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Comparing the Hemodynamic Effects of Spinal Anesthesia in Preeclamptic and Healthy Parturients During Cesarean Section

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Abstract

Background: Despite controversies about the safest anesthetic technique for cesarean delivery in severely preeclamptic women, there is evidence that supports the use of spinal anesthesia in this group of patients.
Objectives: This prospective randomized clinical trial was designed to determine the hemodynamic effects of low-dose spinal bupivacaine and the incidence of spinal anesthesia-associated hypotension in severely preeclamptic and healthy parturients undergoing cesarean sections.
Patients and Methods: Spinal anesthesia was performed with 10 mg (= 2 mL) hyperbaric 0.5% bupivacaine plus 2.5 μg sufentanil in two groups of patients after they received 500 mL of IV lactated Ringer's solution. Heart rate and blood pressure were recorded before spinal anesthesia and at two minutes intervals for 15 minutes after the block, and then every five minutes until the end of the surgery. Hypotension was defined as more than 25% of decline in the mean arterial blood pressure compared to the baseline in both groups (or systolic blood pressure < 100 mmHg in healthy parturients) and was treated with 5 mg IV ephedrine. The total amounts of intravenous administered fluid and the total doses of ephedrine were recorded for each patient as well.
Results: The incidence rate of hypotension among the preeclamptic patients was lower than that of the healthy parturients, despite the former group receiving smaller volumes of intravenous fluids ($P < 0.05$). The total doses of IV ephedrine for treating hypotension were significantly lower among the preeclamptic patients (3.2 mg in preeclamptic patients versus 7.6 mg in normotensive patients) ($P = 0.02$). The one-minute Apgar score was significantly lower for the preeclamptic parturients (8.4 ± 0.7 versus 7.2 ± 1.5) ($P = 0.001$), but there was no significant difference in the five-minute Apgar scores between the two groups.
Conclusions: Our results confirm that low-dose bupivacaine spinal anesthesia is associated with a lower risk of hypotension than previously believed, and it can therefore be safely used in severe preeclamptic women undergoing cesarean delivery.

Keywords: Preeclampsia, Anesthesia, Spinal, Cesarean Section, Hypotension

1. Background

Pregnancy-induced hypertension is a major cause of morbidity and mortality in obstetrics, complicating 3% - 8% of pregnancies. Severe preeclampsia poses a dilemma for anesthesiologists, and there is some controversy about the best anesthetic technique for cesarean delivery in such cases (1, 2). Because of the risks related to airway edema, difficulty with the airway or failed intubation, hypertensive response to direct laryngoscopy, and aspiration pneumonitis, general anesthesia is associated with more untoward outcomes in this particular group of patients (3, 4). When there is no contraindication for performing regional anesthesia, risk-benefit considerations strongly favor neuraxial techniques over general anesthesia for cesarean delivery in cases of severe preeclampsia. Regional anesthesia techniques have been widely used recently, however, spinal anesthesia, once considered contraindicated due to the common belief that the sudden and extensive sympathetic blockade following the subarachnoid block would result in severe hypotension and compromise uteroplacental blood flow in this group of patients (5-8).

Although controversial, some studies have shown the effectiveness of colloid loading on reducing the incidence of hypotension in spinal anesthesia (9, 10), but vasopressor agents and volume loading, which are commonly used to manage spinal anesthesia-induced hypotension, could put the preeclamptic patients at increased risk of hypertension and pulmonary edema (6).

Recent evidence has challenged this view, suggest-

ing that spinal anesthesia may in fact be an appropriate choice for preeclamptic women when cesarean delivery is planned, as long as neuraxial anesthesia is not contraindicated (e.g., coagulopathy, eclampsia with persistent neurologic deficits) (2, 5, 8). Although the relative safety of the subarachnoid block in these patients has been demonstrated, there are few studies that compare the differences in the hemodynamic changes and newborn well-being after single-shot spinal anesthesia between preeclamptic and healthy parturients

2. Objectives

This prospective randomized clinical trial was designed to compare the hemodynamic effects and the incidence of spinal anesthesia-associated hypotension after spinal anesthesia with bupivacaine plus sufentanil in severely preeclamptic versus healthy parturients undergoing cesarean sections.

3. Patients and Methods

After obtaining institutional ethics committee approval, 80 parturients (37 healthy and 43 severely preeclamptic parturients) that were being cared for in our unit from April 2011 to July 2012 were enrolled in the study after providing informed consent. Severe preeclampsia was defined as a systolic arterial blood pressure of 160 mmHg or higher, or a diastolic blood pressure of 110 mmHg or higher, associated with proteinuria > 5 g in 24 hours.

Patients who were excluded were those with coagulopathy (including those with platelet counts < 50,000), placental abruption, severe fetal distress, a history of allergy to local anesthetics, oliguria of less than 500 mL in 24 hours or persistently < 30 mL/hour, cerebral or visual disturbances, pulmonary edema, hemodynamic instability, local infection of the spinal injection site, or refusal of a spinal block.

All patients in the preeclampsia group received a 4 g loading dose of intravenous magnesium sulfate ($MgSO_4$) followed by a 1 g/hour infusion for 24 hours for seizure prophylaxis. Intravenous hydralazine of 5 mg was given at 20-minute intervals to decrease diastolic blood pressure to approximately 90 mmHg.

Before performing spinal anesthesia on each patient, preoperative fluid administration equal to 10 mL/kg of Ringer's lactate solution was administered over the course of 15 - 20 minutes. All patients received 1500 - 2000 mL lactated Ringer's solution after spinal anesthesia and during the operation. The volume of administered fluid was not restricted in the preeclamptic patients because of the contracted intravascular volume in this group of patients and the high incidence of hypotension caused by spinal anesthesia-induced sympathetic blockade. Patients were monitored with standard monitoring devices including automated blood pressure cuffs, electrocardiogram, and pulse oximetry.

Spinal anesthesia was performed with 10 mg hyperbaric 0.5% bupivacaine plus 2.5 - 3 μg sufentanil (2.5 mL volumes) in two groups in the sitting position in the L3-L4 or L4-L5 vertebral interspaces. Each patient was then placed in the supine position with a left lateral tilt of 15-20 degrees. The height of the sensory block was assessed using a pinprick test, and a 10°-15° head down-tilt (Trendelenburg position) was initiated if a T4 sensory level was not achieved at 10 minutes after the spinal injection. After achieving an adequate sensory block (T4 level), the patient was prepared for surgery. Heart rate and blood pressure were recorded before performing spinal anesthesia at two-minute intervals for 15 minutes after the block, and then every five minutes until the end of the surgery. Hypotension was defined as more than 25% decline in mean arterial blood pressure (MAP) compared to the baseline in both groups (or systolic blood pressure (SBP) < 100 mmHg in healthy parturients) and was treated with 5 mg IV ephedrine. The total amounts of intravenous administered fluid and the total doses of ephedrine were recorded as well.

Based on the findings of previous studies, we calculated that at least 38 patients per group were required to show a 25% difference in the incidence of hypotension, with 80% power at the 5% level. Data are presented as number, median and range, mean $\pm$ SD, or percentage as appropriate. Fisher's exact test was used for intergroup comparisons of the incidence of hypotension. Mean values of most of the quantitative study variables were compared by using the unpaired Student's t-test. A P value of less than 0.05 was considered to indicate statistical significance. Data entry and analysis were performed using SPSS software version 16.

4. Results

Eighty patients (severe preeclampsia = 43 and healthy = 37) were studied. Demographic data, the times from spinal injection to delivery, the median sensory blocked levels at the time of incision, the volumes of estimated blood loss, and the surgical durations were similar between the two groups (Table 1).

The mean gestational age and mean one-minute Apgar scores in the patients with severe preeclampsia were significantly lower than those of the healthy parturients (Ta-

Table 1. Maternal, Neonatal, and Anesthetic Considerations[a]

Variable	Healthy	Preeclampsia	P Value
n	37	43	
Age, y	28.1 ± 5	29.3 ± 6.6	0.12
Gestational age, week	38.8 ± 1.2	34.3 ± 3.8	0.00
Base line MAP	101.1±10.1	119.5±15.9	0.02
Upper Sensory Level (Median, Range)	T4 (T2-T5)	T4 (T2-T5)	0.32
IV fluid, mL	2500 ± 0.1	2400 ± 0.2	0.000
Spinal puncture to delivery interval, minute	17.5 ± 2.5	17.1 ± 2.5	0.83
Ephedrine dose, mg	7.5 ± 9.2	3.2 ± 7.8	0.04
APGAR score 1-min (Range)	8.4 ± 0.7, (5 - 10)	7.2 ± 1.5, (2 - 10)	0.001
APGAR score 5-min (Range)	9.4 ± 0.7, (7 - 10)	8.6 ± 1.1, (5 - 10)	0.35

[a]Values are expressed as mean ± SD unless otherwise indicated.

ble 1). However, there was no significant difference in the five-minute APGAR score between the two groups.

The incidence rate of hypotension in the preeclamptic patients (55.8%) was less than that of the healthy parturients (89.2%) (Table 2), despite the former receiving smaller volumes of intravenous fluids (2.4 versus 2.5 lit) (Table 1) (P = 0.001).

Table 2. Incidence of Hypotension and Changes in Blood Pressure After Spinal Anesthesia in the Two Groups

Variable	Healthy	Preeclampsia	P Value
Incidence of MAP hypotension (%)	33 (89.2%)	24 (55.8%)	0.001
Lowest SBP mmHg	98 ± 12.9	116 ± 18.6	0.02
Lowest DBP mmHg	47.5 ± 9.5	66.3 ± 14.1	0.03
Lowest MAP mmHg	64.9 ± 10.1	83.7 ± 14.9	0.008

The SBP, DBP, and MAP measured at the baseline were higher for the patients with preeclampsia, and the mean lowest SBP and MAP measured among the preeclamptic patients were consistently higher than the corresponding values among the healthy parturients (Table 2). Furthermore, the total doses of IV ephedrine for treating hypotension were significantly lower for the preeclamptic patients than for the normotensive patients (3.2 ± 7.8 mg versus 7.5 ± 9.2 mg) (P = 0.04).

5. Discussion

Spinal anesthesia-associated hypotension may occur in up to 64% - 100% of pregnant women undergoing cesarean delivery (2). Severely preeclamptic patients have been considered to be at higher risk of severe hypotension (1, 2, 5-8), and the concern of severe hypotension caused by subarachnoid block may often deter the anesthesiologist from choosing this technique for this group of patients. Epidural anesthesia has traditionally been regarded to be safer for preeclamptic parturients as it does not produce sudden hypotension. However, some studies have shown that the two techniques produce a similar incidence and severity of hypotension in preeclamptic parturients (6, 7, 11).

There is growing interest in using spinal anesthesia on preeclamptic patients because of its simplicity, faster onset, lower dose of injected local anesthetic (which decreases the probability of systemic toxicity), and less tissue trauma caused by the use of a smaller gauge spinal needle (12-14). As a result of this interest, a number of studies have been conducted to show the hemodynamic consequences of spinal anesthesia in patients with preeclampsia. A prospective study by Aya et al. found that the risk of hypotension following spinal anesthesia in preeclamptic patients was significantly lower than the risk among healthy term parturients (17% in preeclamptic parturients and 53% in healthy parturients) (2). In another study, the same author suggested that the risk of hypotension following a subarachnoid block in preeclampsia was related to preeclampsia-associated factors rather than a small uterine size (15).

Similar to the studies by Aya et al., the incidence of hypotension in severely preeclamptic patients undergoing spinal anesthesia for cesarean delivery was found to be significantly lower in comparison to the rate among healthy parturients (55% versus 89%) in our study. Factors such as difference in gestational age, the carrying of a smaller fetus, less aortocaval compression, sympathetic hyperactivity, and high vascular tone might have led to this finding (1, 2, 8, 16). The injection of different doses of bupivacaine (10 mg versus 8 - 12 mg) for the induction of the subarachnoid block and the different criteria for defining hypotension (a 25% versus 30% decline to baseline MAP) might explain why the incidence of hypotension was higher in both groups in our study compared to the corresponding rates in Aya et al.'s study.

According to two other studies conducted by Mendes et al. (17) and Saha et al. (8), the hemodynamic changes and newborn well-being appeared to be comparable in severely preeclamptic and healthy parturients submitted to spinal anesthesia for cesarean section, and spinal anes-

thesia seemed to be a safe option for patients with severe preeclampsia.

The ephedrine requirement for treatment of spinal anesthesia-induced hypotension in preeclampsia has been reported to be lower than that required by healthy parturients (2, 18). Preeclamptics have been reported as requiring significantly less phenylephrine to treat hypotension as well (8). These results were comparable to our findings, in that the total doses of IV ephedrine for treating hypotension were significantly lower for the preeclamptic patients (3.2 ± 7.8 mg) than for the normotensive patients (7.5 ± 9.2 mg) ($P = 0.04$).

There is little evidence in the current literature supporting the use of phenylephrine as the vasopressor of choice in high-risk pregnancies such as those involving preeclampsia (19), so we chose to use ephedrine for treating hypotension in our patients. More studies are needed to investigate the effects of vasopressors while considering the influence on feto-maternal physiology in patients with preeclampsia.

The results of a review by Dyer et al. showed that after spinal anesthesia for cesarean section, patients with preeclampsia had a lower susceptibility to hypotension and less impairment of cardiac output than healthy parturients (20). In a prospective observational study on 15 parturients with severe preeclampsia, no clinically significant change in cardiac output was shown after the subarachnoid block (21). The focus of our study was on the blood pressure changes during spinal anesthesia in the preeclamptic patients, and therefore we did not measure the cardiac output fluctuations in our patients. Further studies with larger sample sizes evaluating cardiac output are needed for better understanding of hemodynamic changes during spinal anesthesia in this group of patients.

It is believed that the incidence of spinal anesthesia-induced hypotension is related to the local anesthetic dose, so one particular strategy to minimize the hemodynamic disruption after spinal anesthesia involves using small intrathecal local anesthetic doses. In a pilot study which compared the hemodynamic consequences of two doses of spinal bupivacaine (7.5 mg versus 10 mg) for cesarean delivery in those with severe preeclampsia, predelivery MAP was lower and the ephedrine requirements were greater in the 10 mg group (22). In another study, Roofthoof and Van de Velde have shown that when low-dose spinal anesthesia (6.5 mg bupivacaine) was administered with sufentanil as part of a combined spinal-epidural (CSE) technique in shorter surgeries (less than 60 minutes), the need for epidural supplementation was rare (23).

The ED95 of intrathecal bupivacaine coadministered with intrathecal 2.5 μg sufentanil using CSE anesthesia for cesarean section in severely preeclamptic patients was reported to be 8.82 mg in another study, and using smaller doses of intrathecal bupivacaine in the patients resulted in a decrease of incidences of maternal hypotension and vasopressor requirements (24). However, no studies have compared CSE with single-shot spinal anesthesia in severe preeclampsia, and further research is needed to elucidate the best strategy to optimize the hemodynamics and uteroplacental perfusion in this particular group of patients.

Considering the neonatal outcomes after various anesthesia techniques in cesarean delivery among preeclamptic patients, no statistically significant difference was found in the one- and five-minute Apgar scores and the umbilical artery blood gas markers between the two groups of patients receiving spinal or general anesthesia (25). Other studies in support of subarachnoid block have also shown that transient neonatal depression and birth asphyxia are more common among preeclamptic women who have received general anesthesia (26). Comparing umbilical arterial fetal base deficit and other markers of maternal and neonatal well-being in 70 preeclamptic patients undergoing cesarean delivery who were randomized into groups receiving either spinal or general anesthesia, the spinal group had a higher mean umbilical arterial base deficit and a lower median umbilical arterial pH, but other markers of a compromised neonatal condition, including the requirement for neonatal resuscitation, an Apgar score < 7, an umbilical arterial pH < 7.2, and the need for neonatal intermittent positive pressure ventilation were the same among the two groups (27). In comparison with healthy subjects, patients with severe preeclampsia had a younger gestational age (34 weeks versus 39 weeks) in our study, which is one of the likely causes of the lower one-minute Apgar scores of the neonates among the first group.

Although there was evidence as early as 1950 that preeclampsia attenuates spinal anesthesia-induced hypotension, it has taken a long time for clinical trials to demonstrate the safety of spinal and CSE anesthesia in preeclamptic parturients. Recently, after five decades of research, the relationship between spinal anesthesia, preeclampsia, and hypotension can be properly acknowledged and put into clinical practice (28). Because of an altered balance of vascular tone, reduced responses to endogenous pressors, and increased synthesis of vasodilator prostaglandins and nitric oxide, the normal pregnant patient is very sensitive to spinal anesthesia. These effects increase dependence on sympathetic vascular tone in normal pregnancy, and this can be the main cause of spinal anesthesia-induced hypotension in healthy parturients, while damaged vascular epithelium results in persistent vasoconstriction in preeclampsia (8, 16).

There is a dramatic increase in the use of spinal anes-

thesia for cesarean delivery in severe preeclampsia that could be related to the documented safety of subarachnoid block in this group of patients. Therefore, single-shot subarachnoid block may be a good choice for cesarean delivery in patients with severe preeclampsia, since it has been shown to be safe for both the mother and the neonate (28).

5.1. Conclusion

Our results have also confirmed that single-shot low-dose bupivacaine spinal anesthesia is associated with a lower risk of hypotension and vasopressor requirements in comparison to the rates of healthy subjects, and could be safely used in patients with severe preeclampsia undergoing cesarean delivery. However, more studies with the CSE technique using smaller doses of local anesthetics and larger sample sizes are suggested. Further research is needed to find the best strategies to optimize hemodynamics and uteroplacental perfusion in severely preeclamptic parturients during spinal anesthesia for cesarean delivery.

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Footnote

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