Intrathecal 0.75% Isobaric Ropivacaine Versus 0.5% Heavy Bupivacaine for Elective Cesarean Delivery: A Randomized Controlled Trial

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ABSTRACT

OBJECTIVE: Ropivacaine, a local anesthetic with duration of action of 2-3 hours, has shown greater selectivity for sensory blockade along with lower systemic toxicity as compared to bupivacaine when used for spinal anesthesia. This study was aimed to compare the intrathecal efficacy and safety of 0.75% isobaric ropivacaine for cesarean delivery with 0.5% heavy bupivacaine in parturients.

MATERIALS AND METHODS: We enrolled 46 parturients of ASA (American Society of Anesthesiologists) grade I-II scheduled for elective cesarean delivery under spinal anesthesia for this prospective randomized control trial. The patients were randomized to receive either 12.5 mg of 0.5% hyperbaric bupivacaine or 24 mg of 0.75% isobaric ropivacaine intrathecally. Intraoperative hemodynamic parameters, characteristics of sensory and motor nerve block, neonatal outcome and maternal adverse effect (such as hypotension, bradycardia, nausea, vomiting, shivering or pruritis) were evaluated.

RESULTS: Baseline demographic variables were similar in the 2 groups (p-value>0.05). Neonatal outcomes were also similar in both the groups. The time to achieve sensory block to T10 (3.2 ± 1.5 vs 2.5 ± 1.3 minutes) or to the maximal level (9.8 ± 3.1 vs 7.9 ± 2.3 minutes) was longer in the ropivacaine group (p-value 0.048) but the median maximal level of sensory block was similar between the two groups (p-value>0.05). Duration of sensory block was shorter in the ropivacaine group (160.5± 22.2 vs 182.3± 30.5 minutes) (p-value 0.03). Duration of motor block was also significantly shorter than bupivacaine group (112.5 ± 45 vs 165.3 ± 26) (p-value 0.004).

CONCLUSION: Spinal anesthesia for elective cesarean delivery with intrathecal 24 mg of 0.75% isobaric ropivacaine provided clinically effective surgical anesthesia of shorter duration without compromising neonatal outcome and can be used as an effective and safe alternative to bupivacaine.

Key Words: Spinal Anesthesia, Isobaric Ropivacaine, Bupivacaine, Cesarean Delivery, APGAR Score

INTRODUCTION

Cesarean delivery is usually conducted under spinal anesthesia with bupivacaine. Ropivacaine, which blocks sensory nerve fibers more readily than motor fibers, is now gaining popularity due to its reduced cardiac toxicity with overdose [1]. Recent studies with intrathecal ropivacaine have demonstrated low cardiovascular and neurotoxic effects, good tolerability and efficacy [2].

The aim of this randomized controlled trial was to compare the efficacy and safety of intrathecal 0.75% isobaric ropivacaine (24 mg) with 0.5% heavy bupivacaine (12.5 mg) for elective cesarean delivery [3]. We selected the ropivacaine dose based on the dose-response study by Khaw et al, which estimated the 95% effective dose (ED 95) of intrathecal ropivacaine

for cesarean delivery to be 26.8 mg (23.6-34.1 mg) [4, 5, 6]. The most novel aspect of our study is the comparison between hyperbaric 0.5% bupivacaine and isobaric 0.75% ropivacaine; such a study has not been conducted before.

METHODS

After approval of Institutional Ethical Committee and written informed consent, 46 full term parturients of American Society of Anesthesiologists (ASA) grade I and II with weight < 80 kg and height between 145 cm to 160 cm, scheduled for elective cesarean delivery under spinal anesthesia, from January 2011 to October 2011, were included in this prospective randomized single-blind study. We selected our patients from Obstetrics and Gynecology ward of our medical college and hospital. Parturients having cardiac or neurologic disease, diabetes, pre-eclampsia or eclampsia, bleeding or coagulation disorder, any obstetric complications or evidence of fetal compromise or suspected fetal abnormality were excluded from the study. The parturients were randomized, according to computer generated number, into two treatment groups of 23 each to receive an intrathecal injection of either 12.5 mg (2.5 ml of 0.5% hyperbaric bupivacaine) or 24 mg (3.2 ml of 0.75% isobaric ropivacaine) [4, 5, 6]. They received premedication with ranitidine 50 mg and metoclopramide 10 mg intravenously (IV) and were preloaded with Ringer's lactate solution 15ml/kg before initiation of the spinal block. The subarachnoid puncture was performed in sitting position with a 25-gauge Quincke spinal needle.

The subarachnoid block was given by midline approach at the L3-4 interspace and study drug was given over 30 seconds based on the group. Immediately after intrathecal injection, patients were placed in supine position. An anesthesiologist, who was blinded regarding which local anesthetic was used, assessed sensory and motor block after the intrathecal injection at 1 and 2 minutes and then subsequently at 2 minute intervals until surgical anesthesia was achieved. The segmental level of sensory block to pin prick was evaluated bilaterally along the midclavicular line by using a short beveled 27-gauge needle. The motor block of both legs was assessed using the modified Bromage scale (0 = full movement, 1= unable to raise extended leg, 2= unable to flex knee, 3= no movement). The induction of anesthesia was considered when at least the T10 dermatome was anesthetized.

Hemodynamic parameters that were monitored included maternal heart rate by electrocardiogram (ECG), blood pressure and oxygen saturation (SpO2). The values were recorded before the induction, every 2 minutes during the first 10 minutes after spinal block, then every 5 minutes during the first hour and then every 10 minutes until the patient was transferred to the recovery room. Oxygen was administered at a rate of 5 L/min via face mask. A significant change in the heart rate or blood pressure was defined as a greater than 20% change from baseline values. Hypotension was treated with intravenous boluses of mephentermine 5 mg and Ringer's lactate solution, and bradycardia with IV atropine. Nausea and vomiting were treated with IV ondansetron. The condition of neonate was evaluated by APGAR scores at 1 and 5 minutes after delivery.

The time to achieve sensory block at T10 level, the maximum cephalad spread of the sensory block, the time to achieve the motor block and the total duration of analgesia were recorded intra-operatively.

Postoperatively, the blocks were assessed at 15 minutes intervals until regression or complete recovery of motor function had occurred. All patients were evaluated for possible adverse effects due to hemodynamic changes and for headache, nausea, vomiting or transient neurologic deficits.

Statistical Analysis

The sample size was decided based on a pilot study with ropivacaine which indicated that approximately 17 patients should be included in each group in order to detect a 30 minute difference in mean duration of motor blockade between the groups for type 1 error of 0.01 and power of 90%. Assuming a 5% dropout rate, the final sample size was set at 46 patients. Statistical analysis was done for comparing observed data by using Student's t-test, Chi-square test and Mann-Whitney U test as applicable, and p-value of <0.05 was considered statistically significant.

RESULTS

The surgical procedure was successful in all enrolled patients. Demographic variables were similar between the two groups. The anesthetic and surgical techniques were standardized for both groups. The neonates had a mean APGAR score >8 and >9 at 1 minute and 5 minute,

	Ropivacaine	Bupivacaine	P-value
Age (year)	29.3± 8.7	28.6 ±7.9	>0.05
Weight (kg)	68.2±6.2	70.6 ± 6.4	>0.05
Height (cm)	155 ±4.5	156±5.5	>0.05
Duration of surgery (minutes)	55 ± 4	58 ± 3	>0.05
ASA grade (I/II)	25/5	24/6	>0.05
APGAR score at 5 minutes	9.4 ±0.3	9.5± 0.27	>0.05

Table 1: Demographic profile and neonatal outcome (mean ± SD)

Parameters (mean± SD)	Ropivacaine	Bupivacaine	P-value
Sensory block - onset time to T10 (minutes)	3.2 + 1.5	2.5 + 1.3	>0.05
Median maximal sensory level	T6 (T2-T10)	T6 (T2-T8)	>0.05
Time taken for maximal block (minutes)	9.8 + 3.1	7.9 + 2.3*	<0.048
Duration of sensory block (minutes)	130.6 + 10.2*	175.8 + 8.6	<0.03
Time taken to complete motor block (minutes)	14.2 + 2.4	9.4 + 3.4	>0.069
Duration of motor block (minutes)	112.5 + 45**	165.3 + 26	<0.004

Table 2: Sensory and motor block profile

T = Thoracic level

*p-value <0.05 significant, **p-value <0.001 highly significant

Adequate level of sensory analgesia was achieved in all patients before surgery. The mean time to achieve sensory block to T10 (3.2 ± 1.5 vs 2.5 ± 1.3 min) or to the maximal level (9.8 ± 3.1 vs 7.9 ± 2.3 min) was longer in the ropivacaine group than in the bupivacaine group (p-value <0.05). In contrast, the median maximal level of sensory block (T6) was similar in both groups. Mean duration of sensory block was shorter in the ropivacaine group than bupivacaine group (160.5 ± 22.2 vs 182.3 ± 30.50 min) (p-value <0.05). Complete motor block of both legs was observed in all patients. Time to achieve complete motor blockade was similar in both groups but of shorter duration in ropivacaine group (112.5± 45 min) than bupivacaine group (165.3 ± 26 min) (p-value <0.001). The quality of intraoperative anesthesia was comparable between the groups [Table 2]. The incidence of hypotension was more frequent in bupivacaine group, 14 (60.8%) patients had one or more episodes of hypotension when compared with 6 (26%) patients in the ropivacaine group (p<0.05).

The maximal percent decrease in mean arterial pressure or heart rate did not differ between the groups. Student's t-test was applied to compare the intraoperative blood pressure changes between the two groups and p-value >0.05 was non significant at every point [Table 3].

The cesarean deliveries under spinal anesthesia were not accompanied by any deleterious effects of hypotension or bradycardia in any parturient. Ten patients developed nausea and vomiting in bupivacaine group as compared to three patients in ropivacaine group. Shivering was reported in 7 patients of bupivacaine group while only 3 patients complained of shivering in ropivacaine group. No patient complained of any neurological symptoms at the postoperative visit [Table 4].

Fischer's exact test was used to compare the postoperative events of both groups. P-value was <0.05 (significant) for all events.

Parameters	**Heart Rate (bpm)**		**Mean arterial pressure (mmHg)**	
Drugs	**Ropivacaine**	**Bupivacaine**	**Ropivacaine**	**Bupivacaine**
Preoperative	86.3 ± 8.6	88.2 ±7.1	90.40 ± 6.8	92.88 + 7.20
1 minute after SA injection	84.6 ± 7.8	86.55± 10.15	88.14 ± 8.37	79.26 ± 9.10
5 minutes	80.45 ± 9.25	82.85 ±11.24	86.01± 9.33	74.48 ± 8.24
10 minutes	78.6 ± 8.4	76.6 ± 9.60	87.61 ± 7.76	78.16 ± 8.84
15 minutes	77.02 ± 8.8	71.4 ±7.56	84.08 ± 6.44	79.60 ± 10.28
20 minutes	74.0 ±10.4	78.17 ± 8.10	84.60 ± 4.78	80.42 ± 9.76
25 minutes	76.07 ±8.92	77.05 ± 10.26	85.22 ± 7.34	82.92 ± 6.54
30 minutes	77.17±10.01	78.24 ± 8.91	84.68 ± 5.58	82.34 ± 8.12
45 minutes	78.80 ±6.78	80.2 ± 8.22	86.16 ± 6.14	82.00 ± 5.67
60 minutes	80.16 ± 9.02	80.01± 8.98	86.28 ± 7.01	84.22 ± 6.58

Table 3: Hemodynamic parameters of heart rate and mean arterial pressure (MAP)

	Ropivacaine (n=23)	**Bupivacaine (n=23)**	**Significance (p-value)**
Hypotension	6	14	<0.027
Bradycardia	2	8	<0.013
Nausea	3	10	<0.028
Shivering	3	7	<0.048

Table 4: Postoperative adverse events

DISCUSSION

Ropivacaine is a new local anesthetic with duration of action of 2-3 hours and can be used for intrathecal administration. Ropivacaine, as compared to bupivacaine, has lower potential for cardiac and central nervous systemic toxic effects and shows greater differentiation between sensory and motor blockade with hemodynamic stability [2]. Several studies have demonstrated the efficacy and tolerability of spinal anesthesia with ropivacaine for cesarean section [5]. Although a hyperbaric formulation of ropivacaine is not commercially available and intrathecal equipotent doses for intrathecal ropivacaine and bupivacaine are still controversial, many researchers have reported ropivacaine to be less potent than bupivacaine [7].

Khaw et al studied the dose-response relationship for spinal ropivacaine and determined the effective doses for ED 50, ED 90 and ED 95 to be 16.7, 24.5 and 26.8 mg, respectively [4, 5]. In the present study, we have used ED 90 (24.5mg) of 0.75% ropivacaine to achieve effective surgical anesthesia for cesarean delivery. The rational for these dose selection was that the duration of action of ropivacaine in spinal anesthesia is approximately 50% to 67% that of bupivacaine [8]. Consistent with our rationale, 24 mg of isobaric 0.75% ropivacaine for elective cesarean delivery was adequate and surgery was completed successfully with no maternal or neonatal adverse effects.

The spread of block during spinal anesthesia is influenced by the mass of the local anesthetic agent and the patient position. In women, the width of the hips is usually larger than the shoulders, resulting in a head down tilt when lying horizontally in the lateral position. This difference may even be more exaggerated in pregnancy. Thus, when a hyperbaric solution is injected with patient in the lateral position, solution may spread in cephalic direction due to gravity. In contrast, an isobaric solution injected in the lateral position would not have such gravity assisted spread. To avoid this gravity-assisted spread in the present study, the intrathecal drugs were given in sitting position.

The bupivacaine group had a faster onset and episodes of hypotension, nausea and vomiting were more frequent than in ropivacaine group. The maximum sensory block height was similar in both groups. In the context for elective cesarean delivery, a small increase in the speed of onset of anesthesia may not be considered clinically important.

On the other hand, the faster onset and higher block probably may have resulted in the increased incidence of hypotension and nausea in hyperbaric bupivacaine. The duration of motor block is shorter in the ropivacaine group with less hemodynamic changes. A more rapid recovery from anesthesia is highly desirable for ambulatory surgery [9, 10]. In our study, the duration of anesthesia with both drugs was adequately effective for cesarean delivery in all parturients and results were consistent with other studies.

The results of our study are consistent with other studies. For example, Whiteside et al compared 15 mg of either 0.5% ropivacine or 0.5% bupivacaine in 8% glucose and reported that ropivacaine provided reliable spinal anesthesia of shorter duration and with less hypotension than bupivacaine [11]. Similarly, McNamee et al reported that intrathecal administration of 17.5 mg plain ropivacaine 0.5% or plain bupivacaine 0.5% resulted in a similar effective spinal anaesthesia for total hip arthroplasty [12].

In the present study, when considering the parturients' evaluation of surgical anesthesia, no significant differences were noted. All cesarean deliveries were free from adverse effects with good neonatal outcome and none of the patients presented with either back pain or neurologic symptoms at subsequent postoperative visit.

CONCLUSION

Spinal anesthesia for elective cesarean delivery with 24 mg of 0.75% isobaric ropivacaine is an effective and safe alternative to bupivacaine. Ropivacaine provided clinically effective surgical anesthesia of shorter duration without compromising neonatal outcome.

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