Low and Ultra-Low CSE Anesthesia in Elective Cesarean Sections. Prospective Randomized and Experimental Study

L. Puertas*, E. Guasch, E. Alsina, A. Dominguez, N. Brogly and F. Gilsanz

Department of Anesthesiology, Hospital Universitario La Paz, Madrid, Spain

Abstract: *Objective*: Regional anesthesia is the preferred technique used in elective cesarean sections. The controversy lies in knowing what dose of local anesthetic allows for the safety of both mother and fetus during the procedure. The combined spinal-epidural technique (CSE) allows the intradural dose to be lowered, ensuring an adequate block through additional epidural doses. Our aim was to study the success of the technique.

Method: We carried out a prospective, randomized study of 102 women scheduled for cesarean section. Our objective was to study the incidence of maternal hypotension, the success of the technique, motor block, and repercussions in parameters of fetal well-being after performing a combined technique (CSE) with low and ultra-low doses of hyperbaric levobupivacaine (LB-5mg *versus* LB-3.75mg) plus epidural extension with 10ml of isobaric levobupivacaine 0.25%.

Results: We found no difference in the incidence of maternal hypotension between our groups. The overall success of the technique was 81.4% directly relating to the length of the surgical procedure. 18.6% of the patients required some type of analgesic booster in the course of the study. We found no difference in the type of neonatal resuscitation used, but there was a statistically significant difference in umbilical cord arterial pH.

Conclusion: The use of low and ultra-low doses can be an alternative in carefully selected cases. The doses used were sufficient for the cesarean section to be performed in the majority of our study subjects. We did not find evident advantages with regard to the incidence of maternal hypotension and we do not believe that the use of ultra-low doses proves beneficial.

Keywords: Local anesthesia, low doses, combined spinal-epidural technique, CSE, cesarean section, maternal hypotension, neonatal resuscitation, fetal pH.

1. INTRODUCTION

Regional anesthesia has become the preferred technique in performing cesarean sections, whether elective or on an emergency basis [1]. Its main advantage consists in the avoidance of a loss of airway control, thus avoiding the ensuing complications. Nevertheless, its main disadvantage is found in the high incidence of maternal hypotension, which affects three women in four [2]. This makes strict monitoring necessary during surgery as well as the administration, sometimes in prophylactic form, of vasopressors such as phenylephrine [3,4] or ephedrine [5,6]. Although the benefits to the mother have been well-documented, the true impact on the newborn is unclear. For that reason, many groups try to reduce the incidence of hypotension secondary to regional anesthetic techniques by reducing the dose of local anesthetic used [5, 7-13]. The advent of combined spinal-epidural (CSE) techniques allow these doses to be lowered, ensuring the safety of the mother at all times. Additionally, CSE allows for analgesia with rapid onset, a more suitable level of relaxation than that obtained through the use of isolated epidural techniques, and the prospect of extending the block both in duration as well as in metameres through the epidural catheter [10, 14].

Our aim was to study the success of the technique as well as compare the incidence of maternal hypotension, the degree of motor block and the repercussions in parameters of fetal well-being utilizing two different levels of spinal doses (low or ultra-low), both with epidural volume extension (EVE) of local anesthetic during elective cesarean section procedures.

2. MATERIALS AND METHODS

The study was carried out in a tertiary hospital with an average of 8000 births (25% cesarean). After receiving the approval of our institution's ethics committee (Adjudication Code 2535) and patient-informed consent, we performed a prospective randomized (computer-generated random list) study comparing two doses of spinal local anesthetic with epidural extension using 10 ml of levobupivacaine 0.25%.

Our inclusion criteria were women between the ages of 18 and 45 yrs, ASA classification I-III, body mass index less than 30 kg/m^2, gestational age of over 36 weeks, singleton pregnancy and category 3-4 of NICE classification [15,16]. Excluded were women who

*Address correspondence to this author at the Department of Anesthesiology, Hospital Universitario La Paz, Madrid, Spain; Tel: +1 (612-3604578); Fax: 917277050; E-mail: laurapuertas@hotmail.com

E-ISSN: 2310-9394/15

presented with any contraindication for the performance of regional anesthesia techniques, such as allergy to local anesthetics or acute coagulopathies, patients with hypertension pathology whether prior to or caused by the pregnancy, gestational or pregestational diabetes, or those with an ASA classification > III, NICE classification 1-2, or body mass index of over 30 kg/m^2.

Sample size calculation was based on the formula for calculating the statistical power for comparison of proportions. To do so, we are assuming an expected incidence of hypotension of 14% in group LB-3.75 [17] and of 35% in group LB-5 [13]. 102 patients were divided into two groups randomized by computer. Upon arrival at the operating room, the patients were monitored in the customary manner (ECG, pulse oximetry and NIBP) and a 16G gauge peripheral line was inserted. All of the patients received co-hydration with 500 cc of Ringer's Lactate. Immediately thereafter the combined spinal (27G) – epidural (18G) block was carried out under strict asepsis, utilizing Braun Espocan + Docking System + Perifix Soft Tip equipment. The regional CSE technique was carried out in a sitting position at level L3-L4 or L4-L5. Immediately after insertion of the epidural catheter, the patient was placed in a left lateral decubitus position with a 15^o Trendelenburg incline for final positioning of the catheter, after which the patient was placed in a supine decubitus position and the agreed-upon dose of 10 ml of isobaric levobupivacaine at 0.25% was administered epidurally. Trendelenburg was maintained for a minimum of 10 minutes up until commencement of surgery. The patients assigned to the group defined as low dose (LB-5) received 5 mg of hyperbaric levobupivacaine plus 25 µg of fentanyl spinally and the patients assigned to the group defined as ultra-low dose (LB-3.75) received 3.75 mg of hyperbaric levobupivacaine and 18 µg of fentanyl spinally. In both cases, 10 ml of levobupivacaine 0.25% were administered epidurally.

The record of hemodynamic parameters: Systolic blood pressure (SBP), Diastolic blood pressure (DBP), heart rate (BPM) and oxygen saturation (SaO_2) were taken at the basal level and at 3, 5, 10, 15 and 20 minutes and every 10 minutes from that time on until surgery was complete. Mean arterial pressure of 20% below basal was considered maternal hypotension, in which case 10mg of ephedrine were administered IV. The level of sensory block (described in Table **1**) was monitored by means of the "pinprick" technique (light, successive pinpricks all along the mid-axillary line) every five minutes from the beginning of the procedure until the end of the operation. The level of motor block was also evaluated according to the modified Bromage scale [17] before placement of the surgical drapes, at the end of the operation, during the time in the PACU, as well as on the following day (as a part of a quality-control routine postoperative visit).

Table 1: Sensory Block Assessment

Pain of Sensitivity Level (Pin-Prick)	Sensory Block
T4	Optimal
T4-T6	Adequate
Above T4	Excessive
Below T6	Insufficient

Analyses were done of the time it took to reach a level of sensory blockade of the T4 dermatome (T° T4); the time of incision (T° Incision), defined as the period from the performance of the combined technique (CSE) until skin incision; the I-D time (incision-delivery or T° ID), defined as the time from the skin incision until the clamping of the umbilical cord; and the total time (T° total), defined as the time from the beginning of the block until the end of the operation. Parameters of fetal well-being were determined by the type of neonatal resuscitation needed, and the umbilical cord arterial pH (Rapidlab® 1245, Bayer Healthcare).

We define "technique success" when the sensory block was optimal or adequate in the first 15 minutes. We define "late onset" (LO) when the sensory block turned out to be insufficient in the 15 minutes following the puncture. In that case, a single epidural booster would be administered with a local anesthetic (10 ml of lidocaine 2%). We define "insufficient dose" (ID) when, despite having achieved a level of block adequate to be able to begin the surgical procedure, some type of booster was needed, whether epidurally prior to fetal extraction (10 ml of lidocaine 2%) or intravenously after the clamping of the umbilical cord (100 µg of fentanyl). We define "technique failure" (TF) when a level adequate to begin was not reached in the first 15 minutes nor after administration of the epidural supplement, in which case the patient would be placed under general anesthesia. We define "global failure" as the sum of LO, ID and TF.

Similarly, complications, undesirable effects or other problems which could arise in the course of the technique were recorded, such as nausea and/or vomiting, pruritus, drowsiness, bradycardia, tremor, accidental dural puncture with the Tuohy needle or

hematic puncture (canalization of an epidural vein with the epidural catheter).

The patients remained under observation in our PACU for 6 hours following the C-section. They were then transferred to the ward after verification of an adequate level of uterine involution, the absence of vaginal bleeding, full recovery from the motor block and an appropriate level of analgesia.

The chosen variables were analyzed by means of the SPSS INC statistical software package, version 11.0, Chicago, Illinois, USA. The numerical variables are described using central tendency statistics, standard deviation, and mean of the differences between distinct moments of the study with 95% confidence intervals. Comparisons were made using t-Student when two groups were being compared or ANOVA when the analysis included three or more groups. The categorical data and proportion are described by means of absolute and relative frequencies expressed in absolute number and percentage. Comparisons were made using a Chi-Square test.

3. RESULTS

The test groups turned out to be homogeneous and therefore comparable in demographic data, surgical times, level of basal pressure, and history of abdominal/pelvic surgery (Table **2**).

Table 2: Demographic Data. Group Homogeneity

LB-5	LB-3.75	LB-5	P
Age years ± SD	32.8 ± 4.8	32.9 ± 5.1	0.94
mean **BMI** ± SD	28.4 ± 3.8	28.0 ± 3.4	0.57
Total T min ± SD	48.5 ± 10.5	49.9 ± 10.4	0.46
T incision min ± SD	13.8 ± 3.3	13.8 ± 4.5	0.98
T I-D min ± SD	20.8 ± 4.9	23 ± 8.7	0.12
T T4 min ± SD	9.1 ± 2.9	8.8 ± 3.3	0.26
SBP basal mmHg ± SD	126.3 ± 14.1	129.8 ± 10.3	0.16
DBP basal mmHg ± SD	79.9 ± 8.0	80.9 ± 9.1	0.56
Prior abdominal/pelvic surgery	23 (26.5%)	27 (26.5%)	0.69

SD: Standard deviation,

LB: Levobupivacaine,

SBP: Systolic blood pressure,

DBP: Diastolic blood pressure,

T: Time,

I-D: Incision-delivery time,

T4: 4th thoracic block sensory level time,

Prior abdominal/pelvic surgery (including cesarean section, myomectomy, cholecystectomy, and appendectomy).

Overall incidence of hypotension in our series was 42.1%. Analyzing each group separately, we found a 41.2% incidence of hypotension among the patients in group LB-3.75 and 43.2% in group LB-5 ($p > 0.05$) (Table **3**).

Table 3: Incidence of Hypotension by Group

	LB-3.75 (n and %)	LB-5 (n and %)
HypoTN no	30 (58.8%)	29 (56.8%)
HypoTN yes	21 (41.2%)	22 (43.2%)

$p > 0.05$, Data shown in number of patients (n) and percentage (%), HypoTN: Arterial blood pressure of 20% below basal.

The total success of the technique was 81.4% when analyzing the two groups as a whole. This means that 38 patients in LB-3.75 and 45 patients in group LB-5 didn't receive any kind of rescue (p=0.126).

If we divide the failures according to typology, we find the following results: Late onset occurred in 2 patients (2%) in LB-3.75 and in 3 patients (3%) in LB-5. Insufficient dose was found in 11 patients (10.8%) in LB-3.75 and in 3 patients (3%) in group LB-5 ($p > 0.05$).

The causes triggering the need for an epidural or intravenous booster followed a similar pattern in group LB-5. Nevertheless, the need for a booster in the LB-3.75 group was primarily due to an insufficient dose (21%). There was no case of “technique failure” as defined above; therefore, it was not necessary to switch any of our patients to general anesthesia.

A history of previous surgery could potentially increase the difficulty of the C-section due to adhesions. The absence of a history of prior abdominal/pelvic surgery was a determining factor in the success of the technique in group LB-5. That is to say, the additional epidural or intravenous booster was only necessary in the patients from group LB-5 with prior abdominal/pelvic surgery (p=0.024). Nevertheless, in group LB-3.75, the duration of the procedure was the determining factor for success (p=0.001). That is to say, the possibility of failure with said dose increases if there is an increase in the length of the surgical procedure (Table **4**).

The level of sensory block was sufficient (above T6) for surgery to commence in more than 90% of the cases. At the end of the operation, it was estimated that the sensory level should be at the level of the T4 dermatome in order to ensure adequate analgesia

Table 4: Relation between Global Failure and Duration of Surgery in LB-3.75 and Global Failure and History of Prior Surgery in LB-5

LB-3.75	Patients: n (%)	Mean Duration Shown in Minutes (SD)
Success	38 (74.5%)	45.57 (8.8)
Global Failure (LO + ID + TF)	13 (25.4%)	57.38 (10.2)

p=0.001.

LB-5	With h/o Prior Surgery: n (%)	Without h/o Prior Surgery: n (%)
Success	21 (41.1)	24 (47.1)
Global Failure (LO + ID + TF)	6 (11.8)	0

p=0.024.

SD: Standard deviation,

LO: Late onset,

ID: Insufficient dose,

TF: Total failure.

during examination of the uterine cavity. At this time, 82.3% of the patients in group LB-5 were still at an appropriate level as opposed to 60% of group LB-3.75 (p=0.027).

Motor block at the end of the operation was linked to the initial dose and the need for epidural booster. 84.3% of group LB-3.75 and 54.9% of group LB-5 left the operating room with a Grade 0 block on the modified Bromage scale. Overall, almost 100% of these patients had not needed any booster through the epidural catheter during the surgery.

We found no difference in the type of neonatal resuscitation required. Nevertheless, we did find statistically significant differences in the umbilical cord arterial pH, being significantly lower in the LB-5 group (Table **5**). The number of samples tested was less than the number of patients included in the study due to technical problems with the samples. We found no difference in the rest of the side effects studied, including the incidence of nausea and/or vomiting.

4. DISCUSSION

The most relevant finding in our study reflects that the decrease in the dose of hyperbaric levobupivacaine did not result in a clinically relevant decrease in the incidence of arterial hypotension. Many authors have tried to adjust the dose of local anesthetic administered, making good use of the advantages offered by the combined spinal-epidural technique.

Table 5: Neonatal Reanimation and pH Per Group

	Rea 1	Rea 2	Rea 3	Rea 4
LB-3.75	48 (94,1)	2 (3,9)	1 (2,0)	0 (0)
LB-5	45 (88,2)	4 (7,8)	2 (3,9)	0 (0)
Total	93 (91,2)	6 (5,9)	3 (2,9)	0 (0)

p=0.57.

Rea 1: No required additional maneuvers,

Rea 2: Required O_2 by facial mask,

Rea 3: Required O_2 by CPAP,

Rea 4: Required endotracheal intubation,

Rea 5: Required inotropic drugs.

	N (%)	Mean	SD	Minimum	Maximum
LB-3.75	35 (67)	7.3	0.04	7.21	7.36
LB-5	44 (84)	7.26	0.06	7.06	7.38
Total	79 (77.4)	7.28	0.06	7.06	7.38

p=0.012.

SD: Standard deviation.

Hence, studies have appeared with doses much lower than the ED50 giving evidence of greater hemodynamic stability [8,9]. Our results line up with the incidence of hypotension shown in previous series. However, we were not able to corroborate the 14% incidence published by the Teoh group, nor did we find significant differences between our groups. We consider that the overall success of the study was due, in part, to the average time in which cesareans are performed in our institution, less than 45 minutes skin to skin. The absence of a history of prior abdominal/pelvic surgery was likewise shown to be a predictive factor for a successful result in group LB-5. Both factors – surgical time and history of prior abdominal/pelvic surgery – are closely connected. Hence, like other authors [11], we consider that duration of surgery is the main limiting factor for success when working with low or ultra-low doses.

The level of analgesia was appropriate in the majority of patients by the beginning of the operation and, although group LB-3.75 required more booster doses to avoid any sensation of pain or discomfort, our total success fell within the levels accepted in the bibliography [13].

We had no case of total failure, which is why it was not necessary to switch any patient to general anesthesia. Such a high rate of success is due to the experience and training of the entire anesthesia team.

The majority of our patients left the operating room with a degree of block of 0 or 1 on the modified Bromage scale. Taking into account the current tendency to be in favor of and potentiate the first contact between mother and child to the extent possible, less motor block could lead to a shorter stay in PACU, which would facilitate earlier mother-child contact. This could be another of the arguments in favor of the use of low or ultra-low doses in those cases which meet the previously described conditions.

Umbilical cord arterial pH values have been proposed as reference parameters to evaluate fetal perfusion and as a reflection of the hemodynamic stability of the mother [1]. However, the limited difference in the data obtained in our study is clinically irrelevant. Perhaps, as pointed out by Reynolds and Seed [18], we consider that it could be a technique to which thought should be given in cases of fetuses in compromising situations, given that there is a fetus, especially in group LB-5 with values of less than 7.10.

The use of ephedrine as vasopressor of choice constituted a limitation to our study. However, we decided to continue with its use in this study given that we had worked with it on prior occasions [13]. Today, however, the use of phenylephrine [19] is well documented in the literature and its administration, based on minimally invasive hemodynamic monitoring, may be the path to “zero hypotension,” which is the goal in cesarean section, in order to achieve an appropriate balance between the mother’s comfort (appropriate anesthesia without nausea and hypotension) and the well-being of the fetus.

The use of low and ultra-low doses does not guarantee the absence of maternal hypotension. Nevertheless, we consider that the combined spinal-epidural technique with low or ultra-low doses could be a good option in cases of women at high risk, in which the mother’s hemodynamic stability is key. We believe it necessary to continue exploring multimodal strategies which allow us to draw closer to the desired goal of “0” maternal hypotension [18].

REFERENCES

[1] Habib AS. Anaesthesia for caesarean delivery of growth-restricted foetuses: a bird in the hand is worth two in the bush. Eur J Anaesthesiol 2013; 30(1): 5-6. http://dx.doi.org/10.1097/EJA.0b013e328357659b

[2] Rout CC, Rocke DA, Levin J, Gouws E and Reddy D. A reevaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. Anesthesiology 1993; 79(2): 262-269. http://dx.doi.org/10.1097/00000542-199308000-00011

[3] Doherty A, Ohashi Y, Downey K and Carvalho JC. Phenylephrine infusion versus bolus regimens during cesarean delivery under spinal anesthesia: a double-blind randomized clinical trial to assess hemodynamic changes. Anesth Analg 2012; 115(6): 1343-1350. http://dx.doi.org/10.1213/ANE.0b013e31826ac3db

[4] Cooper D, Schofield L, Hynd R, Selvan D, Lloyd A, Meek T and Winnard J. Prospective evaluation of systolic arterial pressure control with a phenylephrine infusion regimen during spinal anaesthesia for caesarean section. Int J Obstet Anesth 2012; 21(3): 245-252. http://dx.doi.org/10.1016/j.ijoa.2012.02.009

[5] Van de Velde M, Van Schoubroeck D, Jani J, Teunkens A, Missant C and Deprest J. Combined spinal-epidural anesthesia for cesarean delivery: dose-dependent effects of hyperbaric bupivacaine on maternal hemodynamics. Anesth Analg 2006; 103(1): 187-190, table of contents. http://dx.doi.org/10.1213/01.ane.0000220877.70380.6e

[6] Coppejans HC and Vercauteren MP. Low-dose combined spinal-epidural anesthesia for cesarean delivery: a comparison of three plain local anesthetics. Acta Anaesthesiol Belg 2006; 57(1): 39-43.

[7] Arzola C and Wieczorek PM. Efficacy of low-dose bupivacaine in spinal anaesthesia for Caesarean delivery: systematic review and meta-analysis. Br J Anaesth 2011; 107(3): 308-318. http://dx.doi.org/10.1093/bja/aer200

[8] Leo S, Sng BL, Lim Y and Sia AT. A randomized comparison of low doses of hyperbaric bupivacaine in combined spinal-epidural anesthesia for cesarean delivery. Anesth Analg 2009; 109(5): 1600-1605. http://dx.doi.org/10.1213/ANE.0b013e3181b72d35

[9] Teoh WH and Sia AT. Ultra-low dose combined spinal-epidural anaesthesia for Caesarean section in severe pre-eclampsia. Anaesthesia 2006; 61(5): 511-512. http://dx.doi.org/10.1111/j.1365-2044.2006.04630.x

[10] Lew E, Yeo SW and Thomas E. Combined spinal-epidural anesthesia using epidural volume extension leads to faster motor recovery after elective cesarean delivery: a prospective, randomized, double-blind study. Anesth Analg 2004; 98(3): 810-814, table of contents. http://dx.doi.org/10.1213/01.ANE.0000101987.79454.BC

[11] Koertzen M and Plaat F. Ultra-light combined spinal-epidural anaesthesia. Int J Obstet Anesth 2009; 18(2): 194-195. http://dx.doi.org/10.1016/j.ijoa.2008.12.005

[12] Roofthooft E and Van de Velde M. Low-dose spinal anaesthesia for Caesarean section to prevent spinal-induced hypotension. Curr Opin Anaesthesiol 2008; 21(3): 259-262. http://dx.doi.org/10.1097/ACO.0b013e3282ff5e41

[13] Guasch E, Dominguez A, Alsina E and Gilsanz F. Combined spinal-epidural anesthesia with very low dose hyperbaric levobupivacaine for cesarean section in a preeclamptic patient. Int J Obstet Anesth 2007; 16(1): 91-93. http://dx.doi.org/10.1016/j.ijoa.2006.08.003

[14] Qiu MT, Lin FQ, Fu SK, Zhang HB, Li HH, Zhang LM and Li Q. Combination of low-dose bupivacaine and opioids provides satisfactory analgesia with less intraoperative hypotension for spinal anesthesia in cesarean section. CNS Neurosci Ther 2012; 18(5): 426-432. http://dx.doi.org/10.1111/j.1755-5949.2012.00306.x

[15] Serenius F, Winbo I, Dahlquist G and Kallen B. Regional differences in stillbirth and neonatal death rate in Sweden with a cause-of-death specific analysis. Acta Paediatr 2001; 90(9): 1062-1067. http://dx.doi.org/10.1111/j.1651-2227.2001.tb01364.x

[16] Soltanifar S and Russell R. The National Institute for Health and Clinical Excellence (NICE) guidelines for caesarean section, 2011 update: implications for the anaesthetist. Int J Obstet Anesth 2012; 21(3): 264-272. http://dx.doi.org/10.1016/j.ijoa.2012.03.004

[17] Kucukguclu S, Unlugenc H, Gunenc F, Kuvaki B, Gokmen N, Gunasti S, Guclu S, Yilmaz F and Isik G. The influence of epidural volume extension on spinal block with hyperbaric or plain bupivacaine for Caesarean delivery. Eur J Anaesthesiol 2008; 25(4): 307-313. http://dx.doi.org/10.1017/S0265021507002670

[18] Reynolds F and Seed PT. Anaesthesia for Caesarean section and neonatal acid-base status: a meta-analysis. Anaesthesia 2005; 60(7): 636-653. http://dx.doi.org/10.1111/j.1365-2044.2005.04223.x

[19] Heesen M, Kolhr S, Rossaint R and Straube S. Prophylactic phenylephrine for caesarean section under spinal anaesthesia: systematic review and meta-analysis. Anaesthesia 2014; 69(2): 143-165. http://dx.doi.org/10.1111/anae.12445

Received on 26-08-2015 Accepted on 08-10-2015 Published on 31-12-2015

DOI: http://dx.doi.org/10.14205/2310-9394.2015.03.02.3