

Effects on hypotension incidence: hyperbaric, isobaric, and combinations of bupivacaine for spinal anesthesia in cesarean section

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Aim: To determine if hypotension frequency changes when hyperbaric or isobaric formulations of bupivacaine, or their sequential administrations, are used for cesarean section. Hypotension after spinal anesthesia for cesarean section is common.

Materials and methods: A total of 144 patients who were to undergo cesarean section with spinal anesthesia were allocated into 4 groups. Spinal anesthesia was achieved with 10 mg of hyperbaric bupivacaine in Group H10, sequential 5-mg administrations of hyperbaric and isobaric bupivacaine in Group H5P5, sequential 5-mg administrations of isobaric and hyperbaric bupivacaine in Group P5H5, and 10 mg of isobaric bupivacaine in Group P10. Hemodynamic parameters were determined and the incidence of hypotension, incidence of bradycardia, and amount of ephedrine required to treat hypotension were recorded. Fetal Apgar scores, the pH of the umbilical cord blood, and side effects were also noted.

Results: American Society of Anesthesiologists risk group, surgical duration, and demographic values were similar among the groups. The incidence of hypotension was found to be 69.4%, 66.7%, 75.0%, and 83.3% in the H10, H5P5, P10, and P5H5 groups, respectively. The incidences of hypotension were not significantly different. Bradycardia incidence, ephedrine consumption, the pH of cord blood, and side effects were not different among the groups.

Conclusion: When the dose of local anesthetic is the same, the incidence of spinal-induced hypotension cannot be lowered using hyperbaric, isobaric, or sequential injections of a half dose of bupivacaine for spinal anesthesia during cesarean section.

Key words: Baricity, bupivacaine, spinal anesthesia, cesarean section

Hipotansiyon insidansı üzerine etkiler: sezaryen için spinal anesteziye hiperbarik, isobarik bupivakain ve kombinasyonları

Amaç: Sezaryen için spinal anesteziye hipotansiyon yaygındır. Bu çalışma sezaryende hipotansiyon sıklığının hiperbarik, isobarik bupivakain veya bunların ardışık uygulanması ile değişip değişmediğini araştırmak üzere planlanmıştır.

Yöntem ve gereç: Spinal anestezi ile sezaryen operasyonu geçirecek 144 hasta randomize olarak dört gruba ayrıldı. Spinal anestezi H10 grubunda 10 mg hiperbarik bupivakainle, Grup H5P5'de ardışık 5 mg hiperbarik ve isobarik bupivakain uygulanmasıyla, Grup P5H5'de ardışık 5 mg isobarik hiperbarik ve isobarik bupivakain uygulanmasıyla

Received: 25.10.2010 – Accepted: 15.12.2010

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ve P10 grubunda 10 mg isobarik bupivakainle gerçekleştirildi. Hemodinamik parametreler, hipotansiyon, bradikardi insidansı ve hipotansiyonu tedavi etmek için gereken efedrin miktarı kaydedildi. Fetal Apgar, umbilikal kord kan pH'sı ve yan etkiler de not edildi.

Bulgular: ASA risk grubu, cerrahi süre ve demografik veriler gruplar arasında benzerdi. Hipotansiyon insidansı H10, H5P5, P10 ve P5H5 gruplarında sırasıyla % 69,4, % 66,7, % 75,0 ve % 83,3 olarak bulundu. Hipotansiyon insidansı istatistiksel olarak farklı değildi. Gruplar arasındaki bradikardi insidansı, efedrin tüketimi, kord kan pH'sı ve yan etkiler de farklı değildi.

Sonuç: Lokal anestezi dozları aynı olduğunda, sezaryen operasyonu için spinal anestezide, spinale bağlı hipotansiyon insidansı bupivakainin hiperbarik, isobarik veya yarı dozda ardışık uygulanması ile düşürülemez.

Anahtar sözcükler: Barisite, bupivakain, spinal anestezi, sezaryen

Introduction

Spinal anesthesia has become an increasingly popular technique for cesarean section in many countries over the last few decades. However, the rapid onset of sympathetic block and subsequent hypotension remains a major clinical concern when using the technique. In order to decrease the incidence and severity of hypotension, various attempts have been made to modify the technique and the dose of local anesthetic used (1,2). However, spinal-induced hypotension is the most important side effect, with a reported incidence between 20% and 100% (3-5). Recently, Cesur et al. (6) demonstrated a marked decrease in the incidence of hypotension when 5 mg of isobaric bupivacaine was followed by 5 mg of heavy bupivacaine for spinal anesthesia during cesarean section. They reported that the maternal hypotension frequency decreased from 67% to 14% when 5 mg of isobaric and 5 mg of hyperbaric bupivacaine were used sequentially instead of 10 mg of hyperbaric bupivacaine (7,8). In light of the study mentioned above, we hypothesized that sequential injections of isobaric and hyperbaric bupivacaine would decrease the incidence of hypotension. Therefore, this study was designed to compare the hemodynamic effects of hyperbaric solutions, isobaric solutions, and the sequential administration of hyperbaric and isobaric solutions during cesarean section. The primary outcome was the incidence of hypotension.

Materials and methods

After obtaining the approval of the institutional ethics committee and the informed consent of patients, 144 patients in American Society of Anesthesiologists

(ASA) risk groups I or II who would be undergoing elective or urgent cesarean section with a preference for regional anesthesia were randomly allocated into 1 of 4 groups in this randomized, prospective study. Group H10 received 10 mg of hyperbaric bupivacaine in 2 mL of solution (Marcaine Spinal Heavy, Astra-Zeneca, Sweden), Group H5P5 received 5 mg of hyperbaric bupivacaine followed by 5 mg of plain bupivacaine (Marcaine), Group P5H5 received 5 mg of plain bupivacaine followed by 5 mg of hyperbaric bupivacaine, and Group P10 received 10 mg of plain bupivacaine. Parturients with a singleton pregnancy at 37 to 40 weeks of gestational age and no contraindications to spinal anesthesia were enrolled in the study. Patients who needed immediate surgery according to the decision of the obstetrician, displayed blood loss or preeclampsia, were in active labor, or preferred general anesthesia were not included.

Randomization was achieved by using a random samples table. Parturients received an intravenous cannula at the obstetric ward, and an infusion of lactated Ringer solution at a rate of 10 mL kg⁻¹ h⁻¹ was begun. All parturients were intravenously administered 50 mg of ranitidine and 10 mg of metoclopramide prior to arrival at the operation room. In the operation room, the patients' blood pressure was noninvasively monitored with an electrocardiogram and pulse oximetry. A crystalloid infusion was completed to 1000 mL before attempting the spinal procedure. Infusion continued throughout the operation procedure at a rate of 15 to 20 mL kg⁻¹ h⁻¹. Parturients were placed in a sitting position, and spinal anesthesia was performed at the interspace of either L2-3 or L3-4 at the discretion of the anesthesiologist.

A lumbar puncture was made with a 25-gauge pencil point needle (Pencan, Braun, Melsungen, Germany); when a free flow of cerebrospinal fluid was obtained, a previously prepared local anesthetic was injected with the bevel oriented in the cephalad direction within 30 s. In 2 separate syringes for Groups H5P5 and P5H5, 1 mL of each local anesthetic solution was prepared. Each solution of local anesthetic was injected over 15 s, and changing syringes took about 5 s. Parturients were immediately placed in a supine position, and the operating table was set to a 15° left lateral tilt. The table was returned to a horizontal position before the skin incision was made. Oxygen was administered at a rate of 4 L min⁻¹, and maternal blood pressure was measured every 2 min until 20 min after the injection, and every 5 min thereafter. Hypotension was defined as systolic blood pressure <90 mmHg or as a 20% decrease from the baseline value (the average of 2 values before the spinal anesthesia attempt) (6). Bradycardia was defined as a heart rate lower than 50 beats min⁻¹. Hypotension and bradycardia were treated with 5 mg of ephedrine boluses every 2 min and with 0.01 mg kg atropine, respectively. The incidence of hypotension and the amount of ephedrine and atropine used were recorded. Anesthesiologists performing the block procedure recorded all of the hemodynamic data and assessed sensory and motor blocks. Sensory block was evaluated with cold application and pinprick stimulus using a 3-point scale: 0 = cold, 1 = feel but not cold, 2 = no touch; and 0 = sharp, 1 = blunt, 2 = no touch, respectively. The motor block was evaluated with a modified Bromage scale: 0 = no motor block, 1 = cannot move leg, 2 = cannot flex knee but can move foot, 3 = cannot move foot. Cold sensation was evaluated with an alcohol swab, and pinprick sensation was evaluated with the blunt end of a 22-gauge needle. The upper level of the sensorial block, the time to the maximum level, the 2-segment regression time, the maximum motor block level, and the motor block duration, defined as the time until full recovery, were recorded. Surgery was allowed to begin when the loss of cold sensation was scored as 1 at T6 bilaterally. If sensorial block did not reach the T6 level at the end of 20 min, the patient would be excluded from the study. Patients describing discomfort received a 0.5 mg kg⁻¹ intravenous bolus of propofol before cord clamping and 1 µg

kg⁻¹ fentanyl thereafter. The amount of propofol or fentanyl required was recorded, as well. A fetal blood gas sample was taken from the umbilical cord and analyzed, and the pH values were recorded. A pediatrician evaluated the 1 and 5 min Apgar scores, and they were recorded by an anesthesia resident. At the end of the operation, the surgical duration was determined, and abdominal relaxation was assessed by an obstetrician blinded to the group allocation with a 3-point scale (1 = poor, 2 = fair, 3 = good) and recorded. Analgesia duration was defined as the time from the spinal injection to the time of the patient's first request for pain medication (score of pain greater than 3 on a numeric rating scale, where 0 represented no pain and 10 represented the most painful state).

Power analysis

The major outcome of our study was the incidence of hypotension. Sample size estimation was based on the hypotension incidence reported in a similar study performed by Cesur et al. (6). Using the hypotension incidence (66.7%) determined by Cesur et al. in order to detect a 30% change in the hypotension incidence with an alpha error of 0.05 and a power of 80%, the required sample size was calculated to be at least 33 patients per group. Estimating an approximately 10% drop-out rate, we included 36 patients in each group. The sample size estimation was performed using the Power Calculator (UCLA Department of Statistics, <http://www.stat.ubc.ca/~rollin/stats/ssize>).

Statistical analysis

SPSS 11.5 was used for data analysis. An analysis of distribution was performed using the Kolmogorov-Smirnov test. One-way ANOVA was used to compare parametric variables. The chi-square test was used for nonparametric variables. Numerical data are given as the mean ± standard deviation. Categorical variables are shown as percentages. P < 0.05 was considered statistically significant.

Results

All of the patients completed the study. Patient characteristics and surgical times were similar (Table 1). The anesthesia characteristics are shown in Table 2. The groups were similar in terms of peak dermatome reached (with cold and pinprick modalities), the time required to reach peak dermatome, the motor block

Table 1. Demographic data.

	Group H10 (n = 36)	Group H5P5 (n = 36)	Group P10 (n = 36)	Group P5H5 (n = 36)	P
Age (years) (mean \pm SD)	28.47 \pm 5.07	28.38 \pm 5.23	28.08 \pm 4.88	27.69 \pm 5.96	0.924
Weight (kg) (mean \pm SD)	75.30 \pm 11.37	77.50 \pm 11.21	74.83 \pm 12.21	71.58 \pm 7.63	0.140
Height (cm) (mean \pm SD)	161.77 \pm 6.44	160.75 \pm 5.35	159.75 \pm 4.12	160.77 \pm 5.46	0.473
ASA I/II (n)	27/9	30/6	30/6	27/9	0.786
Duration of surgery (min) (mean \pm SD)	44.58 \pm 15.50	45.13 \pm 11.30	41.86 \pm 9.10	40.44 \pm 8.33	0.253

Table 2. Anesthesia characteristics.

	Group H10 (n = 36)	Group H5P5 (n = 36)	Group P10 (n = 36)	Group P5H5 (n = 36)	P
L2-3/L3-4 (n)	21/15	24/12	18/18	17/19	0.337
Peak dermatome mean (range) (cold)	T3 (C8-T6)	T4 (C8-T6)	T3 (C8-T5)	T4 (C8-T6)	0.176
Peak dermatome mean (range) (pinprick)	T4 (T2-T8)	T5 (T1-T8)	T4 (T1-T6)	T5 (T1-T8)	0.063
Time to peak dermatome level (min) (mean \pm SD)	9.47 \pm 3.57	10.05 \pm 3.56	11.22 \pm 3.32	9.36 \pm 4.01	0.118
Motor block degree, median (range)	3 (2-3)	3 (2-3)	3 (2-3)	3 (2-3)	0.520
Abd muscular relax					0.813
Good (n)	33	32	33	31	
Fair (n)	3	4	3	5	
Poor (n)	0	0	0	0	
Time to 2 dermatome regression (min) (mean \pm SD)	41.86 \pm 19.88	46.80 \pm 23.40	48.14 \pm 20.56	48.90 \pm 29.60	0.761
Duration of motor block (min) (mean \pm SD)	134.86 \pm 38.57	145.83 \pm 32.43	151.81 \pm 29.74	146.67 \pm 27.90	0.161
Analgesia duration (min) (mean \pm SD)	131.87 \pm 40.69	134.46 \pm 39.96	130.17 \pm 42.85	144.16 \pm 78.31	0.742

degree and duration, and the 2-segment regression duration. The surgeons' evaluation of abdominal muscular relaxation was not different among the groups.

The mean neonatal Apgar scores and umbilical cord pH values were similar among the groups (Table 3). Of the 144 patients, 4 had postdural puncture headache; all were treated conservatively with bed rest, hydration, and oral analgesics, which included

caffeine. None required epidural blood patches.

Hypotension incidence, ephedrine consumption, and nausea-vomiting frequencies were similar among the groups (Table 4). A total of 3 patients, 1 in Group H10 and 2 in P5H5 ($P > 0.05$), received atropine for bradycardia treatment. The number of patients requiring supplemental fentanyl or propofol according to the study protocol was not statistically different among the groups (Table 5).

Table 3. Apgar scores and umbilical pH values (mean \pm SD).

	Group H10 (n = 36)	Group H5P5 (n = 36)	Group P10 (n = 36)	Group P5H5 (n = 36)	P
Apgar, 1 min	8.83 \pm 1.38	8.70 \pm 1.14	8.47 \pm 1.31	9.01 \pm 0.98	0.311
Apgar, 5 min	9.86 \pm 0.35	9.70 \pm 0.46	9.72 \pm 0.74	9.69 \pm 0.52	0.543
Fetal pH	7.30 \pm 0.07	7.29 \pm 0.05	7.28 \pm 0.06	7.31 \pm 0.07	0.102

Table 4. Side effects and ephedrine requirements.

	Group H10 (n = 36)	Group H5P5 (n = 36)	Group P10 (n = 36)	Group P5H5 (n = 36)	P
Hypotension (n, %)	25 (69.4%)	24 (66.7%)	27 (75.0%)	30 (83.3%)	0.539
Nausea (n, %)	8 (22.2 %)	10 (27.8%)	15 (41.7%)	18 (50%)	0.092
Vomiting (n, %)	0 (0%)	3 (8.3%)	3 (8.3%)	6 (16.7%)	0.144
Bradycardia (n, %)	3 (8.3%)	5 (13.9%)	2 (5.6%)	2 (5.6%)	0.536
Ephedrine requirement (mg) (mean \pm SD)	12.08 \pm 13.11	12.36 \pm 15.09	11.94 \pm 13.16	13.88 \pm 12.98	0.926

Table 5. Number of patients needing fentanyl or propofol in the groups.

	H10	H5P5	P10	P5H5	P
Fentanyl (n, %)	4 (11.1%)	7 (19.4%)	6 (16.7%)	9 (25.0%)	0.486
Propofol (n, %)	6 (16.7%)	4 (11.1%)	4 (11.1%)	8 (22.2%)	0.501
Fentanyl or propofol (n, %)	9 (25.0%)	7 (19.4%)	8 (22.2%)	12 (33.3%)	0.557

Discussion

The results of our study have demonstrated that spinal anesthesia performed with 10 mg of hyperbaric bupivacaine, isobaric bupivacaine, or a sequential administration of a hyperbaric-isobaric bupivacaine combination did not cause a difference in hypotension frequency.

Previous studies with hyperbaric bupivacaine for spinal anesthesia during cesarean section yielded hypotension frequencies ranging from 4.5% (9) to 100% (10). In an early study by Santos et al. (9), 7.5 to 10 mg (depending on the patient's height) of hyperbaric bupivacaine was used for

spinal anesthesia during cesarean section, and they reported a hypotension incidence of only 4.5%, which was easily treated with a small dose of ephedrine. However, in a study investigating whether a low dose (4 mg) of bupivacaine was advantageous over 10 mg of hyperbaric bupivacaine, the hypotension incidence was found to be 100% in patients treated with 10 mg of bupivacaine (10). Leo et al. (2) studied the hypotension frequency when 7, 8, and 9 mg of hyperbaric bupivacaine was administered as the spinal component of a combined spinal epidural technique for cesarean section. They postulated that lowering the dose of spinally administered bupivacaine in the combined spinal epidural technique decreases

the incidence of hypotension. The hypotension incidences were 30%, 55%, and 70% for the study groups that received 7, 8, and 9 mg of the study drugs, respectively, suggesting a linear relationship with the increase in dose. In our study, hypotension incidence in Group H10 was 69.4%, which is consistent with the previous results (66.7%) obtained by Cesur et al. (6) for the same group. We found that the incidence of hypotension for the 10 mg isobaric bupivacaine group was 75%. The same dose of isobaric bupivacaine was reported to produce an incidence of hypotension of 64% in spinal anesthesia for cesarean section by Russell (11). Besides that by Cesur et al. (6), no other study has been found to which we could directly compare our results regarding hypotension incidence when the hyperbaric and isobaric forms of bupivacaine are administered sequentially. Although we observed an almost identical hypotension incidence for hyperbaric bupivacaine as that found by Cesur et al., we have failed to demonstrate reduced hypotension incidence for the sequential injection method. Other spinal block characteristics, such as peak dermatomal level (median), reported by the mentioned study were T4 and T5 for the hyperbaric and sequential injection groups, respectively, which is the same as in our study. Similarities between the hyperbaric and sequential injection groups also exist for the time to peak dermatomal level (8.2 ± 4.2 and 9.4 ± 3.2 min as originally reported versus 9.47 ± 3.57 and 9.36 ± 4.01 min in our study) and for the motor block durations (140 ± 32.2 and 152 ± 48.2 min as originally reported versus 134.8 ± 38.5 and 146.6 ± 27.9 min in our study).

In his editorial, Russell (7) postulated that the chance effect cannot be ignored as an explanation

for the extraordinary results of the first study. Additionally, he stated that because plain bupivacaine is hypobaric in pregnant women (12), plain bupivacaine is expected to float upwards when the patient is in the sitting position. This expectation of plain bupivacaine to move upwards in the cerebrospinal fluid may be the reason for the higher hypotension frequency in Group H5P5.

One of the differences between the techniques of the 2 studies was the higher usage rate of the L2-L3 interspace for spinal anesthetic injection in our study. The choice of the injection site (either L2-L3 or L3-L4) was left to the discretion of the attending anesthesiologist, and, clearly, there is a chance of misinterpreting the interspace. The site of injection is an important factor that influences the distribution of local anesthetic in cerebrospinal fluid (13). We cannot exclude the effect of this difference on the incidence of hypotension. Second, our study was not double-blinded because we planned to focus on hypotension frequency, which depends on noninvasive blood pressure measurements read directly from the monitor equipment; thus, the bias was not introduced by subjectivity. A third difference between the 2 studies was the type of needle chosen; we used a pencil point needle, whereas the Quincke type was used in the original study.

In conclusion, 10 mg of hyperbaric bupivacaine, isobaric bupivacaine, or their sequential injections in half doses for spinal anesthesia in cesarean section were not different in terms of hypotension incidence. The sequential injection technique with the method described in this study does not offer a benefit for parturients planning to undergo spinal anesthesia for cesarean section.

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