ORIGINAL ARTICLE

Comparison of the maternal and neonatal effects of bupivacaine plus fentanyl and ropivacaine plus fentanyl during cesarean delivery

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Abstract

Purpose: The aim of the present study was to compare the anesthetic efficacy, and fetal and maternal effects of 7.5 mg (1 ml) intrathecal 0.75% hyperbaric ropivacaine + 25 µg (0.5 ml) fentanyl versus 5 mg (l ml) intrathecal 0.5% hyperbaric bupivacaine + 25 µg (0.5 ml) fentanyl in elective cesarean delivery.

Materials and Methods: The study included 40 ASA I–II cases scheduled for cesarean delivery that were randomized into two groups of 20 cases each. Cases in the RF group were administered 0.75% hyperbaric ropivacaine + 25 µg (0.5 ml) fentanyl and those in the BF group were administered 5 mg (l ml) hyperbaric bupivacaine + 25 µg (0.5 ml) fentanyl into the spinal space. The time until spinal anesthesia in the T4 dermatome, overall duration of analgesia, hemodynamic parameters, Apgar score of newborns at 1–5 min, fetal blood gas values (pH, PO2, PCO2, HCO3−, and BE), maternal side effects, the degree of motor block, maternal need for ephedrine, objective pain scale score, and patient satisfaction were recorded in each group.

Results: There were no significant differences between the groups in terms of the parameters evaluated ($P > 0.05$).

Conclusion: In elective cesarean delivery, the combinations of bupivacaine + fentanyl or ropivacaine + fentanyl exhibited similar anesthetic efficacy, and fetal and maternal effects.

Key words: Bupivacaine, cesarean, opioid, ropivacaine

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Introduction

Anesthetic technique must produce adequate surgical anesthesia of adequate duration and minimal maternal and neonatal side effects during cesarean delivery. Spinal anesthesia provides a rapid and reliable anesthetic technique for cesarean section that may provide greater safety than general anesthesia. The principal side effects of spinal anesthesia for cesarean section are a reduction in maternal and uteroplacental blood flow/pressure, maternal pain,[1] and conversion to general anesthesia.[2] Reducing the dose of intrathecal local anesthetic (LA) will improve cardiovascular stability, but may not provide adequate surgical anesthesia. The addition of an opioid will allow the safe reduction of the LA dose with equal success and less severe side effects.[3]

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There are many recommended combinations of LA/opioid for cesarean section spinal anesthesia. Ultra low doses such as 5 mg of bupivacaine with 25 µg of fentanyl have been reported to be adequate.[3] The addition of 0.15 mg of morphine[4] or 10 µg of fentanyl to 15 mg of hyperbaric ropivacaine produced good surgical anesthesia in all cases.

There are studies comparing the concentration and doses of the two drugs used epidurally in cesarean section or spinally in different surgeries.[5-7] We could not find any study with these doses used in cesarean section. So, that the aim of the present study was to compare the anesthetic efficacy, fetal

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and maternal effects of 7.5 mg (1 ml) intrathecal 0.75% hyperbaric ropivacaine + 25 μg (0.5 ml) fentanyl versus 5 mg (l ml) intrathecal 0.5% hyperbaric bupivacaine + 25 μg (0.5 ml) fentanyl in elective cesarean delivery.

Materials and Methods

The study included 40 ASA class I–II pregnant women aged 18–40 years. The study protocol was approved by our institution's ethics committee. The study was randomized, double blind, and with two parallel treatment groups. Pregnant women who gave informed consent to an institutionally approved protocol were studied. Patients were not eligible if there was a history of allergy or sensitivity to amide-type LAs; maternal diabetes; a psychiatric history which could lead to unreliability in the clinical assessment; alcohol, drug, or medication abuse as judged by the investigator; or a contraindication for epidural procedures. Women who had hypotension and expectation of fetal anomaly, and those contraindicated for spinal anesthesia were excluded from the study.

Prior to spinal anesthesia, the women were placed in the 10 degree–15 degree left lateral position in order to reduce aorta-caval pressure, and then 4 l/min of O2 was administered with a face mask and non-invasive arterial pressure, ECG, and peripheral oxygen saturation (SpO2) (Cato Edition Drager, Lubeck, Germany) monitoring were carried out. Before the spinal block, 15 ml/kg/min of Ringer lactate solution was administered as bo.lus for 15 min and infusion was maintained at the rate of 8 ml/kg/h during the procedure. After prehydration infusion, the women were randomized into the RF group ($n = 20$) or BF group ($n = 20$) by random selection of envelops. While in a sitting position after antiseptic cleaning, the intrathecal region was entered from the L3–L4 space using a 26-G needle. After free CSF flow was observed, the RF group was administered 7.5 mg (1 ml) intrathecal 0.75% hyperbaric ropivacaine + 25 μg (0.5 ml) fentanyl, whereas the BF group was administered 5 mg (1 ml) 0.5% hyperbaric bupivacaine + fentanyl 25 μg (0.5 ml). When sensorial block reached the T4 dermatome, the surgical procedure was initiated. The time to reach sensorial block to the T4 dermatome was determined by the pin-prick test.

Heart rate (HR), mean arterial pressure (MAP), and oxygen saturation (SpO2) were recorded before and after block, every 5 min during the perioperative period, and every 10 min during the postoperative period until analgesia was required. HR below 60 bpm was considered bradycardia and a decrease of >30% in MAP, as compared to the preoperative value, was considered hypotension. For bradycardia, i.v. atropine sulfate 0.5 mg was administered, and fluid replacement (colloid) was done and ephedrine (when necessary) was administered for hypotension. In the patients with slight pain of l degree–2 degree, analgesia was given with support. In both groups after babies were delivered, 20 units of oxytocin was administered intravenously. Additionally, 10–20 units of oxytocin was added to each liter of fluid. Blood samples (2 ml) were obtained from the umbilical artery. Blood gas analysis was carried out on the samples using a Stat Profile 9 device (Nova, USA).

Overall duration of analgesia, the degree of motor block (measured with a Bromage scale) at 5-min intervals, objective pain scale score at 10-min intervals (0: Perfect; l: Good; 2: Moderate; 3: Inadequate; 4: Poor-bad), and patient satisfaction with the method (l: Very good; 2: Good; 3: Bad; 4: I will never use it) were recorded. Apgar scores of the newborns were recorded at 1 and 5 min, maternal side effects (headache, tinnitus, bradycardia, hypotension, respiratory depression, nausea and vomiting, itching and urticaria, and head, arm, and chest pain) were evaluated every 5 min, and the dose of ephedrine used and the time until the first need of analgesics were recorded. An Apgar score >7 at 1 and 5 min suggests that the methods do not have any adverse effects on the fetus.

The sample size for the study was calculated with the aim of showing a difference between treatments in duration of motor block, with a mean difference of at least 1 h. The standard deviation of Bromage 1 motor block was assumed to be approximately 1.1 h with 20 patients in each group and using a significance level of 0.05.

SPSS for Windows v. 11.0 was used for statistical evaluation of the data obtained. To evaluate the data, in addition to descriptive statistical methods (frequency, mean, and standard deviation), following the analysis of the distribution of parameters using the Kolmogorov Smirnov test, the *t* test was used for data distributed normally in independent groups and the Mann–Whitney U test was used for groups in which data were not distributed normally. The significance of differences in time was investigated using the *t* test in dependent groups. Correlation coefficients were used to investigate relationships. Results were evaluated at 95% confidence interval and *P* values <0.05 were considered significant.

Results

There were no statistically significant differences in demographic data between the two groups ($P > 0.05$) [Table 1]. The time for analgesia to reach the T4 dermatome and the overall duration of analgesia were not statistically significant ($P > 0.05$) [Table 1].

Table 2 shows the Apgar scores at 1 and 5 min in each group. A significant difference was not observed between the groups with regard to 1- and 5-min Apgar scores ($P > 0.05$).

Table 3 shows that the fetus delivery time and duration of the procedure in both groups were not significantly different ($P > 0.05$).

Fetal blood gas values in both groups are shown in Table 4. There were no statistically significant differences between the groups ($P > 0.05$).

The degree of motor block difference was not statistically significant ($P > 0.05$) [Table 5].

According to the objective pain scale scores, 5 (25%) cases in the RF group and 7 (35%) cases in the BF group did not have pain. In addition, 15 (75%) cases in the RF group and 13 (65%) cases in the BF group complained of slight pain (1 degree–2 degree) that support with sedoanalgesia [Table 6]. Table 7 shows the patient satisfaction with the method in both groups; the difference was not statistically significant ($P > 0.05$).

Regarding hemodynamic parameters, within 10 min of spinal block in the RF group, 3 (10%) cases had bradycardia that responded to atropine and 8 had (16.6%) hypotension that was corrected with fluid replacement. In the BF group, 2 (6.6%) cases had bradycardia (they also had concurrent hypotension) and responded to atropine + fluid replacement, and in 9 cases (16.6%) only hypotension was observed. A significant difference between the groups in terms of atropine and ephedrine doses was not observed ($P > 0.05$), nor was there a difference in SpO2 values ($P > 0.05$).

Respiratory depression and tinnitus did not occur in either group. Nausea was observed in 12 patients in the RF group and in 13 patients in the BF group. In the RF group, 3 patients had bradycardia coexisting with nausea and responded to atropine. In the BF group, nausea was accompanied by bradycardia and hypotension in six patients that responded to atropine + fluid replacement. A significant difference between the groups in terms of maternal side effects was not observed ($P > 0.05$) [Table 8].

Discussion

There were no statistically significant differences in demographic data, the time for analgesia to reach the T4 dermatome, the overall duration of analgesia, 1- and 5-min Apgar scores, fetus delivery time, duration of the procedure, fetal blood gas values, and the degree of motor block between the two groups.

Ideal intrathecal anesthesia for cesarean section is characterized by localized effect, minimal impact on motor function, effect at low doses, minimal maternal and fetal side effects, and reversibility.[8] From prospective trials, it is clear that lowering the spinal dose improves maternal hemodynamic stability. Doses of intrathecal bupivacaine between 5 and 7 mg are

Table 1: Demographic data and the duration of analgesia

Parameters	RF group ($n = 20$)	BF group ($n = 20$)	*P*
Age (years)	30.5 ± 5.2	28.8 ± 5.2	0.61
Weight (kg)	66.76 ± 10.7	63.0 ± 8.6	>0.05
Length (cm)	159.8 ± 4.4	160.3 ± 4.6	>0.05
Pregnancy week	38.9 ± 1	38.4 ± 0.6	0.07
Birth weight (g)	3411.9 ± 361.5	3358.4 ± 482.7	0.65
Time to reach T4 dermatome (min)	4.8 ± 1.1	5.00 ± 1.0	>0.05
Overall duration of analgesia (min)	138.5 ± 12.7	140.4 ± 29.2	>0.05

Values are given as mean ± SD $P < 0.05$ is significant

Table 2: Apgar scores at 1 and 5 min

	RF group ($n = 20$)	BF group ($n = 20$)	*P*
1-min score	8.4 ± 0.5	8.1 ± 0.8	0.45
5-min score	9.7 ± 0.43	9.8 ± 0.3	0.49

Values are given as mean ± SD

Table 3: Duration of operation and delivery time

	RF group ($n = 20$)	BF group ($n = 20$)	*P*
Fetus delivery time (min)	7.7 ± 1.7	7.7 ± 2	0.52
Duration of procedure (min)	43.5 ± 4.8	43.9 ± 5.3	0.51

Values are given as mean ± SD

Table 4: Fetal blood gas values

	RF group ($n = 20$)	BF group ($n = 20$)	*P*
pH	7.4 ± 0.03	7.3 ± 0.02	0.07
PCO_2 (mmHg)	39.2 ± 4.9	41.5 ± 1.1	0.27
PO_2 (mmHg)	27.4 ± 6.1	25.8 ± 5.2	0.32
HCO_3^- (mEq/l)	24.5 ± 2.3	25.5 ± 2.8	0.14
BE_B (mEq/l)	0.88 ± 1.6	0.4 ± 2.21	0.38

Values are given as mean ± SD

Table 5: Degree of motor block

Degree of motor block	RF group ($n = 20$) Number of patients (percentage)	BF group ($n = 20$) Number of patients (percentage)	*P*
1	4 (20.0)	2 (10.0)	>0.05
2	15 (85.0)	15 (75.0)	>0.05
3	1 (5.0)	3 (15.0)	>0.05

Table 6: Objective pain scale scores

Objective pain scale	RF group ($n = 30$) Number of patients (percentage)	BF group ($n = 30$) Number of patients (percentage)	*P*
0 (perfect)	5 (25)	7 (35)	>0.05
1 (moderate)	14 (70)	13 (65)	>0.05
2 (inadequate)	1 (5)	-	>0.05
3 (poor)	-	-	-

Table 7: Patient satisfaction with the method

Patients' satisfaction with the method	RF group ($n = 20$) Number of patients (rate)	BF group ($n = 20$) Number of patients (rate)	*P*
1 (very good)	13 (65)	12 (60)	>0.05
2 (good)	5 (25)	6(30)	>0.05
3 (bad)	1 (5)	1 (5)	>0.05
4 (will never use it again)	1 (5)	1 (5)	>0.05

Table 8: Maternal side effects

Side effects	RF group ($n = 20$) Number of patients (percentage)	BF group ($n = 20$) Number of patients (percentage)	*P*
Bradycardia	3 (10)	2 (6.6)	>0.05
Hypotension	8 (16.6)	9 (13.3)	>0.05
Respiratory depression	None	None	-
Itching, urticaria	13	10	>0.05
Head, arm, and chest pain	2 (6.6)	3 (10)	>0.05
Tinnitus	None	None	-
Nausea and vomiting	12 (40)	13 (43)	>0.05

sufficient to provide effective anesthesia. Complete motor block is, however, seldom achieved and adequate anesthesia is limited in time.[8] Gaffud *et al.*[9] reported that for birth analgesia, the combination of bupivacaine + fentanyl yielded better analgesia than bupivacaine alone.[9] It was reported that the combined use of both drugs provides more rapid and prolonged anesthesia.[9] Fifteen milligrams of hyperbaric ropivacaine would seem a reasonable intrathecal dose for cesarean section. Intrathecal fentanyl (10–25 μg) may provide the best combination of minimal side effects, effective reduction in LA dose, and duration of action.

Different findings have been reported from minimum effective LA dose (MLAD) studies.[10] Several studies have been designed in order to find the optimum dosage of intrathecal LAs for obstetric patients. The MLAD model has been used in the investigation of analgesic requirements in labor. There are a few studies about the use of MLAD model in cesarean section.[11] In a study, it was concluded that the addition of sufentanil reduced the MLAD of both the LAs.[12] In this study, we observed that with the addition of fentanyl, doses of both LAs could be decreased. Further studies concerning this issue can be done.

Bogra *et al.*[13] administered bupivacaine at different doses for spinal anesthesia and reported that the rate of the decrease in systolic arterial blood pressure (SAP) correlated with the dose increase and became more marked with the addition of fentanyl to bupivacaine. Considering that administration of LA also influences the development of hypotension. Knudsen[14] reported that ropivacaine does not have a marked effect on the cardiovascular system, which may be related to its partial vasoconstrictor effect. Likewise, in the present study, keeping the dose of local analgesics as low as possible and administering them at a low rate minimized the hemodynamic side effects. We feel that the hypotension and bradycardia observed in the present study may have been due to the adverse effect of LAs on the afferent conduction system of the heart at the T4 dermatome level, and that sympathetic block and bradycardia may have been associated with the effect of the LA causing sympathetic block. The data of hemodynamic properties obtained in the present study are consistent with those previously reported.

In studies on cesarean section where epidural ropivacaine has been compared to bupivacaine, most have used 0.5% solutions in similar doses and found them equally effective.[15,16] Veneziani and colleagues[17] have compared ropivacaine 0.75% with bupivacaine 0.5%. They found ropivacaine 0.75% with fentanyl clinically superior to bupivacaine 0.5% with fentanyl using similar volumes (and consequently a 50% increase in dose).[17] Bjornestadt and colleagues[18] found plain ropivacaine 0.75% equally effective as bupivacaine 0.5%, but with a 50% increase in the dose of ropivacaine. Both 0.5% and 0.75% ropivacaine appear to be effective solutions for providing epidural anesthesia for cesarean section. Christelis *et al.*[5] found that epidural 0.75 % ropivacaine may be used as an alternative to 0.5% bupivacaine + fentanyl for elective cesarean delivery. In this study, the effectiveness of LA used spinally at that concentration was evaluated. Similar results were observed in studies conducted with epidural route.

In this study, the concentration of the LA was different, but the volume given to the patient was the same. Spread of intrathecal LAs is determined principally by baricity and position of the patient.[19] McLeod *et al.* determined the density of bupivacaine, levobupivacaine, and ropivacaine with and without dextrose at both 23°C and 37°C. They concluded that opioids such as fentanyl are hypobaric (0.9933 mg/ml) and when added to an LA will render the subsequent mixture even more hypobaric. The degree to which this occurs is proportional to the respective densities and volumes of individual drugs.[19] Although changes in density may seem minimal and clinically unnecessary, a change in density as low as 0.0006 mg/ml may influence the spread of LA.[10,19] The baricity of the drugs was not evaluated in this study. But we chose hyperbaric LA solutions. We conclude that baricity studies with this concentration and doses can be performed.

Due to low-level sensorial block in cases that were administered excessive ephedrine, some cases were

administered additional LA from the epidural space; therefore, the increase in ephedrine use was attributed to additional administration of LA.[20,21] In the present study, ephedrine use was similar in both groups.

As in the present study, Ogun *et al.*[4] administered bupivacaine and ropivacaine at equal doses (morphine added) and observed that both agents had similar potency, in terms of sensorial block and postoperative analgesia.

A study concluded that sufficient anesthesia for cesarean delivery as a dose that provided adequate sensory dermatomal anesthesia to pinprick to T7 dermatome.[10] For cesarean delivery, it has been purposed that to achieve optimum conditions for surgery, one should aim to achieve an upper level of sensory anesthesia of T4.[22] But in a previous study, T7 was found to be the optimum anesthesia level which could provide good condition for cesarean section and higher block height probably resulted in the increased incidence of hypotension.[23,24] However, in many studies, though recording sensory block to T6, patients still have a significant incidence of visceral pain when using lower doses, especially when opioids are not added.

In this study, when sensory block reached the T4 dermatome, the surgical procedure was initiated. Pain usually occurred when the fetus was removed and patients mostly described chest pain, which was thought to be due to the stimulation of T4 sympathetic fibers related to stretching the peritoneum. None of the cases experienced 3 degree pain and, as such, did not receive general anesthesia. It shows that the sensory level is lower than T4 for the women to report pain due to peritoneal irritation. The uterus exteriorized during repair in this study. It may have caused pain.

In elective cesarean delivery, a lower degree of motor block with intrathecal anesthesia is desirable. Ogun *et al.* reported that motor block was longer in the bupivacaine group. Similarly, in the present study, motor block duration was longer in the BF group than in the RF group, but the difference was not statistically significant. Differences in the reported results may stem from differences in drug dosage and rate of administration, or differences in the additional opioids used.

Nausea in patients was attributed to stimulation of the chemoreceptor trigger zone caused by opioids, as well as to hypotension.[25] Itching and urticaria were reported to be due to the histamine-releasing effect of opioid drugs.[25] We think that side effects such as nausea, itching, and urticaria that occurred in the present study developed by the same mechanism.

Transfer of drugs to the placenta in general and regional anesthesia influences the fetus directly. Maternal hypotension and vasoconstrictive drugs may lead to fetal hypoxia and acidosis.[26] Intrathecal administration of opioids (i.e. spinal analgesia) has evolved from an experimental model into an important therapy for obstetric analgesia and anesthesia. A small dose of opioid delivered into the CSF provides almost immediate relief from labor pain with minimal risks to the mother and fetus.[27] Apgar scores and blood gas findings were within the normal range in the present study, which is consistent with the data reported in the literature. It is known that intrathecal anesthetic administration can give rise to headache, urinary retention, tinnitus, cauda equina syndrome, and transient neurological syndrome (TNS), depending on the diameter of the caudal needle used.[28] In this study, these side effects were not found.

In conclusion, in view of the fact that intrathecally administered bupivacaine + fentanyl or ropivacaine + fentanyl combinations prolonged the duration of postoperative analgesia and were comfortable for the patients during the perioperative and postoperative periods, and that there was a high level of patient satisfaction, we feel that both combinations of drugs have similar effects in elective cesarean delivery.

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