistically significant.

Results

There were no significant differences in mean age, height, weight, or gestational age among the women in the three groups. Median durations of surgery, induction-delivery times and volumes of prehydration were similar among the groups (Table 1).

All groups had similar baseline SBP and HR values ($p = 0.7$, $p = 0.19$, respectively). Serial SBP and HR values during surgery after the onset of spinal anesthesia among groups are shown in Fig. 1. SBP in group 10 was significantly lower than that in group 5 from 7 min to the end of surgery in most measurements (except at 15, 25 and 35 min), and lower than that in group 7.5 at 7, 11 and 30 min, but there was no significant difference between groups 5 and 7.5 except at 50 min. HR values in group 5 were higher than those in group 10 at 3 min and from 7 to 50 min, and those in group 7.5 at 3 and 25 min. There were significant differences between groups 7.5 and 10 at 13, 15, 30 and 35 min. One patient in group 5, two patients in group 7.5, and five patients in group 10 required atropine for bradycardia ($p = 0.17$).

Table 1 Patient and surgical characteristics

	Group 5	Group 7.5	Group 10
Age (years)	28.9 ± 3.9	29.8 ± 4.6	30.9 ± 3.5
Height (cm)	161 ± 3.2	162.4 ± 3.7	161.8 ± 3.1
Weight (kg)	72.2 ± 8.7	75.3 ± 7.8	74.6 ± 8.4
Gestational age (weeks)	39 (38–40)	39 (38–40)	39 (38–40)
Volume of prehydration (mL)	1262.5 ± 271.8	1310.6 ± 175.1	1283.1 ± 183.7
Duration of surgery (min)	50.3 ± 4.9	49.4 ± 5.9	50.7 ± 5
Induction-delivery time (min)	16.3 ± 2.2	15.8 ± 2.2	16 ± 2.7

Data are presented as mean ± SD or median (range)

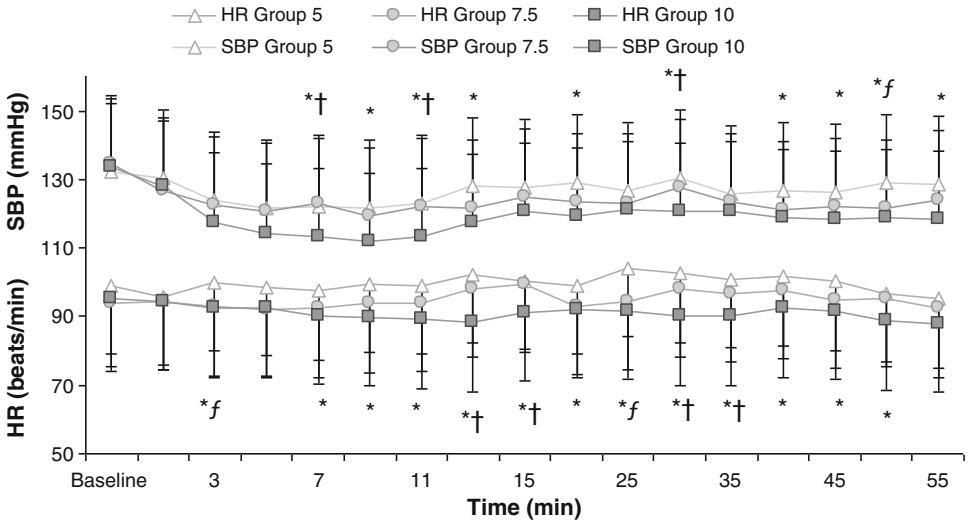

Fig. 1 Hemodynamic differences among groups ($^{f}p < 0.05$ for group 5 versus group 7.5, $^{*}p < 0.05$ for group 5 versus group 10, $^{\dagger}p < 0.05$ for group 7.5 versus group 10

Onset time for motor block was shorter in the levobupivacaine 10 mg group than in the other two. No statistically significant differences were observed between the three groups with respect to times to maximum cephalic spread or motor block Bromage 3 score ($p = 0.4$, $p = 0.2$, respectively). Times of sensory block regression to both two segment regression and T10 were longer in the levobupivacaine 10 mg group than in the other two groups. The degree and duration of motor block were significantly less in group 5 than in groups 7.5 and 10 (Tables 2 and 3).

The incidence of hypotension and the ephedrine dose employed were higher in group 10 than in the other two. Nausea and/or vomiting, itching and bradycardia were similar ($p = 0.1$, $p = 0.2$, $p = 0.17$, respectively). Bradycardia was treated with atropine, but women who had itching, nausea and/or vomiting did not require any treatment. Surgeon and patient satisfaction were greater in group 10 than in the other two groups, and there was a significant difference between groups 5 and 7.5. Only one patient in group 10 was not satisfied due to fetal extraction at delivery, but an epidural bolus dose was not required. Nine patients in group 5 and five patients in group 7.5 needed an epidural bolus dose towards the end of surgery. Seven patients in group 5 and two patients in group 7.5 needed an epidural bolus dose before skin incision due to an inadequate level of anesthesia. The number of patients needing epidural supplementation in each group is shown in Table 4.

Discussion

In this study, we observed that the incidence of hypotension was higher in the levobupivacaine 10 mg group, although this group provided more effective anesthesia and greater patient and surgeon satisfaction with spinal anesthesia compared with the other two groups. Levobupivacaine 5 mg plus fentanyl 25 μg remained inadequate for cesarean section under spinal anesthesia owing to the higher epidural dose required. Levobupivacaine 7.5 mg plus fentanyl 15 μg was found to be suitable due to the lower incidence of hypotension than when levobupivacaine 10 mg plus fentanyl 10 μg was used, and the reduced need for epidural supplementation than when levobupivacaine 5 mg plus fentanyl 25 μg was employed.

The density of the anesthetic solution and the position of the patient are the most important factors affecting intrathecal drug spread [16]. Compared with plain solutions, the use of hyperbaric local anesthetics results in not only a more predictable cephalad spread but also increased

Table 2 Motor and sensory block characteristics among the groups

	Group 5	Group 7.5	Group 10	*p* values		
				5 versus 7.5	5 versus 10	7.5 versus 10
Sensory block						
Time to maximum cephalic spread (min)	8.7 ± 1.9	8.9 ± 1.6	9.5 ± 2.3	ND	ND	ND
Maximum sensory block height	T4 (3–12)	T4 (3–10)	T4 (2–5)	ND	<0.0001	0.005
Number of parturients with T5 or above dermatome (*n*)	33	38	40	ND	0.01	ND
Time to two segment regression (min)	41.9 ± 10	50 ± 16.5	72.8 ± 26	0.03	<0.0001	<0.0001
Motor block						
Onset time of motor block to Bromage 1	3.6 ± 1.1	3.1 ± 1.2	2.5 ± 1	0.02	<0.0001	0.02
Maximum motor block score (Bromage)	2 (0–3)	3 (0–3)	3 (1–3)	0.02	<0.0001	0.006
Modified Bromage scale 0/1/2/3 (*n*)	5/2/20/13	1/3/13/23	0/1/5/34	ND	<0.0001	ND
Time to motor block Bromage 3 score (min)	10.1 ± 3	8.7 ± 3	8.2 ± 3.2	ND	ND	ND

Data are presented as mean ± SD, median (range) or number of patients (*n*). *ND* no difference ($p > 0.05$)

Onset times of sensory block, times to motor block Bromage 3 score, and times to maximum cephalic spread were similar among groups ($p = 0.23$, $p = 0.21$, $p = 0.4$, respectively)

Table 3 Recovery characteristics among the groups

	Patients, including those who received epidural supplementation (except before skin incision)			Patients without epidural supplementation		
	Group 5 (*n*:33)	Group 7.5 (*n*:38)	Group 10 (*n*:40)	Group 5 (*n*:24)	Group 7.5 (*n*:33)	Group 10 (*n*:40)
Time to recede to T10 (min)	78.7 ± 15.9*	96.6 ± 22.5	125.2 ± 17.9†	71.7 ± 11.1^{f}	90.7 ± 17.5	125.2 ± 17.9†
	78 (57–128)	92.5 (65–142)	125.5 (85–165)	67 (57–95)	90 (65–128)	125.5 (85–165)
Time for recovery to Bromage 0 (min)	63.4 ± 9.9*	75.5 ± 15.2	108.8 ± 18†	58.5 ± 7.2^{f}	71.8 ± 12.1	108.8 ± 18†
	61 (45–83)	75 (55–115)	112.5 (60–135)	58 (45–75)	70 (55–95)	112.5 (60–135)

Data are presented as mean (SD) or median (range)

* $p < 0.001$ for group 5 versus group 7.5

^{f} $p < 0.0001$ for group 5 versus group 7.5

† $p < 0.0001$ for group 10 versus groups 5 and 7.5

Table 4 Side effects and patient and surgeon satisfaction

	Group 5	Group 7.5	Group 10	*p* values		
				5 versus 7.5	5 versus 10	7.5 versus 10
Hypotension (%, *n*)	12.5 (5)	17.5 (7)	42.5 (17)	ND	0.005	0.027
Nausea and/or vomiting (%, *n*)	7.5 (3)	10 (4)	22.5 (9)	ND	ND	ND
Itching (%, *n*)	15 (6)	7.5 (3)	5 (2)	ND	ND	ND
Bradycardia (%, *n*)	2.5 (1)	5 (2)	12.5 (5)	ND	ND	ND
Total number of epidural supplementations (%, *n*)	40 (16)	17.5 (7)	0 (0)	0.04	<0.0001	0.01
Mean ephedrine dose (mg)	0.8 ± 2.5	1 ± 2.3	3.2 ± 4.1	ND	0.003	0.005
Number of VAS ≥ 4 (%, *n*)	40 (16)	17.5 (7)	0 (0)	0.04	<0.0001	0.01
Surgical conditions (poor/fair/good/excellent) (*n*)	6/10/14/10	3/6/18/13	1/1/11/27	ND	<0.0001	0.01
Patient satisfaction (not satisfied/moderate/good/very good) (*n*)	8/7/8/17	2/6/20/12	1/1/9/29	0.02	0.004	0.002

Data are presented as mean (SD), or % (*n*)

ND no difference ($p > 0.05$)

duration of the clinically useful block, and leads to more rapid regression of the sensory block and recovery from motor block [17]. Sen et al. [18] compared the same doses of hyperbaric and isobaric levobupivacaine and found that the speed of onset and offsets of motor and sensory block were significantly faster with hyperbaric levobupivacaine, although the hemodynamic parameters and incidences of adverse effects were similar. However, according to a report by Van Gessel et al. [19], the decrease in mean arterial pressure was significantly more severe in the hyperbaric (30%) than in the isobaric (18%) or hypobaric (14%) solutions. Another study reported that the hyperbaric group was associated with an increased incidence of hypotension compared with the plain group [20]. The slower and more limited cephalad spread of the sensory block may explain the reduced incidence and/or severity of hypotension. However, the reduced spread may have increased the need for epidural supplementation [21]. Adding an opioid to the local anesthetic may confer a local anesthetic-sparing effect and lead to a shorter onset time for sensory block and a prolongation of the duration of the sensory block without affecting the motor block, reducing the incidence of intraoperative pain. The opioid interrupts pain transmission in the dorsal horn while the local anesthetic blocks conduction in the motor and sensory nerves [3, 5, 12, 22]. In the first study on levobupivacaine with fentanyl, Lee et al. [5] compared the clinical efficacy, motor block and hemodynamic effects of using 2.6 mL of 0.5% levobupivacaine and 2.3 mL of 0.5% levobupivacaine with fentanyl 15 μg during urological surgery, and showed that levobupivacaine with fentanyl was as effective as levobupivacaine alone. In a study, 0.5% levobupivacaine (2.5 mL) and 0.5% levopubivacaine (2.2 mL) with fentanyl (0.3 mL) for elective transurethral resection were compared [12]. The highest level of sensory block was T9 in the levobupivacaine group and T6 in the levobupivacaine with fentanyl group, and the duration of motor block was shorter in the one including fentanyl. Parpaglioni et al. [3] demonstrated that the minimum local anesthetic doses were 10.65 mg in the levobupivacaine group and 4.73 mg in the levobupivacaine with 3.3 μg sufentanil group. The onset time for sensory block was reduced when sufentanil was used as an adjunct to levobupivacaine (23.4 vs. 10.3 min), and the regression time to the T10 sensory level was significantly prolonged in the levobupivacaine with sufentanil group (118 vs. 89.4 min). When compared with Parpaglioni's study [3], however, this regression time in the levobupivacaine with sufentanil group was longer than those for groups 5 and 7.5 in our study. The reason for this difference might be the duration of action, which is shorter for fentanyl than sufentanil [23]. As all of the groups received opioid, we found that onset and maximum cephalic spread times were similar among the groups, while maximum sensory block height was greater in group 10. The motor block was more intensive in groups that had a higher dose of local anesthetic, as expected since the lower incidence of complete motor block was related to the lower dose of local anesthetic used [24]. In addition, the epidural supplements may prolong motor and sensory block at the end of the procedure [21, 25]. Thus, we evaluated the recovery motor and sensory blocks of the patients statistically with regard to whether they received intraoperative epidural supplementation or not. Bremerich et al. [13] found that, compared to 7.5 mg levobupivacaine, 10 and 12.5 mg levobupivacaine prolonged the duration of effective analgesia postoperatively (45 vs. 81 and 96 min, respectively). These authors recommended 10 mg levobupivacaine for parturients undergoing elective cesarean section with spinal anesthesia, because parturients receiving 7.5 mg levobupivacaine 40% required supplementary intravenous opioid analgesics intraoperatively. However, we observed that less epidural supplementation was needed in the levobupivacaine 7.5 group. Adding opioid to levobupivacaine might be the reason for this. Gautier et al. [8] demonstrated that anesthesia was effective in 80% of patients receiving 8 mg levobupivacaine with 2.5 μg sufentanil. In studies with bupivacaine, adequate surgical anesthesia has usually been reported in parturients receiving 5 mg of bupivacaine to which 25 mg of fentanyl were added [26]. However, levobupivacaine is less potent than bupivacaine [27]. Thus, unlike the study of Ben David et al. [26], we could have found inadequate surgical anesthesia and an enhanced need for epidural supplementation when using levobupivacaine 5 mg plus fentanyl 25 μg. Moreover, Guasch et al. [28] determined that the requirement for rescue analgesia was higher in the group receiving 5 mg of levobupivacaine with 25 μg fentanyl, just as we observed in our results (46 vs. 40%).

The dose of opioid added to the local anesthetic for sensory analgesia is also important [2, 4, 29]. Chu et al. [29] studied 0.5% hyperbaric bupivacaine assosiated with different doses of fentanyl (7.5, 10, 12.5, and 15 μg) for spinal anesthesia. While all of the patients in the 12.5 and 15 μg fentanyl groups experienced excellent intraoperative and postoperative analgesia, 7.5 μg did not produce actual clinical effects. Furthermore, Goel et al. [4] compared three different doses of intrathecal fentanyl (7.5, 10 or 12.5 μg) in combination with low-dose bupivacaine to identify the minimum effective dose of intrathecal fentanyl. They found that the group receiving fentanyl 7.5 μg had a significantly higher number of failed blocks (almost 27%). Therefore, considering these studies, we preferred to use at least 10 μg of fentanyl.

Hypotension is correlated with the degree of sympathetic block. When the concentration of the anesthetic solution decreases, the drug concentration penetrating to

the nerves is reduced, and the sympathetic block can be less intense [25, 30]. Furthermore, opioids also yield a reduced sympathetic block, resulting in a lower incidence of hypotension [3]. Parpaglioni et al. [31] determined that the percentage of patients who showed hypotension was 38.5% in the levobupivacaine- alone group. Another study by the same authors [3] established that the percentages of patients showing hypotension were 43.3% in the levobupivacaine group and 20.4% in the levobupivacaine with sufentanil group. In our study, the incidence of hypotension was similar to that seen in the studies by Parpaglioni et al. [3, 31], and the incidence of hypotension increased with the dose of local anesthetic. In contrast, Luck et al. [17] reported that the incidence of hypotension was 30% in the 15 mg levobupivacaine group. Moreover, Lee et al. [5] compared the hemodynamic effects of using 2.6 mL of 0.5% levobupivacaine alone and 2.3 mL of 0.5% levobupivacaine with fentanyl (0.3 mL) in old patients. The incidence of hypotension was 12% in the group including fentanyl, and 4% in the levobupivacaine-alone group. In these studies with old patients, hypotension was defined as a decrease in the systolic blood pressure of more than 30% from the baseline. The higher incidence of hypotension in our study might be due to the different definition of hypotension used here, and because all of our patients were young, fit parturients. Some factors, such as sex, age, pregnancy, and illness, may affect the intrathecal spread of local anesthetics [16].

The analgesic benefits of intrathecal opioid should be balanced against its side effects, namely nausea and vomiting, sedation and itching, which are dose-related. In particular, higher doses are associated with increased itching [2]. In our study, the incidence of itching was very low and no treatment was needed. When other side-effects were evaluated, we found a higher incidence of nausea and/or vomiting with levobupivacaine 10 mg, but there was no statistical difference among the groups. Nausea or vomiting after spinal anesthesia may be caused by hypotension or fentanyl use. In the present study, the higher incidence of nausea may be related to the higher incidence of hypotension with levobupivacaine 10 mg. Brizzi et al. [1] demonstrated that the incidences of vomiting and bradycardia were 12 and 24%, respectively, in the spinal group with 7.5 or 8 mg of levobupivacaine and 5 μg sufentanil. We found fewer adverse effects such as nausea, vomiting and hypotension than in the study of Brizzi et al. [1]. The reason might be the use of different opioids or high doses.

There are certain limitations of our study. For instance, we did not measure the densities of the solutions. Opioids such as fentanyl are hypobaric, and when added to a local anesthetic they will render the subsequent mixture even more hypobaric. In addition, we did not record the time from administration of neuraxial block to initial requirement of postoperative analgesic.

In this comparative study of three different doses of levobupivacaine with fentanyl, 10 mg of levobupivacaine with 10 μg fentanyl provided fast and effective induction of surgical anesthesia for elective cesarean section. Yet, the incidence of maternal hypotension was higher in this group compared with the other two. 7.5 mg of levobupivacaine with 15 μg fentanyl were found to be more suitable as they led to a lower incidence of hypotension than 10 mg of levobupivacaine with 10 μg fentanyl and less epidural supplementation than 5 mg of levobupivacaine with 25 μg fentanyl. We believe that 7.5 mg of levobupivacaine with 15 μg fentanyl should be used in the CSE technique, as this combination may be insufficient for spinal anesthesia alone.

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