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Effect of Spinal Low Dose Bupivacaine-Sufentanyl for Cesarean Section in Preeclamptic Parturients on Neonatal Outcome.

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Abstract:

Background: We studied markers of both neonatal and maternal hemodynamic condition in preeclamptic patients receiving spinal anesthesia for cesarean section and evaluated primary neonatal outcome with Apgar scores.
Methods: 44 preeclamptic patients randomized into two groups of 22 patients were enrolled in this trial in Tabriz Alzahra Hospital. The trials were conducted from December 2005 to August 2006. In group A, spinal anesthesia was performed with 6mg of bupivacaine and 3.3 µg of sufentanyl, while Group B received 12mg of bupivacaine alone. Hypotension was treated with intravenous ephedrine boluses of 2.5-5 mg, up to maximum of 50 mg. After delivery, 1st and 5th minute Apgar scores were evaluated and umbilical arterial blood gas samples were drawn and analyzed.
Results: All patients had satisfactory anesthesia. Five of 22 patients in group A required 5mg of ephedrine, while 17 of the 22 patients in group B required ephedrine. There was no significant between group differences for 1st and 5th minute Apgar scores (P=0.760, P=0.349) and umbilical arterial blood gas markers (p>0.05).
Conclusion: A 6mg dose of bupivacaine in combination with 3.3 µg of sufentanyl provided satisfactory spinal anesthesia for cesarean section in preeclamptic patients, and caused substantially less hypotension than 12 mg of bupivacaine alone. There was no difference in immediate neonatal outcome, as assessed by Apgar scores and neonatal pH and base deficit.

Keywords: Preeclampsia, spinal anesthesia, Bupivacaine, sufentanyl, Neonatal Outcome

Introduction:

Women with severe preeclampsia commonly require delivery by cesarean section.[1, 2] Regional techniques reduce the risk of airway complications and avoid the hemodynamic changes associated with laryngoscopy and intubation.[3] The optimal anesthetic technique for cesarean section in severely preeclamptic women remains controversial. Recent clinical practice indicates that spinal anesthesia in the absence of contraindications is safe.[4] It appears that preeclamptic patients exhibit less hypotension during spinal anesthesia than normal patients.[5-10] Therefore, the use of a single shot of spinal anesthesia is considered acceptable by many investigators.[11-15] Because uterine blood flow decreases during maternal hypotension, and may compromise neonatal wellbeing [16], one method of minimizing this effect utilizes small doses of local anesthetics. Although the use of a single low dose of local anesthetic for spinal blockade may limit hypotension, it may not provide acceptable anesthesia.[6, 7]

In addition, the intrathecal use of opioids in combination with a low dose local anesthetic may decrease the incidence and severity of spinal anesthesia-induced hypotension and would likely improve the quality of intra and postoperative analgesia.[13-14]

This study seeks to evaluate the neonatal effects of adding sufentanyl to a small-dose bupivacaine (Marcaine) for spinal anesthesia in preeclamptic parturients undergoing cesarean section.

Methods:

After obtaining informed consent and approval from the hospital Ethics committee, 44 preeclamptic parturients scheduled for cesarean section under spinal anesthesia were randomized into two groups of 22 patients. Parturients with blood pressure >140/90 mm Hg and proteinuria 2g/24h were enrolled in this study. Exclusion criteria were patient refusal or any other contraindication to spinal anesthesia, patients with cardiovascular or pulmonary disease, diabetes and patients with central nervous system disorders, seizure, coagulopathy, or HELLP syndrome. Parturients were randomly assigned into two groups defined by the spinal injectate. This study was performed in Alzahra Hospital from December 2005 to August 2006.

In group A, patients received 6mg of 0.5% hyperbaric bupivacaine and 3.3 µg of sufentanyl, while patients in group B received 12mg of bupivacaine alone. Bupivacaine 0.5% in glucose was prepared by adding 4mg of glucose 50% to 20ml of bupivacaine 0.5%. In both groups, distilled water was added to the drug mixture making a total of 2.5ml. Both the anesthesiologist and data collection personnel were blinded to the contents of each syringe, as well as to the patient's assessment and care. Antepartum management included seizure prophylaxis in patients with severe preeclampsia, and consisted of magnesium sulfate (MgSO4) administered as a loading dose of 4g intravenously, followed by 1g/hour intravenously. Hydralazine was administered intravenously as a vasodilator for additional blood pressure control

according to a standardized protocol that was identical in both groups. During the 15-30 minutes before spinal anesthesia, each patient received a rapid infusion of 8 ml/kg of Ringer's solution in the left lateral position during the 15-30 minutes before spinal anesthesia and blocking. Baseline blood pressure and heart rate values were recorded. Spinal anesthesia (SA) was performed in the sitting position using a 25-gauge Quincke type needle in the L3 – L4 interspace. After aspiration of 0.5 ml of cerebrospinal fluid, the local anesthetic solution was administered over 10-15 seconds. The patients were immediately returned to the supine position with left uterine displacement. The operation table was positioned the patien'ts head facing 15-30 degrees down. Each patient received 40% O2 by face mask. Standard monitoring included continuous electrocardiogram, pulse oximetry, and automated non-invasive blood pressure.

Vital signs were recorded every minute up to the birth of the neonate and every five minute thereafter. Pinprick testing was used to establish onset of block and block height. For the purpose of the study, hypotension was defined as a systolic blood pressure decrease of more than 30% from baseline. Hypotension was treated promptly by increasing uterine displacement and the rate of fluid administration. If hypotension persisted despite these measures, 5mg of ephedrine was injected and repeated if needed. Patients received a total of 1500-2000 ml of Ringer's solution during the course of surgery.

Vital signs, frequency of hypotension, total ephedrine dose for each patient, and intraoperative patient complaints such as pain, nausea, and vomiting were recorded. A 0.625 mg dose of droperidol was used to treat nausea and vomiting. Neonatal assessment included 1st and 5th minute Apgar scores and umbilical arterial pH and base deficit. The condition of the neonates was assessed by Apgar score at the 1st and 5th minute after delivery and an umbilical artery blood sample was drawn for blood gas analysis. All mothers received oxytocin by continuous infusion after delivery. Return of sensory and motor function was assessed at 15 minute intervals until complete recovery from anesthesia. Statistical analysis was performed using SPSS 13. Results were considered significant at $P< 0.05$.

Results:

There were 22 patients in each group. There were no differences between the demographic characteristics of patients in the two groups (table 1), or in baseline systemic blood pressure (157.91 16.920 in group B versus 155.23 13.73 in group A) ($p>0.05$). 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, along with their ratio to the baseline pressures, which were 71.2% and 59.5% in Group A versus 64.5% and 53.5% for group B. This data had no clinical significance.

Five patients in Group A and 17 patients in Group B required ephedrine. However, the frequency of ephedrine administration in incremental doses was 19 in group B versus 5 in group A. This difference was clinically significant (p=0.0001), however, there wasn't any significant difference in GCS scores (Glascow Coma Scale) between the two groups. Mean value of Spo2 in group A was 94.45±3.47 and was 93.56±3.78 in group B, which was not clinically significant.

Neonatal outcome is showed in table 3. There were no significant between- group differences in 1st and 5th minute Apgar scores (P=0.760, P=0.349) or in umbilical arterial blood gas values (P>0.05).

Nausea was experienced by 12 patients in Group B and by three patients in Group A (P<0.01). Eight of the patients in Group B and none of the patients in Group A had vomiting. Postoperative follow–up revealed uneventful recovery in all patients, with the exception of three in Group A who complained of pruritus and who were treated with antihistaminic drugs (P>0.05).

Table 1: Demographic data

Variables	Group A	Group B
Age	30.41±5.23	29.32±6.03
Weight	78.95±9.28	76.62±11.88
Gravidity	1.91±1.15	1.79±1.87
Gestational age	33.59±2.57	33.52±2.85
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, P 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 two groups

Variables	Group A	Group B	P value
1st apgar score	7.80±1.34	7.90±1.15	0.760
5th apgar score	8.83±0.37	7.26±0.56	0.349
PH	7.26±0.27	7.26±0.70	0.906
PCO2	46.63±10.48	44.97±10.56	0.850
BD*	5.27±2.63	5.01±3.62	0.683
HCO3	21.46±2.44	22.42±4.39	0.340

Data are mean ± SD., P<0.05 was significant , *Base deficit.

Discussion:

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

The appropriate sensory level for cesarean section is T4. A high level of block may influence the maternal hemodynamics due to increasing sympathetic block with accompanying hypotension.[5-7] The use of single shot low dosage local anesthetic, defined as lower than 10mg of bupivacaine for SA (spinal anesthesia), not only reduced hypotension but also produced reliable anesthesia, even in parturients. The addition of an intrathecal opioid may reduce the dose requirements for local anesthetics and provide satisfactory anesthesia on the basis of a synergistic analgesic effect between opioids and local anesthetics.[8-11] There was no difference in sensory level between the two groups in this study. Also, the quality of analgesia due to the addition of the opioid to the local anesthetic was satisfactory.

This study demonstrated that the use of a low dose of bupivacaine plus sufentanil in SA (6µg bupivacaine plus 3.3 µg sufentanyl) for cesarean section in preeclamptic parturients provides adequate surgical anesthesia and incurs a low level of hypotension. In the group A, five patients experienced hypotension and in these patients a single dose of 5mg ephedrine sufficed. This was in contrast to the marked reduction in blood pressure and the significant ephedrine requirements seen in the group receiving spinal anesthesia with the higher dose of bupivacaine (Table2).

Antoin et al. showed that patients with severe preeclampsia experience less hypotension than healthy parturients during spinal anesthesia with low dose bupivacaine plus intrathecal sufentanil. Aya et al. demonstrated that the risk of hypotension and ephedrine use was less

than that in a preterm group of healthy patients. They concluded that preeclampsia associated factors, rather than a smaller uterine, accounted for the frequent incidence of spinal hypotension in preeclamptic patients. In this study, although the incidence of hypotension was higher in group B, it had no apparent deleterious effect on the mother or her neonate.[2]

In this study, patients received 8ml/kg of Ringer's solution preoperatively. 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.[17]

Ephedrine is probably the most commonly used drug for the treatment of hypotension during a cesarean section. Ephedrine does not have detrimental effects on uterine blood flow, which supports its use as a suitable treatment for hypotension of spinal anesthesia in the parturients. In spite of this, systemic vasoconstriction and an accelerated response to vasopresors in preeclamptic parturients limits its use in large doses in this group.[16, 18]

In this study, ephedrine was used in incremental doses which started at 5mg. Nausea and vomiting during spinal anesthesia was evident and may be related to a postural hypotension and hypoxemia of the vomiting center. Excessive rise in blood pressure following administration of a vasopressor can also produce nausea.[8] This problem is unpleasant during surgery. In this study, the incidence of nausea and vomiting in group A was 3 and 0, and in group B was 12 and 5, respectively (table3), and the differences were found to be significant ($P<0.05$). This difference showed that nausea and vomiting were higher in group B than Group A, who also appeared more hypotensive following administration of spinal anesthesia. We concluded that the most probable cause of nausea and vomiting is hypotension rather than other causes such as intrathecal sufentanyl . This is particularly true in low doses.

After delivery, the most common method used to detect neonatal condition is the 1st and 5th minute Apgar scores, though the most accurate and predictive measurement 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 newborns at risk of fetal hypoxia are Apgar score less than seven at the 1st and 5th minute, neonatal umbilical PH less than 7.20, and an umbilical arterial base deficit greater than 10 mmol.[3, 19, 20] In this study, 1st and 5th Apgar scores and umbilical arterial acid-base values were evaluated. There were no significant differences in PH, base deficit, HCO3, PaCO2 values, and in 1st and 5th Apgar scores between the two groups. Five neonates in group A, and six neonates in group B had 1st minute scores less than seven, but their 5th minute scores became nine after resuscitation (positive pressure ventilation, stimulation and free flow of oxygen) (Table3). Robert et al. compared general to

spinal anesthesia for cesarean delivery in preeclamptic patients with no reassuring fetal heart rate trace and showed that the hemodynamic changes of the mothers were similar in both groups, though the 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 the spinal group compared to the general group. They did not find any correlation between ephedrine use (associated with hypotension) and base deficit values and concluded that the clinical significance of these results remains to be established.

Shifman and Filippovich's study contains data of retrospective observation studies on 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.(7)

In our study, we found that although baseline systemic blood pressure was slightly higher in group B, the difference was not significant. Several preeclamptic parturients undergoing spinal anesthesia with small doses of bupivacaine alone experienced more hypotension than parturients in the bupivacaine-sufentanil group, but the hemodynamic instability was transient and did not influence the neonatal outcome.

In conclusion, a 6 mg dose of bupivacaine in combination with 3.3 µg of sufentanil provided acceptable spinal anesthesia for cesarean section in preeclamptic patients. The low dose of bupivacaine–sufentanil caused less hypotension than 12mg of bupivacaine alone and nearly eliminated the need for vasopressor supports of blood pressure. In addition, it also decreased the incidence of nausea and vomiting, without negatively influencing neonatal outcome.

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