Title:

Preperitoneal ropivacaine in the management of postoperative pain in post-cesarean section patients.

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Abstract

Background: Post-surgical pain in cesarean section negatively influences the mother-child binomial.

Objective: The objective of this study was to evaluate postoperative pain in post-cesarean section patients with preperitoneal ropivacaine..

Methods: Randomized, double-blind, controlled clinical trial. We include female patients, 18 to 40 years old, with full-term pregnancy and elective or scheduled cesarean section, randomized into two groups. Group A (n=41) received preperitoneal ropivacaine, 225 mg, during cesarean section. Group B (n=41) without application of ropivacaine. Ketorolac was administered to all of them every 8 hours (h). Postoperative pain was evaluated with the VAS scale (visual analogue scale) at 0, 2, 6, 12, 18 and 24 h after surgery and follow-up 10 days after surgery.

Results: In all evaluations, group A patients presented pain to a lesser extent when compared to those in group B (p=0.0003, < 0.0001, 0.0003, 0.02, 0.002, 0.005, respectively). Only one patient in group A required rescue analgesics, as opposed to 17 in group B (p=0.001). There were no adverse events in both groups.

Conclusions: Preperitoneal ropivacaine infiltration in cesarean section is effective as postoperative analgesia, being a fast, simple and safe procedure.

Keywords: postoperative analgesia, Cesarean delivery, Peritoneum, Randomized trial, Ropivacaine.

INTRODUCTION

Post-surgical pain has been widely studied but scientific evidence indicates that less than half of the patients report adequate pain relief (1).

The rate of caesarean sections has increased exponentially (2), with pain management being of great relevance in this type of surgical intervention since inadequate postoperative pain control negatively influences the early initiation of exclusive breastfeeding, increases hospital stay and postpartum depression (3). It can also cause respiratory, cardiovascular, gastrointestinal, immunological, muscular, hematological, psychological and renal complications (4).

The etiology of pain in abdominal surgery is multifactorial, including that related to peritoneal manipulation (5, 6, 7), for which some studies report that infiltration of the surgical site provides adequate pain relief (8, 9).

Currently, a multimodal approach is being carried out for pain management, using local anesthetics for wound infiltration (10, 11, 12), spraying of the anesthetic (13), infiltration of the same through a catheter (14) and preperitoneal infiltration (15), which have shown a reduction in postoperative pain. These techniques being safe and economical, with few adverse effects (16).

Bupivacaine and ropivacaine are used for the management of postoperative pain, the latter having less cardio and neurotoxicity, as well as faster elimination, which makes it safer and a good alternative in postoperative anesthesia[15,16]. The intention of the present study is to demonstrate the adequate control of postoperative pain with the use of preperitoneal ropivacaine in post cesarean section patients.

MATERIAL Y METHODS.

Randomized, double-blind, controlled clinical trial, in the Unidad Médica de Alta Especialidad No. 48, Hospital de Gíneco-Pediatría, of third level of healthcare. The study was approved by the unit's Research Ethics Committee and Local Health Research Committee, with registration number R-2018-1002-046. Informed consent was requested from all participants.

We included women between the age of 18 and 40 years, with full-term pregnancy and who underwent a planned or elective cesarean section with a mid-infraumbilical incision. Patients with chronic diseases, placental disorders, infections, allergies to anesthetics, those with contraindication to regional anesthesia, obstetric emergency, history of drug abuse or inability to understand the visual analog scale were not included.

The patients were randomly assigned, by simple random sampling, into two groups (A and B), in accordance with a table of random numbers; both the patients and the interviewer were blinded. Preperitoneal ropivacaine was administered in group A, while group B (control) did not receive this. Clinical data such as age, weight, height, body mass index, weeks of pregnancy, gestations and number of caesarean sections were obtained. Regarding the anesthetic procedure, all patients

underwent a pre-anesthetic evaluation. In the operating room, they were administered regional anesthesia through L2 - L3 epidural block, with 2% lidocaine with epinephrine, at a dose of 4 mg per kg of body weight, with a latency time of 10 to 15 minutes. The cesarean section was performed with the conventional technique, with a mid-infraumbilical incision in the skin and a Kerr-type incision in the uterus, the hysterorrhaphy was sutured in three planes. Before proceeding with the closure of the surgical wound, patients in group A received preperitoneal ropivacaine. The perincisional parietal peritoneum (subfascial) was located and taken with four Kelly forceps, a 22 G needle was inserted, up to 2 cm deep over the edge of the peritoneum, in the preperitoneal space and at an angle of 45 °, 30 ml were infiltrated of ropivacaine 0.75%, corresponding to 225 mg total (7.5 mg / ml bottle). The presence of adverse events was monitored at all times. Finally, the surgical wound was sutured by planes. In group B patients, the conventional cesarean section was performed in the same way as previously explained, but without the application of ropivacaine. No substance was administered as a placebo.

In all patients, both in group A and group B, during the postoperative period, the intensity of pain was evaluated using the VAS scale (On this scale, the intensity of pain is represented in a 10 cm line, at one end features the phrase “no pain” which corresponds to 0 and at the opposite end “the worst pain imaginable” which corresponds to 10)[17]. Pain intensity records were made at the end of the surgery (0 hours), at 2, 6,12,18 and 24 hours after surgery. In both study groups, ketorolac was indicated, at a dose of 30 mg intravenously every 8 hours. In the cases of patients who require rescue doses, due to the presence of pain, the following analgesics were administered, according to the persistence of pain, in the order in which they are mentioned, paracetamol and tramadol (intravenous route).

The time elapsed between the end of the surgery until the start of ambulation and the days of hospital stay were evaluated. At hospital discharge, all patients were arranged to meet for check-up 10 days after surgery to assess the surgical wound, as well as the presence of some type of complication.

In the statistical analysis, we reported frequencies, percentages, and descriptive statistics. The comparison of nominal variables between the groups was carried out with the chi-square test and

Fisher's exact test, as well as, for numerical variables, with the Mann-Whitney U test. Kruskal Wallis test, to compare variables between the study groups. Assumption of normality tests were performed (Shapiro-Wilk W, Anderson-Darling, Martinez-Iglewicz, Kolmogorov-Smirnov, D'Agostino Skewness, D'Agostino Kurtosis, D'Agostino Omnibus), without showing normal distribution, therefore the results are expressed in a median and 95% confidence intervals. Statistical significance was considered with a value of $p < 0.05$. We used the NCSS Copyright 2020, LLC y Epidat 3.1. statistical packages.

RESULTS

We included 82 pregnant women distributed in two groups of 41 patients each. Considering the entire sample, the age range of the patients was from 18 to 40 years, with a median age of 28 (CI 95% 27-29) years, BMI 27.8 kg/m^2 (CI 95% 26.9-28.3), pregnancies 2 (CI 95% 2-2), cesarean sections 2 (CI 95% 2-2) and gestational age of 39 weeks (CI 95% 39-39). There was no significant difference between the two groups in terms of general characteristics (Table I).

When evaluating pain between both groups, we highlighted that patients in group A perceived significantly less pain than those in group B (table II). In group A, only one patient required rescue analgesics, as opposed to 17 in group B (table III).

There was no significant difference in terms regarding days of hospital stay between the study groups, 2 (CI 95% 2-2) days for each one. There was no record of any adverse events in both groups during the hospital stay and at the 10-day follow-up.

DISCUSSION

In this study, it is demonstrated that preperitoneal ropivacaine infiltration in cesarean section is effective as postoperative analgesia.

This clinical trial shows that patients in the group who received preperitoneal ropivacaine presented better analgesia than those who did not, something similar to that published by Thomas D. et al (15) who compared the administration of bupivacaine in two groups through a different route (subcutaneous y preperitoneal), observing better analgesia more frequently in the patients of the last group, although without presenting statistical significance.

We observed similarity of our results with those of the study by *Öz* M et al. (13) who, after the application of ropivacaine, identified similar analgesia in relation to the control group. Perhaps this similarity is due to the route of administration of the drug and its bioavailability, so future research should be carried out comparing both routes of administration.

There are studies that analyzed ropivacaine (14) and bupivacaine (20) through different routes of administration than the one used in the present trial and that have achieved pain control similar to that reported in our study.

In the present investigation, we did not observe adverse effects (seromas, wound dehiscence, hematomas, neurotoxicity or hemodynamic alterations) in the experimental group, which confers safety with the dose of ropivacaine used and the methodology for its instillation as in the *Öz* M et al study (13). This is due to the fact that ropivacaine is a much safer analgesics than others due to its later diffusion and its easy elimination (17, 18). In a previous study where bupivacaine was used, seromas, nausea and vomiting were reported (20).

We did not assess immediate adherence or early initiation of breastfeeding, futhermore we also used standard doses of ropivacaine for all patients; for which reason it is proposed that future research should analyze these points, in addition to applying the ropivacaine calculated according to the weight of the patients.

Table I. General characteristics of the two study groups.

Variables	Group A n = 41	Group B n = 41	p
Age (years)	28 (27-31)	27 (24-30)	0.20
BMI (kg/ m^2)	27.6 (26.8-28.3)	28 (26.7-28.3)	0.66
Births(n)	2 (2-3)	2 (2-3)	0.52
Cesarean sections (n)	2 (2-2)	2 (1-2)	0.56
Gestational age (weeks)	39 (38.5-39)	39 (38.5-39.6)	0.60

Values expressed in median and 95% confidence intervals (IC 95%). Mann Whitney U test.
BMI: Body Mass Index; n= number; kg= kilograms; m^2= meter squared.

Table II. Pain assessment in both groups.

Timing of Pain Assessment (hours)	Group A *n* = 41		Group B *n* = 41		*p*
	With pain	Without pain	With pain	Without pain	
0	1 (2.4)	40 (97.6)	14 (34.2)	27 (65.8)	0.0006
2	3 (7.3)	38 (92.7)	29 (70.7)	12 (29.3)	<0.0001
6	23 (56)	18 (44)	38 (92.7)	3 (7.3)	0.0003
12	33 (80.5)	8 (19.5)	40 (97.6)	1 (2.4)	0.029
18	32 (78)	9 (22)	41 (100)	0	0.0024
24	27 (65.8)	14 (34.2)	38 (92.7)	3 (7.3)	0.0053

Values expressed in frequencies and percentages (%). Fisher's exact test.

Table III. Use of rescue analgesics according to the study group.

Use of rescue analgesics	Group A n = 41(%)	Group B n = 41(%)
Yes	1 (2.4)	17 (41.4)
No	40 (97.6)	24 (58.6)

Values expressed in frequencies and percentages. Fisher's exact test. p= 0.001

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