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International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo



CLINICAL ARTICLE

Effect of combined spinal–epidural analgesia versus epidural analgesia on labor and delivery duration

Javier Pascual-Ramirez ^{a,*}, Javier Haya ^b, Faustino R. Pérez-López ^c, Silvia Gil-Trujillo ^a, Rosa A. Garrido-Esteban ^b, Ginés Bernal ^a

^a Anesthesiology Department, Ciudad Real University General Hospital, Ciudad Real, Spain

^b Obstetrics and Gynecology Department, Ciudad Real University General Hospital, Ciudad Real, Spain

^c Obstetrics and Gynecology Department, University of Zaragoza Clinic Hospital, Zaragoza, Spain

ARTICLE INFO

Article history:

Received 4 February 2011

Received in revised form 3 April 2011

Accepted 27 May 2011

Keywords:

Combined spinal–epidural analgesia

Labor and delivery duration

Labor epidural analgesia

Morphine spinal analgesia

Randomized trial

ABSTRACT

Objective: To determine whether combined spinal–epidural analgesia (CSEA) can decrease the known epidural effect of lengthening delivery. **Methods:** Between April and May 2010, 144 women undergoing childbirth in hospital with epidural pain relief were randomized to receive either low-dose epidural analgesia (LEA) or CSEA. The spinal component included 2.5 mg of bupivacaine, 25 µg of fentanyl, and 200 µg of morphine. The epidural component of the CSEA procedure was started once pain returned. The primary outcome was total labor duration measured from the time of initiation of labor analgesia to delivery. **Results:** The difference in duration between LEA (n=72) and CSEA (n=72) was 5 minutes for labor ($P=0.82$), 2 minutes for delivery ($P=0.60$), and 7 minutes for total labor duration ($P=0.75$). The combined group used less levobupivacaine ($P<0.001$) and had lower sensory blockade at the dermatomal level ($P=0.037$). Women in the CSEA group had a higher incidence of pruritus ($P=0.002$) and lightheadedness ($P=0.02$) during labor; and a higher incidence of pruritus ($P=0.002$), nausea–vomiting ($P=0.026$), and drowsiness ($P=0.003$) in the postpartum period. **Conclusion:** As compared with LEA, CSEA did not shorten the duration of labor length; however, it did reduce levobupivacaine consumption and motor weakness.

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1. Introduction

Pain control and satisfaction are obvious advantages of neuraxial analgesics for parturients. The traditional, local, anesthetic-based epidural procedure for labor has been associated with prolonged stage II, more frequent use of oxytocin augmentation, and increased incidence of instrumental vaginal delivery [1]. These effects have been attributed to impairment of the down-bearing Ferguson–Harris reflex, which is due to motor nerve blockade by the local anesthetic [2]. Low-dose epidural analgesia (LEA) and combined spinal–epidural analgesia (CSEA) may reduce these adverse effects. The American Society of Anesthesiologists (ASA) 2007 Practice Guidelines for Obstetric Anesthesia states that CSEA provides fast and effective analgesia, although its effects on duration of labor and motor block are equivocal [3].

We considered that, as compared with LEA alone, the combination of a short-onset opioid (fentanyl) with a long-lasting (morphine) opioid for spinal labor analgesia, followed by epidural analgesia should provide (1) longer periods without local anesthetic, use of more diluted local anesthetic, and less risk of motor-associated

weakness; (2) shorter total labor duration; and (3) better pain control and satisfaction (owing to increased mobility). Our primary goal was (2)—that is, to achieve shorter total labor durations.

The aim of the present study was to assess whether the underlying analgesia provided by the spinal component in a CSEA procedure allowed the anesthesia provider to manage the epidural component with a smaller amount of local anesthetic in order to shorten total labor duration, rather than to study any intrinsic influence of intrathecal opiates on labor. Our intervention choice necessarily included intrathecal morphine as a long-lasting agent to achieve the first goal (and consequently the second and third goals). Most previous studies of CSEA have used fentanyl and sufentanil as intrathecal opiates; these drugs were considered too short-acting to achieve the first goal.

2. Materials and methods

Between April 1, 2010 and May 25, 2010, 144 women undergoing childbirth with epidural pain relief at Ciudad Real University General Hospital, Ciudad Real, Spain, were enrolled in a randomized study. The study was approved by the hospital research and ethical boards, and eligible women gave written informed consent.

The sample size was based on the length of labor since the block was started (229 ± 115 minutes), as measured in a previous study of

* Corresponding author at: C/Besana, 2b Miguelturra, 13170 Ciudad Real, Spain. Tel.: +34 654516075/26240455.

E-mail address: pascrub@hotmail.com (J. Pascual-Ramirez).

pure epidural procedures in a mixed parity population. Considering a clinically significant time difference of 60 minutes, a power of 80% (two-sided test), and a significance level of 95%, 58 individuals would be required in each group. Allowing for a cesarean delivery rate of 20% and post-recruitment lose of 5%, we recruited 72 individuals per group.

Eligible individuals had to meet at least 2 out of 3 criteria (in addition to analgesia request): regular contractions every 2–3 minutes, cervical effacement, and cervix dilation of 2 cm. The exclusion criteria were estimated fetal weight of less than 2500 g or more than 4500 g; gestational age of less than 35 weeks; non-singleton; non-vertex presentation; ASA category 3 mother; body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) of 35 or higher before pregnancy; and neuromuscular disease. Major complications of the neuraxial procedure (e.g., wet tap, high block, subdural block, respiratory depression of the mother) were considered for exclusion after the patient was recruited.

Allocation to either the LEA or the CSEA procedure was done by opaque, sealed, computer-generated, numbered envelopes. The parturient and the obstetrician were blind to the procedure. Nurses were not aware of the content of the envelope, but were allowed to observe the procedure. Seven anesthesia providers took care of the parturients.

The CSEA procedure was performed with a needle (27G) through needle (18G Tuohy) technique (Braun, Melsungen, Germany). It was started with an intrathecal standard mixture of 0.20 mg of morphine; 25 µg of fentanyl, and 2.5 mg of hyperbaric bupivacaine. An epidural catheter was left in place and used when pain returned. The epidural component of the CSEA procedure was started on a second request for analgesia: 0.125% or 0.25% levobupivacaine with 0–50 µg of fentanyl. The LEA procedure was started with 10 mL of 0.125% or 0.25% levobupivacaine and 50 µg of fentanyl. An epidural infusion of 0.1% or 0.125% levobupivacaine was started after the epidural bolus.

The epidural infusion concentration was 0.1% or 0.125%; the infusion rate was 8 mL per hour; and the fentanyl dose was 0 or 2 µg/mL. The anesthesia provider always had 2 options—a high or low levobupivacaine concentration for bolus and drip, and fentanyl or no fentanyl—based on clinical data such as labor stage, gestational age, dermatome level, motor strength, and pain of the parturient. Because of the underlying effects of the spinal opiate, it was conceivable that the epidural component of CSEA (as opposed to LEA) could be run at the lower composition if the same requirements were applied to both groups in terms of pain control. Before allocation, all patients in both groups were treated intravenously with 10 mg of metoclopramide and 4 mg of ondansetron to diminish the nausea and pruritus associated with intrathecal administration of morphine.

The “intermediate anesthetic” outcomes included bolus and infusion volume, and dilution of levobupivacaine, fentanyl dose, sensory level of dermatome to cold measured by a chloroethyl jet, and motor weakness measured with the Bromage scale (1, elevate hips; 2, flexes knees; 3, moves feet; 4, no movement of legs) [4].

The main outcome was the total duration of labor (i.e. labor plus delivery) after initiation of the procedure. Women receiving CSEA had a cervical exam performed immediately before the epidural bolus was given to assess labor progression under spinal analgesia. All other cervical exams were decided by the obstetrician. The obstetric outcomes were delivery mode and labor complications (1-sided analgesia, nausea, tremor, pruritus, fever, low blood pressure, and lightheadedness).

Non-anesthesia-related personnel completed the pain and satisfaction questionnaire according to the numeric rating score (NRS; where 0 is no pain and 10 is the worst pain imaginable) [5] (1) at the first request for analgesia; (2) at 20–30 minutes after the initial procedure; (3) for the most representative point of the stage-I period; and (4) for the most representative point of the stage-II period. On

postpartum day 1, participants were asked whether they had any complaints during labor or after delivery, and about their satisfaction with the analgesic support. The choices were simple and understandable to any given cultural level of the parturient: “perfect”, “good”, “fair”, and “bad”. They were asked whether they would like to repeat the procedure for their next labor and delivery, even in the case that the discomforts (nausea, vomiting, pruritus, weakness, lightheadedness) experienced might be due to the analgesic technique.

Continuous variables were tested with Student *t* test and ordinals were tested with the Mann–Whitney test (Wilcoxon for repeated variables in the same groups). Categorical variables were tested with the χ^2 or Fisher exact test. A Kaplan–Meier plot of time-dependent birth was generated, and the Mantel–Cox test was used to compare the difference between the curves. A risk ratio (RR) with 95% confidence interval (CI) was calculated for continuous variables. A *P* value of less than 0.05 was considered to be significant. A Cox regression was also performed as multivariate analysis. Variables with a *P* value of less than 0.25 in the univariate analysis and those with an “a priori” clinical significance were included in the initial proportional hazards Cox regression model. PASW 18 (SPSS, Chicago, IL, USA) and Epidat 3.1 (SERGAS–WHO, Geneva, Switzerland) statistical computer packages were used for data analysis.

3. Results

Among 144 women enrolled in the study, 1 participant in the CSEA group received an intrathecal dose of morphine 3 times higher than the planned dose; and for 1 participant in the LEA group, the procedure was not completed owing to technical difficulties. These 2 participants were kept in their assigned groups to preserve the intention-to-treat analysis (Fig. 1).

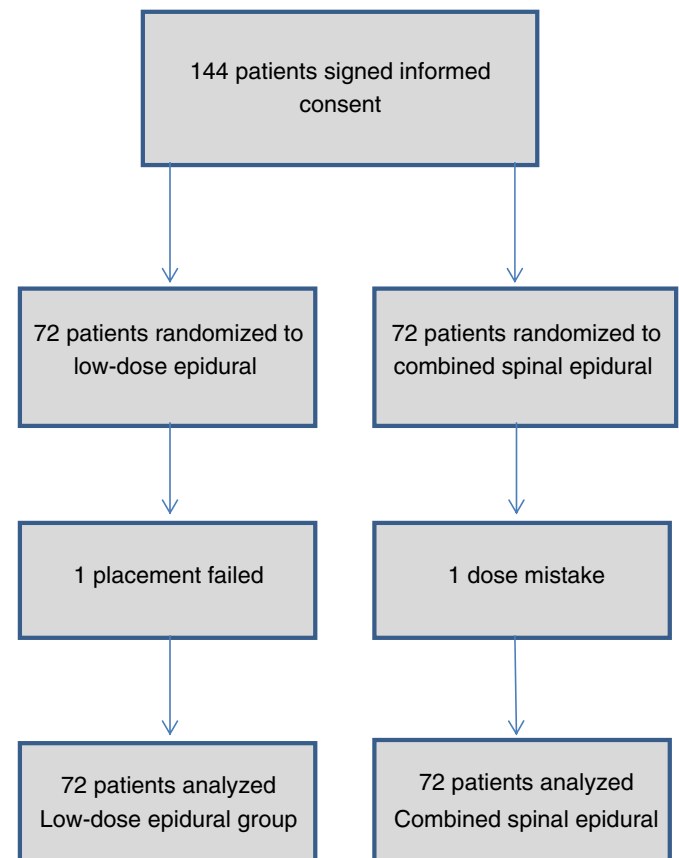


Fig. 1. Flow chart of patient recruitment, assignment, and intervention.

Table 1 shows the baseline characteristics of the participants. There were no significant differences among the 2 groups in baseline personal or obstetric characteristics.

There were no significant differences between the 2 procedures in duration outcomes, including stage I, stage II and total labor duration (Table 2). Labor and delivery durations lasting up to 300 minutes (5 hours) were identical among the 2 groups (Fig. 2). After this point in time, there was a non-significant (Mantel–Cox test, $P=0.095$) retardation in labor and delivery for participants given CSEA.

The average time duration of opioid spinal until further analgesia was requested was 113 ± 93 minutes, which represents 53.8% of stage-I time for the CSEA-treated group. Thirteen patients in the CSEA group did not request further anesthesia; 4 of these 13 women delivered by cesarean. Cervical examination of women in the CSEA group at the point of the second request for analgesia showed a small but significant ($P=0.045$) progression of labor from a median of 3 cm (interquartile difference 2–4 cm) to a median of 4 cm (interquartile 2–6 cm) during the time under intrathecal opioid analgesia.

Multivariate analysis showed that no analgesia-related factors were associated with total labor duration. Risk factors for prolonged total labor duration included nulliparity ($P=0.015$) and partum induction ($P<0.001$). Analysis of the subgroup of nulliparous women showed even shorter time differences (Table 2): 2 minutes for labor, 3 minutes for delivery, and 3 minutes for total labor duration.

Table 3 shows the secondary anesthetic outcomes. The procedure was started at a similar stage of labor. Thirteen patients included in the CSEA treatment did not ask for further analgesia after the initial intrathecal bolus. The dilution, volume, and fentanyl dose for both the bolus and the infusion were lower for the epidural component of the CSEA technique as compared with LEA. The sensory dermatomal level to cold measured by chloroethyl jet was higher among women who underwent the LEA procedure, but there was no significant difference in motor blockade measured with the Bromage scale.

Obstetric outcomes were similar among both groups (Table 3). The number of complications attributable to the analgesic technique were higher in the CSEA group both during ($P=0.025$) and after ($P<0.001$) labor and delivery. The particular complications noted were pruritus,

Table 1
Baseline characteristics of the participants.^a

	LEA (n = 72)	CSEA (n = 72)	P value
Age, years	31 ± 5	29 ± 6	0.11
Height, cm	162 ± 6	163 ± 6	0.88
Weight, kg	75.8 ± 10.3	4.5 ± 12.6	0.65
Gestational age at delivery, weeks	39 ± 2	39 ± 1	0.17
Cervical dilation, cm ^b			
Median (Q1–Q3) ^c	3 (2–4)	3 (2–4)	0.64
Latent phase (≤4 cm)	59 (78)	60 (80)	0.97
Newborn weight, g	3254 ± 370	3285 ± 456	0.60
Parity			0.93
Nullipara	38 (52.8)	38 (52.8)	
Primipara	26 (36.1)	25 (34.7)	
Multipara	9 (12.5)	10 (13.9)	
Labor type ^d			0.20
Spontaneous	22 (30.5)	28 (38.8)	
Augmented	29 (40.3)	30 (41.6)	
Induced	22 (30.5)	15 (20.8)	
Comorbidities/history			
Previous cesarean	0 (0.0)	5 (6.9)	0.12
Gestational diabetes	6 (8.3)	2 (2.8)	0.27
Gestational hypertension	3 (4.2)	1 (1.4)	0.61
Low back pain	6 (4.2)	3 (4.2)	0.49

Abbreviations: LEA, local anesthetic epidural; CSEA, combined spinal–epidural analgesia.

^a Values are given as mean ± SD or number (percentage) unless stated otherwise.

^b At initiation of the procedure.

^c Interquartile range.

^d Labor type as it was at the initiation time; labor type could change afterwards (e.g., spontaneous could be converted to augmented).

Table 2
Primary outcomes: time in minutes since the neuraxial block was started.

	LEA (n = 72)		CSEA (n = 72)		P value
	n	Mean ± SD	n	Mean ± SD	
Total population analysis					
Stage I period	63	204 ± 109	58	212 ± 133	0.85
Stage II period	62	42 ± 32	57	43 ± 34	0.60
Total labor duration	62	246 ± 112	57	255 ± 144	0.77
Nulliparous subgroup analysis					
Stage I period	34	237 ± 109	30	239 ± 142	0.94
Stage II period	33	48 ± 32	29	51 ± 34	0.76
Total labor duration	33	282 ± 113	29	185 ± 145	0.91

Abbreviations: LEA, local anesthetic epidural; CSEA, combined spinal–epidural analgesia.

nausea, and drowsiness (Table 4). Naloxone use for these adverse effects was not required among women in the LEA-treated group. By contrast, it was necessary for 8 CSEA-treated patients: 3 women during labor, and 5 women during the postpartum.

NRS-rated pain was significantly different ($P=0.002$) between the groups during stage II, with lower scores for the CSEA procedure (Table 4). By contrast, satisfaction about the analgesic support was higher among women in the LEA group during dilatation, but there was no difference during delivery.

4. Discussion

The main study hypothesis about total labor duration was clearly rejected because there were no differences in duration at all (Table 2). The subgroup of CSEA-treated patients who were able to deliver without an epidural component had a shorter stage I (67 minutes), stage II (22 minutes), and total labor duration (86 minutes), as compared with the remaining CSEA-treated patients. However, these differences were not significant, and are not likely to represent a benefit of spinal opiates. It is plausible that the women who had short labors in the CSEA group simply did not have a chance to ask for the second component of the CSEA. During the period under spinal analgesia for the CSEA procedure, dilatation progressed from 3 cm to 4 cm: this seems a poor achievement, considering that it accounted

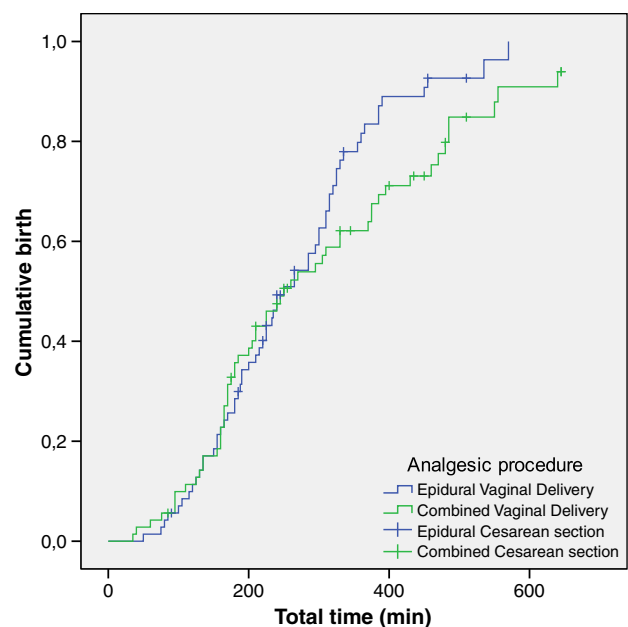


Fig. 2. Kaplan–Meier birth curve showing cumulative vaginal delivery and cesarean delivery rates in both epidural and combined groups.

Table 3
Secondary outcomes.

	LEA (n = 71)	CSEA (n = 71)	P value
Total l-bupivacaine consumption, mg	53.69 ± 13.04	36.77 ± 13.7	0.001
Total fentanyl consumption, µg	74.4 ± 12.1	37.7 ± 22.5	0.002
Dermatome level 30 min after technique, median (Q1–Q3) ^a	T10 (T7–T10)	T10 (T8–L1)	0.037
Initial Bromage after epidural			0.490
Median (Q1–Q3) ^a	1 (1–1)	1 (1–1)	
Score “1”	65 (92.9)	65 (92.6)	
Score “2”	5 (7.1)	3 (4.4)	
Score “3” and “4”	0 (0)	0 (0)	
Oxytocin			
No. taking maximal dose	49 (69.0)	44 (62.0)	0.690
Mean dose, mU/min	21.1 ± 12.1	21.6 ± 12.6	0.870
Bromage score by end of stage I			0.057
Median (Q1–Q3) ^a	1 (1–2)	1 (1–1)	
Score “1”	37 (67.3)	43 (84.3)	
Score “2”	17 (30.9)	6 (11.8)	
Score “3”	1 (1.8)	2 (3.9)	
Score “4”	0	0	
Delivery mode			
Cesarean delivery	10 (14.1)	15 (21.1)	0.270
Indication for cesarean			
Progression arrest	8 (11.1)	9 (12.5)	0.570
Nonreassuring fetal status	2 (2.8)	6 (8.3)	0.410
Vaginal delivery			
Spontaneous	57 (79.2)	54 (75)	0.680
Instrumental	4 (5.6)	2 (2.8)	
Apgar score, median (Q1–Q3) ^a			
1-minute score	9 (9–9)	9 (9–9)	0.660
5-minute score	10 (9–10)	10 (10–10)	0.650
Labor complications			
One-sided analgesia	6 (8.4)	2 (2.8)	0.270
Nausea	4 (5.6)	8 (11.2)	0.360
Tremor	3 (4.2)	0	0.240
Pruritus	4 (5.6)	18 (25.3)	0.002
Fever	2 (2.8)	2 (2.8)	1.00
Low blood pressure	2 (2.8)	2 (2.8)	1.00
Lightheadedness	0	10 (14.1)	0.020
Postpartum complication			
Low back pain	4 (5.6)	5 (7.0)	1.00
Leg weakness	1 (1.4)	1 (1.4)	1.00
Nausea	3 (5.6)	12 (28.1)	0.026
Pruritus	3 (4.2)	20 (28.1)	0.002
Urinary retention	2 (2.8)	2 (2.8)	1.00
Drowsiness	3 (4.2)	19 (26.7)	0.003

Abbreviations: LAE, local anesthetic epidural; CSEA, combined spinal–epidural analgesia.

^a Interquartile range.

for 50% of the duration of stage I (113 out of 210 minutes), but no comparison with the LEA group is available.

Neuraxial analgesia in nulliparous women has been associated with a slower active labor [6]. These data have been largely supported by observational studies about the first and second stages [7]. Evidence from randomized control trials suggests that only the second stage is prolonged by epidural analgesia, and is not conclusive about the first stage [1].

A systematic review [8] did not make conclusions about the total duration of labor with CSEA versus LEA because usually this outcome is not the primary one and is under-reported. Nevertheless, most of the available data do not show differences in labor duration [9–13]. The COMET trial [9] was close to demonstrating a shorter labor time of more than 60 minutes for LEA ($p=0.06$) and CSEA ($P=0.15$), as compared with traditional epidural. Tsen et al. [14] found faster cervical dilation with a sufentanil spinal, but their high proportion of cesarean delivery (>30%) downsized their sample ($n=34$ versus $n=32$). Bhagwat et al. [15] found that the first stage was 75 minutes shorter in their intrathecal fentanyl group compared with epidural bupivacaine ($n=30$ versus $n=30$). Wong et al. [16] compared intrathecal fentanyl with systemic hydromorphone and found that labor was 90-minutes shorter with the former intervention.

Table 4
Pain numeric rating scale and overall satisfaction with analgesic procedure.

	LEA (n = 71)	CSEA (n = 71)	LEA	CSEA	P value
	Number (percentage)		Median (Q1–Q3)		
NRS before analgesia			8 (7–10)	8 (7–9)	0.610
NRS after initial procedure			2 (0–4)	4 (0–7)	0.200
Stage I NRS			2 (0–4)	1 (0–4)	0.820
Stage II NRS			3 (0–7)	0 (0–4)	0.002
Initial satisfaction			1 (1–2)	2 (1–2)	0.004
Perfect	42 (59.2)	26 (36.3)			
Good	25 (35.2)	33 (46.5)			
Fair	3 (4.2)	11 (15.5)			
Bad	1 (1.4)	1 (1.4)			
Stage I satisfaction			1 (1–2)	2 (1–2)	0.005
Perfect	43 (60.6)	24 (34.4)			
Good	21 (29.6)	37 (52.9)			
Fair	5 (7.0)	8 (11.4)			
Bad	2 (2.8)	1 (1.4)			
Stage II satisfaction			2 (1–3)	2 (1–2)	0.400
Perfect	22 (36.1)	22 (39.3)			
Good	18 (29.5)	21 (37.5)			
Fair	17 (27.9)	9 (16.1)			
Bad	4 (6.6)	4 (7.1)			
Patient would not repeat analgesic procedure next time	1 (1.4)	4 (5.6)			0.170

Abbreviation: NRS, numeric rating scale for pain.

^a Interquartile range.

Only 3 randomized controlled trials of CSEA versus epidural intervention have included intrathecal morphine in the CSEA procedure: Abouleish et al. [17] ($n=40$; morphine dose, 0.2 mg) found prolonged stages I and II; Caldwell et al. [18] ($n=26$; dose, 0.25 mg) did not control for time; and Culha et al. [19] ($n=20$; dose, 0.1 mg) found a shorter first stage among women in the CSEA group including intrathecal morphine. These randomized controlled trials were probably underpowered to draw reliable conclusions. Studies of CSEA that did not include morphine have not reached unequivocal conclusions, and do not necessarily apply to CSEA interventions including morphine.

The intermediate goal of the present study, which was to use a smaller volume and concentration of epidural local anesthetic in the CSEA group, was sufficiently achieved, as has been described elsewhere [20]. In fact, 13 patients treated by CSEA did not request further analgesia after intrathecal opioid administration. Levobupivacaine consumption (53.69 mg versus 36.77 mg, $P=0.001$) and fentanyl consumption (74.4 µg versus 37.7 µg, $P=0.002$) were lower in the CSEA group. The dermatome sensitive level was lower for CSEA. Therefore, the prior condition to prove the hypothesis—what we termed “intermediate anesthetic” outcomes—was essentially achieved (Table 3).

The loss of abdominal wall strength associated with local anesthetics during pushing efforts may be compensated by pelvic relaxation favoring the progress of labor. This would explain the lack of shortening of labor or delivery among women in the CSEA-treated as compared with the LEA-treated group. A similar absence of this time-sparing effect has been reported in a study comparing early start LEA with late start LEA [21].

A systematic review pointed out that a higher rate of pruritus is associated with CSEA, but found no difference in nausea, vomiting, drowsiness, or lightheadedness [9]. The higher proportion of postpartum complications in the present study may be due to the long-lasting central effects of intrathecal morphine, as pointed out in a meta-analysis [22]. Naloxone was rarely used in the present study because the preventive protocol for pruritus and nausea [23] minimized the impact of these adverse effects.

During dilatation, there was no significant difference in pain control but satisfaction was worse among women in the CSEA group because they were experiencing discomfort owing to adverse effects of the intrathecal morphine (nausea, pruritus, drowsiness) as compared with LEA patients. During delivery, pain control was better among women in the CSEA group because they had the epidural component in use at that point in time, blocking breakthrough pain as previously described [24].

The present study has several limitations. First, the patients and obstetricians were blind to the allocated procedure, but the analgesia providers and nurses were not. Second, the protocol did not tightly fix the epidural components, but instead considered high and low options and analyzed the result as an intermediate outcome (the spinal opiate was supposed to allow the anesthesia provider to choose the low option). This was a prior condition to prove the main hypothesis, but certainly might introduce variability in the results. Using a fixed protocol for the epidural component would have increased the chances of proving the hypothesis, but at the risk of having many patients with inadequate pain relief and satisfaction. Last, the population was not limited to nulliparous patients: this could be a source of variability but increased the external validation and clinical applicability of the results.

Despite these limitations, the present results discourage the assumption that CSEA with intrathecal morphine–fentanyl favors the progression of labor and delivery better than LEA. Intrathecal morphine–fentanyl was used in the interventions, and the conclusions may not apply to other intrathecal opiates.

Conflict of interest

The authors have no conflicts of interest.

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