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Effects of Varying Doses of Spinal 0.25% Hyperbaric Bupivacaine on Visceral Pain in Cesarean Section

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The present study investigated the safety and efficacy of 0.25% hyperbaric bupivacaine on the incidence of visceral pain during cesarean section performed under subarachnoid anesthesia. Sixty patients who were scheduled for elective cesarean section, allocated randomly to one of three groups, according to patient's height. Group 1, 2 and 3 received 3.2-3.6 mL (8-9 mg), 3.6-4.0 mL (9-10 mg) and 4.0-4.4 mL (10-11 mg) of 0.25% hyperbaric bupivacaine, respectively. There was no difference in the incidence of visceral pain between three groups ($p > 0.05$), but the quality of intraoperative analgesia, as needs for general anesthesia or high dose of supplementary fentanyl, was significantly lower in group 3 than groups 1 and 2 ($p < 0.05$). In conclusion, hyperbaric 0.25% bupivacaine in the dose of 10-11 mg is safe and effective in obtaining better quality of block in cesarean section, in order of reducing the severity of visceral pain.

Key words: Bupivacaine, visceral pain, spinal anesthesia, cesarean

INTRODUCTION

Spinal anesthesia is an appropriate choice for most cesarean sections. Bupivacaine used frequently for this purpose and T₄ sensory block level is recommended. (Miller *et al.*, 2005; Chestnut, 2004) Although this level could be obtained with clinically using doses (0.5% bupivacaine, 7.5-10 mg), but parturients usually experience some discomforts other than sharp surgical pain that require supplementary analgesia, because of visceral pain during surgery (Chung *et al.*, 1996; Pedersen *et al.*, 1989). Visceral pain was defined as silent and dull pain, sensation of pressure that poorly defined, diffused or referred to another area and headache that can or can not be accompanied by nausea and vomiting (Echevarria *et al.*, 1996). Mechanisms and pathophysiology of visceral pain were not completely understood. Leaving parasympathetic nervous system of abdomen unblocked, as in spinal anesthesia, is the most popular explanation for visceral pain.

Recently, several reports, have suggested that, increasing the total dose of bupivacaine could probably reduce the incidence of visceral pain. But this high dose can significantly increase the complications such as severe hypotension (Choi *et al.*, 2000; Alahuhtas *et al.*, 1990; Hirabayashi *et al.*, 1995).

Chung *et al.* (1996) observed that, increasing the volume of injected drug as 0.25% bupivacaine could decrease the incidence or severity of visceral pain. In the present study, we investigate the safety and efficacy of different volumes of 0.25% bupivacaine in 5% glucose on visceral pain in cesarean section done under spinal anesthesia.

MATERIALS AND METHODS

We studied 60 term parturients with ASA (American Society of Anesthesiologists) class I or II, underwent elective cesarean section, with spinal anesthesia. The study was approved by the Hospital Ethics Committee and written informed consent was obtained from all patients. Parturients who had obstetric complications or evidence of fetal compromise were excluded. Patients were allocated randomly to one of three groups according to their heights. Group 1 had 20 mothers were 155-165 cm tall and were given 3.2-3.6 mL (8-9 mg) of 0.25% bupivacaine in 5% glucose. In Group 2 and 3, the corresponding bupivacaine volumes were 3.6-4.0 mL (9-10 mg) and 4.0-4.4 mL (10-11 mg), respectively. Hyperbaric bupivacaine solution 0.25% was made with the same volume of 0.5% bupivacaine hydrochloride and 10% glucose monohydrate. All subarachnoid blocks performed by one anesthesiologist and data were collected by two

registers who were blinded to the solutions. All parturients received an infusion of 1000 mL lactated Ringer's solution over 15-30 min before anesthesia. They were also given ephedrine 40 mg, i.m, approximately 10 min before subarachnoid injection. Subarachnoid injections were performed in right lateral decubitus position with a 23-gauge Quincke spinal needle, using a midline approach at L₃-L₄ or L₄-L₅ interspace. Predetermined volume of bupivacaine was injected over 20-30 sec, without barbotage. After injection, the mothers were immediately turned supine with left lateral displacement and head rested on a pillow. We elevated parturient's legs 10-15 degree. The spread of sensory block to pinprick was measured at 2 min intervals during the first 10 min and every 5 min thereafter. The degree of motor block of low extremities was also assessed at the same intervals, using modified Bromage scale: 0 = no paralysis, 1 = unable to raise the extended leg, 2 = unable to flex knee and 3 = unable to flex ankle. Maternal arterial pressure and heart rate were recorded every minute until delivery and every 5 min thereafter, using automated noninvasive device.

Hypotension (systolic arterial pressure less than 100 mmHg or 20% reduction in systolic arterial pressure from baseline) (Miller *et al.*, 2005) was treated promptly by increasing of uterine displacement, or fluid administration. If hypotension persisted despite these measures, ephedrine 5-10 mg was given 4 times and repeated as needed. Oxygen 6 L min⁻¹ was administered routinely by face mask. Nausea and vomiting not related to hypotension, was treated with dropridol 0.625 mg 4 times.

The incidence and frequency of complications were noted. The efficacy of intraoperative analgesia was assessed by the following four categories, (Chung *et al.*, 1996) excellent = no discomfort during the procedure, good = mild discomfort but not required any systemic analgesia, fair = pain that required additional analgesia and poor = moderate to severe pain that needed more than 100 µg fentanyl or general anesthesia. When patient complained of pain, fentanyl 50 µg was given 4 times and repeated as need. Diazepam 5 mg, (4 times) was administered if the patient requested to sleep after birth of the baby. The condition of neonates was assessed by apgar score at 1st and 5th min after delivery. All mothers received oxytocin 20 unit and cephalosporin 1 g by continuous infusion after delivery. All data were expressed as number or mean (SD or range) and were analyzed using ANOVA followed by Tukey's test for parametric data and chi-square test with Yates' correction. The Kruskal-Wallis followed by the Mann-Whitney U-test for nonparametric data. p<0.05 was considered statistically significant.

RESULTS

There were no statistically significant difference in age, weight, height and gestational age between three groups, but significant difference was in gravidity between group 3 with group 1 and 2 (ANOVA, $p = 0.012$) (Table 1). There was not any significant difference in basic systolic arterial pressure and heart rate, but basic systolic pressure (ANOVA one way, $p = 0.014$) and mean systolic arterial pressure in group 3 were higher significantly than group 2 (independent t-test $p = 0.002$).

During monitoring of BP in the first 30 min of surgery, the decrease in blood pressure in 6th min postanesthesia was significant in all groups ($p = 0.01$) but there was not any difference in hypotension between each group with the other. Maximum changes of systolic arterial pressures (Kruskall-Wallis, $p = 0.57$), heart rates, needs for ephedrine injection ($p = 0.81$) or its dosage ($p = 0.17$) didn't change significantly between groups. Comparing of arterial pressures in different min with basic systolic pressure, showed that, there was a significant difference in 4th min postanesthesia ($p = 0.04$, t test for paired sample), this difference is related to the hypotension in group 2 in compared with group 1. Heart rate at 2nd, 4th, 6th, 10th and 15th min after anesthesia had significant difference in compare with basic HR between groups. There were significant differences in mean sensory block

level in min 20, 25 and 30 between groups but not between two groups with each other. Also, the difference in peak sensory block level was not significant between groups ($p = 0.14$). Mean Motor block in 10th min post anesthesia, showed significant difference between groups with each other. However it was noted that, despite the correlation of block severity in all three groups, after 10 min, the degree of stabilization (SD) was very high in group 3, such that all patients in this group had grade 3 of motor block. There was not any difference in onset time of sensory or motor block and the time from onset to T_6 level achieved (allowing to surgical incision) between groups, but only in one patient of group 1, the sensory level was T_7 , such that, she was received additional dose of analgesia (fentanyl+katamine) in 35th min of anesthesia. None of patients of all groups had pain at incision time, unless, in one case, spinal anesthesia replace with general anesthesia and tracheal intubation, because of the onset of pain.

There were no differences in the time from onset of block to delivery, time from incision to delivery (clamping of umbilical cord), operation time and apgar score of neonates at 5th min, between groups. But 1st min apgar had significant difference between groups ($p = 0.017$). But there was not any difference in every two groups with each other. Of course 1st min apgar was always higher than 7 (Table 2).

Table 1: Demographic data in three-group Mean (SD) and range

Group	Group 1 (3.2-3.6 mL)	Group 2 (3.6-4.0 mL)	Group 3 (4.0-4.4 mL)	p-value
Age (year)	23.5 (4.4) (18-36) n = 20	24.9 (5.2) (17-36) n = 20	27.0 (5.7) (18-37) n = 20	0.11
Height (cm)	159.65 (3.80) (155-165) n = 20	159.00 (3.52) (155-165) n = 20	159.80 (3.86) (155-165) n = 20	0.77
Weight (kg)	68.4 (12.26) (55-93) n = 20	67.6 (8.52) (52-81) n = 20	74.7 (11.18) (54-90) n = 20	0.08
Gestational age (week)	39.2 (1.29) (36-41) n = 17	39.4 (0.8) (38-40) n = 18	39.4 (0.7) (38-40) n = 18	0.08
Gravidity	1.5 (0.9) (1-4) n = 20	1.9 (0.8) (1-3) n = 20	1.7 (1.7) (1-7) n = 20	0.012

Table 2: Mean (SD) and the range of variables

Group	Group 1	Group 2	Group 3	p-value
Time before peak sensory block level achieved (min)	7.52 (5.69) (2-25) n = 19	6.80 (5.27) (2-20) n = 20	6.20 (4.39) (2-20) n = 20	$p = 0.72$
Time before peak motor block level achieved (min)	5.21 (5.33) (2-25) n = 19	3.80 (1.82) (2-8) n = 20	4.50 (2.58) (2-10) n = 20	$p = 0.14$
Time from incision to clamping of the cord	95.5 (23.81) (60-150) n = 18	83.2 (29.61) (40-150) n = 20	78.7 (25.17) (45-120) n = 20	$p = 0.88$
Operation time (min)	48.42 (10.80) (30-75) n = 19	48.0 (12.50) (30-90) n = 20	48.5 (9.88) (30-95) n = 20	$p = 0.98$
Apgar score:				
1st min	1.0 (0.84) (7-10) n = 19	9.6 (0.59) (8-10) n = 20	9.6 (0.50) (9-10) n = 18	$p = 0.017$
5th min	9.8 (0.31) (9-10) n = 19	10 (0.0) (10-10) n = 20	10 (0.0) (10-10) n = 18	$p = 0.13$



Fig. 1: Percent of different qualities of sensory block

Comparing of the quality of anesthesia as the incidence of visceral pain showed no significant difference between groups ($p = 0.027$, kruskall-wallis, chi-square) (Fig. 1) There were not any correlation between visceral pain and gravidity, age, weight, peak motor and sensory block level, HR and BP changes, but it was significant correlation between it and the percent of hypertension (Mann-Whitney test, $p = 0.013$).

DISCUSSION

Our study showed that 0.25% hyperbaric bupivacaine in the range of 10-11 mg can provide satisfactory sensory block and decreases the severity of visceral pain in cesarean section. With this dosage, defect in sensory and motor block can decrease without any rapid and deteriorous decreasing in arterial blood pressure.

Between demographic variables, although there was not any correlation in gravidity and the incidence of visceral pain, however, it must be considered that gravidity can present mothers culture, experiencing of previous anesthesia, her anxiety and psychological status which can affect the occurrence of visceral pain. Thus, it appears that mother's training programs before and during pregnancy and before anesthesia, can reduce these problems.

Recently a few studies discussed about new properties of bupivacaine which are different from those mentioned earlier. Unlike lidocaine, sympathetic block level is the same as sensory block with hyperbaric bupivacaine and as the dose increases, sensory and sympathetic blocks reach a plateau and the quality of block will be better without any increasing in complications (Fig. 1) (Chung *et al.*, 1996; Echevarria *et al.*, 1996).

In our study the incidence of hypotension was not different between groups (15.7, 30 and 25% in group 1, 2 and 3, respectively). Pedersen *et al.* (1989) found the same results, such that the incidence of hypotension in

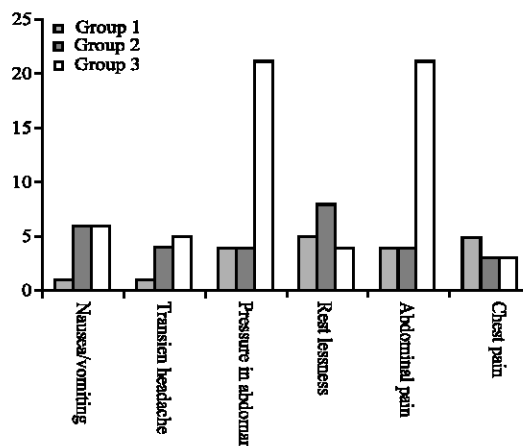


Fig. 2: Percent of different complaints in three group

the two group of patients candidate for cesarean section under spinal anesthesia (10-12 mg in group 1 and 7.5-10 mg in group 2) was 22-24%, (Petersen *et al.*, 1989) but Chung *et al.* (1996) showed the high incidence of hypotension (40-75%) in a similar study with the same dosage and volumes of 0.25% hyperbaric bupivacaine. In our study we elevated parturient's legs 10-15 degree that can probably decrease early hypotension and influence surgical status with relaxing abdominal Rectus muscles. Relative to basic blood pressure, the greatest decrease was in 4th min of puncture and unlike lidocaine the onset of hypotension is slow and controllable.

Bradycardia which is a serious complication of spinal anesthesia (Miller *et al.*, 2005) didn't occur in our study, however Chung *et al.* (1996) reported a 26% incidence of bradycardia in their study. The reason for this discrepancy is not well known. Although, it has been reported that unlike tetracaine, in subarachnoid injection of hyperbaric bupivacaine, the plasma level of catecholamines elevate and this is probably the reason for the low incidence of bradycardia.

T₄ sensory block level usually recommended for cesarean section (Miller *et al.*, 2005), but despite of it, many parturients have several complaints (Fig. 2), which are needed for supplementary treatment. In our study, all mothers had at least T₆ sensory block level, none of them had pain or discomfort at the incision time, but in one case the spinal anesthesia replace with general anesthesia, because of the onset of pain. Achieving T₄ block level, is significantly predictable in group 2 (3.6-4.0 mL) and group 3 (4.0-4.4 mL) than group 1 (3.2-3.6 mL) and the variance is lower in group 3 than group 2.

Cesarean section is a lower abdomen operation, however, pressures and tractions, applied to the upper part of the abdomen for fetal extraction and, on the other

hand, shedding of blood and amniotic fluid to the abdomen cavity, high traction of fallopian tube mesentery at the time of uterine extraction or cleaning of abdomen cavity from blood, all can excite the upper abdomen regions and this problems, need for higher sensory block levels which can be easily accomplished with clinically using doses, but the quality of block will be varied with different doses (Chung *et al.*, 1996). Petersen achieved the same sensory block level with 7.5-10 mg and 10-12 mg of 0.5% hyperbaric bupivacaine, but the incidence of visceral pain was significantly low with 10-12 mg (31.6 versus 70.5%) (Pedersen *et al.*, 1989).

Chung *et al.* (1996) found the low incidence of visceral pain and the need for supplementary analgesic treatment in group 2 (3.6-4.0 mL) and group 3 (4.0-4.4 mL) than group 1 (3.2-3.6 mL). But in our study there was no difference in visceral pain between three groups.

Supplementary analgesia (Inhalational or interval) currently recommended in spinal anesthesia. If the quality of anesthesia is referred to the defect in the severity of block, it was seen that this defect will be decline with increasing the dose of the drug and will be controlled easily with minimal interventions (assurance of mother, intravenous administration of low dose analgesics or sedatives). But in spite of achieving the same sensory block level with high volumes, the defect in the severity of block in low volumes will be more and needs for aggressive supplemental treatment, such that from 6 patients which were received general anesthesia or more than 100 µg fentanyl and considered as weak quality of sensory block (Fig. 2), 5 patients was from group 1 (3.2-3.6 mL) and one patient was from group 2 (3.6-4.0 mL) and none of patients of group 3 need for this aggressive treatment. It was resulted that better and predictable quality of sensory block will be achieved with increasing volumes of the drug.

CONCLUSIONS

Increasing volumes of 0.25% hyperbaric bupivacaine may be a safe and effective method for decreasing visceral complaints of mothers undergoing cesarean section with spinal anesthesia.

It was needed for more studies and researches about visceral pain. For this reason, with regard to several physiologic, anatomic, surgical, medical, neurological and psychological aspects, which affect visceral pain and can not be controlled only by anesthesiologist, it appears that a team works with a wide range of responsibility and teaching programs from prepartum to immediately before and after anesthesia is required.

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