KASTAMONU MEDICAL JOURNAL

Original Article

DOI: 10.51271/KMJ-0151

Kastamonu Med J. 2024;4(3):96-101.

Comparison of the efficacy of two different doses of low-dose bupivacaine for spinal anesthesia in patients undergoing cesarean operations on anesthesia quality and intraoperative hemodynamic parameters

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Received: 29/05/2024 ◆ **Accepted**: 01/07/2024 ◆ **Published**: 01/09/2024

ABSTRACT

Aims: The primary aim of this study was to investigate the effects of two different low-dose bupivacaine used in cesarean operations on intraoperative hemodynamic parameters, and the secondary aim was to evaluate the time of anesthesia onset, motor block scores, and the need for vasopressor agent.

Methods: This prospective randomized double-blind study was performed on 72 pregnant women who underwent cesarean surgery. We randomized the patients into two groups, Group A and Group B, and performed a combined spino-epidural anesthesia. Group A received a solution containing 5 mg isobaric bupivacaine+15µg fentanyl+0.5 isotonic (total volume 1.8 ml) and Group B received a solution containing 7.5 mg bupivacaine+15µg fentanyl (total volume 1.8 ml) over a period of 30 seconds. Vital signs were recorded before the spinal anesthesia and perioperatively. Demographic data, hemodynamic parameters, vital signs and side effects, operation duration, time interval from spinal injection to placement in the supine position, Apgar scores, time interval from spinal injection to delivery, analgesia duration, the degree of motor block immediately before the surgery and at the end of the operation, maximum block level, time for sensory block to reach T6 dermatome level after spinal injection and postoperative side effects were recorded. We recorded the postoperative time to resolution of motor block and the time to regression of sensory block to T10.

Results: There was no statistically significant difference between the two groups in terms of demographic data, anesthesia duration, surgery duration, time interval from spinal injection to placement in the supine position, time interval from spinal injection to delivery, analgesia duration, time for sensory block to reach T10, T6, and T4 dermatomes, 1- and 5-minute (min) Apgar scores, and preoperative Bromage scores. While the mean time to resolution of motor block was 159.69±65.72 min in Group B, the mean time to resolution of motor block was 123.13±64.93 min in Group A and the difference was statistically significant (p=0.02). Hypotension was observed in 19 patients (52.77%) in group A and 29 patients (80.55%) in group B (p=0.012). A statistically significant difference was detected between the two groups in terms of the need for vasopressor agent and the amount of ephedrine used (p=0.012, p=0.021, respectively). Postoperative Bromage score was 1.25±0.93 in group A while it was 2.47±1.27 in group B (p=0.000).

Conclusion: In patients undergoing CS, we found that intrathecal administration of 5 mg isobaric bupivacaine combined with 15 mcg fentanyl and 0.5 ml isotonic not only provided adequate anesthesia but also better-preserved hemodynamic stability and significantly shortened the time to resolution of motor block. We believe that this dose can be used safely in patients undergoing CS. Further studies using varying intrathecal bupivacaine doses are necessary to validate our findings.

Keywords: Cesarean, spinal anesthesia, low-dose bupivacaine, hemodynamics

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Cite this article as: Doymuş Ö, Dostbil A, Aksoy M, İnce İ, Cimilli Şenocak G. Comparison of the efficacy of two different doses of low-dose bupivacaine for spinal anesthesia in patients undergoing cesarean operations on anesthesia quality and intraoperative hemodynamic parameters. *Kastamonu Med J.* 2024;4(3):96-101.

INTRODUCTION

Spinal anesthesia (SA) is currently the most commonly used regional anesthesia technique for cesarean section (CS) procedures, as it provides a rapid and intense sensory block.[1] Spinal anesthesia-induced hypotension is the most commonly observed complication. Intraoperative hypotension causes nausea, dizziness, and impaired utero-placental blood flow in the mother and may lead to neonatal acidosis and fetal death.[2-4] In the recent years, the use of combined spino-epidural anesthesia has become increasingly common in CS procedures.

In the application of combined spinal-epidural anesthesia (CSEA), different techniques in terms of both the dosage and administration of medications are used by clinicians. Techniques such as administration of low-dose local anesthetics, combined use of local anesthetics and opioids, and epidural volume extension have been used. One of these techniques is the use of low-concentration medication in spinal anesthesia, and if this medication is inadequate, elevation of anesthesia level by subsequently administering epidural fluids. It is unclear whether epidural fluid administered together with low-dose spinal anesthesia affects the onset of anesthesia. This method may not be suitable for emergency cesarean delivery, which requires more rapid action. While the use of low-dose local anesthetic in CSEA might decrease the severity of hypotension, it might lead to intraoperative pain and shorter anesthesia duration.[5-7] Providing effective analgesia after CS enables the mother to be active and free depending on the needs of the newborn infant and allows the mother to be psychologically better.[6]

Bupivacaine is the most commonly used agent in cesarean operation, and while hyperbaric and hypobaric bupivacaine provides effective anesthesia and adequate analgesia duration, its high doses are associated with hypotension.[3,8] Use of low-dose bupivacaine decreases hypotension and nausea but leads to shorter motor block and analgesia duration.[9,10] Use of intratechal opioid in combination with low-dose bupivacaine (5-9 mg) can provide adequate anesthesia and leads to less hemodynamic changes.[5,10,11]

In this study, the aim was to evaluate the effect of two different low-dose bupivacaine in combined spino-epidural anesthesia in cesarean operations on intraoperative hemodynamics. The primary aim was to assess the need for ephedrine, and the secondary aim was to evaluate the time of anesthesia onset, motor block scores and the need for a vasopressor agent.

METHODS

For this prospective randomized double-blind study, Atatürk University, Faculty of Medicine Research Hospital Clinical Researches Ethics Committee approval (Date: 28.09.2017, Decision No: 8) and verbal informed consent of the patients were obtained. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study was performed on 72 pregnant women between 16-50 years of age, who were ASA II, between 150-180 cm height, had a BMI<40 kg/m², and were planned to undergo elective cesarean operation. Those with a history of emergency obstetric surgery, pregnancy-induced hypertension, severe systemic disease, multiple gestations, fetal or placental abnormalities, hypersensitivity or allergy, contraindications to neuroaxial anesthesia, impaired coagulation, infection at the injection site, and refused to participate into the study were excluded from the study. Patients were transferred to operation room and routine monitoring comprising electrocardiogram (ECG), peripheric oxygen saturation (SpO_2) and non-invasive blood pressure was performed. Using 18 G branula, intravenous (IV) vascular access was established. During the surgery, Isolyte S was administered at an infusion rate of 10 ml/kg/h, but no preload and co-load fluids were administered. Using sealed envelope system, randomization was performed and the patients were randomly divided into two groups, group A and group B. The using needle-through-needle technique, combined spino-epidural anesthesia was administered to pregnant women while in seated position. The skin was sterilized and local infiltration was performed using 2% lidocaine. Using loss-of-resistance technique, 18 Gauge Tuohy needle (BBraunPerican® 88x1.3 mm, Melsungen/Germany) was inserted using midline approach between L3-L4 or L4-L5, and epidural space was identified. Then, dura was punctured by inserting a 27 Gauge pencil point needle (BBraunPencan® 138.5x0.42 mm, Melsungen/Germany) through the Tuohy needle. After observing the flow of cerebrospinal fluid, a solution containing 5 mg isobaric bupivacaine+15 µg fentanyl+0.5 ml isotonic was administered to Group A and a solution containing 7.5 mg bupivacaine+15 µg fentanyl was administered to Group B through the spinal needle over a period of 30 seconds. Spinal needle was removed. Through the Tuohy needle, epidural catheter (20 G BBraunPerifix® 1000X0.45 mm, Melsungen/Germany) was inserted 3 cm into the epidural space. Patients were immediately made to lie supine with a wedge beneath the right hip, to tilt the pelvis 15° to the left. Using a chronometer, procedure durations were recorded. Other researchers collecting intraoperative and postoperative data were blind to the group of the patient they evaluated. During the operation, the room temperature was maintained at 24°C. In order to conserve the patients' body temperature, warming blankets were used, and all fluids administered during the surgery were at room temperature. Oxygen was administered via a face mask at a flow rate of 4 l/min to the patients in the supine position.

Patients' blood pressure and heart rate were recorded before the administration of spinal anesthesia, and these values were considered basal values. The same parameters were recorded every 2 minutes (min) within the first 20 min after spinal anesthesia, and then, every 15 min until the surgery was over. Hypotension was described as systolic blood pressure dropping below 20% of the basal value, and when hypotension occurred, 5 mg ephedrine was administered initially. When perfusion could not be restored, 3 mg ephedrine was administered every 2 minutes until normal blood pressure was restored. Bradycardia was described as a heart rate below 50 beats/min and when it occurred, it was treated with 1 mg iv atropine.

Sensory block level was assessed using cold discrimination by examining the respective dermatomes when the patient was placed in supine position after applying the coolpack bilaterally at 1-minute intervals until the sensory block level reached T6, and then at 2-minute intervals until the maximum block level was attained. If the sensory block level did not reach T6 or if the patient felt pain during the skin incision, spinal anesthesia was considered unsuccessful. In that case, 5 ml of a solution containing 15 ml 2% lidocaine+2 ml bicarbonate+2 ml fentanyl+1 ml 1/200000 adrenaline (Lidocaine-Aritmal® 2% ml ampulla, 100 mg, Osel İlaç Sanayi, İstanbul, Turkiye/Fentanyl-Talinat® 10 ml ampulla, 0.5 mg, Vem İlaç, İstanbul, Turkiye/

Bicarbonate-Sodium Bicarbonate 8.4% molar 10 ml, Galen İlaç, İstanbul/ Adrenaline- Adrenaline ¼ mg 1 ml, Galen İlaç, İstanbul) was administered via epidural catheter. If adequate block could not be attained despite the administration of this solution, general anesthesia was used, and the patient was excluded from the study.

The efficacy of anesthesia was evaluated based on criteria including the motor block of the patient's lower extremity, muscle relaxation, and whether the patient felt pain during the skin incision and abdominal exploration. Motor block was identified based on the following criteria: 0=able to lift extended leg; 1=able to freely flex the knee; 2=unable to flex the knee but can move the ankle; 3=unable to move the ankle but toes are still active; 4=no movement at the lower extremity.

Muscle relaxation was evaluated using a subjective scale based on the surgeon's comments: good (satisfactory), poor (insufficient but operation is possible), very poor (more anesthetic interventions are required to continue the operation).

Pain during skin incision and abdominal exploration was graded as none, moderate (tolerable pain) and severe (intolerable pain). When the patient felt abdominal pain or discomfort during the surgery, administration of 50 µg fentanyl was planned.

Parameters such as demographic data, intraoperative hemodynamics, intraoperative and postoperative complications, need for vasopressor agents, operation, anesthesia, and analgesia (time from spinal injection to onset of pain and time until the need for analgesics) were recorded. Additionally, spinal time from injection to placement in the supine position, pain, abdominal discomfort, 1- and 5-minute appearance, pulse, grimace, activity and respiration (APGAR) scores, time from spinal injection to birth, degree of motor block just before and after surgery, time to resolution of motor block (time to move both legs), maximum block level, time for sensory block to reach T6 dermatome level after spinal injection, and the need for epidural drug application were recorded. Postoperatively, the patient was transferred to PACU, and sensory and motor block levels were assessed at every 15 minutes. The time to resolution of motor block and the time to regression of sensory block to T10, time to lift extended leg, and the time to the onset of pain were recorded.

Statistics Analysis

The primary aim of this study was to reduce the need for ephedrine. In the preliminary study performed for this purpose, it was found that the difference between the arithmetic means of the amounts of ephedrine used in group A and B was 3.30 mg, and the standard deviation was 4.30 in group A and 4.79 in group B. Assuming an α=0.05, β=0.20, with a power of 80%, the number of patients per group was calculated as 32. In our study, we included 36 patients in each of the two groups.

For statistical analyses, SPSS 22 software package (IBM, Armonk, New York, USA) package was used. Numerical data were presented as mean and standard deviation, categorical data were presented as numbers and percentages. If conditions for parametric analysis were met when analyzing numerical data and intergroup differences, Independent Samples T test was used, if not, the Mann-Whitney U test was used, and when analyzing categorical data, the chi-square test was used. A p value <0.05 was considered statistically significant.

RESULTS

A total of 72 patients were included in the study. There was no difference between the groups in terms of demographic data, operation duration, and anesthesia duration (p>0.05). Analgesia duration was 166.09±64.93 min in group A whereas it was 166.09±64.93 min in group B, and there was no statistically significant difference between the groups in terms of analgesia duration (p>0.65). Time to motor block resolution was 123.13±64.93 min in group A while it was 159.69±65.72 min in group B. Time to motor block resolution for pregnant women in group A was statistically significantly shorter than Group B (p=0.02, Table 1).

Table 1. Demographic characteristics, anesthesia duration, operation duration analgesia duration and time to resolution of motor block

	Group A (n=36)	Group B (n=36)	p
Age (years)	31.38±5.07	31.36±4.98	0.981
Height (cm)	161.44±6.13	163.05±5.65	0.250
Weight[27]	77.52±10.86	77.02±9.03	0.832
BMI (kg/m²)	29.70±3.86	29.02±3.35	0.428
Anesthesia duration (min)	52.30±11.28	52.08±10.30	0.931
Operation duration (min)	39.44±11.46	38.27±9.20	0.635
Time to resolution of motor block (min)	123.13±64.93	159.69±65.72	0.02[b]

[a]All values were presented as mean±SD. [b]p<0.05, [a]All values were presented as mean±SD, SD: Standard deviation, BMI: Body mass index, min: Minimum

Changes in systolic blood pressure, diastolic blood pressure and heart rate between groups over time are shown in the figure (Figure 1, Figure 2, Figure 3).

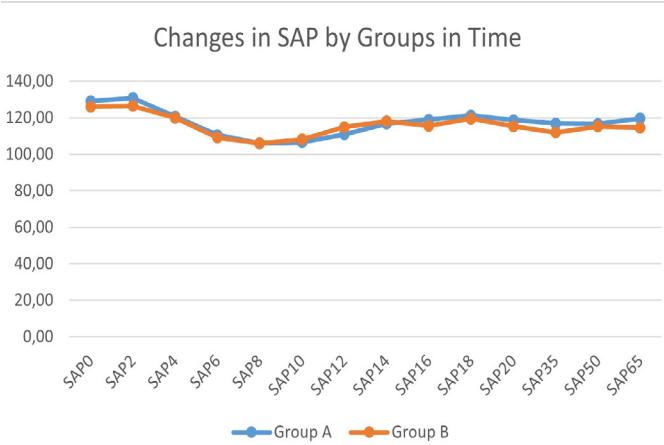

Figure 1. Changes in SAP by groups in time

SAP: Contractility

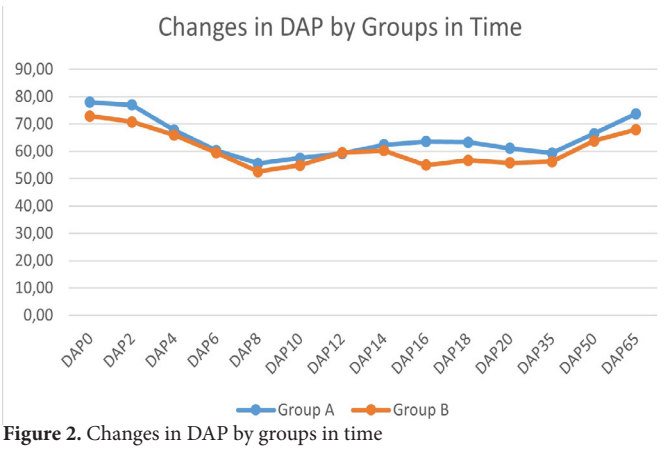

Figure 2. Changes in DAP by groups in time

DAP: Arterial tone

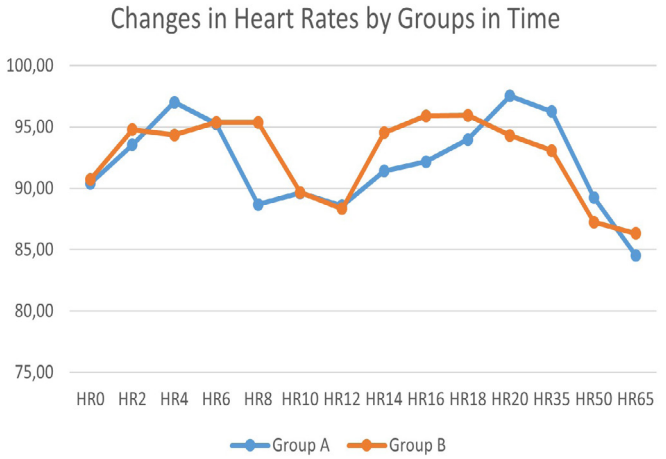

Figure 3. Changes in heart rate by groups in time

There was no difference between the groups in terms of preoperative Bromage scores (p=0.310). Postoperative Bromage score was 1.25±0.93 in group A, whereas it was 2.47±1.27 in group B. Postoperative Bromage scores of pregnant women in Group A were statistically significantly lower than Group B (p<0.05, Table 2).

Table 2. Preoperative and postoperative bromage scores

	Group A (n=36)	Group B (n=36)	p
Preoperative Bromage score	1.55±0.84	1.75±0.76	.310
Postoperative Bromage score	1.25± 0.93	2.47±1.27	.000[b]

[a]All values were presented as mean±SD, [b]p<0.05, SD: Standard deviation

Hypotension was observed in 19 cases (52.77%) in group A and 29 cases (80.55%) in group B. The incidence of hypotension in pregnant women in group A was statistically significantly lower than group B (p=0.012). While side effects or complications such as nausea, itching and SpO_2<95% were not observed in any of the groups, no statistically significant difference was detected between the groups in terms of the incidence of bradycardia and incidence of nausea (p>0.05, Table 3).

Table 3. Intraoperative hemodynamics and complications[a]

	Group A (n=36)	Group B (n=36)	p
Hypotension % (N/n)	52.77 (19/36)	80.55 (29/36)	.012[b]
Bradycardia % (N/n)	2.77 (1/36)	5.55 (2/36)	.555
Nausea % (N/n)	16.66 (6/36)	13.88 (5/36)	.743
Vomiting % (N/n)	0/36	0/36	-
Itching % (N/n)	0/36	0/36	-
SpO_2 <95% (N/n)	0/36	0/36	-

[a]All data were presented as mean±SD and %, N: Number of patients with complication [b]p<0.05, SD: Standard deviation

The need for vasopressor agent and the amount of ephedrine used were lower in group A (52.77%) than group B (80.55%) (p=0.012, p=0.032, respectively Table 4).

Table 4. Amount and need for vasopressor agent

	Group A (n=36)	Group B (n=36)	p
Need for vasopressor agent % (N/n)	52.77 (19/36)	80.55 (29/36)	.012[a]
Amount of vasopressor agent median (min-max) (mg)[b]	5 (0-11)	8 (0-18)	.032[a]

[a]p<0.05 [b] Median (min-max), N: Number of cases in need of vasopressor agent, min: Minimum, max: Maximum

There was no statistically significant difference between the groups in terms of the time for sensory block to reach T10, T6 and T4 dermatome (p=0.671, p=0.468, p=0.579, respectively). The time for sensory block to reach T10 dermatome was 5.16±2.28 min in Group A, whereas it was 4.94±2.12 min in group B. The time for sensory block to reach T6 dermatome was 7.72±3.82 min in group A, whereas it was 7.16±2.50 min in group B; and the time for sensory block to reach T4 dermatome was 9.72±4.39 min in group A while it was 9.22±3.09 min in group B. When neonatal outcomes were evaluated, no statistically significant difference could be detected between the two groups in terms of 1-minute and 5-minute APGAR scores (p=0.494, p=0.673, respectively, Table 5).

Table 5. The mean times for sensory block to reach T10, T6 and T4 dermatomes and neonatal outcomes[a]

	Group A (n=36)	Group B (n=36)	p
Time to reach T10 (min)	5.16±2.28	4.94±2.12	.671
Time to reach T6 (min)	7.72±3.82	7.16±2.50	.468
Time to reach T4 (min)	9.72±4.39	9.22±3.09	.579
1-min APGAR	8.38±0.76	8.25±0.93	.494
5-min APGAR[b]	10 (8-10)	10 (9-10)	.673

[a]All data were presented as mean±SD, [b]Median (min-max), SD: Standard deviation, min: Minimum, APGAR: Appearance, pulse, grimace, activity and respiration

DISCUSSION

In this study, we found that hypotension incidence was lower, the amount of vasopressor agent needed was lower, and the time to resolution of motor block was shorter in the group administered low dose local anesthetic.

Hypotension is a common outcome of the sympathetic nerve block caused by spinal anesthesia used in cesarean delivery. Spinal anesthesia-induced hypotension is a common problem in cesarean delivery if preventive measures are lacking. In order to reduce the incidence and severity of hypotension, approaches such as left lateral tilt position, crystalloid and colloid infusion, prophylactic administration of vasopressor agents have been used. None of these strategies have been able to fully treat spinal anesthesia-induced hypotension. Therefore, reducing the dose of local anesthetics used in spinal anesthesia was recommended to decrease the severity and incidence of hypotension.[1,12,13]

In the study by Chandra et al.,[14] adequacy of anesthesia, time to resolution of motor block and spinal anesthesia-induced side effects were recorded. No difference in terms of hypotension incidence was detected between patients who were given 5 mg bupivacaine and 7.5 mg bupivacaine. In the study by Ben David et al.,[11] hypotension was observed in more patients in the high-dose bupivacaine group and higher amount of ephedrine use was detected. In our study, hypotension occurred in more patients in group B than group A. Higher amount of ephedrine was used in group B than group A. We suggest that hypotension incidence and the amount of vasopressor agent used can be reduced by using bupivacaine at a lower dose.

Dyspnea during cesarean delivery is a tentative marker of spinal anesthesia-induced high sensory block. Dyspnea might occur as a result of the atrophy of thoracic proprioception or partial block of abdominal and intercostal muscles.[15] In the study by Kimoto et al.,[16] dyspnea incidence was higher in the group receiving 12.5 mg bupivacaine than the groups receiving 5, 7.5 and 10 mg bupivacaine. In our study, dyspnea was not observed in any of the patients.

In cesarean operations, nausea and vomiting are very frequently observed events that cause patient discomfort. Hypotension is the most common problem associated with nausea and vomiting during a cesarean operation. Moreover, vagal hyperactivity, visceral pain, and the use of iv opioids and uterotonic agenst may lead to nausea and vomiting. The incidence of intraoperative nausea and vomiting might be reduced by preventing hypotension, minimizing the amount of iv and neuroaxial opioids, and improving the quality of the block.[17,18]

In the study by Jung Hyang Lee et al.,[19] sufentanil and fentanyl were added to 0.5% bupivacaine. In terms of the complications observed, the incidence of nausea and itching was higher in the group that received 20 µg fentanyl than the control group and the group that received 2.5 µg sufentanil, and the difference was statistically significant, whereas no difference was reported between the groups in terms of other complications such as vomiting, shivering, and hypotension. In our study, vomiting and itching were not observed in any of the patients. In the study by Mebazaa et al.,[20] the incidence of hypotension and nausea was higher in the group that received 10 mg bupivacaine. In our study, there was no difference between the groups in terms of the incidence of nausea and low-dose local anesthetic and opioid were used. As a result, the incidence of spinal anesthesia-induced complications was lower.

Rapidly ascending sensory block levels lead to a high incidence of hypotension following spinal anesthesia in cesarean deliveries. This increases the risk of maternal distress and fetal anoxia. Hypotension is believed to have the potential to cause abnormalities in fetal acid-base balance by leading to reduced utero-placental perfusion. Various studies have revealed that spinal anesthesia-induced hypotension incidence is higher after a sensory block at a level ≥T5 or at the T4 level during delivery. The fact that nerve fibers affecting the vasomotor tone of the arterial and venous vessels arise from T5-L1 and that cardioaccelerator fibers arise from T1-T4 corroborate these findings.[21,22]

Turhanoğlu et al.[23] could not find any association between the time of sensory block to reach T6 dermatome and bupivacaine amount. They reported that 1- and 5-minute APGAR scores were similar in both groups. Bryson et al.[24] could not find any association between bupivacaine dose and APGAR scores. In our study, both groups were similar in terms of APGAR scores. Our findings were in concordance with the literature.

It is well known that drug dose affects both the sensory and motor block duration and has a significant effect on the severity of hypotension. Low concentrations of local anesthetics used in spinal anesthesia are associated with less sensorial and motor block. This contributes to early mobilization.[25] Leo et al.[26] found that the level of block was lower in patients who received lower doses of bupivacaine. Mebazaa et al.[20] found that the time to regression of sensory block to T10 dermatome and time to resolution of motor block were shorter in the low-dose bupivacaine group. Ben David et al.[11] found that block level was higher and Bromage scores were higher in patients who received high-dose bupivacaine. In our study, time to resolution of motor block was shorter in group A than group B. We assumed that the high amount of local anesthetic used in group B might have contributed to the late resolution of motor block. Postoperative Bromage scores were lower in group A than group B. Lower Bromage scores were obtained in the group that received lower amount of local anesthetic. Despite the low dose of drug, adequate level of anesthesia was attained.

Limitation

Our research has certain limitations. A major limitation of our investigation was the relatively small patient sample size and the absence of a multi-center approach. The assessment of hemodynamic parameters using noninvasive methods posed another constraint. Furthermore, a better assessment could have been made using blood gas parameters in addition to the APGAR score to better see the effect of hemodynamic variables on neonatal variables.

CONCLUSION

In patients undergoing CS, we found that intrathecal administration of 5 mg isobaric bupivacaine combined with 15 mcg fentanyl and 0.5 ml isotonic not only provided adequate anesthesia but also better-preserved hemodynamic stability and significantly shortened the time to resolution of motor block. We believe that this dose can be used safely in patients undergoing CS. Further studies using varying intrathecal bupivacaine doses are necessary to validate our findings.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Atatürk University, Faculty of Medicine Research Hospital Clinical Researches Ethics Committee (Date: 28.09.2017, Decision No: 8).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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