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Original Article

Hyperbaric Spinal Ropivacaine for Cesarean Delivery: The Optimal Dose in Chinese Women

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ABSTRACT

Background: Earlier studies demonstrated that the intrathecal ropivacaine could be used to provide quality anesthesia with advantages of lesser hypotension and quicker recovery compared to bupivacaine for cesarean delivery. However, the optimal dose of spinal ropivacaine in obstetric patients varies greatly in different reports. Here we designed a randomized double-blind study to determine the optimal dose of spinal ropivacaine for elective cesarean delivery in China.

Methods: A total of 500 healthy primiparas who underwent elective cesarean delivery were randomly divided into five groups, 100 primiparas in each group. Participants received hyperbaric ropivacaine in the subarachnoid with 10, 12, 14, 16 or 18 mg at 0.2 mL/second as groups R10, R12, R14, R16, and R18 respectively. The speed of onset, duration of sensory and motor block, the satisfaction of the mother and surgeon, incidences of hypotension, bradycardia, nausea and vomiting, supplement of intravenous analgesics, use of vasoactive drugs and neonatal Apgar score were all recorded. A dose was considered effective if an upper sensory level to the pinprick of T6 or above was achieved and no intravenous supplements were required. The median effective dose (ED50) and ED95 were determined by a logistic regression model.

Results: Totally, 492 patients completed the study. All the participants in the study were comparable with respect to age, weight, and height. The average duration of the surgery was 40 minutes. The mean time to achieve T6 sensory block was significantly shorter in Group R18 compared to R10 (2 ± 0.8 min vs. 3.05 ± 1.2 min, $P < 0.05$). Accordingly, the duration of sensory block (regression to T12) was markedly longer in Group R18 than R10 (151.3 ± 30.7 min vs. 92.3 ± 30.5 min, $P < 0.05$). Importantly, the perfect patients' satisfaction was much higher in Group R18 than R10 (100% vs. 66%, $P < 0.05$), same as surgeons' satisfaction (100% vs. 49%, $P < 0.05$). The incidence of hypotension in Group R16 was higher than R10 ($P < 0.05$). Moreover, the incidence of hypotension in Group R18 was higher than R10, R12 and R14 ($P < 0.05$). The incidences of nausea in Groups R16 and R18 were higher than R10 and R12 ($P < 0.05$). The incidence of vomiting in Group R18 was higher than Groups R10 and R12 ($P < 0.05$). The ED50 was 9.7 mg (95% confidence interval [CI], 8.9 to 10.3) and ED95 was 14.3 (95% CI, 13.7 to 15.3) mg.

Conclusion: The dose of 14 mg of hyperbaric ropivacaine for spinal anesthesia can provide a satisfying anesthetic effect, with fewer occurrences of intraoperative adverse events during a cesarean delivery for Chinese women. (Funded by the Department of Anesthesiology, Obstetrics and Gynecology Hospital to Nanjing Medical University, Nanjing, China.)

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Combined spinal-epidural anesthesia is currently the most commonly used anesthesia method for cesarean delivery in China (1). It provides effective anesthesia and sufficient muscle relaxation for the cesarean delivery (2). It can also provide an option for post-cesarean analgesia via epidural. Ropivacaine has less toxicity to the central nervous and cardiovascular systems than that of the commonly used bupivacaine (3). In addition, Ropivacaine has fewer side effects, less motor blockage and shorter recovery time after the operation (4). Thus, it could be an ideal local anesthetic for obstetric anesthesia. However, little research exists regarding the optimal dosage of spinal hyperbaric ropivacaine for obstetrics. Thus, we conducted this dose-finding study to determine an optimal dose of hyperbaric ropivacaine for spinal anesthesia in a large-sample study to provide a reference for clinical practice in China.

METHODS

Inclusion Criteria

The study was approved by the hospital ethics committee and all participants signed informed consent. The study enrolled 500 healthy primiparas with no obstetric complications who underwent an elective cesarean delivery in our hospital from October 2014 to June 2015.

Anesthetic Techniques

All patients were hydrated with 500 mL sodium lactate Ringer's solution before spinal anesthesia. Vital signs were routinely monitored, including electrocardiogram (ECG), blood pressure (BP), heart rate (HR), and pulse oxygen saturation (SpO_2). After entering the operation room, the patient's BP was monitored when she was in a sitting position and again 5 minutes after resuming a supine position. Patients with a difference in blood pressure greater than 30% were excluded from the study, based on their apparent tendency for supine hypotension. Patients were randomly assigned into five groups (n = 100 per group) and received hyperbaric ropivacaine (0.75% ropivacaine + 0.5 mL of 10% glucose) at a dose of 10, 12, 14, 16, or 18 mg respectively. Combined spinal and epidural (CSE) was placed in a left lateral decubitus position at L3-4 interval. Hyperbaric ropivacaine was injected over 6s after dilution with outflow cerebrospinal fluid to 3 mL via a spinal needle. An epidural catheter was then inserted in place. After CSE placement, all patients took a left uterine displacement position of 20-30°, and the level operating bed was adjusted to control the anesthesia level below T4. Blood pressure lower than 30% of the baseline or a systolic blood pressure less than 90 mmHg were defined as hypotension, and ephedrine (6-10 mg) or phenylephrine (50-100 mg) were given as treatment. A heart rate of less than 55 beats/min was treated with 0.3 mg atropine. If the anesthetic effect was not sufficient at the time of closure (Visual Analogue Scale/Score, VAS ⩾ 4), the rescue measurements include intravenous administration of 30 mg of ketamine, and/or 5-10 ml of 2% lidocaine was given via the epidural catheter. If there was a minor discomfort during the surgery, (VAS ⩾ 1 but VAS ⩽ 3), the patient was given ketamine 20-30 mg or sufentanil 5-10 μg intravenously.

Data Collection

The primary outcomes are successful spinal sensory and motor blocks and adequate anesthesia for the surgery. The dose was considered successful if a sensory block T6 was achieved, and there was no need for additional analgesia or conversion to general anesthesia during cesarean delivery. The sensory level was assessed using an acupuncture needle. The times to achieve T6 level and to recess to T12 were recorded as spinal onset time and recovery time. The motor block was assessed using a modified Bromage grading score, where 0 = no motor block; 1 = partial block (just able to move knees, but cannot lift lower limbs); 2 = almost complete block (able to move feet only); and, 3 = complete block (unable to move feet or knees). The time elapsed from the maximum Bromage Score to the lowest Bromage Score is the duration of motor block.

The patient satisfaction and surgical satisfaction with spinal anesthesia were assessed as follows: Patient satisfaction score: 0 points = unsuccessful, inadequate analgesia (VAS ⩾ 7), general anesthesia required to complete surgery; 1 point = not satisfied, poor analgesia (VAS 4-6), and need for supplemental analgesic drugs (ketamine or sufentanil) and use of epidural; 2

Table 1. Comparison of Onset Time and the Duration of Sensory and Motor Block in Each Group.

Group	N	Spinal Onset Time (s)	Sensory Block Duration (min)	Motor Block Duration (min)
R10	94	183 ± 72	92.27 ± 30.52	62.74 ± 24.54
R12	98	149 ± 63	101.87 ± 25.47	92.43 ± 26.65
R14	100	144 ± 54[a]	122.29 ± 28.33[a]	101.58 ± 28.27[a]
R16	100	123 ± 55[ab]	147.46 ± 32.15[abc]	123.42 ± 35.47[abc]
R18	100	118 ± 49[abc]	151.27 ± 30.56[abc]	148.67 ± 42.24[abc]

Data were presented as mean ± standard deviation. Compared with R10, [a]P < 0.05; Compared with R12, [b]P < 0.05; Compared with R14, [c]P < 0.05.

Table 2. The Patient Satisfaction Score and Surgical Satisfaction Score in Each Group.

Group	N	Patient Satisfaction Score				Surgical Satisfaction Score			
		3	2	1	0	3	2	1	0
R10	100	21	45	28	6	12	37	45	6
R12	100	68[a]	17[a]	13[a]	2[a]	35[a]	52[a]	11[a]	2[a]
R14	100	90[ab]	9[ab]	1[ab]	0[a]	82[ab]	13[ab]	5[ab]	0[a]
R16	100	98[abc]	2[abc]	0[ab]	0[a]	93[abc]	6[abc]	1[abc]	0[a]
R18	100	97[abc]	3[abc]	0[ab]	0[a]	92[abc]	8[abc]	0[abc]	0[a]

Data presented as incident of group: N. Compared with R10, [a]P < 0.05. Compared with R12, [b]P < 0.05; Compared with R14, [c]P < 0.05.

points = anesthetized almost adequately (VAS 1-3), but intravenous sedatives required for anxiety or agitation during anesthesia and surgery; 3 points = satisfied (VAS ≤1), patients were comfort. Surgical satisfaction score: 0 points = the anesthetic effect is poor and operation cannot be completed; 1 point = the operation can be performed, but poor analgesic and no muscle relaxant effect; 2 points = anesthetic and analgesic effects are satisfactory, poor muscle relaxation; 3 points = surgical condition, anesthetic, analgesic, and muscle relaxation effects are satisfactory.

The secondary outcomes include the incidence of nausea and vomiting, Apgar scores, use of vasoactive medications (ephedrine or deoxyadrenaline) and postoperative neurological complications for 48 hours.

Statistical Analysis

The SPSS software (version 13.0, IBM) was used for statistical analysis. One-way analysis of variance (ANOVA) was used for comparison among groups. A chi-square test was used for count data. The $P < 0.05$ was considered statistically significant.

The dose-response relation for spinal ropivacaine was determined using probit analysis (5). An effective dose (success) was defined as a dose that provided adequate sensory dermatomal anesthesia to pinprick to T6 or higher required no intravenous supplement for surgery to be completed.

RESULTS

A total of 500 healthy primiparas enrolled in the study and 492 participants finished the study. The initial block levels were not achieved and thus not included in calculations in 8 patients (6 in Group R10 and 2 in Group R12). There were no significant differences in age, height, weight and operation time among the five groups ($P > 0.05$).

The spinal onset time is shorter and the duration is longer in higher dose groups in a dose-dependent relationship (Table 1). Achieving T6 sensory block was quicker in groups receiving 14 mg or more than in those receiving 10 or 12 mg. ($P < 0.05$). Furthermore, the duration of sensory and motor block in Groups R14, R16 and R18 were longer than group R10 ($p < 0.05$), and Groups R16 and R18 were longer than Groups R12 and R14 ($P < 0.05$).

The patients' satisfaction scores and surgeons'

Table 3. The Use of Vasoactive Drugs, Intravenous Drugs and Adverse Reactions in Each Group.

Group	N	Atropine	Ephedrine	Deoxyepinephrine	Intravenous Drugs	Hypotension	Nausea	Vomiting
R10	94	0	2(2.1)	6(6.4)	42(44.7)	8(8.5)	2(2.1)	0
R12	98	1(1.0)	3(3.1)	10(10.2)	17(17.3)[a]	13(13.3)	3(3.1)	0
R14	100	1(1.0)	4(4.0)	13(13.0)	5(5.0)[ab]	17(17.0)[a]	8(8.0)	1(1.0)
R16	100	2(2.0)	6(6.0)	14(14.0)[a]	1(1.0)[abc]	20(20.0)[ab]	13(13.0)[abc]	3(3.0)
R18	100	5(5.0)[a]	11(11.0)[abcd]	21(21.0)[abcd]	1(1.0)[abc]	32(32.0)[abc]	21(21.0)[abc]	6(6.0)[abc]

Data presented as "n (%)". Compared with R10, [a]$P < 0.05$; Compared with R12, [b]$P < 0.05$; Compared with R14, [c]$P < 0.05$. Compared with R16, [d]$P < 0.05$.

satisfaction scores in Groups R14, R16 and R18 were higher than those in Groups R10 and R12 (Table 2). In contrast, the use of intravenous supplement pain medicine was more frequent in Group R10 and R12 than in Groups R14, R16 and R18 ($P < 0.05$, Table 3).

The highest dose of ropivacaine in Group R18 resulted in the highest incidence of hypotension (need for use of ephedrine and deoxyepinephrine) than in the other four groups ($P < 0.05$). The incidence of nausea in Groups R16 and R18 was higher than in Groups R10, R12 and R14 ($P < 0.05$), and the incidence of vomiting was also higher in group R18 than in groups R10, R12 and R14 ($P < 0.05$, Table 3). The median effective dose (ED50) was 9.7 mg (95% confidence interval [CI], 8.9 to 10.3) and ED95 was 14.3 mg (95% CI, 13.7 to 15.3).

Apgar scores at 1 minute and 5 minutes after birth did not differ significantly among the five groups ($P > 0.05$).

DISCUSSION

Choice of the best local anesthetics for cesarean delivery could be difficult. Ropivacaine is a relatively new local anesthetic. Compared with bupivacaine, it has low cardiotoxicity. In addition, it also has peripheral vasoconstrictor effects, and the advantages of less motor block (6). At present, it has been widely used for neuraxial anesthesia and analgesia. Madhuri reported that the optimal dose of ropivacaine for cesarean delivery in a range of 15-20 mg (7). Khaw et al. studied 80 cases of cesarean delivery using plain ropivacaine spinal anesthesia and observed an ED50 of 16.7 mg, and an ED95 of 26.8 mg (5). Other clinical studies using plain ropivacaine have also described wide variability of block height and a frequent incidence of insufficient cephalic spread requiring supplementary anesthesia or conversion to general anesthesia (8, 9). However, evidence from studies of other local anesthetics suggests that the addition of glucose would improve reliability and might enable a smaller dose to be used. The addition of glucose to intrathecal ropivacaine was investigated by Whiteside et al. (10), who reported that solutions of ropivacaine 15 mg in glucose 1% and 5% had greater cephalic spread and less block variability compared with plain solutions. Interestingly, Chen found that when hyperbaric ropivacaine was used in spinal anesthesia, the ED50 was 10.37 mg and the ED95 was 15.39 mg in a Chinese population (11), and our study found that the ED50 was 9.7 mg and ED95 was 14.3 mg.

Our present study found that reducing the dose of spinal anesthesia ropivacaine can reduce the incidence of maternal hypotension, reduce the use of vasopressors, reduce the incidence of nausea and shorten post-anesthesia care unit (PACU) stay, improving the overall satisfaction of patients. However, if ropivacaine dose is too low, it often results in maternal discomfort, intraoperative pain, the possibility of anesthesia failure, and may even have to convert to general anesthesia. This study showed that a subarachnoid ropivacaine dosage of 12 mg and less than 12 mg cannot guarantee a satisfactory anesthetic effect, requiring rescue treatment with an intravenous supplement of pain medicine to treat or conversion to general anesthesia.

When the dose was increased to 16 mg, the anesthetic effect was improved significantly, along with the satisfaction of patients and surgeons. Due to the increased dosage, the inci-

dence of hypotension, nausea and vomiting increased. Gaiser et al. found that epidural infusion of 8-12 mL of 0.25% ropivacaine achieved a T10 dermatomal sensory level, also resulted in detectable blood concentrations of ropivacaine in the maternal arterial blood and umbilical vein blood after delivery of the fetus (12). Thus, we believe that spinal ropivacaine has near zero systemic absorption and it is safe for the fetus.

In summary, in the combined spinal-epidural anesthesia for cesarean delivery, the optimal dose of 14 mg of hyperbaric ropivacaine provided effective spinal anesthesia with fewer side effects compared to higher doses. This dosage is safe to the fetus.

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The authors have no other potential conflicts of interest for this work.

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