



COMPARISM BETWEEN THE EFFECTS OF SPINAL ANESTHESIA IN PATIENTS WITH PRE-ECLAMPSIA AND HEALTHY PATIENTS DURING CESAREAN SECTION

Dr. Duraid Jameel Kareem*, Dr. Khlood Ahmad Shihab and Dr. Raed Majeed Yaseen

¹C.A.B.M.S, Department of Anaesthesia and General Surgery, Baquba's Pain Management Center, Baqua Teaching Hospital, Diyala Health Directorate, Iraq.

^{2,3}Diploma in Anesthesia, Department of Anaesthesia and General Surgery, Baquba's Pain Management Center, Baqua Teaching Hospital, Diyala Health Directorate, Iraq.

***Corresponding author: Dr. Duraid Jameel Kareem**

C.A.B.M.S, Department of Anaesthesia and General Surgery, Baquba's Pain Management Center, Baqua Teaching Hospital, Diyala Health Directorate, Iraq.

Article Received on 03/06/2018

Article Revised on 24/06/2018

Article Accepted on 15/07/2018

ABSTRACT

Background: Spinal anesthesia is widely regarded as a reasonable anesthetic option for cesarean delivery in severe pre-eclampsia, provided there is no contraindication to neur-axial anesthesia, 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. In this review, we describe the advantages and limitations of spinal anesthesia in the setting of severe preeclampsia and the evidence guiding intraoperative hemodynamic management. **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: In our study we performed:** Spinal anesthesia with 7.5 mg (= 1.5 mL) hyperbaric 0.5% bupivacaine plus 25 µg fentanyl in two groups of patients after they received 500 mL of IV lactated Ringer's solution. At start, 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 < 100mm Hg in healthy parturients) and was treated with 5 mg IV ephedrine. We have been recorded the total amounts of intravenous administered fluid and the total doses of ephedrine for each patient as well. **Results:** For both groups, the incidence rate of hypotension among the pre-eclamptic patients was lower than that of the healthy parturients, despite the former group receiving smaller volumes of intravenous fluids (P< 0.05). Compared with healthy parturients, those with severe preeclampsia experience less frequent, less severe spinal-induced hypotension. However, this hypotension is typically easily treated and short lived, and no studies have demonstrated clinically significant differences in outcomes when spinal anesthesia is compared with epidural or general anesthesia. The total doses of IV ephedrine for treating hypotension were significantly lower among the pre-eclamptic patients (2.8mg in preeclamptic patients versus 7mg in normotensive patients) (P = 0.02), The one-minute Apgar score was significantly lower for the pre-eclamptic 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:** In my study, the 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 pre-eclamptic women undergoing cesarean delivery.

KEYWORDS: Preeclampsia, Anesthesia, Spinal, Cesarean Section, Hypotension.

1. BACKGROUND

It is well known that pregnancy-induced hypertension is a major cause of morbidity and mortality in obstetrics, complicating 2% -9% 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] 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 sub-arachnoid block would result in severe hypotension and compromise utero-placental 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

vasoconstrictor 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, suggesting that spinal anesthesia may in fact be an appropriate choice for pre-eclamptic 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 fentanyl in severely preeclamptic versus healthy parturients undergoing cesarean sections.

3. PATIENTS AND METHODS

After obtaining institutional ethics committee approval, 70 parturients (32 healthy and 38 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, 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 5 g loading dose of intravenous magnesium sulfate (Mg SO₄) followed by a 1 g/hour infusion for 24 hours for seizure prophylaxis. Intravenous hydralazine of 7 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 15 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 pre-eclamptic 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 7.5 mg hyperbaric 0.5% bupivacaine plus 25 - 30 µg fentanyl (2.5mL 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 5mg 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 29 patients per group were required to show a 25% difference in the incidence of hypotension. 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.

4. RESULTS

Seventy patients (severe preeclampsia=38 and healthy=32) were studied. All data used in the comparison 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 (Table 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 (52.6%) was less than that of the healthy parturients (87.5%) (Table 2), despite the former receiving smaller volumes of intravenous fluids (2.2 versus 2.3 lit) (Table 1). 2 Anesth Pain Med. 2016; 6(3):e11519.

Table 1: Maternal, Neonatal, and Anesthetic Considerations^a

Variable	Healthy	Preeclampsia
n	32	38
Age, y	28±4	29±6
Gestational (age.week)	37.8±1.4	33.9±3.7
Base line MAP	101.2±8.1	118.9±15.5
Spinal puncture to delivery interval, (minute)	17.1±2.6	17.2±2.4
Upper Sensory Level (Median, Range)	T4(T2-T5)	T4(T2-T5)
Ephedrine dose, mg	7.3-9.1	3.1-7.6
IV fluid, mL	2300 ± 0.1	2200 ± 0.2
APGAR score 5-min (Range)	9.4±0.7(7-10)	8.6±1.1,(5-10)
APGAR score 1-min (Range)	8.3±0.7,(5-10)	7.3±1.3,(3-10)

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 (3.1_7.6 mg versus 7.3_9.1 mg). *Anesth Pain Med.* 2016; 6(3):e11519.

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

Variable	Healthy	Preeclampsia
Incidence of MAP hypotension (%)	28(87.5%)	20(52.6%)
Lowest(SBP) mmHg	96±12.8	115±17.5
Lowest (MAP) mmHg	64.5±10.2	82.9±14.6
Lowest (DBP) mmHg	46.3±8.8	65.4±13.9

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] 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] 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 anesthesia seemed to be a safe option for patients with severe preeclampsia.^[2,18] we chose to use ephedrine for treating hypotension in our patients as there is little evidence in the current literature supporting the use of phenylephrine as the vasopressor of choice in high-risk pregnancies. Preeclamptic patients 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 (3.1_7.6 mg) than for

the normotensive patients (7.3_9.1 mg).^[19] More studies are needed to investigate the effects of vasopressors while considering. The influence on fetomaternal 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.

The focus of our study was on the blood pressure changes during spinal anesthesia in the preeclamptic patients, and 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 and showed that those patients had a lower susceptibility to hypotension and less impairment of cardiac output than healthy parturients.^[20]

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.^[21] 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.^[22]

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.^[23]

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 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.^[24]

In comparison with healthy subjects, patients with severe preeclampsia had a younger gestational age (32 weeks versus 37 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. 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 anesthesia 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] Spinal anesthesia affords quicker onset of anesthesia than epidural or CSE anesthesia, which is a critical advantage in emergency situations.

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. Further research is needed to find the best strategies to optimize hemodynamics and utero-placental perfusion in severely preeclamptic parturients during spinal anesthesia for cesarean delivery.

ACKNOWLEDGMENTS

We would like to thank our patients and the operating room staff of AL-batoul teaching hospital for their help.

REFERENCES

1. Flood P, Rollins MD. In: Anesthesia for obstetrics. 8th ed. Miller RD, editor. Philadelphia: Saunders, 2015; 2344–8.
2. Aya AG, Mangin R, Vialles N, Ferrer JM, Robert C, Ripart J, et al. Patients with severe preeclampsia experience less hypotension during spinal anesthesia

- for elective cesarean delivery than healthy parturients: a prospective cohort comparison. *Anesth Analg*, 2003; 97(3): 867–72. [PubMed: 12933418].
3. Pournajafian A, Rokhtabnak F, Kholdbarin A, Ghodrati M, Ghavam S. Comparison of remifentanyl and fentanyl regarding hemodynamic changes due to endotracheal intubation in preeclamptic parturient candidate for cesarean delivery. *Anesth Pain Med*, 2012; 2(2): 90–3. doi: 10.5812/aapm.6884. [PubMed: 24223345].
4. Chumpathong S, Sirithanetbhol S, Salakij B, Visalyaputra S, Parakkamodom S, Wataganara T. Maternal and neonatal outcomes in women with severe pre-eclampsia undergoing cesarean section: a 10-year retrospective study from a single tertiary care center: anesthetic point of view. *J Matern Fetal Neonatal Med*, 2016; 1–5. doi: 10.3109/14767058.2016.1159674. [PubMed: 26952582].
5. Santos AC, Birnbach DJ. Spinal anesthesia for cesarean delivery in severely preeclamptic women: don't throw out the baby with the bathwater! *Anesth Analg*, 2005; 101(3): 859–61. doi: 10.1213/01.ANE.0000175218.75396.82. [PubMed: 16116004].
6. Hood D, Curry RRN. Spinal versus Epidural Anesthesia for cesarean section in severely preeclamptic patients: A retrospective survey. *Anesthesiol*, 1999; 90(5): 1276–82.
7. Visalyaputra S, Rodanant O, Somboonviboon W, Tantivitayatan K, Thienthong S, Saengchote W. Spinal versus epidural anesthesia for cesarean delivery in severe preeclampsia: a prospective randomized, multicenter study. *Anesth Analg*, 2005; 101(3): 862–8. doi: 10.1213/01.ANE.0000160535.95678.34. [PubMed: 16116005] table of contents.
8. Saha D, Ghosh S, Bhattacharyya S, Mallik S, Pal R, Niyogi M, et al. Comparison of hemodynamic response and vasopressor requirement following spinal anaesthesia between normotensive and severe preeclamptic women undergoing caesarean section: A prospective study. *J Obstet Anaesth Critical Care*, 2013; 3(1): 23.
9. Alimian M, Mohseni M, Safaeian R, Faiz SH, Majedi MA. Comparison of hydroxyethyl starch 6% and crystalloids for preloading in elective caesarean section under spinal anesthesia. *Med Arch*, 2014; 68(4): 279–81. doi: 10.5455/medarh.2014.68.279-281. [PubMed: 25568553].
10. Fathi M, Imani F, Joudi M, Goodarzi V. Comparison Between the Effects of Ringer's Lactate and Hydroxyethyl Starch on Hemodynamic Parameters After Spinal Anesthesia: A Randomized Clinical Trial. *Anesth Pain Med*, 2013; 2(3): 127–33. doi: 10.5812/aapm.7850. [PubMed: 24244923].
11. Hood DD, Boese PA. Epidural and Spinal Anesthesia for Elective Cesarean Section in Severely Pre-Eclamptic Parturients. *Reg Anesth*, 1992; 17(1): 35.

12. Van de Velde M, Berends N, Spitz B, Teunkens A, Vandermeersch E. Lowdose combined spinal-epidural anaesthesia vs. conventional epidural anaesthesia for Caesarean section in pre-eclampsia: a retrospective analysis. *Eur J Anaesthesiol*, 2004; 21(6): 454–9. [PubMed: 15248625].
13. Berends N, Teunkens A, Vandermeersch E, Van de Velde M. A randomized trial comparing low-dose combined spinal-epidural anesthesia and conventional epidural anesthesia for cesarean section in severe preeclampsia. *Acta Anaesthesiol Belg*, 2005; 56(2): 155–62. [PubMed: 16013660].
14. Chaudhary S, Salhotra R. Subarachnoid block for caesarean section in severe preeclampsia. *J Anaesthesiol Clin Pharmacol*, 2011; 27(2): 169–73. doi: 10.4103/0970-9185.81821. [PubMed: 21772674].
15. Aya AG, Vialles N, Tanoubi I, Mangin R, Ferrer JM, Robert C, et al. Spinal anesthesia-induced hypotension: a risk comparison between patients with severe preeclampsia and healthy women undergoing preterm cesarean delivery. *Anesth Analg*, 2005; 101(3): 869–75. doi: 10.1213/01.ANE.0000175229.98493.2B. [PubMed: 16116006] table of contents.
16. Sharwood-Smith G, Drummond GB. Hypotension in obstetric spinal anaesthesia: a lesson from pre-eclampsia. *Br J Anaesth*, 2009; 102(3): 291–4. doi: 10.1093/bja/aep003. [PubMed: 19218369].
17. Mendes FF, Hennemann G, Luft A, Farias C, Braga S. Hemodynamic effects of spinal anesthesia for cesarean section are equivalent in severely preeclamptic and healthy parturients. *J Anesthe Clinic Re*, 2012; 2011.
1. Clark VA, Sharwood-Smith GH, Stewart AV. Ephedrine requirements are reduced during spinal anaesthesia for caesarean section in preeclampsia. *Int J Obstet Anesth*, 2005; 14(1): 9–13. doi:10.1016/j.ijoa.2004.08.002. [PubMed: 15627532].
18. Nag DS, Samaddar DP, Chatterjee A, Kumar H, Dembla A. Vasopressors in obstetric anesthesia: A current perspective. *World J Clin Cases*, 2015; 3(1): 58–64. doi:10.12998/wjcc.v3.i1.58. [PubMed: 25610851].
19. Dyer RA, Piercy JL, Reed AR. The role of the anaesthetist in the management of the pre-eclamptic patient. *Curr Opin Anaesthesiol*, 2007; 20(3): 168–74. doi:10.1097/ACO.0b013e328136c1ac. [PubMed: 17479015].
20. Jain K, Makkar JK, Yadanappudi S, Anbarasan I, Gander S. Two doses of spinal bupivacaine for caesarean delivery in severe preeclampsia: a pilot study. *Int J Obstet Anesth*, 2012; 21(2): 195–6. doi: 10.1016/j.ijoa.2011.12.010. [PubMed: 22341891].
21. Moslemi F, Rasooli S. Comparison of spinal versus general anaesthesia for caesarean delivery in patients with severe preeclampsia. *J Med Sci*, 2007; 7: 1044–8.
22. Ajuzieogu OV, Ezike HA, Amucheazi AO, Enwereji J. A retrospective study of the outcome of cesarean section for women with severe preeclampsia in a third world setting. *Saudi J Anaesth*, 2011; 5(1): 15–8. doi: 10.4103/1658-354X.76480. [PubMed: 21655010].
23. Dyer RA, Els I, Farbas J, Torr GJ, Schoeman LK, James MF. Prospective, randomized trial comparing general with spinal anesthesia for cesarean delivery in preeclamptic patients with a nonreassuring fetal heart trace. *Anesthesiology*, 2003; 99(3): 561–9.