Original Article

Intrathecal Ropivacaine in Cesarean Delivery

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Abstract

Objective: The aim of the present study was to evaluate the optimum dose of ropivacaine by comparing three different dosing regimens of isobaric ropivacaine 1% (naropin 10 mg/ml, Astra Zeneca) administered intrathecally and to demonstrate the effects of anesthesia in pregnant women scheduled for cesarean section. **Patients and Methods**: Sixty ASA grade I-II patients were scheduled to undergo elective cesarean sections under spinal anesthesia. The patients were randomly assigned into three groups. Group 1 received 15 mg ropivacaine 1%, Group 2 received 20 mg ropivacaine 1%, and Group 3 received 25 mg ropivacaine 1%. **Results:** Intraoperative hemodynamic variables were not significantly different between the three groups, and sensory block time, motor block time and time to reach maximal sensory block time, and motor block time were similar between the three groups. The time to two-segment regression of sensory block was longer in Group 3 compared to other groups, and the difference was statistically significant ($p < 0.05$). The motor block time was longer with higher doses of ropivacaine; however, the difference was not statistically significant. **Conclusion:** Ropivacaine administration produced rapid induction of anesthesia and satisfactory anesthesia level, ropivacaine 15 mg and 20 mg dosing regimens are satisfactory for spinal anesthesia.

Keywords: *Ropivacaine, spinal anesthesia, intrathecal, cesarean section*

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Introduction

Ropivacaine (1-propyl-2", 6"-pipecoloxylidide) is an amino amide local anesthetic (LA) drug that chemically and pharmacodynamically resembles bupivacaine.[1] Ropivacaine is an enantiomer whose intrathecal administration has been investigated.

In epidural and spinal anesthesia, ropivacaine offers shorter motor blockage time compared to bupivacaine.[2] In animal studies, ropivacaine was shown to decrease spinal cord blood flow, but it showed no neurotoxic effects, and ropivacaine was reported to be safe for intrathecal administration.[3,4] The clinical studies show that ropivacaine is less potent than bupivacaine, and doses ranged between 8 and 22.5 mg after intrathecal administration.[5-7]

There are studies to show optimal dosing for intrathecal ropivacaine; however, it is still an active area of research.

The aim of the present prospective study was to evaluate the optimum dose of ropivacaine by comparing three different dosing regimens of isobaric ropivacaine 1% administered intrathecally and to demonstrate the effects of anesthesia in pregnant women scheduled for cesarean section also the effects of the drug on newborns.

Methods

Sixty pregnant women aged between 16 and 45 years with gestational age of more than 36 weeks and who have American Society of Anesthesiologist physical status I-II were included in the study at Akdeniz University Hospital in Antalya, Turkey. The written informed consent of the patients was provided before their participation in the study. The patients that refused regional anesthesia and those with prolonged prothrombin time, activated partial thromboplastin time,

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thrombocytopenia, systemic diseases (i.e., diabetes mellitus, preeclampsia, and hypertension), or lumber disc pathologies were excluded from the study. After obtaining approval from the University Hospitals ethics committee, the patients were randomly assigned in to three groups. Group 1, 2, and 3 received 15 mg, 20 mg, and 25 mg isobaric ropivacaine 1% intrathecally. The solutions were prepared in equal volumes (3 ml) by addition of 0.9% NaCl to plain ropivacaine. The study variables of hemodynamic parameters, systolic arterial blood pressure, diastolic arterial blood pressure, heart rate and SPO2 values, anesthetic complications, sensory and motor block times, the time to first analgesic requirement ,VAS scores, umbilical blood gas analysis, and Apgar scores of the newborns, were recorded and analyzed. The patients were moved into the operating room and monitorized with the multiscan (Sony) 100s monitor for ECG (heart rate), noninvasive systolic arterial blood pressure, diastolic arterial blood pressure, peripheric oxygen saturation (SPO2), and administered with intravenous NaCl 0.9% at a dose of 15 ml/kg within 15 minutes before the spinal anesthesia. The spinal puncture was performed while the patients were placed on either the left or right lateral decubitus position. The L3-4 interspace was determined, and a 25-gauge Whitacre-point spinal needle (Braun spinal needle) was advanced until free fluid (cerebrospinal fluid) return was established. The ropivacaine 0.1% solution was administered in three different doses and then the spinal needle was removed. The patients were brought into a supine position, and then the operation was initiated. and diastolic arterial blood pressure, heart rate, and SPO2, were recorded at 1 min, 3 min, 5 min, 10 min, 15 min, 30 min, and 45 min during the skin incision, after delivery of baby, and at the end of surgery. Hypotension was defined as systolic blood pressure to drop under 90 mmHg or a 20% decline from baseline. Hypotension was treated with 5 mg bolus doses of intravenous ephedrine. Bradycardia was defined as the heart rate < 50 beat per minute, and it was treated with 0.5 mg IV atropine. The presence of nausea, vomiting, and shivering were also recorded during the operation and were treated with IV antiemetics and IV sedatives (midazolam), and the patients were treated according to complications. No patient was excluded from the study due to the side effects of drug or insufficient spinal anesthesia.

The sensorial blockage level of anesthesia was assessed using the pin-prick test at 1 min, 3 min, 5 min, 10 min, and 15 min after drug injection and every 10 min during the surgery and the values were recorded. The level of sensory block was assessed bilaterally along the mid-clavicular line by the loss of pinprick sensation and was performed using a 17 G needle. A sensory level to pin-prick was assessed by the Hollmen scale: 0 = ability to appreciate a pinprick as sharp; 1 = ability to appreciate a pinprick as less sharp; 2 = inability to appreciate a pinprick as sharp (analgesia); and 3 = inability to appreciate a pin touching (anesthesia).

The onset time of sensory block was the time for sensory block to develop to T10 (thoracic ten) level and maximum sensory block time was the time for sensory block to develop to T4 (thoracic four) level. The motor blockage level of anesthesia in the lower limbs was determined according to the Bromage scale. The Bromage scale: 0 = able to lift extended leg at hip; 1 = able to flex knee but not lift extended leg; 2 = able to move foot only; and 3 = unable to move foot. The onset of motor block time was time to motor block to develop Bromage 1, and maximal motor block time was time to motor block of Bromage 3. The operation was initiated when the sensory block reached to the level of the thoracic fourth to sixth dermatome.

Blood samples were collected from the umbilical artery and umbilical vein; blood gas analysis was performed to measure PH, PO2, PCO2, HCO3, and SpO2. The Apgar scores of the infants were evaluated at 1 min and 5 min, and birth weights of the infants were recorded.

In the post-anesthesia care unit, duration of sensory block time and motor block time of the patients were evaluated. The time to two-segment regression of sensory block time was regarded as the duration of sensory block, and duration of motor block time was regarded as the time to regress to Bromage 2. The patients were asked to rate the pain level on a 10 cm linear visual analogue scale (visual analogue scale; VAS = 0 no pain, and VAS = 10 severe pain). The patients were administered with a non-steroidal anti-inflammatory drug (NSAID) (tenoxicam 20 MG po), if postoperative pain was more than three on a VAS, and this was recorded as the time to first analgesic requirement. In the first 24 hours after the operation, the patients were asked to report any complications such as headache and urinary retention.

In the present study, statistical analysis of hemodynamic variables, age, weight, height, and gestational age were expressed as mean standard deviation (SD). One-way analysis of variance was used to compare variables between the groups, intragroup comparison of the variables was performed by the paired samples *t*-test ($p < 0.05$ means statistical significant), and chi-square test was used to analyze the complications.

Results

Demographic variables did not significantly differ

Table 1: Demographic variables of the study groups (mean ± SD)

Groups	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)
Age (Years)	29.05 ± 4.08	30.70 ± 4.55	27.00 ± 3.35
Height (cm)	163.15 ± 3.88	164.65 ± 4.14	163 ± 3.54
Weight (kg)	79.8 ± 9.11	78.00 ± 10.93	74.75 ± 8.49
Gestational age (week)	37.85 ± 1.13	37.90 ± 1.41	38.15 ± 1.04
Birth weight (gr)	3236.6	3341	3303

Table 2: Comparison of sensory block time between the three groups (mean ± SD)

Groups	Group I (n = 20)	Group II (n = 20)	Group III (n = 20)
Onset of the sensory block time (min)	1.0	1.0	1.0
Maximum sensory block time (min)	6.60 ± 3.20	8.30 ± 4.23	7.95 ± 4.37
Time to two-segment regression of sensory block (min)	127.8 ± 43.22	141.40 ± 36.94	163.10 ± 49.68*

*p <0.05(statistically significant difference)

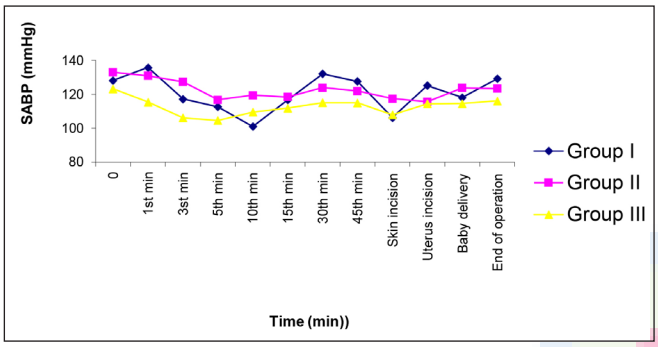

Figure 1: Systolic arterial blood pressure (SABP) of the groups

between the three groups (p > 0.05) as illustrated in Table 1.

Systolic arterial blood pressure measurements of groups during the operation did not significantly differ between the three groups, and the difference was not significant statistically (p > 0.05) [Figure 1]

Diastolic arterial blood pressure measurements of the groups during the operation did not significantly differ between the three groups, and the difference was not significant statistically (p > 0.05) [Figure 2].

The heart rate measurements of groups during the operation did not significantly differ between the three groups, and the difference was not significant statistically (p > 0.05) [Figure 3].

The onset time of sensory block was defined as a bilateral sensory block to develop to dermatome T10 level within 1 min of intrathecal drug administration for the three groups. The maximum sensory block time to dermatome T4 level was similar in the three groups, and there was no statistically significant difference between the groups (p > 0.05). The time to two-segment regression of sensory block was longer in Group 3 compared to other groups, and the difference was statistically significant (p < 0.05) [Table 2].

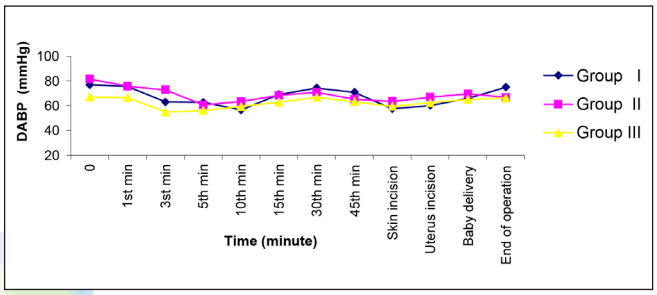

Figure 2: Diastolic arterial blood pressure (DABP) of groups

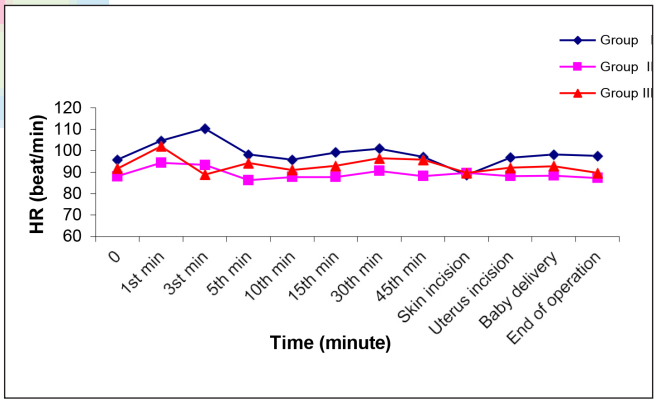

Figure 3: The peripheric oxygen saturation of groups (SPO2)

The onset of motor block (Bromage 1) and the time to reach maximum motor block (Bromage 3) were similar in the three groups, and there was no statistically significant difference between the groups (p > 0.05). As shown in Table 3, the motor block time (time to regress to Bromage 2) was longer with higher doses of ropivacaine; however, the difference did not reach statistical significance (p > 0.05).

Hypotension was observed in eight, eight, and ten patients in Group 1, Group 2, and Group 3, respectively, and they were treated with intravenous bolus doses of 5 mg ephedrine. Ephedrine requirement was significantly

Table 3: Comparison of the motor block time between the three groups (mean ± SD)

Groups	Group I (*n* = 20)	Group II (*n* = 20)	Group III (*n* = 20)
Onset of the motor block (min)	1.4 ± 0.82	1.6 ± 1.14	1.45 ± 2.01
Maximum motor block time (min)	5.5 ± 4.81	8.05 ± 3.95	5.40 ± 4.07
Motor block time to regress to Bromage 2 (min)	117.95 ± 53.72	137.15 ± 53.27	143.45 ± 60.27

Table 4: The complications associated with spinal anesthesia

Groups	Group I (*n* = 20)	Group II (*n* = 20)	Group III (*n* = 20)
hypotension	*n* =8	*n* =8	*n* =10
bradycardia	*n* =2		
Allergic reactions	*n* =1		
shivering		*n* =1	
headache	*n* =1		*n* =1
Nausea	*n* =1	*n* =3	*n* =5

Table 5: Comparison of time to first analgesic requirement and VAS scores between the groups (mean ± SD)

Groups	Group I (*n* = 20)	Group II (*n* = 20)	Group III (*n* = 20)
Time to first analgesic requirement (min)	149.35 ± 12.21	216.50 ± 39.06	197.25 ± 34.77
VAS	4.20 ± 1.05	3.40 ± 1.35	3.85 ± 1.22

Table 6: Umbilical artery blood gas analysis

Group	pH	PCO2	PO2	HCO3	SpO2
I	7.33	46.91 ± 7.79	19.00 ± 9.08	25.67± 2.73	28.25±20.60
II	7.33	47.33 ± 3.87	17.04 ± 4.92	25.63 ± 3.18	22.60 ± 12.93
III	7.32	43.60± 7.75	19.48 ± 4.57	24.67 ± 2.42	28.58 ± 12.92

Table 7: Umbilical vein blood gas analysis

Group	pH	PCO2	PO2	HCO3	SpO2
I	7.35	41.86 ± 4.76	26.24 ± 6.21	24.61 ± 3.71	45.43 ± 14.89
II	7.37	39.13 ± 8.58	30.68 ± 11.33	25.60 ± 3.11	54.07 ± 20.58
III	7.37	40.21 ± 5.85	28.88 ± 9.60	24.72 ± 2.31	50.19 ± 19.43

higher in Group 3 compared to the other two groups that was significant statistically ($p < 0.05$). Bradycardia was observed only in two patients in Group 1 and treated with 0.5 mg intravenous atropine. Allergic reactions were observed only in one patient in Group 1 and treated with the administration of intravenous antihistamines. Shivering was observed in one patient in Group 2, and headache was observed within 24 hours in one patient in Group 1 and one patient in Group 3 and treated with IV hydration and NSAID (tenoxicam 20 mg po). Nausea and vomiting were observed in one patient in Group 1, three patients in Group 2, and five patients in Group 3, and all were treated with intravenous administration of 10 mg metoclopramide. We have not observed any urinary retention and neurological side effects [Table 4]. The rates of complications except hypotension and ephedrine requirement were not significantly different between the three groups ($p > 0.05$).

The time to first analgesic requirement was longer in Group 2 and shorter in Group 1; however, the difference was not statistically significant ($p > 0.05$). The VAS scores were similar, and there were no difference between the groups statistically ($p > 0.05$) [Table 5].

Umbilical artery and vein blood gas analysis were within normal limits, and fetal acidosis was not observed in any groups (pH < 7.20) ($p > 0.05$) [Tables 6 and 7].

Apgar scores in 1 min and 5 min were Group I: 7.9, Group II :8.05, and Group III: 8.1, and there were not any significant difference statistically ($p > 0.05$).

Discussion

The optimal dosing regimen for intrathecal administration of isobaric ropivacaine is still an active area of research. Ropivacaine is not approved for intrathecal use even though it has not shown any neurotoxic effects in clinical studies at dosages of 8-22.5 mg.[5] The clinical studies did not report neurological side effects associated with the intrathecal administration of ropivacaine.[5,6]

In cesarean section, the baricity of LA and position of the patient affect the level of nerve block. In the lateral position, hyperbaric LA solutions have more cephalic spread compared to isobaric LA solutions.[8,9]

The 50% effective dose (ED50) and the estimated 95% effective dose (ED95) of spinal plain ropivacaine alone for cesarean delivery were 16.7 and 26.8 mg, respectively.[10]

Khaw *et al.* used intrathecal ropivacaine administration in cesarean sections, in which the study evaluated the spread of anesthesia using the pin-prick test. The anesthesia was considered unsuccessful if the patient reported pain. In comparison to successful spinal anesthesia, the study reported incomplete motor block. The study concluded that sensory block as well as cephalic spread of LA depended on the amount of LA administered into the intrathecal space.[11]

In studies that evaluated intrathecal administration of 15–25 mg isobaric ropivacaine, the motor block time was shown to be related to the dose administered.[6,12-14] In another study, incremental doses of ropivacaine were found to be responsible for a longer motor block time.[11] During a cesarean section, muscle relaxation is an important part of surgery, whereas a shorter motor block time facilitates early mobilization.[13] The present study used equal volumes (3 ml) of isobaric ropivacaine 15 mg, 20 mg, and 25 mg, and onset of sensory block and motor block was similar in all the three groups; however, sensory and motor block times were longer with higher ropivacaine doses. The increments in the LA dose were associated with increases in sensory and motor block times and a longer time to the first analgesic requirement.

Linda *et al.* showed the vasoconstrictor effects of ropivacaine on spinal pial veins, for which administration of vasoconstrictor agents such as epinephrine is not required in order to provide sustained analgesia.[15-17] In the present study, isobaric ropivacaine 1% was administered intrathecally, and addition of a vasoconstrictor agent to LA solution was not required, and a sufficient level of anesthesia was achieved in all of the patients.

In the study by Evans *et al.*, Apgar scores of the infants (Apgar score > 7 at 1 min and 5 min) and umbilical artery blood gas analysis (pH > 7.20) were more favorable in the regional anesthesia group compared to general anesthesia group.[18] In other studies, the Apgar scores of the infants were higher in the regional anesthesia group compared to the general anesthesia group.[19,20] In the present study, the Apgar scores and the results of umbilical artery blood gas analysis were within normal limits in the three groups, and fetal acidosis was not observed (pH < 7.20).

The pregnant women are at increased risk of developing deep venous thrombosis in the postpartum period. The most important risk factor for venous thromboembolism is immobilization, and early mobilization in the postpartum period prevents deep venous thrombosis and pulmonary embolism.[21] Ropivacaine is a less potent agent in inducing motor block and allows early mobilization in the postpartum period. In the present study, the motor block time was longer with higher doses of ropivacaine, and our patients were mobilized in the early period.

Wong *et al.*, concluded that either 18.75 mg (2.5 ml) or 22.5 mg (3 ml) 0.75% glucose-free ropivacaine could provide spinal anesthesia of the same efficacy and safety for Caesarean section in Chinese women.[21] Ogun *et al.* suggested that intrathecal isobaric ropivacaine 0.5% 15 mg plus morphine 150 μg provided sufficient anesthesia for Caesarean delivery and the ropivacaine–morphine combination resulted in a shorter motor block, similar sensory and postoperative analgesia with respect to the same combination of bupivacaine–morphine.[22] In our study, although we used plain ropivacaine that was glucose free and we did not make any analgesic combinations, we achieved sufficient spinal anesthesia.

Hypotension is an important maternal and fetal complication occurring after intrathecal administration of anesthetic agents.[13,14] In the present study, 25 mg ropivacaine dose caused maternal hypotension that is detrimental to fetus by decreased placental blood flow, and ephedrine requirement was significantly higher. However, 15 mg and 20 mg doses were associated with maternal hypotension but did not necessitate high ephedrine doses, and patients were hemodynamically more stable. In the present study, nausea, vomiting, and shivering were also recorded during the operation; however, no neurological adverse events were observed during and after the operation associated with the intrathecal administration of isobaric ropivacaine.

Conclusions

In the present study, hemodynamic parameters, anesthetic complications, sensory and motor block times, time to first analgesic requirement, VAS scores, umbilical artery blood gas analysis, and Apgar scores of the infants were compared between the three groups. We conclude that anesthesia with 25 mg ropivacaine required intravenous administration of ephedrine due to decreases in systemic blood pressure. Although the induction of anesthesia was fast and a sufficient level of anesthesia was achieved in the three groups, 15 mg and 20 mg ropivacaine dosing regimens were satisfactory for spinal anesthesia

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Conflicts of interest

There are no conflicts of interest

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