

# Hemodynamic Effects of Spinal Anesthesia for Cesarean Section are Equivalent in Severely Preeclamptic and Healthy Parturients

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## Introduction

The optimal anesthetic technique for cesarean delivery in severely preeclamptic women remains controversial [1]. Given that failure to vasodilate is a common factor in preeclampsia, neuraxial blockade during labor and delivery appears to be a logical choice. Even though some authors still recommend epidural anesthesia as the method of choice in patients with severe preeclampsia [2], recent studies suggest that spinal anesthesia is also safe in these patients [3-7].

Of notice, studies comparing the hemodynamic response of severely preeclamptic patients to that of healthy parturients undergoing spinal anesthesia for cesarean section have suggested that hypotension is in fact less common in the former group, further opposing earlier assumptions [3,4]. However none of these studies followed standardized protocols for hypertension management and spinal anesthesia.

Therefore, the present study was carried out in an effort to compare the hemodynamic changes and newborn well-being in patients with severe preeclampsia and healthy parturients undergoing spinal anesthesia for cesarean section. Our hypothesis is that patients severely preeclamptic submitted to spinal anesthesia for cesarean sections have that the same degree of hypotension that healthy patients present.

## Patients and Methods

After approval by the Institutional Review Board, severely preeclamptic and healthy parturients scheduled to have elective cesarean delivery under regional anesthesia were studied during the 1-yr period from November, 2008 to December, 2009. The severely preeclamptic group (PE) was comprised by patients with systolic arterial blood pressure (SBP)  $\geq 160$  mmHg or diastolic arterial blood pressure (DBP)  $\geq 110$  mmHg and proteinuria  $\geq 100$  mg/dL. Patients with coagulopathy, abruptio placentae, placenta previa, HELLP syndrome, pulmonary oedema, cord prolapse and severe fetal distress were excluded from the study.

To be considered eligible patients had to meet all of the following inclusion criteria: singleton pregnancy, semi-elective or elective cesarean section, absence of labor (because labor can decrease the incidence of hypotension related to neuraxial anesthesia [1], absence of any coexisting co-morbid such as diabetes or renal impairment, no contraindication to neuraxial anesthesia and negative history of allergies to local anesthetics or morphine.

The following healthy parturient (HP group) scheduled for elective cesarean section was selected after each PE was enrolled. Exclusion criteria for the HP group were: previous hypertension, cardiac disease, renal disease and thrombocytopenia ( $<100.000$  platelets/mm<sup>3</sup>).

The PE group received a 4 g loading dose of intravenous magnesium sulfate (MgSO<sub>4</sub>) followed by 1g/h for 24hrs for seizure prophylaxis. Intravenous hydralazine 5mg was given at 20-min intervals to decrease DBP to approximately 90 mmHg. The interval between the administration of the last dose of magnesium sulfate and the start of cesarean section was at least 60 minutes.

Preoperative fluid administration, which was limited to 500 mL of Ringer's lactate solution, was given upon arrival in the operating room, over 20 minutes. All patients received supplemental oxygen at 5 L/min by facemask. The patients were monitored with standard devices including automated blood pressure cuff, electrocardiogram, and pulse oximetry. Spinal anesthesia was performed with patients seated, with a 27-gauge Quincke spinal needle, via midline approach between L2-L3 or L3-L4 interspinous spaces. After observing the flow of cerebrospinal fluid, 2.2 mL of 0.5% hyperbaric bupivacaine with 0.1 mg of preservative-free morphine was injected into the subarachnoid space. The patient was then put in a supine position with left uterine displacement with a modified Crawford wedge under the right flank. After the injection of the anesthetic, all patients received IV Ringer's lactate solution at 100 mL/h<sup>8</sup>.

Arterial blood pressure assessment was started before performing the spinal anesthesia and was carried out every 2 minutes. Arterial hypotension was defined as a 30% or greater decrease from baseline systolic blood pressure, and was treated with ephedrine 5mg IV bolus every 2 minutes until blood pressure was restored. Ephedrine use and total dose were recorded for each patient. Newborn APGAR scores were assigned by neonatologists not participating in the study. Gestational age was determined by means of early prenatal ultrasonography.

Data are presented as mean (SD), median or number (percentage) as appropriate. X<sup>2</sup> test or Fisher's exact test was used for qualitative variables, the ANOVA test was used for analysis of the time course study of blood pressure over the study period and unpaired Student's t-test for intragroup and intergroup comparisons, or its non-parametric equivalent, was used for quantitative variables. Type I error was set at 0.05 without adjustment for multiple hypothesis testing because these comparisons over time were only for the purpose of exploratory analysis. Sample size to identify a difference between groups of at least 10% in the mean drop of systolic pressure, at a standard deviation of 12% in each group, was calculated as at least 16 patients per group for a type I error (alpha) of 5% and a type II error (beta) of 10%.

All statistical data analysis was performed using SPSS version 11.5 (SPSS, Chicago, IL).

## Results

Overall, 40 patients were included in the study, 20 in the PE and

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20 HP group. One patient was excluded from the PE group due to protocol violation. Demographic maternal and neonatal characteristics are depicted in Table 1. Patients in the PE group had higher mean body weight ( $P = 0.04$ ), lower gestational age ( $P = 0.003$ ) and their newborns had lower birth weights ( $P = 0.006$ ; Table 1).

Table 2 presents the data on hemodynamic parameters and vasopressor use. There was no statistically significant difference between the 2 groups regarding the occurrence of hypotension, ephedrine use or total ephedrine dose. The mean drop in systolic blood pressure was 27.5% in the PE group and 24.2% in the HP group ( $P = 0.21$ ). Diastolic blood pressure decreased by 33.1% and 35.9% in the PE and HP groups, respectively ( $P = 0.31$ ; Table 2).

	Severe Preeclampsia	Healthy Parturients	P
Age (years)	24.8 ± 5.8	25.2 ± 6.2	0.83 #
Body weight (kg)	79.1 ± 15.7	69.4 ± 12.3	0.04 #
Height (cm)	160.2 ± 5.6	157.1 ± 7.5	0.15 #
Number of pregnancies	2.26 ± 1.59	2.95 ± 1.95	0.23 #
Gestational age (weeks)	35.9 ± 2.9	38.6 ± 2.3	0.003 #
Newborn birth weight (g)	2596 ± 733	3182 ± 511	0.006 #
1-minute APGAR	7.79 ± 1.13	8.25 ± 1.0	0.20 *
5-minute APGAR	8.79 ± 0.85	9.20 ± 0.76	0.12 *

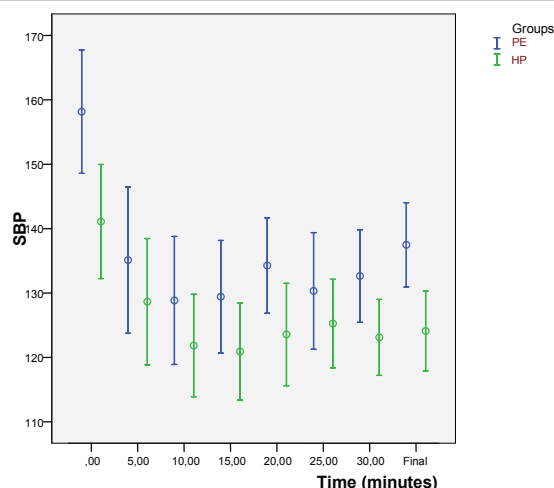
# Data are mean ± SD, \* median (range). Unpaired Student's t-test; Mann-Whitney U-test; Chi-square test, Fisher's exact test.

**Table 1:** Demographic Maternal and Neonatal Characteristics.

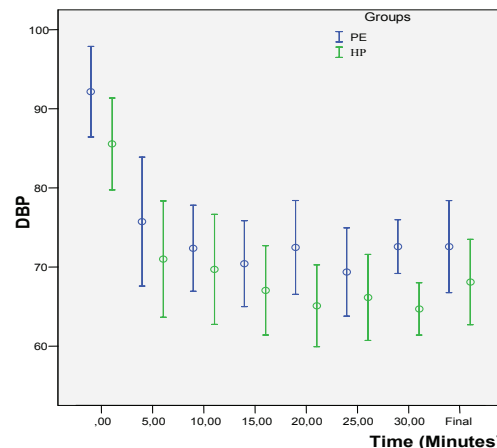
	Severe Preeclamptic	Healthy Parturients	P
Baseline SBP (mmHg)	158.2 ± 19.9	141.1 ± 18.9	0.009 #
Lowest SBP (mmHg)	114.1 ± 18.4	107.6 ± 16.7	0.25 #
SBP decrease (%)	-27.6 ± 10.3	-24.2 ± 12.4	0.21 #
Baseline DBP (mmHg)	92.2 ± 11.9	85.5 ± 12.4	0.09 #
Lowest DBP (mmHg)	61.2 ± 11.4	54.2 ± 10.1	0.047 #
Mean total ephedrine dose (mg)	11.0 ± 9.5	12.2 ± 11.4	0.83 #
Hypotension, n (%)	16 (84%)	14 (70%)	0.45 *

Data are mean ± SD, \* n (%). Unpaired Student's t-test; Mann-Whitney U-test; Chi-square test, Fisher's exact test. SBP = systolic blood pressure; DBP = diastolic blood pressure.

**Table 2.** Hemodynamic Parameters and Vasopressor Use.



**Figure 1:** Systolic blood pressure variations. Mean (95% CI). SBP – Systolic blood pressure. PE = severe preeclampsia; HP = healthy parturients.



**Figure 2:** Diastolic blood pressure variations. Mean (95% CI). DBP – Diastolic blood pressure. PE = severe preeclampsia; HP = healthy parturients.

Mean SBP was significantly higher in the PE group at baseline, 20 minutes, 30 minutes, and at the end of the procedure (Figure 1). The PE group also exhibited higher mean DBP at baseline, 30 minutes, and at the end of cesarean section (Figure 2).

There were no difference between APGAR indices in 1 and 5 minutes.

## Discussion

The present study evaluated the hemodynamic response of patients with severe preeclampsia submitted to spinal anesthesia for cesarean section to that of healthy parturients. There was no significant difference between these two groups regarding the occurrence of hypotension, decrease of blood pressure, vasopressor use, mean total vasopressor dose or newborn well-being. Severely preeclamptic patients showed significantly higher systolic and diastolic blood pressures before, throughout and at the end of cesarean section.

Upon comparing the hemodynamic effects of spinal anesthesia in severely preeclamptic and term healthy parturients, Aya et al. [3] found that the incidence of clinically significant hypotension was 6-fold smaller in severely preeclamptic patients. However, hypertension treatment, fluid administration and anesthetic dose used were not standardized in their study, which may significantly alter the hemodynamic response related to the neuraxial blockade, making proper interpretation of the data very difficult.

In spite of the methodological shortcomings two hypotheses emerged to explain the findings by Aya et al. firstly, preeclampsia-associated factors could be implicated. Secondly, provided that the healthy parturients in such study had more advanced gestational age and their newborn's body weight was significantly higher, the possibility that a lesser degree of aortocaval compression had been responsible for the smaller frequency of hypotension in the severe preeclampsia group was also considered [9].

In order to elucidate whether severe preeclampsia intrinsically affected the hemodynamic response to spinal anesthesia the same group compared severe preeclamptics to preterm women with comparable newborn weight who were also being submitted to spinal anesthesia for cesarean section [4]. Hypotension was half as common in preeclamptic

patients, which supports the existence of preeclampsia-associated factors. On the other hand, while preeclamptic patients required less ephedrine than women in the preterm group to restore blood pressure to baseline levels, the magnitude of the decrease in systolic, diastolic, and mean arterial blood pressure was similar between groups. Importantly, the latter study also lacked standardization of methodology and, therefore, the aforementioned caveats are again applicable.

Even though the studies by Aya et al. are concordantly attesting for the safety of spinal anesthesia in severely preeclamptic patients divergent results were found with regard to the difference in incidence of hypotension and BP change between preeclamptic and healthy patients. We believe that the dissimilar patient samples and particularly the lack of standardization of hypertension management and anesthetic protocol in their studies accounts for such.

Upon considering that both groups exhibited similar hemodynamic responses it must be taken into account that the severe preeclampsia group had received magnesium sulfate and hydralazine, and could, therefore, be expected to exhibit greater decreases in blood pressure. The absence of such effect can be regarded as additional evidence to the existence of an intrinsic role of preeclampsia in decreasing the occurrence of hypotension.

Adding further evidence to the safety of spinal anesthesia, Dyer et al., using lithium dilution cardiac output monitoring in severely preeclamptic patients, showed that neither spinal anesthesia nor treatment of hypotension with modest doses of phenylephrine reduces maternal cardiac output during caesarean section, further supporting the safety of neuraxial blockade in this patient population [6].

Regarding fetal well-being, it had been theorized that the sympathectomy attributable to spinal anesthesia could significantly decrease uteroplacental blood flow in preeclampsia and, thereafter, lead to worse neonatal outcomes. Conversely, several studies supporting the safety of spinal anesthesia in these patients have been published, and neuraxial anesthesia for labor pain relief has even been shown to increase placental blood flow in patients with severe preeclampsia [10]. While epidural anesthesia may in fact provide modestly superior hemodynamic stability, due to the more gradual onset of sympathectomy, there seems to be no differences between the two techniques in neonatal outcome [8]. Even though uteroplacental perfusion was not directly assessed, the present study shows that the Apgar score, a clinical marker of uteroplacental blood flow, is similar in severely preeclamptic and healthy parturients submitted to spinal anesthesia for cesarean section. This important finding agrees with the current literature in attesting the neonatal safety of spinal anesthesia in severe preeclampsia.

The present study is not without limitations. Its small sample size and lack of direct measurements of cardiac output or uteroplacental blood flow should be noted. On the other hand, a few strengths distinguish it from previous efforts. We were able to prospectively evaluate not only patients' hemodynamic response but also newborn well-being in consecutive patients subjected to a standardized anesthetic protocol.

In conclusion, the hemodynamic changes and newborn well-being appear to be comparable in severely preeclamptic and healthy parturients submitted to spinal anesthesia for cesarean section. While the exact pathophysiologic mechanisms involved are yet to be determined and further, larger studies are necessary before irrevocable conclusions can be drawn, spinal anesthesia seems to be a safe option for patients with severe preeclampsia undergoing cesarean section.

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