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# Effects of Levobupivacaine at Different Doses with Fentanyl added on Intrathecal Anaesthesia for Cesarean Section

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## Abstract

**Aim:** The main aim of this study is to investigate the effect of levobupivacaine at different doses with fentanyl added on intrathecal anaesthesia in cesarean section.

**Materials and methods:** This study is randomized, prospective and double-blind. Patients were divided into 3 groups (n=24 per group). Group 1: 11 mg levobupivacaine intrathecal, Group 2: 8 mg levobupivacaine+25 microgram fentanyl intrathecal and Group 3: 6 mg levobupivacaine+25 mg fentanyl intrathecal. Spinal anaesthesia start time, sensorial block time, motor block time, satisfaction of surgeon, satisfaction of patient, and analgesic consumption was recorded. The three groups were compared in terms of these values.

**Results:** Motor block time in Group 1 was statistically longer than Group 3. Additional analgesic requirements in Group 1 were statistically less than Group 2 and 3 at the end of surgery.

**Conclusion:** CSEA is gold standard for cesarean section. If local anesthetic dose is reduced anesthetic quality decreases, analgesic requirements increase and motor block recovery is shortened.

**Keywords:** Combined spinal epidural anaesthesia; Levobupivacaine; Fentanyl; Patient-controlled analgesia

for caesarean surgeries [1]. Some studies have been designed to find the best balance between the lowest dose required to prevent fetal and maternal side effects and good quality analgesia and to find the best dose of intrathecal local anaesthetic [2,3]. Currently, the low-dose opioid levobupivacaine is used; for example, it has been shown to reach sufficient analgesia without increasing side effects like rostral spread of block, motor block, maternal hemodynamic disorders and reduced uteroplacental blood flow developing afterwards [3-6]. Low-dose intrathecal local anaesthetic and epidural volume expansion ensure the possibility of forming sufficient anaesthesia level and may be used for neuraxial anaesthesia in risky pregnancies [7]. One of these local anaesthetics used at low dose of levobupivacaine, with same enantiomer and same pharmacological properties as bupivacaine but with less cardiotoxic and neurotoxic effects, has begun to be used for spinal and epidural anaesthesia [8]. Levobupivacaine ensures sufficient sensory block for caesareans, forms motor block with shorter duration, had less cardiac toxicity with excess dose and as a result is a good alternative to bupivacaine [9,10]. Intrathecal opioids are combined with local anaesthetics to reduce side effects and lengthen effect duration of local anaesthetics. Most of the time this combination lengthens quality and duration of postoperative analgesia, does not affect the APGAR of newborns after caesarean and provides a more comfortable birth [11].

One of the methods to reduce postoperative pain is patient-controlled analgesia. Benefits for sufficient treatment of postoperative pain have been shown [12,13]. Levobupivacaine is a local anaesthetic used for both intrathecal anaesthesia and for postoperative epidural analgesia with the PCA method [14].

## Introduction

Caesarean births are among the surgical interventions requiring very close teamwork between anaesthesiologists and surgeon, with the basic aim being a rapid birth without fetal or maternal side effects [1]. Caesarean anaesthesia uses general and regional anaesthesia techniques. Regional techniques are reliable for obstetric anaesthesia and are commonly-used anaesthesia methods. Neuraxial blocks are the gold standard

In this study, we planned to compare the effect of levobupivacaine or levobupivacaine+fentanyl at different doses with intrathecal administration to patients with planned elective caesarean operations. Comparisons of maternal spinal anaesthesia onset duration, sensory block duration, motor block duration, patient satisfaction, surgeon satisfaction and analgesic requirements during surgery and in the postoperative first 24 hours were made.

## Materials and Methods

This study was completed after receiving ethics committee permission from the local ethics committee, including patients with planned elective caesarean operation in the birth ward linked to the department of obstetrics and gynaecology who provided written informed consent. The study was randomized, prospective and double-blind and was completed in accordance with the Helsinki declaration of human rights. In an 8-case pilot study, we found time to reach T4 after spinal anaesthesia was  $4.2 \pm 1.6$  minutes in Group 1 and  $5.3 \pm 0.6$  minutes in Group 2. In order to find the 1.1 difference between the two groups significant with type 1 error 0.05 and test power of 0.8, each group required a minimum of 21 subjects.

### The exclusion criteria

- Caesarean surgeries of non-term pregnancies
- Multiple pregnancies
- Abnormalities of the fetus
- Maternal medical situations that may affect the fetus
- Cases with classification above ASA II
- Drug-addicted pregnant cases
- Body mass index >35
- Atopic body
- Situations preventing spinal-epidural anaesthesia
- Cases who did not wish to have regional techniques administered.

### The inclusion criteria

- Elective caesarean section surgeries
- Term pregnancies (37-41 weeks)
- No fetal distress.

Cases without premedication were given information about combined spinal epidural anaesthesia (CSEA) and patient-controlled analgesia (PCA) before being taken to the operation room. The PCA device was prepared with solution content of 100 ml physiologic serum, with 13 ml removed and 10 ml levobupivacaine+3 ml fentanyl inserted. PCA device settings were loading dose 10 ml, bolus dose 10 ml, basal infusion 10 ml, lock time 20 minutes and 4-hour limit of 80 ml. Loading dose was administered to patients with VAS value of 5 and above. Postoperative analgesic requirements were determined fully by the patients themselves in line with their own needs.

Patients taken to the operating room had electrocardiography, non-invasive arterial pressure (AP) and peripheral pulse oximetry (SpO<sub>2</sub>) monitoring performed. A twenty-gauge venous cannula was used to enter the antecubital vein, with 500 ml volume infused within 20 minutes, then continued with 10 ml/kg/hr physiologic serum infusion. All pregnant cases were placed in sitting position, with the skin of the intervention site cleaned with polyvinyl pyrrolidone and then local anesthetic infiltration with 2% lidocaine on the skin and sub dermal of the L3-4 or L4-5 interval. All patients had the CSEA technique used. An 18 G

Tuohy epidural needle (Espocan+Docking System+perifix mSoft Tip-Braun® Combine Spinal Epidural Set) was used to reach the epidural interval using the resistance-loss technique on the midline. Later a 27 G (Spinoca, Braun®) or 26 G (Atraucan 26 G 3×1/2, Braun®) spinal needle was used to enter the subarachnoid interval and after observing cerebrospinal fluid (CSF) medications were administered in group forms using a previously-prepared randomization program on a computer. To ensure a double-blind feature, the study solution was prepared by a different anaesthesiologist. Another anaesthesiologist who did not know the content of the solution injected the solution intrathecal within 30 seconds.

**Group 1:** 11 mg levobupivacaine (Chirocaine 50 mg/10 ml AbbVie, Takeda Pharmaceuticals Norway)=2.1 cc

**Group 2:** 8 mg levobupivacaine (Chirocaine 50 mg/10 ml AbbVie, Takeda Pharmaceuticals Norway)+25 µg Fentanyl (fentanyl, Braun, Germany)+isotonic=2.1 ml

**Group 3:** 6 mg levobupivacaine (Chirocaine 50 mg/10 ml AbbVie, Takeda Pharmaceuticals Norway)+25 µg Fentanyl (fentanyl, Braun, Germany)+isotonic=2.1 cc

After ensuring spinal anaesthesia, the epidural catheter was passed through the Tuohy needle and remained 3 cm within the epidural interval. Ensuring the skin entry site of the catheter remained sterile it was fixed at the waist and back and the tip of the catheter was placed on the right shoulder after inserting a bacteria filter. After this procedure, patients were placed in supine position and the operating table was placed in position with head 15° up and 20° to the left. To ensure sensorial block and motor block reached maximum levels, 20 minutes wait was ensured and then 2 ml 2% lidocaine+1 µg adrenaline mixture was administered through the catheter to examine whether there was an increase in heart rate (HR) and block level and confirm the position of the catheter. With CSEA procedure finished, the patient in supine position was administered free oxygen through a mask at 4 ml/min.

Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), heart rate (HR) and SpO<sub>2</sub> values were measured after spinal anaesthesia was administered, and every 2 minutes for the first 20 minutes. Then measurements were made every 5 minutes until the end of surgery. At the end of surgery measurements were made every 15 minutes until sensorial block fully ended. The time to reach T4 was recorded with the pin-prick test using a double-tipped 25-gauge needle on the mid-clavicular line with at most 20 minutes wait time. Patients who did not reach T4 level sensorial block within twenty minutes were excluded from the study. Patients with T4 sensorial block at the end of twenty minutes had surgery begun and PCA began. Duration to the beginning and end of surgery were recorded. The analgesia amount consumed up to the end of surgery and within the postop first 24 hours was recorded.

Surgeon satisfaction was evaluated by the surgical team using a 4-point scale.

1: Perfect (in terms of muscle relaxation, and patient movement) (No movement and ++++ muscle relaxation), 2: Good (in terms of muscle relaxation, and patient movement) (+ movement and +++ muscle relaxation), 3: Moderate (in terms of muscle relaxation, and patient movement) (++ movement and ++ muscle relaxation), 4: Weak (in terms of muscle relaxation, and patient movement) (+++ movement and + muscle relaxation) [15].

Patient satisfaction was assessed by patients using a 4-point scale:

1: Patient very satisfied, 2: unhappy with some things but satisfied, 3: not satisfied but not emergency analgesic requirements and 4: not satisfied with emergency analgesic requirements [2].

All patients waited 20 minutes after spinal anaesthesia was administered. Sensorial block was bilaterally assessed with time to reach T4 recorded. The regression time from T4-T6 was recorded. Patients had sensory block level and motor block level recorded 5 minutes after the procedure.

The sensorial block level, AP, HR and SpO<sub>2</sub> of patients were monitored and assessed in the postoperative recovery room. After the procedure ended, the duration to regress from T4 sensorial block to T6 was recorded as the sensory block duration. The duration until motor block completely ended after the procedure was recorded as motor block duration. When sensory and motor block fully ended patients were sent to the ward.

If HR of patients dropped below 60 beats/minute, 0.5 mg atropine was administered intravenously. A 20% fall in systolic arterial pressure from basal values was assessed as hypotension and 5-10 mg ephedrine bolus was administered intravenous. A 20% increase in systolic arterial pressure from basal values was assessed as hypertension. In this situation, patients were requested to use the PCA. Side effects developing preoperatively of nausea, vomiting, pruritus, respiratory depression and low saturation were recorded. Patients who continued with nausea-vomiting in spite of resolved hypotension were administered 8 mg ondansetron IV. If pruritus was allergic-based, pheniramine hydrogen maleate 22.7 mg IV was administered and if pruritus was due to neuraxial opioid 20 mg propofol IV was administered [16-18].

## Statistical analysis

Statistical analysis used the SPSS 11.5 for Windows program. Normal distribution of data was assessed with the Kolmogorov-Smirnov test. Variables with normal distribution were assessed with one-way analysis of variance from the parametric tests and if statistically significant differences were found, the post-hoc Tukey test was used to find which group caused the difference. Results are given as mean  $\pm$  SD. The chi-square test was used to compare categorical variables and results are given as % (n). For all tests,  $p < 0.05$  was accepted as statistically significant.

## Results

Comparison of patients included in the groups in terms of age, height, weight and gestational week did not observe any statistically significant differences between the 3 groups (**Table 1**).

Patients included the groups had no statistically significant differences observed between the 3 groups when compared in terms of time for sensorial block to reach T4 segment after spinal anaesthesia administration and sensorial block durations.

When patients included in the groups are compared in terms of motor block duration, there were statistically significant differences between the 3 groups. The motor block duration in Group 1 was statistically significantly longer compared to Group 3 ( $p = 0.014$ ) (**Table 2**).

**Table 1** Demographic data of patients included in the groups (mean  $\pm$  SD).

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

When patients included in the groups are compared in terms of patient numbers developing complications, there were no statistically significant differences between the 3 groups in terms of nausea, vomiting, additional medication requirements, bradycardia and hypotension (**Table 3**). However, there were statistically significant differences observed between the 3 groups in terms of pruritus ( $p < 0.001$ ).

When the 3 groups are compared separately in terms of itching, there were statistically significant differences between Groups 1 and 2 and between Groups 1 and 3 ( $p < 0.001$  and  $p < 0.001$ ).

The number of patients with pruritus in Groups 2 and 3 were higher than in Group 1. No patient had allergic-related itching. In all patients, pruritus was due to neuraxial opioid. All patients had pruritus treated with 20 mg propofol.

When spinal anaesthesia quality was assessed by the surgeon, there were no statistically significant differences in terms of moderate and poor-quality spinal anaesthesia numbers (**Table 4**). However, there were statistically significant differences between the groups in terms of numbers with perfect and good quality spinal anaesthesia.

When groups are compared in terms of perfect quality, there were statistically significant differences between Groups 1 and 3 and between Groups 2 and 3 ( $p = 0.002$  and  $p = 0.001$ ).

Groups 1 and 2 had more perfect quality compared to Group 3 according to surgeons. When groups are compared in terms of good-quality, there were statistically significant differences between Groups 1 and 3 and Groups 2 and 3 ( $p=0.001$  and  $p=0.001$ ). Group 3 had more good quality compared to Groups 1 and 2 according to surgeons.

**Table 2** Time to reach T4 sensorial block after spinal anaesthesia, sensorial block duration and motor block duration in patients included in the groups (mean  $\pm$  SD).

Time	Group 1	Group 2	Group 3	p-value
Time to reach T4 sensorial block after spinal anaesthesia (duration to onset of spinal anaesthesia) (minutes)	7.2 $\pm$ 4.12	8.4 $\pm$ 2.98	6.6 $\pm$ 4.53	0.265
Sensorial block duration (minutes)	65 $\pm$ 2.23	68.4 $\pm$ 2.67	57 $\pm$ 1.12	0.111
Motor block duration (minutes)	106 $\pm$ 12.8	88 $\pm$ 13.9	82 $\pm$ 9.6	0.03*

**Table 3** Comparison of complications developing in patients included in the groups (n%).

Complications		Group 1	Group 2	Group 3	p-value
Vomiting	+	21(31.3%)	22(32.8%)	24(35.8%)	0.222
	-	3(60%)	2(40%)	0(0%)	
Sedation requirements	+	23(33.3%)	24(34.8%)	22(31.9%)	0.352
	-	1(33.3%)	0(0%)	2(66.7%)	
Nausea	+	16(28.6%)	20(35.7%)	20(35.7%)	0.276
	-	8(50%)	4(25%)	4(25%)	
Pruritus	+	24(55.8%)	10(23.3%)	9(20.9%)	<0.001*
	-	0(0%)	14(48.3%)	15(51.7%)	
Bradycardia	+	21(31.3%)	22(32.8%)	24(35.8%)	0.222
	-	3(60%)	2(40%)	0(0%)	
Hypotension	+	11(30.6%)	12(33.3%)	13(36.1%)	0.846
	-	13(36.1%)	12(33.3%)	11(30.6%)	
*Statistically significant difference					

Spinal anaesthesia quality when assessed by patients had no statistically significant differences in terms of patient numbers who were not satisfied but did not require analgesia and who were not satisfied and required analgesia (**Table 5**).

However, there were statistically significant differences between the satisfied patient numbers in the groups.

**Table 5** Comparison of patient satisfaction in the groups (n%).

Patient satisfaction		Group 1	Group 2	Group 3	p-value
Satisfied	+	5(22.7%)	4(18.2%)	13(59.1%)	0.008*

When groups are compared in terms of satisfied patient numbers, there were statistically significant differences between Groups 1 and 2 and between Groups 1 and 3 ( $p=0.009$  and  $p=0.007$ ). The number of satisfied patients was higher in Groups 1 and 2 compared to Group 3.

When groups are compared in terms of analgesic amounts used in the PCA, the analgesic amounts used until the end of surgery were statistically significantly low in Group 1 compared to Groups 2 and 3 ( $p=0.024$ ). The analgesic amount used from the start of PCA in the first 24 hours postoperative was not statistically different when the groups were compared. When patients are compared in terms of duration of surgery, there were not statistically significant differences between the groups (**Table 6**).

**Table 4** Comparison of anaesthesia quality in patients included in the groups by surgeon assessment (n%).

Quality		Group 1	Group 2	Group 3	p-value
Perfect	+	4(22.2%)	2(11.1%)	12(66.7%)	0.002*
	-	20(37%)	22(40.7%)	12(22.7%)	
Good	+	22(37.3%)	22(37.3%)	15(25.4%)	0.010*
	-	2(15.4%)	2(15.4%)	9(69.2%)	
Moderate	+	23(33.3%)	24(34.8%)	22(31.9%)	0.352
	-	1(33.3%)	0(0%)	2(66.7%)	
Weak	+	23(32.9%)	24(34.3%)	23(32.9%)	0.598
	-	1(50%)	0(0%)	1(50%)	
*Statistically significant difference					

When all three groups are compared in terms of APGAR values used to assess new-borns, there was no statistically significant difference ( $p=0.067$ ). Statistical analysis of measurements performed every 2 minutes for the first 20 minutes after spinal anaesthesia was administered, every 5 minutes until the end of surgery and every 15 minutes until the end of sensorial block, there were not statistically significant differences found.

Spinal anaesthesia did not take in 1 patient in Group 1, 4 patients in Group 2 and 2 patients in Group 3, and general anaesthesia was administered. In 3 patients in Group 3 spinal anaesthesia formed but general anaesthesia was administered as patients continued to move. Three patients in Group 3 required deep sedation.

One patient in Group 1 could not have the epidural interval entered and general anaesthesia was administered. All these patients were excluded from the study. There is no difference between these three groups in terms of cost.

	-	19(38%)	20(40%)	11(22%)	
Satisfied a little	+	20(35.7%)	20(35.7%)	16(28.6%)	0.276
	-	4(25%)	4(25%)	8(50%)	
Not satisfied (but no analgesic requirements)	+	23(34.3%)	24(25.8%)	20(29.9%)	0.061
	-	1(20%)	0(0%)	4(80%)	
Not satisfied (analgesic required)	+	23(33.3%)	24(34.8%)	22(31.8%)	0.352
	-	1(33.3%)	0(0%)	2(66.7%)	

\*Statistically significant difference

**Table 6** Comparison of medications used in PCA and surgical durations in the groups (mean  $\pm$  SD).

Comparison of medications	Group 1	Group 2	Group 3	p-value
Analgesic amount used from beginning of PCA until end of surgery (ml)	7 $\pm$ 3.2	17.3 $\pm$ 3.1	24.8 $\pm$ 2.6	0.015*
Analgesic amount used from beginning of PCA until 24 hours postop (ml)	260.8 $\pm$ 14.8	271 $\pm$ 12.1	266 $\pm$ 10.5	0.123
Duration of surgery (minutes)	37 $\pm$ 8.6	38 $\pm$ 7.1	35 $\pm$ 6.8	0.067

\*Statistically significant difference

## Discussion

For caesarean surgeries it is important to create quality anaesthesia with optimum analgesia for the mother while ensuring sufficient muscle relaxation for the surgeon to perform surgery. At the same time, it is important to use appropriate doses of local anaesthetic and opioid mixtures for central block to set anaesthesia level and analgesia quality preventing disruption of fetal physiology, increase the onset rate of anaesthesia and reduce side effects [19]. At this point, there is a need to find medication combinations that create the desired ideal conditions. For comfortable CSE anaesthesia for caesarean operations, there is no definite consensus about the levobupivacaine and opioid dose needed and studies continue on this topic. D Ambrosia et al. used two different concentrations of 0.25% and 0.5% intrathecal levobupivacaine in two different patient groups and found no differences in terms of side effects and hemodynamic changes [1]. However, they observed the use of low concentration of levobupivacaine reduced the absence of motor block. In our study, we used 11 mg isobaric levobupivacaine intrathecal in Group 1 and we did not observe insufficient spinal anaesthesia in a total of 24 patients. In terms of APGAR values used to assess new-borns, there was no statistically significant difference between the three groups ( $p=0.067$ ). We did not assess neonatal cord blood gases in our study.

The study by Bidikar et al. used 7.5 mg levobupivacaine (0.5%)+12.5 mcg fentanyl and 10 mg levobupivacaine (0.5%) and ensured sufficient anaesthesia [20]. They stated the group with added fentanyl had short-duration motor block and better hemodynamic. In our study, we observed no difference between Groups 1 and 2 in terms of anaesthesia sufficiency.

One of the unwanted postop side effects in pregnant cases is long duration of motor block. Liao et al. administered intrathecal bupivacaine to one group and levobupivacaine to another group [21]. They identified the onset duration of motor block was long with levobupivacaine administration, but motor block regression duration was short. A study found that when intrathecal levobupivacaine is used, the duration of motor block regression is shorter compared to the use of bupivacaine [22].

A study administered spinal anaesthesia with levobupivacaine and bupivacaine and observed no statistically significant differences between sensory block onset duration (12  $\pm$  6 min and 9  $\pm$  5 min), motor block onset duration (11  $\pm$  6 min and 8  $\pm$  4 min) and motor block end duration (256  $\pm$  86 min and 245  $\pm$  86 min) [23]. In our study, the time to reach T4 was found to be 7.2  $\pm$  4.12 minutes in Group 1, 8.4  $\pm$  2.98 minutes in Group 2 and 6.6  $\pm$  4.53 minutes in Group 3. Motor block duration was 106  $\pm$  12.8 minutes in Group 1, 88  $\pm$  13.9 minutes in Group 2 and 82  $\pm$  9.6 minutes in Group 3.

When a study using levobupivacaine and levobupivacaine with added morphine for spinal anaesthesia aims in caesarean surgery was assessed by patients in terms of anaesthesia quality, there were no statistically significant differences between the two groups [24]. In our study, when anaesthesia quality is assessed by surgeons, there were statistically significant differences between the groups, with statistically significantly more perfect patients in Groups 1 and 2 compared to Group 3. When assessed for patient satisfaction, there were statistically significantly more satisfied patients in Groups 1 and 2 compared to Group 3. We think that as the dose of local anaesthetic reduces, surgeon and patient satisfaction reduce.

A study of patients with spinal anaesthesia using ropivacaine and ropivacaine+fentanyl found pruritus was

statistically significantly higher in the group with fentanyl [25]. Adding 25 mcg fentanyl, we identified the pruritus rate as 48.3% in Group 2 and 51.7% in Group 3. Pruritus was not observed at all in the first group, which supports the study by Kallio et al. [25]. Pruritus occurring in our patients was within their limits, and generally widely observed in the anterior region of the chest.

A study by Matsota et al. used diluted local anaesthetics of 1.5% levobupivacaine, 1.5% ropivacaine and 1.5% ropivacaine +2 µg/ml fentanyl in PCA for caesarean sections and considered they provided successful postoperative analgesia [14]. In the study, though there was equal local anaesthetic consumption in the 1.5% ropivacaine+2 µg/mL fentanyl groups, they observed higher patient satisfaction. In our study, analgesic consumption until the end of surgery was statistically significantly low in Group 1 compared to Groups 2 and 3. This situation leads to the consideration that as local anaesthetic dose reduces the patients feel low anaesthesia quality during surgical manipulation and this may explain the increase in analgesic requirements. However, there were no statistically significant differences between the groups in terms of analgesic amount consumed in the first 24 hours postoperative. This leads to the consideration those analgesic requirements in the first 24 hours postop is not affected by intrathecal use of low-dose opioids and local anaesthetic doses.

## Conclusion

In conclusion, when the three groups are compared in terms of onset of spinal anaesthesia and sensorial block duration, no statistically significant difference was observed. In terms of the surgeon, anaesthesia quality was statistically higher in Groups 1 and 2 compared to Group 3. For patient satisfaction, Groups 1 and 2 had statistically higher satisfaction compared to Group 3. The number of patients with intraoperative pruritus was statistically higher in Groups 2 and 3 compared to Group 1. The amount of analgesic consumed until the end of surgery in Group 1 was significantly lower compared to Groups 2 and 3; however, there was no statistically significant difference between the groups in terms of analgesia consumption in the first 24 hours postop. As dose of local anesthetic increases, anaesthesia quality increases, analgesic medication requirements reduce, surgeon quality and patient satisfaction increased and there was no difference between the groups in terms of side effects, but pruritus was increased in the groups administered opioid. We think administration of CSEA with intrathecal 11 mg levobupivacaine is an appropriate dose for caesarean surgery providing comfortable anaesthesia, sufficient analgesia and a pruritus-free operation.

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