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Maternal Hemodynamic and Neonatal Outcome in Preeclamptic Parturients Udergoing Cesarean Section with Small Dose Bupivacaine-Sufentanyl Spinal Anesthesia

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Abstract: We studied both markers of neonatal condition and maternal hemodynamic in preeclamptic patients receiving spinal anesthesia for cesarean section. Forty four preeclamptic patients were randomized to two groups of 22 patients in this double-blind and case-controlled trial study. Group A received a spinal anesthetic of bupivacaine 6 mg plus sufentanyl 3.3 μg and Group B received 12 mg bupivacaine. Hypotension was defined as a 30% decrease in systolic and diastolic pressure from baseline. Hypotension was treated with intravenous ephedrine boluses 2/5-5 mg up to maximum 50 mg. After delivery, neonatal 1st and 5th apgar scores were evaluated and umbilical arterial blood gas samples were taken and analyzed. All patients had satisfactory anesthesia. About 5 of 22 patients in group A required ephedrine, a single dose of 5 mg. About 17 of 22 patients in group B required vasopressor support of blood pressure. First and 5th apgar scores ($p = 0.760, 0.349$) and umbilical arterial blood gas markers (PH, PCO_2, HCO_3, BE) showed no deference between 2 groups ($p>0.05$). A small-dose of 6 mg bupivacaine in combination with 3.3 μg sufentanyl provides satisfactory spinal anesthesia for cesarean section in the preeclamptic patients and caused dramatically less hypotension than 12 mg bupivacaine. Also, neonatal apgar score and umbilical arterial blood markers are not influenced it.

Key words: Preeclampsia, spinal anesthesia, bupivacaine, sufentanyl, neonatal outcome

INTRODUCTION

Women with severe preeclampsia commonly require delivery by cesarean section (Claire *et al*., 2001; Antoine *et al*., 2003). Regional techniques also reduce the risk of airway complications and avoid the hemodynamically ractions associated with laryngoscopy and intubation (Miller, 2005; Dyer *et al*., 2003). The optimal anesthetic technique for cesarean delivery in severely preeclamtic women remains controversial. Recent clinical practices, however, indicate that spinal anesthesia can be and is, safely used (Antoine *et al*., 2003; Dyer *et al*., 2003). The use of spinal anesthesia in preeclamptic parturients is of considerable benefit. Although, spinal anesthesia may be avoided in these patients because of the risk of severe hypotension, however, it appears that blood pressure changes during spinal anesthesia in patients with preeclampsia are not different from those that occur in normal patients (Santos and Birnbach, 2005; Sharwood *et al*., 1999; Santos and Birnbach, 2003; Shifman and Filipprovich, 2003; Marcel *et al*., 1998; Chestnut, 2004; Chiu *et al*., 2003; Mandal and Surapaneni, 2004). Therefore, the use of a single shot spinal anesthesia considered acceptable by some experts and they attempt to minimize hypotension of spinal anesthesia and its possible adverse effects on the fetus/newborn (Jain *et al*., 2004; Ramanathan *et al*., 2001; Ben-David *et al*., 2005; Dahlgren *et al*., 1997; Lim *et al*., 2004). Because uterine blood flow decreases during maternal hypotension and compromise neonatal wellbeing (Chestnut, 2004; Karinen *et al*., 1996). One approach is to minimize hypotension by using very small doses of local anesthetics. However, although, the use of a single shot low dosage local anesthetic for spinal blockade may limit hypotension, it may not provide acceptable anesthesia (Santos and Birnbach, 2003; Shifman and Filipprovich, 2003; Chestnut, 2004).

In this regard, intrathecaly use of opioids with low dose local anesthetic can decrease the incidence and severity of spinal anesthesia-induced hypotension and likely improve the quality of intra and postoperative analgesia (Jain *et al*., 2004; Ramanathan *et al*., 2001; Ben-David *et al*., 2005; Dahlgren *et al*., 1997; Lim *et al*., 2004).

It was therefore, decided to study maternal hemodynamics and evaluate the neonatal effects of adding sufentanyl to small-dose bupivacaine for spinal anesthesia in preeclamptic parturients undergoing cesarean section.

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MATERIALS AND METHODS

Forty four preeclamptic parturients were candidated for cesarean section with spinal anesthesia randomized into 2 groups of 22 patients. Parturients with blood pressure >140/90 mm Hg and proteinuria 2 g per 24 h were chosen for this study. Exclusion criteria were patient refusal or any other relative contraindication to spinal anesthesia, patients with cardiovascular and pulmonary disease, diabetics and patients with CNS disorders, seizure, coagulopathy and HELLP syndrome. Parturients were randomly assigned to 2 groups defined by the spinal injectate. This study was done in Alzahra Hospital during 2006 and last 1 year.

After obtaining written informed consent of the subjects, group A were given 6 mg bupivacaine 0.5% in glucose, plus 3.3 μg sufentanyl and Group B, received 12 μg bupivacaine 0.5% in glucose. Bupivacaine 0.5% in glucose was prepared by adding 4 mg glucose 50% to 20 mL bupivacaine 0.5%. In both groups, distilled water added to drug mixture for making drug volume 2.5 mL in total. The syringe was prepared by one researcher and it was administered by second anesthetists, who were performed subarachnoid blocks and remained blinded to its contents patient's assessment, care and data recording done by blind observer. The antepartum management include seizure prophylaxis in patients with severe preeclampsia and consisted of magnesium sulfate (mgso4) administered as a loading dose of 4 g intravenously, followed by 1 g hourly intravenously. Hydralazine was administered intravenously as a vasodilatator for additional blood pressure control against a standardized protocol that was identical in both groups. Previous use of other agents (α-methyl dopa, Dexamethasone) was recorded. Before block, each patient received a rapid infusion of 8 mL kg^{-1} of ringer's solution, in left lateral position during 15-30 min and the baseline blood pressure, heart rate, were noted. After prep and drep of the back of patient, subarachnoid injection was performed in the sitting position using a 25 gauge needle positioned midline at the L3-L4 interspace. After aspiration of 0.5 mL of CSF the local anesthetic drug was injected in spinal space during 10-15 sec (if no blood was aspirated). After completion of injections the patients were immediately returned to the supine position and the operating bed positioned in 15-30° head down, with left uterine displacement. The parturients head was rested on a pillow. Each patient received 6-8 L min^{-1} O_2 by face mask. Standard monitoring include continuous ECG, pulseoximetry, maternal BP and HR.

The vital signs were recorded every 1 min up to the birth of neonate and then every 5 min with using an automated noninvasive device. Pinprick testing in the right side of body was used to establish onset and peak level of blockade. For the purpose of the study, hypotension was defined as a systolic blood pressure decrease of >30% from baseline. Hypotension was treated promptly by increasing uterine displacement and the rate of fluid administration. If hypotension persisted despite these measures, ephedrine 2.5-5 mg was injected and repeated as needed. Patients received 1500-2000 mL of ringer solution during whole surgery.

The vital sings, number of hypotension measurements, total ephedrine dose for each patient and intraoperative patient complaints of pain, nausea and vomiting were recorded. Ondancetrone 2-4 mg was used to treat nausea or vomiting. The condition of the neonates was assessed by apgar score at 1 and 5 min after delivery and umbilical artery blood sample was taken for blood gas analysis. All mothers received oxytocin by continuous infusion after delivery. Return of sensory and motor function was assessed at 15 min intervals until complete recovery from anesthesia. Statistical analysis was performed using SPSS 13. Analyzes of variance was used to analyze demographic data. The nondepended t-test and χ^2-test and fisher exact test were used to analyze data. Results were considered significant at $p<0.05$. The type of study was interventional comparison.

RESULTS

There were 22 patients in each of the 2 groups. There were no differences between the demographic characteristics of the 2 groups (Table 1).

Though, baseline systemic blood pressure was slightly higher in group B, this was not a significant difference (157.91±16.920 in group B versus 155.23±13.73 in group A). No patients in either group complained of intraoperative pain or required supplemental analgesics intraoperatively. Peak sensory block level was similar in both groups.

The lowest recorded systolic and diastolic blood pressures are reported in Table 2 as well as their percentages of the baseline pressures. For group A these were 71.2 and 59.5% versus 64.5 and 53.5%, respectively for group B.

Table 1: Demographic data

Variables	Group A bupiracaine 6 mg + sufentanyl 3.3 μg	Group B bupiracaine 12 mg
Agev	30.41±5.230	29.32±6.030
Weight	78.95±9.280	76.62±11.88
Gravidity	1.91±1.150	1.79±1.870
Gestational age	33.59±2.570	33.52±2.850
Operating time	62.11±10.84	66.29±14.73
Base line heart rate	102.91±16.15	103.64±12.38
Base line systolic pressure	155.23±13.73	157.91±16.92
Base line diastolic pressure	95.91±10.30	99.86±14.01

Data are mean±SD unless other wise indicated, p-value was not significant for all variables

Table 2: Study data

Variables	Group A	Group B	p-value
Peak level of block	T (5.7±1.146)	T (5.7±1.225)	0.058
Patients having Pain during surgery	0	0	
Patients experienced hypotension	6	14	0.34
Lowest systolic pressure	109.8±14.5	100.8±13.0	0.037
Lowest/baseline systolic pressure	0.712±0.113 (71/2%)	0.645±0.100 (64.5%)	0.042
Lowest diastolic pressure	57.1±12.2	52.2±7.6	0.117
Lowest/baseline diastolic pressure	0.599±0.127 (59.97%)	0.535±0.101 (55.5%)	0.072
Number of patients treated for hypotension	6	11	0.597
Number of ephedrine injection	5	19	0.0001

Data are mean±SD unless other wise indicated; $p<0.05$ was significant

Table 3: Neonatal condition markers in 2 groups

Variables	Group A bupiracaine 6 mg + Sufentanyl 3.3 μg	Group B bupiracaine 12 mg	p-value
1st apgar score	7.80±1.340	7.90±1.150	0.760
5th apgar score	8.83±0.370	7.26±0.560	0.349
pH	7.26±0.270	7.26±0.700	0.906
PCO_2	46.63±10.48	44.97±10.56	0.850
BE*	5.27±2.630	5.01±3.620	0.683
HCO_3	21.46±2.440	22.42±4.390	0.340

Data are mean±SD unless other wise indicated; $p<0.05$ was significant; *Base deficit

Table 3: Side effects

	Group A (n = 22)	Group B (n = 22)	p-value
Nausea	3	12	0.01
Vomiting	0	5	0.29
Pruritis	3	0	

$p<0.05$ was significant

In group A 5 of 22 patients and in group B 17 of 22 patients experienced hypotension according to the protocol definition of hypotension. About 17 patients in Group B and 5 patients, in group A required treatment with ephedrine. However, numbers of ephedrine administration in incremental doses were 19 times in group B versus 5 times in group A and this difference is significant ($p = 0.0001$).

Neonatal condition markers presented in Table 3. There was not any significant deference in 1st and 5th min apgar scores ($p = 0.760, 0.349$) and blood gas values of neonatal umbilical artery between 2 groups ($p>0.05$).

Nausea was seen in 12 patients of group B and 3 patients of group A. Also, 8 patients in group B and no patient in group A had vomiting. Postoperative follow-up revealed uneventful recovery in all patients unless, 3 patients of group A complained of pruritis and treated with antihistamine (Table 4).

DISCUSSION

The current study addressed the issue of neonatal outcome, while also comparing hemodynamic data in the 2 groups. It is likely that there are many influences on neonatal outcome after cesarean delivery in preeclampsia. These including severity of maternal and fetal condition, anesthesia and surgical management. Fetal development is related to gestational age and to chronic uteroplacental insufficiency, which results in intrauterine growth restriction. In addition any acute maternal deterioration may impact unfavorably on fetal outcome. All of these, allowed us to assess the influence of anesthesia independently.

In this study, the equivalence is seen between the 2 groups in terms of demographic and clinical data, severity of maternal diseases and gestational age. Most of neonates were preterm according to the gestational age.

One of the most important factors, in the spinal anesthesia is sensory block level. The appropriate sensory level for cesarean section is T_4. High level of block may influence the hemodynamic of the mothers with higher sympathetic block with more lessen the mothers BP (Sharwood *et al*., 1999; Santos and Birnbach, 2003; Shifman and Filipprovich, 2003; Marcel *et al*., 1998; Chestnut, 2004; Chiu *et al*., 2003; Mandal and Surapaneni, 2004; Jain *et al*., 2004; Ramanathan *et al*., 2001; Ben-David *et al*., 2005; Dahlgren *et al*., 1997; Lim *et al*., 2004). Pregnant patients require less local anesthetic because of increase sensitivity of nerve fibers for local anesthetics, the reduced amount of CSF and the effect of the gravid uterus on cephalad spread of intrathecally injected substances (Mille, 2005; Sharwood *et al*., 1995; Chestnut, 2004). But the use of single shot low dosage local anesthetic (<10 mg bupivacaine) for spinal blockade although, can limit hypotension but, may not been possible to develop a reliable anesthesia even in parturients. However, the addition of an opioids intrathecally to local anesthetic reduce the dose requirements, because of a potent synergistic analgesic effect of it and local anesthetic and provide satisfactory anesthesia (Marcel *et al*., 1998; Chestnut, 2004; Chiu *et al*., 2003; Mandal and Surapaneni, 2004; Jain *et al*., 2004; Ramanathan *et al*., 2001; Ben-David *et al*., 2005; Dahlgren *et al*., 1997; Lim *et al*., 2004). There were not differences in sensory level between 2 groups in this study. Also, the quality of analgesia was satisfactory, due to adding of opioid to the local anesthetic.

This study demonstrate that the use of a minidose bupivacaine plus sufentanyl spinal anesthetic (6 μg bupivacaine plus 3.3 μg sufentanyl) for cesarean section in preeclamptic parturients provides successful anesthesia and incurs a minimum of hypotension. In the minidose, group 5 of 22 patients experienced hypotension and in these patients a single dose of 5 mg ephedrine sufficed. This stood in contrast to the marked reduction in blood pressure and the significant vasopressor requirements seen in the group receiving spinal anesthetic of bupivacaine 12 mg (17 of 22 patients in group B).

In one study, Antoine *et al.* (2003) showed that patients with severe preeclampsia experience less hypotension during spinal anesthesia with low dose bupivacaine plus sufentanyl intrathecally than healthy parturients. They also demonstrated that the risk of hypotension and ephedrine use was less than that in the preterm group. They concluded that preeclampsia associated factors, rather than a smaller uterine was account for the infrequent incidence of spinal hypotension in preeclamptic patients (Antoine *et al.*, 2003). In this study, although the incidence of hypotension was higher in group B but it was with out any dangerous effect on the mother or her neonate.

The intravenous fluid preload of 8 mL kg^{-1} Ringer's solution used in this study. Fluid administration may prevent a decrease in central venous pressure and may diminish or even reverse the decrease in cardiac index and contribute to the lower incidence and severity of hypotension in preeclamptic patients undergoing spinal anesthesia (Chestnut, 2004; Clark *et al.*, 2005).

Ephedrine probably is most commonly used in cesarean section. It dose not have detrimental effect on uterine blood flow, thus, it is widely to use as a vasopressor for treatment of hypotension due to spinal anesthesia in the parturients, but systemic vasoconstriction and accelerated response to vasopressors in preeclamptic parturients limited it to use in large doses in these patient (Clark *et al.*, 2005; Cooper and Mowbray, 2004). In this study, ephedrine was used in incremental doses and started with 5 mg. Nausea and vomiting during spinal anesthesia may be related to a postural hypotension and hypoxemia of the vomiting center. Excessive rise in blood pressure following administration of a vasopressor is also produce nausea (Miller, 2005; Marcel *et al.*, 1998). This problem is unpleasant during surgery. In this study, incidence of nausea and vomiting in group A (mini dose group) was 3 and 0 and in group B was 12 and 5, respectively and the differences were significant.

This difference showed that nausea and vomiting were higher in group B than group A, which were more hypotensive following administration of spinal anesthesia. We conclude that the more possible cause of nausea and vomiting is hypotension than other causes such as intrathecal sufentanyl especially in these lower doses.

After delivery, the most common method used to detecting neonatal condition is 1st and 5th min apgar scores. Also, the more accurate and predictive measure, is neonatal umbilical arterial acid-base values. The primary outcome measure is mean neonatal umbilical arterial base deficit and this is a more specific index of the metabolic component of acid-base balance. Accepted criteria used to identify newborn infants at risk of fetal hypoxia are apgar score <7 at 1 and 5 min, neonatal umbilical pH <7.20 and umbilical arterial base deficit >0 (Miller, 2005; Dyer *et al.*, 2003; Okafor and Okezie, 2005; Helbo-Hansen *et al.*, 1993). In this study, 1st and 5th apgar scores and umbilical arterial acid-base values were evaluated. According to Table 3, there were not seen significant differences in pH, base deficit, HCO_3 and $PaCO_2$ values and 1st and 5th apgar scores, between groups. Five neonate in group A and 6 neonate in group B, had 1st scores <7, but their 5 min scores become 9 after resuscitation (positive pressure ventilation, stimulation and free flow oxygen). Robert *et al.* (2002) compared general with spinal anesthesia for cesarean delivery in preeclamptic patients with a no reassuring fetal heart rate trace and showed that the hemodynamic of the mothers was similar in both groups, but median neonatal umbilical artery pH was lower (7.20 versus 7.25) and mean neonatal arterial base deficit was higher (7.13 versus 4.24) in spinal group than general group, but they were not find any correlation between ephedrine use (associated with hypotension) and base deficit values. They concluded that the clinical significance of these results remains to be established (Robert *et al.*, 2002).

Shifman and Filipprovich (2003) study contains retrospective data of 54 cases with subarachnoid anesthetic management for cesarean section in preeclampsia. The results showed that no complications were detected in mothers and fetuses of the experimental group and confirmed the safety of this method in patients with preeclampsia (Shifman and Filipprovich , 2003).

According to this study, we found that although, baseline systemic blood pressure were slightly higher in group B, but this was not a significant difference, also, it has not any dangerous effect on the mother or her neonate. We conclude that severe preeclamptic

parturients undergoing spinal anesthesia, with small dose of bupivacaine-sufentanyl, experience less and transient hypotension than bupivacaine group and these minor changes do not influence neonatal outcome.

CONCLUSION

Minidose of 6 mg bupivacaine in combination with 3.3 μg sufentanyl provides acceptable spinal anesthesia for cesarean section in preeclamptic patients. The minidose bupivacaine-sufentanyl caused less hypotension than 12 mg bupivacaine and nearly eliminated the need for vasopressor supports of blood pressure and decreases the incidence of nausea and vomiting. The neonatal outcome in 2 groups is same.

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