Revista Colombiana de Anestesiología
Colombian Journal of Anesthesiology
www.revcolanest.com.co

Brief Academy

Comments on "effective dose 50% (ED50) and effective dose 95% (ED95) of intrathecal bupivacaine in morbidly obese patients undergoing cesarean delivery"☆

Comentario sobre "dosis efectiva 50% (DE50) y dosis efectiva 95% (DE95) de bupivacaína intratecal en pacientes obesas mórbidas en cesárea"

*Javier Bastidas, Eduardo Kattan, Hector J. Lacassie**

Division of Anesthesiology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Chile

ARTICLE INFO

Article history:
Received 19 June 2015
Accepted 7 February 2016

Introduction

This work presents a critical analysis of the article by Carvalho et al.[1]

A decreased dose of local anesthetics is recommended when administering subarachnoid anesthesia in a caesarian section for obese patients.[2] Magnetic resonance imaging studies have shown a decrease in the volume of cerebrospinal fluid in this population[3] due to the distension of the epidural veins and the pressure exerted on the dural sac by the increase in soft tissues in the epidural space, which makes the effects of local neuraxial anesthetics unpredictable.[1]

While it has been demonstrated that no relationship exists between the height of spinal anesthesia block and body mass index (BMI) for cesarian section,[4,5] these studies do not examine the morbidly obese in particular.

Objective of the study

To determine the effective dose 50% (ED50) and the effective dose 95% (ED95) of intrathecal bupivacaine associated with opioids in the cesarean section of morbidly obese patients.

☆ Please cite this article as: Bastidas J, Kattan E, Lacassie HJ. Comentario sobre "dosis efectiva 50% (DE50) y dosis efectiva 95% (DE95) de bupivacaína intratecal en pacientes obesas mórbidas en cesárea". Rev Colomb Anestesiol. 2016;44:242–244.

* *Corresponding author at*: Marcoleta 367, 3er piso, Departamento de Anestesiología, Hospital Clínico Universidad Católica, Santiago, Chile.
E-mail address: lacassie@med.puc.cl (H.J. Lacassie).

Study design

A prospective, randomized, unicentric and double-blind study was designed. Previous authorization from the Ethics committee was obtained and 42 morbidly obese pregnant women were recruited (body mass index (BMI) > 40 ($kg\,m^{-2}$)) who were undergoing a single birth, past 37 weeks of gestation and scheduled for an elective cesarean section.

The patients were randomly assigned to seven dose groups of the hyperbaric bupivacaine 0.75%: 5, 6, 7, 8, 9, 10 and 11 mg associated with a fixed dose of fentanyl 10 μg (in 0.2 ml) and morphine 200 μg (0.4 ml) administered intrathecally. The spinal–epidural anesthetic technique was used. Each group included at least 5 patients.

The primary outcome was the success or failure of the "induction component", defined as sensory blockade at a T6 level or higher 10 min after intrathecal anesthesia was administered; and the "operation component", defined as an anesthetic blockade that did not require analgesic supplementation.

The secondary outcomes were blood pressure, dose of phenylephrine used in hemodynamic management, intraoperative pain, incidence of nausea/vomiting, maternal satisfaction and time lapsed from the end of surgery until transfer to recovery.

Results

All 42 patients enrolled and randomly assigned completed the study and are included in the analysis. All groups were composed of 6 patients except the 8 and 11 mg groups, which were made up of 5 and 7 patients respectively. The demographic and obstetric characteristics were similar among all groups, as well as the surgical duration with an average of 61 min (CI 95%: 56–75 min).

The ED50 and ED95 (CI95%) were 9.8 mg (8.6–11.0) and 15 mg (10.0–20.0) respectively for the "operation component". The "induction component" could not be measured due to its initial success and low failure rate.

The highest failure rate in the "operation component" occurred with small doses with an average failure time of 47 min (IC 95%: 20–62 min). The time required to reach a T6 sensory blockade was 8 ± 2 min, regardless of the dose used.

There were no differences in pain levels among different groups at the time of surgical incision, uterine exteriorization, fetal extraction and closure. There was an indirect correlation between the dose of bupivacaine administered and the pain in uterine exteriorization ($R = -0.44$, $p = 0.016$). All groups achieved a 100% patient satisfaction rate. The period of recovery was 74 ± 20 min with no variation among groups.

Reviewers' commentary

A prospective, unicentric, randomized study blinded to both patients and physicians was conducted. The initial demographic variables were similar. It was not interrupted prematurely and the protocol was completed in 100% of patients. It is worth noting that there is no mention of conflicts of interest, funding sources, or whether the outcome assessor was blinded. It is also worth highlighting that the study did not use a "normal weight" control group, but rather, figures reported by Ginosar et al.[6] This work was also not originally intended for comparison with non-obese patients (Brendan Carvalho, Cali, Colombia, personal communication, June 2015). These points carry a higher risk of bias for the study.

Another weakness of the study is the small sample size, which had adequate statistical power to fulfill the main objective. However, it is not sufficient in finding significant differences to fulfill the secondary objectives.

This is the first study that calculates ED50 and ED95 of spinal anesthesia for use in morbidly obese patients in cesarean delivery. The logistical regression employed to determine ED50 and ED95 has been amplified using medical literature. However, through this method, ED50 is obtained with higher precision than ED95, since it is extrapolated from the plateau located in the top portion of the curve. This is why the ED95 obtained is 15 mg, higher than the group studied with the highest dose (11 mg). It is important to note that the 15 mg dose of bupivacaine has not been tested, so its use is not recommended.

The authors state that the ED50 and ED95 values are similar to those of normal weight patients. However, a control group was not used to support this statement and is only based on a previous study, which could lead to further bias. Even though it was conducted by the same group of researchers with a similar methodology, equal results cannot be concluded. However, these results are concordant with previous research which has estimated the intrathecal dose of bupivacaine in cesarean delivery to be similar between obese and non-obese patients.[7]

The highest failure rate was reported when using low doses of local anesthesia, which is concordant with the meta-analysis conducted by Arzola et al., who determined that using doses lower than 8 mg of intrathecal bupivacaine increases the risk of intraoperative pain by 3.75 times (CI 95% 2.38–5.92) along with an increased risk of nausea, whereas converting to general anesthesia reduces the necessary number to cause harm to only 4 patients (CI 95%: 2–7).[8] The potential switch to general anesthesia is especially important since the management of the obese patient's airway presents a greater challenge. As a consequence, we do not recommend decreasing the dose in morbidly obese patients unless the anesthesia is reinforced by an epidural catheter. Lastly, it is always necessary to consider the experience of the surgical team with regards to technique and duration of the procedure.

As for the secondary outcomes, duration times for surgery and the period of recovery were similar among groups; this finding is repeated in measuring the time needed to reach a T6 sensory level. There were no differences in the pain level among groups and in the moment of surgical incision, uterine exteriorization, fetal extraction and closure. However, the study does not have sufficient statistical power to determine differences in these outcomes.

To complement these findings, a recent study has demonstrated a higher incidence of high spinal block in super obese patients (CMI above 50 $kg\,m^{-2}$), with no such incidence in lower weight ranges.[9] This demonstrates that not all obese patients should receive the same treatment.

This study provides us a guide for administering spinal anesthesia in the cesarean delivery of morbidly obese patients. If we decide to decrease the dose of local anesthesia compared to that of non-obese patients, this decision must be backed by a technique that allows flexibility in the duration of anesthesia, such as an epidural catheter. Decreasing the dose only increases the risk of failure of the spinal anesthesia and carries a subsequent risk of having to switch to general anesthesia in a patient with potentially difficult airways. The ED95 values (15 mg) can be interpreted as a mathematical extrapolation, and as such are not clinically reasonable or recommended. Therefore, in patients with unusual anthropometry, it is perfectly reasonable to use a technique that offers flexibility in anesthetic management and allows for a titrated dose, such as the combined spinal–epidural technique.

Funding

The authors did not receive sponsorship to carry out this article.

Conflicts of interest

The authors have no conflicts of interest to declare.

REFERENCES

1. Carvalho B, Collins J, Drover DR, Atkinson Ralls L, Riley ET. ED(50) and ED(95) of intrathecal bupivacaine in morbidly obese patients undergoing cesarean delivery. Anesthesiology. 2011;114:529–35.
2. D'Angelo R, Dewan D. Obesity. In: Chestnut D, Polley L, Tsen L, Wong C, editors. Chestnut's obstetric anesthesia: principles and practice. 4th ed. Philadelphia, PA: Mosby Elsevier; 2009. p. 1079–93.
3. Hogan QH, Prost R, Kulier A, Taylor ML, Liu S, Mark L. Magnetic resonance imaging of cerebrospinal fluid volume and the influence of body habitus and abdominal pressure. Anesthesiology. 1996;84:1341–9.
4. Norris MC. Height, weight, and the spread of subarachnoid hyperbaric bupivacaine in the term parturient. Anesth Analg. 1988;67:555–8.
5. Norris MC. Patient variables and the subarachnoid spread of hyperbaric bupivacaine in the term parturient. Anesthesiology. 1990;72:478–82.
6. Ginosar Y, Mirikatani E, Drover DR, Cohen SE, Riley ET. ED50 and ED95 of intrathecal hyperbaric bupivacaine coadministered with opioids for cesarean delivery. Anesthesiology. 2004;100:676–82.
7. Lee Y, Balki M, Parkes R, Carvalho JC. Dose requirement of intrathecal bupivacaine for cesarean delivery is similar in obese and normal weight women. Rev Bras Anestesiol. 2009;59:674–83.
8. Arzola C, Wieczorek PM. Efficacy of low-dose bupivacaine in spinal anaesthesia for caesarean delivery: systematic review and meta-analysis. Br J Anaesth. 2011;107:308–18.
9. Einhorn L, Akushevich I, Habib A. Intrathecal bupivacaine dose for cesarean delivery is not reduced in obese compared to non-obese parturients. In: ASA Meeting. 2014. p. A4206.