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CLINICAL TRIAL REPORT

Norepinephrine or Phenylephrine to Prevent Spinal Anesthesia-Induced Hypotension During Cesarean Section: A Double-Blinded, Randomized, Controlled Study of Fetal Cerebral Perfusion

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Purpose: Spinal anesthesia-induced hypotension can cause detrimental effects on both the mother and the fetus, and it remains a significant concern in obstetric anesthesia. The use of vasopressors is considered the most reliable and effective approach. Previous studies have shown that norepinephrine appears to be superior to phenylephrine in maintaining maternal heart rate and cardiac output. Therefore, we hypothesize that norepinephrine is more effective than phenylephrine in maintaining neonatal cerebral perfusion when used to prevent spinal anesthesia-induced hypotension.

Patients and Methods: This study is a prospective, double-blinded, randomized trial. We enrolled 216 singleton parturients who were scheduled for elective cesarean delivery. The patients received a prophylactic intravenous infusion of either norepinephrine (0.08 μg/kg/min) or phenylephrine (0.5 μg/kg/min). Maternal cardiac output was not routinely monitored during the study period. Fetal ultrasound examinations were performed, with blood velocity measured in the middle cerebral artery and umbilical artery, and the cerebroplacental ratio calculated.

Results: Ninety subjects were ultimately analyzed in each group. The changes in blood velocity in the middle cerebral artery and umbilical artery, as well as the calculated cerebroplacental ratio at 3 and 6 minutes after spinal anesthesia, did not differ significantly between the two groups. The estimated difference of ΔCPR in two groups was - 0.01 (95% CI, −0.05–0.02, P = 0.491) at 3 minutes and was 0.02 (95% CI, −0.01–0.07, P = 0.204) at 6 minutes.

Conclusion: Prophylactic infusion of norepinephrine or phenylephrine at comparable doses has similar effects on fetal cerebral perfusion.

Keywords: norepinephrine, phenylephrine, hypotension, fetal cerebral perfusion

Introduction

Spinal anesthesia-induced hypotension (SAIH) during cesarean delivery can result in a series of detrimental effects on both maternal and neonatal outcomes.[1,2] The prevention and management of this complication remain a major challenge in obstetric anesthesia. Among various strategies, vasopressors administration is considered the most reliable and effective approach for managing SAIH.[3,4] Although phenylephrine is widely used in obstetric anesthesia, its effects on maternal heart rate (HR) and cardiac output (CO) have raised concerns.[5] Norepinephrine, a potent α-adrenergic receptor

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agonist with additional β-adrenergic receptor activity, mitigates bradycardia and better maintains CO, making it a promising alternative to phenylephrine.[2,6]

Previous studies on the prevention of SAIH during cesarean delivery have primarily focused on maternal hemodynamic parameters.[7,8] In recent years, increasing attention has been directed toward neonatal outcomes.[9,10] Umbilical artery pH (UA-pH) is commonly used as an objective measure for assessing neonatal outcomes.[10,11] However, UA-pH cannot provide a comprehensive assessment of fetal hemodynamics, particularly fetal cerebral perfusion, which critically influences cerebral oxygen supply and long-term neurodevelopment. Fetal cerebral perfusion is influenced by multiple factors, including gestational age, maternal comorbidities, fetal vascular resistance, fetal intrinsic autoregulatory mechanisms, fetal cerebral protective effects. In this study, fetal cerebral perfusion was assessed by measuring the blood velocity in the middle cerebral artery (MCA) and umbilical artery (UA), along with calculating the cerebroplacental ratio (CPR), using standardized ultrasound measurements in healthy singleton pregnancies. These ultrasound-derived indicators are recognized as critical predictors of adverse pregnancy outcomes,[12,13] demonstrating high sensitivity and accuracy in detecting fetal hypoxia.[14] And to clarify, the CPR offers a more comprehensive and reliable assessment of fetal well-being compared to the isolated evaluation of UA pulsation index (PI) or MCA PI. By integrating these measurements, CPR effectively eliminates common external confounding factors, minimizes measurement errors, and provides a more realistic and objective evaluation of fetal intrauterine conditions. Particularly in compromised pregnancies where fetal hypoxia is present, the study drug effects on cerebral hemodynamics may assume greater clinical significance.

The aim of this prospective, randomized, double-blind study was to compare the effects of prophylactic norepinephrine versus phenylephrine infusion on fetal cerebral perfusion during spinal anesthesia for cesarean delivery, assessed noninvasively using Doppler ultrasound. Based on previous studies demonstrating norepinephrine's superior ability to maintain maternal cardiac output,[2,6] we hypothesized that norepinephrine is more effective than phenylephrine in maintaining fetal cerebral perfusion during the management of maternal SAIH.

Material and Methods

Study Design and Patient Enrollment

This randomized, double-blinded clinical trial was conducted at the Women's Hospital, School of Medicine, Zhejiang University. The study was registered at the Chinese Clinical Trial Registry (www.chictr.org.cn; registration no. ChiCTR2300077137; registration date: October 31, 2023) and approval for the study was obtained from the Institutional Clinical Research Ethical Review Board (IRB-20230290-R).

We enrolled singleton pregnant women aged 18–40 years scheduled for elective cesarean delivery under combined spinal-epidural anesthesia. All participants were informed of the purpose of the study and gave their written informed consent. Exclusion criteria included: (1) failure or refusal to provide informed consent; (2) contraindications to norepinephrine or phenylephrine use; (3) allergy to ropivacaine; (4) fetal abnormalities; (5) obesity (body mass index > 35kg/m2); (6) obstetric complications, such as hypertension, preeclampsia, cardiovascular disease; (7) preterm rupture of the membranes; (8) contraindications to neuraxial anesthesia; and (9) participation in other clinical studies.

Randomization and Blinding

Before starting the study, a computer-generated random number sequence for 200 codes was created using SPSS software, version 23.0 (IBM Corp), with a block size of 4 to randomize subjects into two equal-sized groups. The random number codes were placed into the sealed, opaque, sequentially numbered envelopes by a research assistant not involved in patient management or data collection. Meanwhile, the research assistant was responsible for preparing the study drugs. Besides, all other members of the study team were blinded to the group allocation.

Anesthesia Management

Upon arrival in the operating room, the standard monitoring was applied using the Detax Ohmeda S/5 monitor, including noninvasive blood pressure (BP), pulse oximetry, and electrocardiography. The baseline BP was determined by averaging three consecutive readings taken at 1-minute intervals, with a difference of less than 10% between readings. The baseline

values of the ratio of systolic to end-diastolic blood velocity (S/D), the resistance index (RI) and the PI for MCA and UA were measured by the same sonographer using the same ultrasound device and standardized measurement protocol at the bedside before anesthesia. All baseline measurements were obtained in the supine position.

The patient was placed in the left lateral position. Combined spinal-epidural anesthesia was initiated in the L3-4 intervertebral space using the needle-through-needle technique. The 18-gauge epidural needle was advanced into the epidural space, and then a 27-gauge spinal needle was used in the same intervertebral space through the epidural needle to penetrate the dura mater. After confirming the free flow of cerebrospinal fluid, a total of 3 mL (15 mg) hyperbaric ropivacaine (1.5 mL ropivacaine 1% +1 mL glucose 10% +0.5 mL normal saline) was injected into the subarachnoid space at a rate of 1 mL/10 s. Subsequently, an epidural catheter was inserted 3–4 cm in the epidural space. If cerebrospinal fluid outflow was absent or inadequate, epidural anesthesia was performed only, and such cases were excluded from the study. Next, the patient was returned to the supine position and given oxygen at a rate of 5 L/min via a face mask.

During the period from intrathecal injection to fetal delivery, maternal BP, SpO2 and HR were monitored once every 1 minute, and the rest of the study time were measured once every 3 minutes. Meanwhile, a rapid crystalloid co-load (10 mL/kg of lactated Ringer's solution) was administered using gravity to achieve the maximal possible flow rate. Simultaneously with intrathecal injection, we commenced continuous intravenous infusion of the study drug via a standardized 50 mL syringe pump. The infusion rate was maintained at 0.01 mL/kg/min, corresponding to 0.08 μg/kg/min for norepinephrine or 0.5 μg/kg/min for phenylephrine.

Fetal ultrasound examination was conducted at the bedside by the sonographer at 3 and 6 minutes after intrathecal injection. Following this, an 18-gauge epidural needle core was utilized to confirm the sensory levels. The surgical procedure was initiated only after the sensory level had reached the T6 level. After delivery, UA and umbilical vein (UV) blood were collected for blood gas analysis. Additionally, Apgar scores at 1 and 5 minutes were also recorded.

Hypotension was defined as systolic blood pressure (SBP) $\leq$ 80% of the baseline value or SBP $\leq$ 90 mmHg. Hypertension was defined as SBP $\geq$ 120% of the baseline value. Bradycardia was defined as HR < 50 beats/min. Adverse outcomes during the study period were actively managed. When hypotension occurred in the absence of bradycardia, intravenous injection of 1 mL of the study drug was administered. When hypertension occurred, the study drug infusion was discontinued and restarted when the SBP returned to < 120% of the baseline value. If bradycardia occurred accompanied by hypotension, a single bolus of 6 mg ephedrine was injected intravenously. If bradycardia occurred only, the study drug infusion was discontinued until the HR $\geq$ 50 beats/min. And if bradycardia persisted for 2 minutes without recovery, a single bolus of 0.5 mg atropine was injected intravenously.

Data Collection and Outcome Assessment

The demographic data and obstetric characteristics were collected. The primary outcomes were the blood velocity of the MCA and UA at 3 and 6 minutes after spinal anesthesia, as well as the calculated CPR. Secondary outcomes included maternal adverse outcomes, such as hypotension, bradycardia, hypertension, nausea and vomiting, as well as neonatal outcomes, including blood gas analysis of neonatal UA and UV, Apgar scores at 1 and 5 minutes and the neonatal ward admission. Additionally, the sensory block level, total volume of vasopressor given at delivery, total fluid intake before delivery and intervals from spinal drug administration to neonatal delivery were also recorded.

Statistical Analysis

Sample size was calculated using PASS 6.0 (NCSS, LLC, Kaysville, UT, USA). Because of the lack of comparative studies on the effects of norepinephrine and phenylephrine for prevention of hypotension induced by spinal anaesthesia on fetal cerebral perfusion, we calculated the sample size based on the changes in maternal cardiac output in a previous study. The study demonstrated that the changes in maternal cardiac output were 102.7% and 93.8% in parturients who received norepinephrine and phenylephrine, respectively, for the prevention of hypotension.[15] Based on this, we estimated that a sample size of 88 patients per group with an alpha error of 0.05 would provide 90% power. Considering a 20% dropout rate, the sample size was increased to 100 per group.

Data analysis was performed using SPSS software, version 23.0 (IBM Corp) (Supplementary Material 1). The normality test of the data was conducted first using the Shapiro–Wilk (SW) test. Nonnormally distributed data were analyzed with the Mann–Whitney *U*-test and presented as the median (interquartile range). Normally distributed data were analyzed with Student's *t*-test and presented as the mean ± standard deviation. Categorical data were analyzed using the chi-square test and presented as the number (%).

Results

The subject recruitment diagram is shown in Figure 1. We recruited a total of 216 patients, and ultimately, a total of 180 parturients completed the study and were available for final statistical analysis, with 90 parturients in norepinephrine group (Group NE) and 90 in phenylephrine group (Group PE). The subject characteristics are shown in Table 1. The demographic data and obstetric characteristics were similar among groups, indicating that the baseline characteristics of the two groups are balanced.

The primary outcomes are presented in Table 2 and the CPR trends are presented in Figure 2. The baseline values of CPR, which are calculated as the ratio of MCAPI/UAPI, as well as the values of CPR at 3 and 6 minutes after spinal anesthesia are comparable between the two groups. The changes in CPR at 3 and 6 minutes after spinal anesthesia were comparable between the two groups. The estimated difference of ΔCPR in two groups was - 0.01 (95% CI, −0.05–0.02, P = 0.491) at 3 minutes and was 0.02 (95% CI, −0.01–0.07, P = 0.204) at 6 minutes. Additionally, the blood velocity of the MCA and UA were similar between the groups.

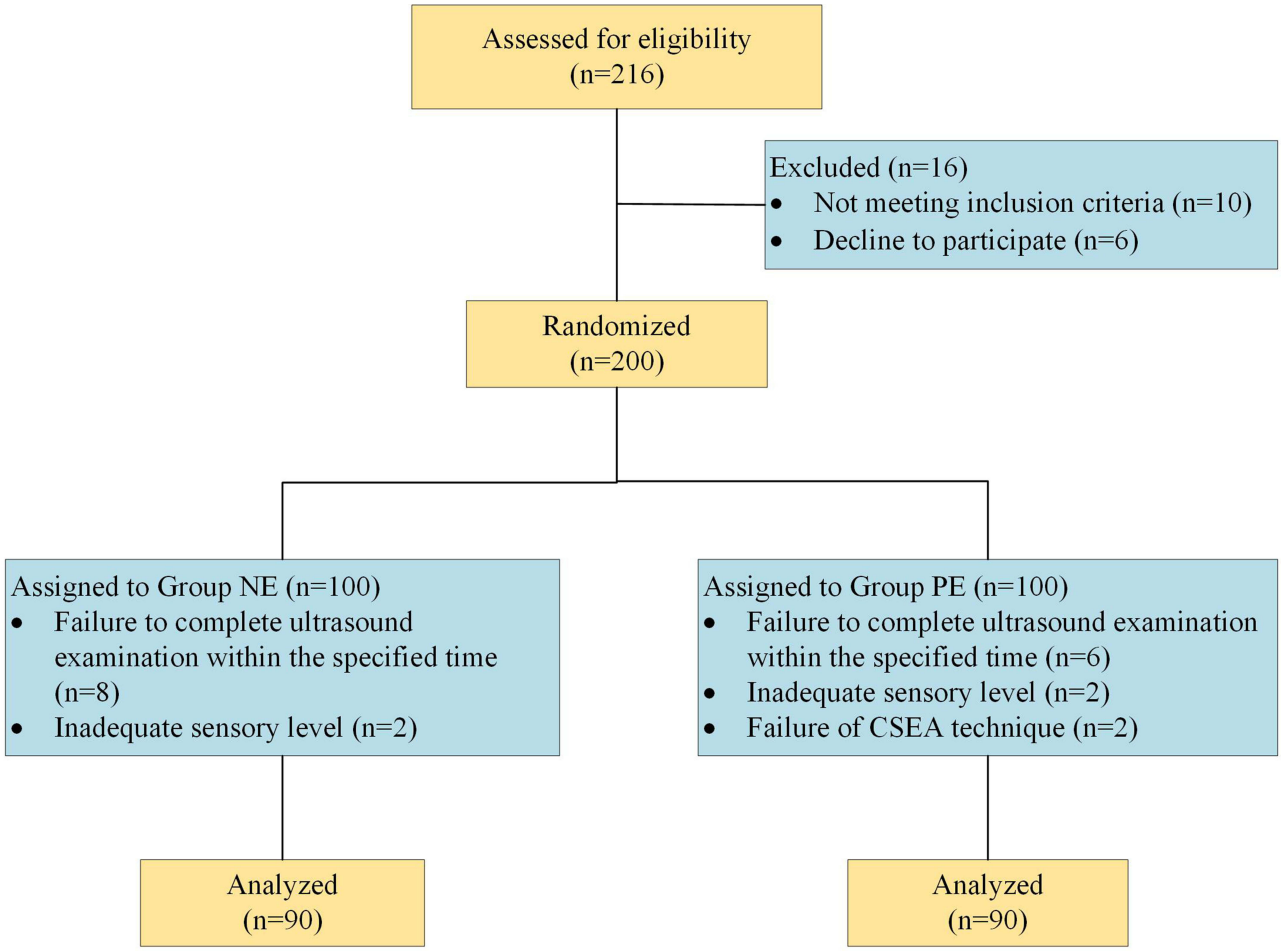

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flowchart showing patient recruitment.

Table 1 Demographic and Obstetric Characteristics

	Group NE (n = 90)	Group PE (n = 90)	P-Value
Age (years)	32 ± 4	33 ± 4	0.586
Height (cm)	160 (7.0)	160 (5.5)	0.069
Weight (kg)	68.17 ± 8.62	70.15 ± 8.54	0.125
Gestation (weeks)	38 (1)	38 (1)	0.462
Gravidity	2 (2)	2 (2)	0.846
Parity	0 (1)	1 (1)	0.571
Previous cesareans	0 (1)	0 (1)	0.925

Notes: Data are presented as mean ± standard deviation or median (interquartile range) for continuous variables.
Abbreviations: NE, norepinephrine; PE, phenylephrine.

Table 2 Outcome of MCA and UA Blood Flow

	Group NE (n = 90)	Group PE (n = 90)	Estimated Difference, (95% CI)	*P*-Value
CPR				
Baseline	1.84 (0.22)	1.85 (0.17)	−0.01 (−0.05, 0.04)	0.706
3min after subarachnoid block	1.80 (0.18)	1.82 (0.17)	0.00 (−0.04, 0.05)	0.870
6min after subarachnoid block	1.78 (0.20)	1.77 (0.20)	0.02 (−0.02, 0.06)	0.399
ΔCPR at 3min	0.01 (0.18)	0.01 (0.10)	−0.01 (−0.05, 0.02)	0.491
ΔCPR at 6min	−0.19 (0.17)	−0.03 (0.16)	0.02 (−0.01, 0.07)	0.204
MCA-S/D				
Baseline	4.16 (0.73)	4.17 (0.86)	0.00 (−0.08, 0.12)	0.999
3min after subarachnoid block	4.26 (0.85)	4.22 (1.09)	0.00 (−0.13, 0.18)	0.933
6min after subarachnoid block	4.26 (0.90)	4.25 (1.18)	−0.01 (−0.17, 0.18)	0.882
MCA-RI				
Baseline	0.74 (0.09)	0.73 (0.09)	0.00 (−0.03, 0.02)	0.721
3min after subarachnoid block	0.75 (0.14)	0.75 (0.14)	0.00 (−0.02, 0.03)	0.936
6min after subarachnoid block	0.75 (0.14)	0.75 (0.14)	0.00 (−0.02, 0.02)	0.932
MCA-PI				
Baseline	1.39 (0.16)	1.42 (0.16)	−0.03 (−0.07, 0.01)	0.177
3min after subarachnoid block	1.38 (0.14)	1.39 (0.17)	−0.03 (−0.07, 0.01)	0.169
6min after subarachnoid block	1.38 (0.16)	1.38 (0.16)	−0.01 (−0.04, 0.02)	0.543
UA-S/D				
Baseline	2.18 (1.04)	2.17 (1.05)	−0.01 (−0.17, 0.10)	0.762
3min after subarachnoid block	2.28 (0.92)	2.26 (1.10)	0.01 (−0.13, 0.15)	0.825

(*Continued*)

Table 2 (Continued).

	Group NE (n = 90)	Group PE (n = 90)	Estimated Difference, (95% CI)	*P*-Value
6min after subarachnoid block	2.35 (0.96)	2.31 (1.01)	0.04 (−0.10, 0.20)	0.518
UA-RI				
Baseline	0.55 (0.14)	0.55 (0.12)	0.00 (−0.03, 0.03)	0.835
3min after subarachnoid block	0.58 (0.11)	0.56 (0.13)	0.00 (−0.02, 0.03)	0.697
6min after subarachnoid block	0.58 (0.13)	0.58 (0.12)	−0.01 (−0.03, 0.02)	0.462
UA-PI				
Baseline	0.76 (0.12)	0.78 (0.11)	−0.01 (−0.03, 0.02)	0.520
3min after subarachnoid block	0.78 (0.08)	0.79 (0.09)	−0.01 (−0.04, 0.01)	0.199
6min after subarachnoid block	0.79 (0.09)	0.81 (0.09)	−0.01 (−0.04, 0.00)	0.171

Notes: Data are presented as median (interquartile range) for continuous variables. The 95% CI was calculated using the Hodges-Lehmann method.
Abbreviations: NE, norepinephrine; PE, phenylephrine; MCA, middle cerebral artery; UA, umbilical artery; CPR, cerebroplacental ratio; S/D, ratio of systolic to end-diastolic blood velocity; RI, resistance index; PI, pulsation index; CI, confidence interval.

The intraoperative details are shown in Table 3. There were no significant differences in the incidences of hypotension, hypertension, nausea and vomiting between the groups. However, the incidence of maternal bradycardia in Group PE was significantly greater than that in Group NE (9 in Group PE and 2 in Group NE) (P = 0.03). Additionally, sensory block level, total volume of vasopressor given at delivery, total fluid intake before delivery and the time from subarachnoid block to fetal delivery between the two groups were comparable. And only one patient per group received 6 mg ephedrine, with no associated fetal compromise. Neonatal outcomes, including the UA and UV blood gases and Apgar scores are similar between groups (Table 4).

Discussion

The findings of this study revealed no statistically significant differences in the primary outcome [blood velocity of the MCA and UA at 3 and 6 minutes after spinal anesthesia, as well as the CPR], following continuous infusion of either norepinephrine (0.08 μg/kg/min) or phenylephrine (0.5 μg/kg/min) for preventing SAIH during cesarean section. The

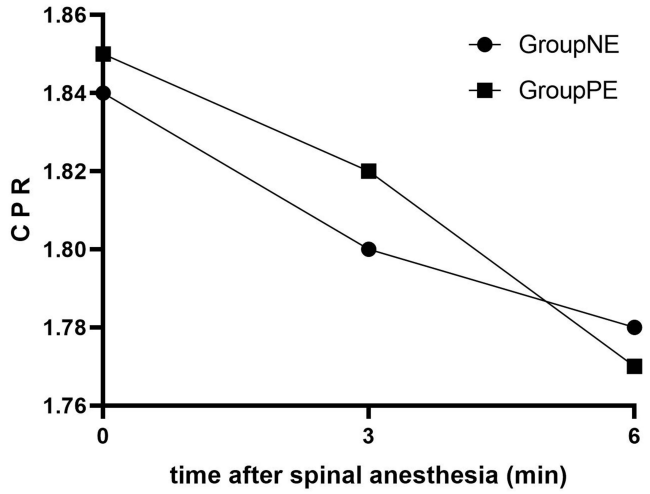

Figure 2 Cerebroplacental Ratio (CPR) Trends Following Spinal Anesthesia. The chart illustrates changes in CPR at 0 min (baseline), 3 min and 6min after spinal anesthesia.

Table 3 Intraoperative Details

	Group NE (n=90)	Group PE (n=90)	*P*-Value
Hypotension (%)	6 (6.7)	8 (8.9)	0.578
Bradycardia (%)	2 (2.2)	9 (10.0)	0.03
Hypertension (%)	4 (4.4)	6 (6.7)	0.515
Nausea (%)	5 (5.6)	9 (10.0)	0.266
Vomiting (%)	0 (0.0)	1 (1.1)	>0.999
Total volume of vasopressor given at delivery (mL)	9.10 ± 1.49	9.55 ± 1.59	0.052
Total fluid intake before delivery (mL)	482 ± 86.	502 ± 85	0.125
Sensory block level (T)	5 (1)	5 (1)	0.088
T4 (%)	26 (29.5)	39 (44.8)	
T5 (%)	45 (51.1)	33 (37.9)	
T6 (%)	17 (19.3)	15 (17.2)	
Time from subarachnoid block to fetal delivery(min)	13 (1)	14 (2)	0.142

Notes: Data are presented as mean ± standard deviation or median (interquartile range) for continuous variables or number (%) for categorical variables.
Abbreviations: NE, norepinephrine; PE, phenylephrine.

Table 4 Neonatal Outcome

	Group NE (n=90)	Group PE (n=90)	*P*-Value
Apgar score			
At 1min after birth	10 (0)	10 (0)	0.966
At 5min after birth	10 (0)	10 (0)	0.156
Umbilical arterial blood gases			
pH	7.29 (0.03)	7.29 (0.02)	0.279
Lac	2.10 (0.80)	1.99 (1.05)	0.858
BE	−1.80 (1.86)	−1.80 (1.40)	0.906
PaO_{22}	19.4 (3.2)	18.9 (3.8)	0.439
$PaCO_2$	53.2 ± 2.9	53.5 ± 3.7	0.606
Umbilical venous blood gases			
pH	7.34 (0.02)	7.34 (0.02)	0.930
Lac	1.50 (0.87)	1.50 (0.70)	0.613
BE	−1.58 (1.26)	−1.58 (1.25)	0.951
PaO_2	28.7 (5.0)	29.0 (4.4)	0.912
$PaCO_2$	43.2 (4.0)	43.4 (4.9)	0.911
Neonatal weight (g)	3334 ± 370	3324 ± 415	0.874
Neonatology department admission (%)	8 (9.4)	10 (11.1)	0.711

Notes: Data are presented as mean ± standard deviation or median (interquartile range) for continuous variables or number (%) for categorical variables.
Abbreviations: NE, norepinephrine; PE, phenylephrine.

secondary outcome measures related to maternal and neonatal outcomes, hemodynamic effects and vasopressor requirements also showed no significant differences between the two groups. The incidence of bradycardia was significantly higher in the PE group compared to the NE group.

The current study builds upon a previous work by our group in which we found that spinal anesthesia combined with prophylactic infusion of equivalent doses of norepinephrine or phenylephrine produces comparable effects on fetal HR and CO.[16] Compared to that study, this research focuses on changes in fetal cerebral perfusion. Fetal cerebral perfusion is influenced not only by maternal blood pressure but also by multiple factors, including fetal local vascular resistance, fetal self-regulation mechanisms, and fetal cerebral protective effects. Additionally, the effects of norepinephrine and phenylephrine crossing the placenta on the fetus are unknown.

The UA and MCA are the most commonly used vessels to understand placental resistance and determine fetal hemodynamic changes. MCA is the most abundant blood vessel in cerebral hemispheres, which directly reflects the supply of fetal intracranial blood circulation. By detecting the parameters of fetal middle cerebral artery blood flow, clinicians can identify the presence of the fetal hypoxia and fetal anemia. The CPR, calculated as the ratio of MCAPI/UAPI, is used to assess fetal intrauterine status by evaluating the balance between cerebral and placental blood flow.[14] Compared to fetal HR and CO, CPR offers significant advantages by providing a comprehensive assessment of fetal hemodynamics, sensitively detecting early signs of hypoxia, dynamically evaluating placental function, and demonstrating strong correlations with adverse perinatal outcomes. Hence, CPR holds a substantial clinical value in fetal monitoring, especially in assessing intrauterine fetal status and predicting pregnancy outcomes.[14,17] Of course, CPR assessment has certain limitations. Specifically, it requires simultaneous measurement of blood flow in both the MCA and UA, which can be time-consuming. However, in our study, all Doppler measurements were performed by the same experienced sonographers, ensuring both efficiency and accuracy without disrupting standard clinical workflows.

This study found no significant difference in CPR between the NE and PE groups. The most likely explanation is that the combination of prophylactic vasopressor infusion and fluid co-loading effectively prevents SAIH, thereby mitigating the range of adverse effects associated with hypotension on the fetus. It is well established that SAIH adversely affects neonatal outcomes. Both the severity of hypotension and the cumulative duration of hypotensive episodes are associated with fetal acidemia and lowered Apgar scores.[2,18] Therefore, timely intervention to address the severity and duration of hypotension, rather than focusing solely on its incidence, may hold greater clinical significance. In the current study, BP was measured every minute from the initiation of spinal anesthesia until delivery, and hypotension was promptly managed upon detection with either a 6 mg ephedrine bolus or 1 mL of the study drug, depending on the presence or absence of concurrent bradycardia. As a result, no adverse neonatal outcomes were observed in either group.

We observed that the incidence of bradycardia was significantly higher in the PE group compared to the NE group, which is consistent with findings from numerous previous studies.[19,20] All cases of bradycardia were promptly managed and no serious adverse maternal or neonatal outcomes were observed. Meanwhile, there was no significant difference in CPR between the two groups. Although studies have demonstrated that maternal HR and CO directly influence placental blood perfusion and indirectly affect fetal hemodynamics,[21] research specifically examining the direct association between maternal hemodynamics and fetal CPR remains limited. Other studies have shown that in the early stages of fetal hypoxia, the fetus maintains hemodynamic stability through its compensatory mechanism, known as the "brain-sparing effect" which may result in Doppler ultrasound parameters of the MCA and UA remaining within the normal range.[22,23] In the current study, the average time from subarachnoid block to fetal delivery was only 13 to 14 minutes. Consequently, the slowdown of the maternal HR had a very limited impact on placental blood perfusion, as well as the blood flow in the MCA and the UA. This might also be a key explanation for the absence of significant differences in the CPR between the two groups. Further investigation is required to determine whether variations in delivery time (from subarachnoid block to fetal delivery) could lead to differences in CPR.

Prophylactic continuous infusion of vasopressors is currently the widely recommended strategy in clinical practice for preventing hypotension following obstetric spinal anesthesia.[2,24] The initial infusion doses of norepinephrine (0.08 μg/kg/min) and phenylephrine (0.5 μg/kg/min) were selected in this study based on two prior dose-response studies which established the 90% effective dose (ED90) for preventing SAIH during cesarean delivery were 0.08 μg/kg/min and 0.54 μg/kg/min, respectively.[25,26] However, these ED90 values were derived using probit regression rather than directly

measuring a 10% incidence of hypotension at these doses. Therefore, the maternal and fetal effects of norepinephrine (0.08 μg/kg/min) and phenylephrine (0.54 μg/kg/min) require further verification and comparison through clinical trials. The incidence of hypotension in the NE and PE groups of this study was 6.7% and 8.9%, respectively. These findings indicate that the previously estimated ED90 values for norepinephrine and phenylephrine were relatively accurate.

Our study has several limitations. First, the inclusion criteria limited the study to healthy parturients undergoing elective cesarean delivery. This homogeneity in the study population may limit applicability to populations with complications, such as preeclampsia or fetal growth restriction. However, CPR is an important monitoring indicator in high-risk pregnancies (such as acute fetal distress, preeclampsia, cardiovascular diseases, and fetal anomalies). Through dynamic monitoring of CPR, it facilitates the early identification of potential risks, optimization of clinical management, and reduction of perinatal complications.[27,28] Secondly, although we have presented confidence intervals for the primary outcomes, which provide a clear sense of the range of plausible effects, we did not conduct a pilot study. When calculating the sample size, owing to the absence of comparative studies on the effects of norepinephrine and phenylephrine in preventing SAIH on fetal cerebral perfusion, the estimation was based on changes in maternal CO, which may introduce some degree of bias. Thirdly, this study did not measure maternal cardiac output, making it impossible to analyze the correlation between changes in fetal cerebral perfusion and maternal CO.

Conclusion

In conclusion, the prophylactic infusion of equivalent doses of phenylephrine and norepinephrine had similar effects on fetal CPR following spinal anesthesia. Neither vasopressor caused significant adverse effects on fetal circulation or neonatal outcomes. Further research is required to evaluate the effects of spinal anesthesia combined with these vasopressors on fetal outcomes in pregnancies complicated by maternal comorbidities.

Data Sharing Statement

The data that support the findings of the study are available from the corresponding author upon reasonable request.

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Disclosure

The authors report no conflicts of interest in this work.

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