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Comparison of median effective concentration of ropivacaine in multiparas or primiparas during epidural labor analgesia

STROBE compliant

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Abstract

The documents on the median effective concentration of local analgesic were many in primiparas during labor analgesia. However, the studies were fewer in multiparas. To explore the analgesic requirements in multiparas during epidural labor analgesia, we investigated the median effective concentration of ropivacaine with 2 μg/mL fentanyl for epidural labor analgesia in multiparas.

Sixty-two women were recruited and assigned to the primipara group and multipara group in this prospective study. All the parturients received ropivacaine combined with 2 μg/mL fentanyl for epidural labor analgesia. The concentration of ropivacaine was determined by the up and down method and an initial concentration was set as 0.1% with a 0.01% interval. Effective analgesia was defined as the visual analog scale (VAS) ≤3 within 30 minutes after epidural administration when cervical dilatation is about 2 cm. The median effective concentration of ropivacaine was calculated by the up and down sequential method. The pain intensity was assessed using VAS. Hemodynamic parameters, the labor stages, and neonatal Apgar scores were recorded. Umbilical artery blood was drawn to analyze. The side effects, if any, were also recorded.

The median effective concentration of ropivacaine was 0.057% (95% confidence interval [CI], 0.051–0.064%) in primiparas during epidural labor analgesia, and 0.068% (95% CI, 0.063–0.072%) in multiparas during epidural labor analgesia, there was significant difference between the groups ($P = .02$).

This study indicated that the median effective concentration of ropivacaine with fentanyl for epidural labor analgesia was 0.068% (95% CI, 0.063–0.072%) and increased in multiparas compared with the primiparas (www.chictr.org.cn, registration number: ChiCTR-1800016486)

Abbreviations: ASA = American Society of Anesthesiologists, BP = blood pressure, CI = confidence interval, HR = heart rate, SpO_2 = pulse oxygen saturation, VAS = visual analog score.

Keywords: ropivacaine, fentanyl, epidural, labor analgesia

1. Introduction

Epidural analgesia is a common pain relief technique during labor and is popular with the parturients. The low dose of ropivacaine is widely used for epidural analgesia during labor with less adverse events.[1–3] However, most of studies on labor analgesia are relation with the primiparas.[4–6] So far as we know, the studies on analgesic requirements are fewer in multiparas. We investigated and compared the effective concentrations of epidural ropivacaine for labor analgesia in multiparas and primiparas.

2. Methods

The ethics committee of Jiaxing University Women's and Children's Hospital approved the study (Chairman Prof Liu)

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The study was registered with the Chinese Clinical Trials Registry, registration number: ChiCTR-1800016486.

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on June 1, 2018, and a written informed consent was signed by all parturients. The trial was registered prior to patient enrollment at www.chictr.org.cn (ChiCTR-1800016486). Sixty-two full-term singleton women aged 20 to 35 years were included in this single-blind study. Exclusion criteria were as follows: patients with the severe cardiopulmonary disease, cervical dilatation >3 cm, height <150 cm or >175 cm, induced labor, contraindications to epidural block and patients undergoing cesarean section or epidural analgesia. At last, 30 multiparas were assigned to the multipara group (Group M), and 30 primiparas were assigned to the primipara group (Group P).

Upon arrival in delivery room, vital signs including noninvasive arterial blood pressure (BP), heart rate (HR), and pulse oxygen saturation (SpO_2) were monitored at 5-minute intervals for women. After venous access was established, Ringer's solutions were infused at a rate of 2 mL/kg/h. Parturients were positioned in the left lateral position, the epidural puncture was performed at the estimated level of L_2-L_3 interspace with an 18-G epidural needle using loss of resistance to air technique when cervical dilation was about 2 cm. Subsequently, an epidural catheter was inserted 4 cm cephalad into epidural space and patients were turned supine. Three milliliters of 1.5% lidocaine was given as a test dose to exclude the epidural catheter in the subarachnoid space, then 10 mL of mixed solutions (ropivacaine +2 μg/mL fentanyl) was given as loading dose. The initial concentration of ropivacaine was set as 0.1% with concentration adjustment interval of 0.01%. The concentration of ropivacaine in the next patient was decided by the analgesic effect of the last patient. Effective analgesia was defined as the visual analog scores (VASs) ≤3 within 30 minutes after epidural administration. If analgesic effect of the last woman was adequate, the concentration of ropivacaine for the next woman was decreased by 0.01%

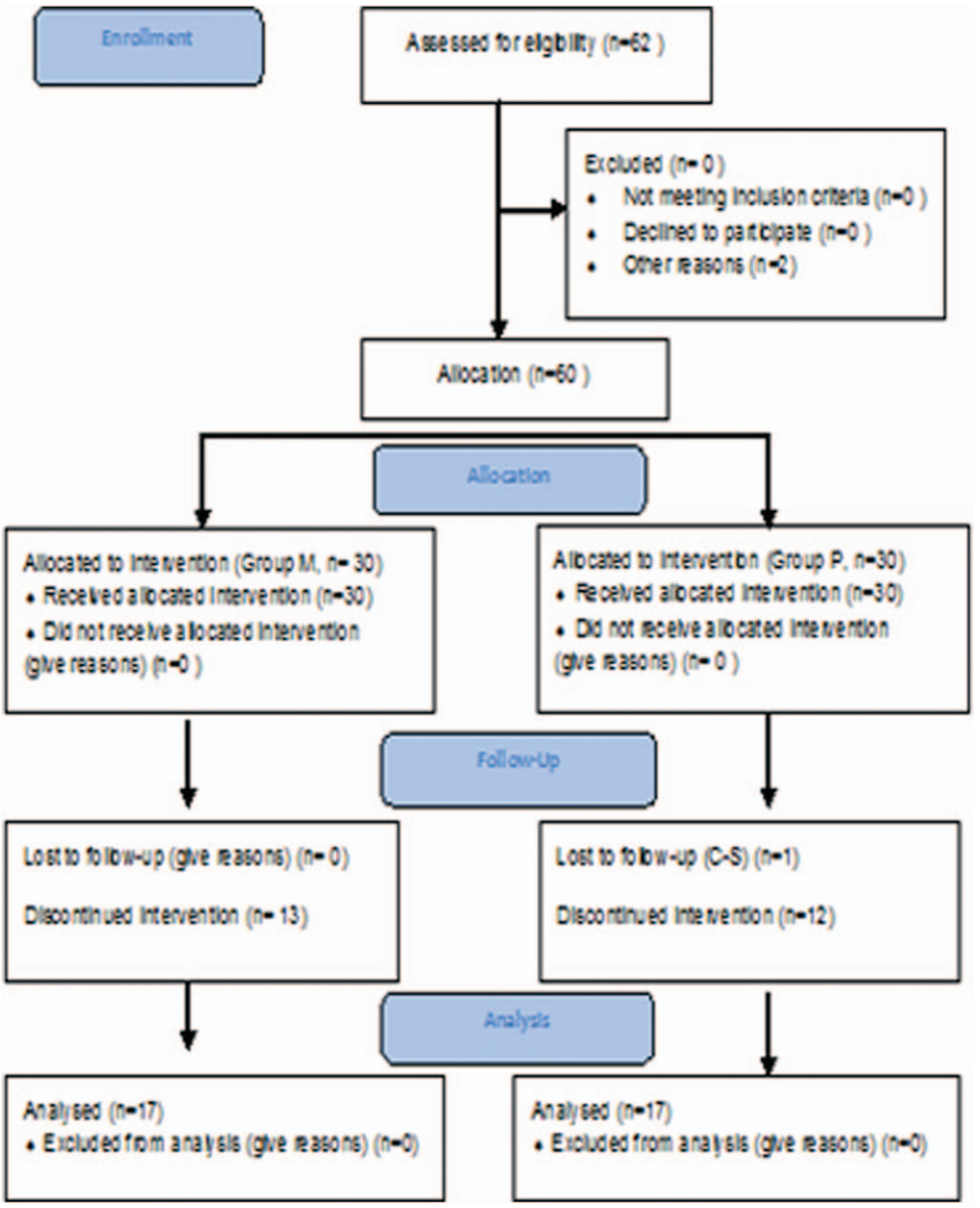

Figure 1. The flow diagram of study.

interval. If analgesic effect of the last woman was inadequate, the concentration of ropivacaine for the next patient was increased at 0.01% interval. The analgesic solutions consisting of 0.1% ropivacaine and 2 μg/mL fentanyl were started continuous infusion 30 minutes after epidural injection with a patient-controlled analgesia pump (background dose of 6 mL/h, lockout time intervals of 20 minutes and a bolus dose of 6 mL). A bolus dose was administrated when VSA >7 in both groups. Additional 10 mL of 1% lidocaine was administrated to rescue if VAS was >4 within 30 minutes after epidural administration, otherwise, excluded from this study.

2.1. Measurements

The BP, HR, SpO_2, duration of labor stages, and Apgar scores were recorded. The maximum block level of sensation was measured using alcohol cotton at 1-minute interval. Umbilical artery blood gas was analyzed immediately after delivery. The analgesic effect was evaluated after epidural administration using VAS (0 = no pain, 10 = maximum pain). Motor block was assessed using Bromage scale (0 = no motor block, 1 = unable to move hip, 2 = unable to move hip and knee, 3 = unable to move hip, knee, and ankle). The adverse events such as hypotension, pruritus, nausea, and vomiting were noted. Respiratory depression was defined as SpO_2 <91% lasting for 30 seconds without inhaling oxygen and respiratory rate <10 breaths/minute. The hypotension was defined as a systolic BP was below 80% of the baseline value.

2.2. Statistical analysis

The VAS value within 30 minutes after epidural analgesia was the primary outcome. As 6 pairs of reversal of sequence were achieved using an up and down method,[7] Twenty-two cases of patients in each group were need in this study and 30 patients were enrolled to allow for dropouts. Numerical variables were presented as mean and standard deviation. Categorical variables were presented as numbers. Parameters distributed normally were analyzed using *t* test and parameters non-normally distributed were analyzed using nonparametric Mann–Whitney *U* test. Categorical parameters were analyzed using the Chi-squared test. A $P < .05$ was considered as significant difference.

3. Results

The flow diagram of study is shown in Figure 1. A total of 62 parturients were enrolled in this clinical study and 59 women finished the study, 2 women were excluded from this study for cervical dilatation >3 cm and 1 woman was excluded for cesarean section. There were no significant differences in characteristics of the parturients between the 2 groups (Table 1).

Table 1

Characteristics of parturients.

Index	Group M (n = 30)	Group P (n = 29)	*P*-value
Age, yr	29.4 ± 4.2	27.8 ± 3.4	.11
Weight, kg	68.2 ± 4.8	70.5 ± 5.1	.28
Height, cm	160 ± 2.5	159 ± 3.2	.12
Gestational age, wk	38.8 ± 1.4	39.3 ± 1.2	.15

Data are presented as mean ± standard deviation.
Group M = multipara group, Group P = primipara group.

Table 2

Data of parturients with effective epidural analgesia.

Index	Group M (n = 17)	Group P (n = 17)	*P*-value
History of receiving epidural analgesia	Yes	No	–
Onset time of analgesia, min	16.5 ± 4.2	15.4 ± 3.8	.93
The maximum sensory block level	T8 [T6–T9]	T8 [T6–T10]	.81
VAS values before analgesia	6.9 ± 1.5	7.1 ± 1.6	.62
Cervical dilatation 30 min after analgesia, cm	2.29 ± 0.47	2.17 ± 0.39	.43
Bolus	4 [1–6]	2 [0–3]	<.01
Bromage score	0 [<1]	0 [<1]	.99
Duration of the first stage, min	274.5 ± 56.8	412.7 ± 61.5	<.01*
Duration of second stage, min	28.6 ± 5.2	36.1 ± 6.8	<.01*
Blood loss, mL	191.6 ± 17.5	186.5 ± 15.8	.42
Apgar score at 1st min	8.6 ± 0.6	8.7 ± 0.5	.18
Apgar score at 5th min	9.5 ± 0.7	9.7 ± 0.6	.76

Data are presented as mean ± standard deviation, median [range], or numbers.
Group M = multipara group, Group P = primipara group, VAS = visual analog score.

The characteristics of effective epidural analgesia are presented in Table 2. Rescue bolus was greater in multipara group than those in primipara group ($P < .01$). The onset time of analgesia and maximum level of sensory block were similar between the 2 groups ($P > .05$). All Bromage score values were below 1 in both groups and no motor block was observed. There were no significant differences in terms of the delivery modes, Apgar scores, and umbilical arterial pH immediately after delivery between the 2 groups ($P > .05$). No significant differences were observed in terms of hypotension, pruritus, nausea, and omitting between the 2 groups (Table 3, $P > .05$).

The sequential doses of epidural ropivacaine with fentanyl are shown in Figure 2. The median effective concentration of ropivacaine was 0.068% (95% confidence interval [CI], 0.063–0.072%) in multiparas, and 0.057% (95% CI, 0.051–0.064%) in primiparas. There were significant differences between the 2 groups ($P < .05$).

4. Discussion

In this study, we found that the median effective concentration of ropivacaine with fentanyl was 0.057% (95% CI, 0.051–0.064%) in primiparas during labor analgesia and the median effective concentration of ropivacaine with fentanyl in multiparas was 0.068% (95% CI, 0.063–0.072%) in multiparas.

The median effective dose represents a dose that produces a positive effect on 50% of individual. It is decided by the up and down sequential method. The median effective concentration of epidural ropivacaine in combination with opioids has been

Table 3

Adverse events of effective epidural analgesia.

Index	Group M (n = 17)	Group P (n = 17)	*P*-value
Nausea and vomiting	1 (5.9%)	1 (5.6%)	.99
Pruritus	1 (5.9%)	0 (0)	.99
Hypotension	1 (5.9%)	1 (5.6%)	.99
Fetal heart rate <120 beats/min	0	0	.99
Respiratory depression	0	0	.99
Shivering	0	1 (5.6%)	.99

Data are presented as mean ± standard deviation or numbers (%).
Group M = multipara group, Group P = primipara group.

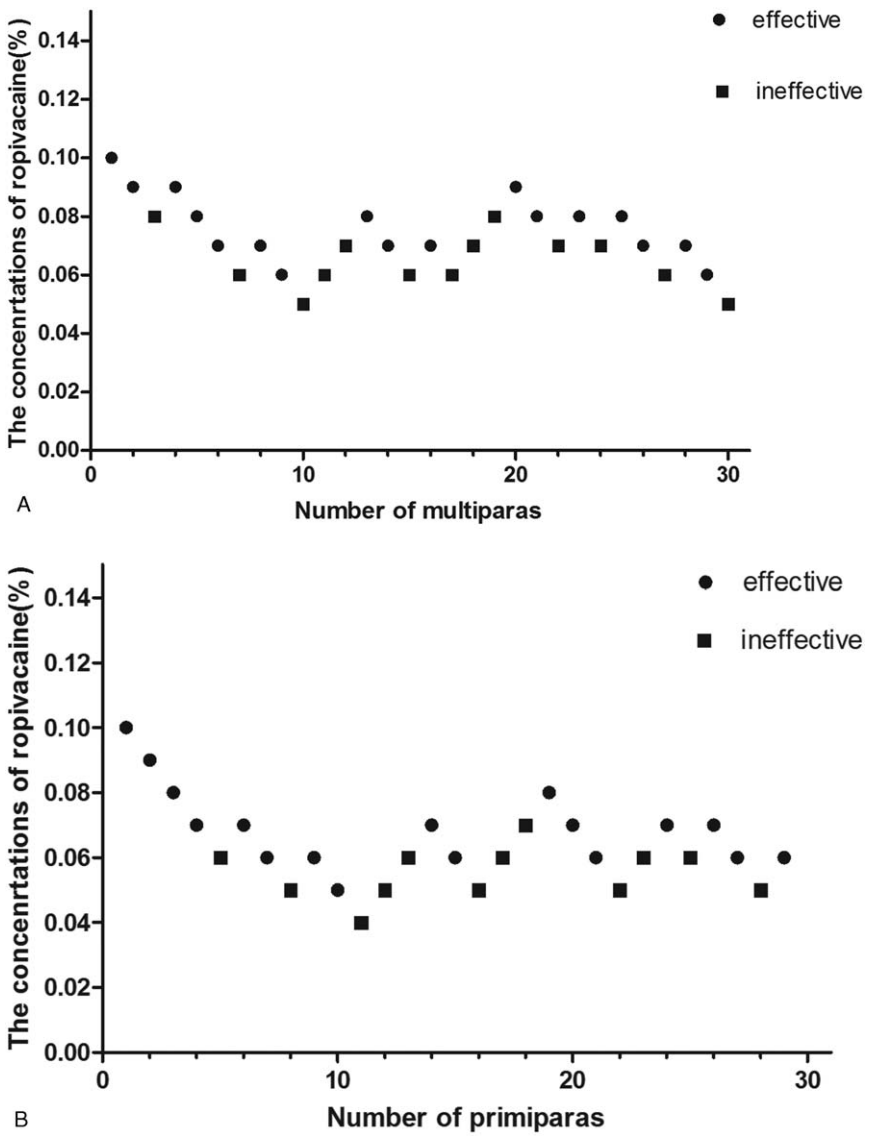

Figure 2. (A) The concentrations of epidural ropivacaine using the up and down method in primiparas. "●" represents an effective analgesia and "■" represents an ineffective analgesia. (B) The concentrations of epidural ropivacaine using the up and down method in multiparas. "●" represents an effective analgesia and "■" represents an ineffective analgesia.

investigated in primiparas in previous study,[8,9] but the studies on the median effective concentration of epidural ropivacaine are fewer in multiparas. The median effective concentration of ropivacaine coadministered with fentanyl 2 μg/mL was 0.057% in primiparas, while the median effective concentration of ropivacaine coadministered with fentanyl was 0.068% in multiparas in our study. Compared with the primiparas, the median effective concentration of epidural ropivacaine with fentanyl in multiparas increased obviously. The documents reported that the patients having psychogenic pain, significantly increased prevalence compared to the patients who suffered from illnesses or pain. Moreover, the patients, who suffered from psychogenic pain, were susceptible to pain.[10,11] Their findings might be to explain this problem that analgesic requirements were increased in multiparas in our study. Additionally, the increase in the median effective concentration of ropivacaine was relevant to the history of epidural analgesia in multiparas during labor. Agaram et al[12] reported that cervical dilatation >7 cm, a history of opioid tolerance and a previous failed epidural increased the odds ratio for inadequate pain relief by logistic regression. The odds ratio for inadequate pain relief would increase in the multiparas ever received epidural labor analgesia when receiving epidural analgesia again as opioid tolerance and a previous failed epidural analgesia or inadequate pain relief. Finally, epidural adhesion after receiving epidural analgesia would affect the analgesic effects. The median effective concentration of ropivacaine was greater in multiparas compared to the primiparas; that was to say, the analgesia demand increased in multiparas during labor analgesia as the previous pain experiences from labor in multiparas caused psychogenic pains. Some studies indicated that only 50% to 66% was effective in parturients undergoing spinal surgery during epidural labor analgesia.[13,14] Recent research was showed that the analgesic requirements hourly did not increase in parturients after spinal

surgery compared with the parturients without undergoing spinal surgery, but postoperative changes of epidural space would more or less affect the analgesic effects.[15]

There are some limitations in this study. Firstly, the median effective concentration was calculated using the formula other than regression analysis, the different methods would impact the results. Secondly, some multiparas underwent epidural labor analgesia, it would affect analgesic effects. At last, further study is needed by the larger sample size.

In summary, this study indicated that the median effective concentration of ropivacaine with 2 μg/mL fentanyl for epidural labor analgesia was 0.068% (95% CI, 0.063–0.072%) and increased in multiparas compared with the primiparas.

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Correction

The first author's name first appeared incorrectly as Qinghua Qeng. It has been corrected and now appears as Qinghua Peng.

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