

RETRACTED ARTICLE: Effects of Prophylactic Infusion of Equivalent Doses of Norepinephrine and Phenylephrine in Preventing Spinal Anesthesia-Induced Hypotension During Cesarean Delivery on Fetal and Maternal Outcomes: A Dual-Center, Non-Inferiority Controlled Trial

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Background: Numerous studies have compared the effects of norepinephrine and phenylephrine on maternal and neonatal outcomes during cesarean delivery. However, the infusion rates are often based on clinical experience, resulting in non-equivalent doses. We aimed to compare the effects of norepinephrine and phenylephrine at equivalent doses on fetal and maternal outcomes, and assess their efficacy at the 90% effective dose (ED_{90}).

Methods: A total of 100 parturients scheduled for cesarean delivery were randomly allocated to receive either 0.10 $\mu\text{g/kg/min}$ norepinephrine (Group NE) or 0.60 $\mu\text{g/kg/min}$ phenylephrine (Group PE) to prevent spinal anesthesia-induced hypotension. The primary endpoint was neonatal umbilical arterial (UA) pH and the incidence of maternal hypotension, while secondary endpoints included hemodynamic changes within the first 15 minutes, maternal adverse events, and additional neonatal measures.

Results: Of the 95 subjects who completed the study, the UA pH in Group NE (7.296 ± 0.041) was found to be non-inferior to Group PE (7.292 ± 0.040), with a mean difference of 0.003 [95% confidence interval (CI): -0.016 to 0.022 ; $P = 0.009$]. The incidences of hypotension (NE: 8.3% vs PE: 10.6%, $P = 0.701$), hypertension, nausea, and vomiting were comparable between groups. However, bradycardia incidence was significantly reduced in Group NE compared to Group PE (2.1% vs 12.8%, $P = 0.046$). The two groups showed no significant difference in systolic blood pressure (SBP) at most time points within the first 15 minutes, except at 7 minutes. Group NE also had a higher heart rate (HR) than Group PE in most measurements. Both groups showed similar neonatal outcomes.

Conclusion: Prophylactic infusion of 0.10 $\mu\text{g/kg/min}$ norepinephrine was non-inferior to 0.60 $\mu\text{g/kg/min}$ phenylephrine in terms of neonatal UA pH. These findings further support the safety of norepinephrine in obstetric anesthesia, although additional research is warranted to assess its long-term maternal and neonatal outcomes.

Keywords: cesarean delivery, norepinephrine, phenylephrine, hypotension, umbilical arterial pH, non-inferiority

Introduction

Spinal anesthesia-induced hypotension (SAIH) is a frequent complication in cesarean delivery, potentially leading to a variety of adverse effects on both mothers and neonates.^{1,2} The use of vasopressors is widely regarded as the most reliable and effective method for preventing and treating SAIH.^{3,4} Studies have shown that continuous prophylactic

infusion of vasopressors provides more stable hemodynamics than single intravenous boluses.^{5,6} However, controversies remain regarding the optimal vasopressor and initial infusion dose.

Phenylephrine has long been the first-choice vasopressor in obstetrics because of its effective control over maternal blood pressure and favorable neonatal outcomes.⁷ However, its dose-dependent effects on maternal heart rate (HR) and cardiac output (CO) have raised notable concerns.⁸ Norepinephrine, a potent α 1-adrenergic agonist and mild β 1-adrenergic agonist, enhances HR and CO, making it a compelling alternative to phenylephrine.^{7,9}

Previous studies on phenylephrine and norepinephrine for preventing SAIH during cesarean delivery have primarily focused on maternal hemodynamics,^{10,11} while recent research has shifted towards assessing their impact on neonatal outcomes.^{12,13} Currently, umbilical artery (UA) pH value analysis is frequently used as an objective indicator of neonatal outcomes.^{12,14}

It is notable that in numerous studies, the initial vasopressor infusion doses were based on the authors' clinical experience rather than robust evidence from the literature, which may result in inequivalent dosages and potential discrepancies in outcomes.^{15,16} In our previous work, a dose of 0.097 μ g/kg/min was determined as the 50% effective dose (ED₅₀) for prophylactic norepinephrine infusion in combination with a 10 mL/kg of crystalloid coload to prevent SAIH during cesarean delivery.¹⁷ Likewise, a dose-response study determined the ED₅₀ for phenylephrine as 0.54 μ g/kg/min,¹⁸ with its relative potency ratio to norepinephrine estimated at approximately 1:6.^{15,19} For ease of comparison and calculation, we considered that the initial infusion rates of 0.10 μ g/kg/min for norepinephrine and 0.60 μ g/kg/min for phenylephrine as appropriate dosing regimens.

This study aimed to compare the maternal and fetal outcomes following prophylactic infusion of norepinephrine and phenylephrine at equivalent doses. We hypothesize that norepinephrine infusion would be non-inferior to phenylephrine infusion in maintaining neonatal acid-base status and preventing maternal hypotension.

Methods

Study Design and Patient Enrolment

This dual-center, randomized, non-inferiority controlled study was conducted at Wenling Maternity and Child Health Care Hospital (Taizhou, China) and Affiliated Xiaoshan Hospital of Hangzhou Normal University (Hangzhou, China), following approval from the Institutional Clinical Research Ethics Review Boards of both institutions (No. 2024-IRB-101 and No. 2023-IRB-015). The study followed the principles of the Declaration of Helsinki and adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines. Written informed consent was acquired from each participant. This study was registered at the Chinese Clinical Trial Registry (accessible at www.chictr.org.cn, with the registration No. ChiCTR2400087985, and the registration date being August 8, 2024). The eligible participants were American Society of Anesthesiologists (ASA) participants with a physical status of less than III, aged 18–40 years and had singleton pregnancies of at least 37 weeks, and scheduled for elective cesarean delivery between August 10 and December 10, 2024. Exclusion criteria were as follows: contraindications to regional anesthesia, allergy to phenylephrine or norepinephrine, height < 150 cm or > 170 cm, obesity (body mass index ≥ 35 kg/m²), multiple gestation, diabetes mellitus, hypertensive disorders of pregnancy, cardiovascular disease, placenta previa, ruptured membranes, and significant coexisting maternal disease.

Randomization and Blinding

Using computer-generated randomization codes, parturients were allocated in a 1:1 ratio to receive an infusion of either 0.10 μ g/kg/min norepinephrine (Group NE) or 0.60 μ g/kg/min phenylephrine (Group PE) for intraoperative blood pressure maintenance. Randomization codes were stored in opaque envelopes, sequentially numbered to ensure concealment. The sealed envelope was opened by a nurse anesthetist with no involvement in the trial, who then prepared a 50 mL syringe labeled study drug containing norepinephrine [dose: maternal weight (kg) $\times$ 6 μ g] or phenylephrine [dose: maternal weight (kg) $\times$ 36 μ g], both diluted in 0.9% saline to a total volume of 50 mL. The prepared study drug was given to the anesthesiologist managing data collection, who administered it at a fixed rate of 50 mL/h. Additionally, bolus doses for treatment of hypotension (6 μ g norepinephrine or 100 μ g phenylephrine) were prepared in identical 10 mL syringes labeled “rescue vasopressor” by the same nurse anesthetist, ensuring allocation concealment for both the anesthesiologist and parturients.

Anesthesia Management and Intervention

Participants fasted for a minimum of 8 hours prior to the surgery, without receiving any preoperative medications. An 18-gauge intravenous catheter was inserted into the left forearm vein, and no preload fluid was administered in the waiting area. Once entering the operating room, parturients were placed in the supine position with the leftward displacement of the uterus. Subsequently, routine monitoring involved non-invasive blood pressure (NIBP), pulse oximetry, and a five-lead electrocardiogram was performed. NIBP was measured every 2 minutes following a brief period of calmness. Baseline values were derived from the average of three consecutive systolic blood pressure (SBP) and HR readings, ensuring a variation of less than 10%.

Combined spinal-epidural anesthesia was performed at the L3–4 intervertebral space with the parturient in the left lateral decubitus position, using the needle-through-needle method. Following the correct positioning of the 18-gauge epidural needle, a 27-gauge spinal needle was advanced into the subarachnoid space via the epidural needle. Upon confirming cerebrospinal fluid reflux, 3 mL (15 mg) of hyperbaric ropivacaine (comprising 2 mL of 0.75% ropivacaine, and 1 mL of 10% dextrose) was administered into the subarachnoid space at a controlled rate of 1 mL every 10 seconds, directed upward. Subsequently, the spinal needle was then removed, and an epidural catheter was inserted into the epidural space, advanced 3–4 cm toward the cephalad direction. The parturient was repositioned to the supine position, and oxygen supplementation at 5 L/min was provided through a face mask. Simultaneously with the intrathecal injection, 10 mL/kg of lactated Ringer's solution was rapidly co-loaded over 10–15 minutes at the maximum possible rate under gravity, and then adjusted to slow infusion to maintain venous patency. Meanwhile, study drug infusions (norepinephrine at 0.10 µg/kg/min and phenylephrine at 0.60 µg/kg/min) were delivered via an infusion pump at 50 mL/h through a three-way stopcock attached to the parturient's intravenous cannula. NIBP readings were taken every minute post-intrathecal injection and every three minutes after delivery. Sensory block was evaluated using an 18-gauge blunt epidural needle at 5 and 10 minutes after intrathecal injection with success defined as T6 or above. Unsuccessful blockade resulted in disqualification, with the next eligible participant enrolled according to the randomization code.

Upon fetal delivery, arterial and venous blood samples were collected by the obstetrician from the double-clamped segment of the umbilical cord and analyzed within 30 seconds using a blood gas analyzer by an assistant blinded to the group allocation. Additionally, Apgar scores were assessed by a pediatrician who was also unaware of the group assignment.

The study period spanned from the start of the intrathecal injection to neonatal delivery. Hypotension, defined as SBP $\leq$ 80% of baseline, was treated with 6 µg norepinephrine in Group NE and 100 µg phenylephrine in Group PE.^{20,21} If there was no response in SBP within 2 minutes after the first dose, additional vasopressor boluses were given until SBP $\geq$ 90% of the baseline value. Hypertension, defined as SBP $\geq$ 120% of baseline, was controlled by pausing the infusion and resuming it once SBP dropped below 120% of baseline. Bradycardia, defined as HR $<$ 60 beats/min. In such cases, the infusion of vasopressors was stopped and resumed once the HR returned to $\geq$ 60 beats/min. If bradycardia persisted for more than 2 minutes, an intravenous dose of atropine (0.5 mg) was administered.

Data Collection and Outcome Assessment

The demographic data along with the obstetric characteristics were recorded. The primary endpoint of this study was umbilical arterial (UA) pH and the occurrence of maternal hypotension throughout the study period.

Secondary endpoints included hemodynamic parameter changes (SBP and HR) within the first 15 minutes, demographic characteristics (including age, height, weight, sensory block level, the interval from spinal anesthesia to delivery, and the total vasopressor volume administered before delivery), maternal adverse events [such as severe hypotension (defined as a decrease of $\geq$ 40% of baseline SBP), bradycardia, reactive hypertension, nausea and vomiting], and other measures of neonatal outcomes (including additional analysis of blood gases within the umbilical artery and vein, and Apgar scores).

Sample Size Estimation

The sample size calculation utilized non-inferiority tests for two means (differences), conducted with PASS 11.0.1 (NCSS, LLC, Kaysville, Utah). Based on a previous study, the mean UA pH was 7.33, with a standard deviation (SD) of 0.03 when phenylephrine was infused at 0.54 µg/kg/min.¹⁴ Using these data, we determined that to achieve 90% power

with an alpha of 0.05 for rejecting the null hypothesis of a UA pH decrease of 0.02 units or more in the Group NE compared to the Group PE, would require a sample size of 40 subjects per group. Considering potential dropouts or incomplete data, the sample size was increased by 25%, resulting in 50 subjects per group.

Statistical Analysis

Data were analyzed using SPSS for Windows (version 22.0) and GraphPad Prism software (version 8.0.2). The Shapiro–Wilk test was applied to assess the normality of continuous variables. Normally distributed variables were evaluated with the independent-samples Student's *t*-test and presented as mean $\pm$ SD, while non-normally distributed variables were assessed with the Mann–Whitney *U*-test and presented as median (with quartiles). Frequency data were compared using either the chi-square test or Fisher's exact test, as appropriate, and presented as numbers (%). A *p* value < 0.05 was defined as statistically significant.

Results

A total of 118 participants underwent screening, with 18 excluded (7 opted not to participate, and 11 failed to meet the inclusion criteria). Subsequently, 100 participants were randomized and allocated equally to Group NE (*n* = 50) and Group PE (*n* = 50). After excluding cases of failed spinal anesthesia and unsuccessful collection of umbilical cord blood samples, the final analysis included 48 participants in Group NE and 47 in Group PE (Figure 1). Maternal data and

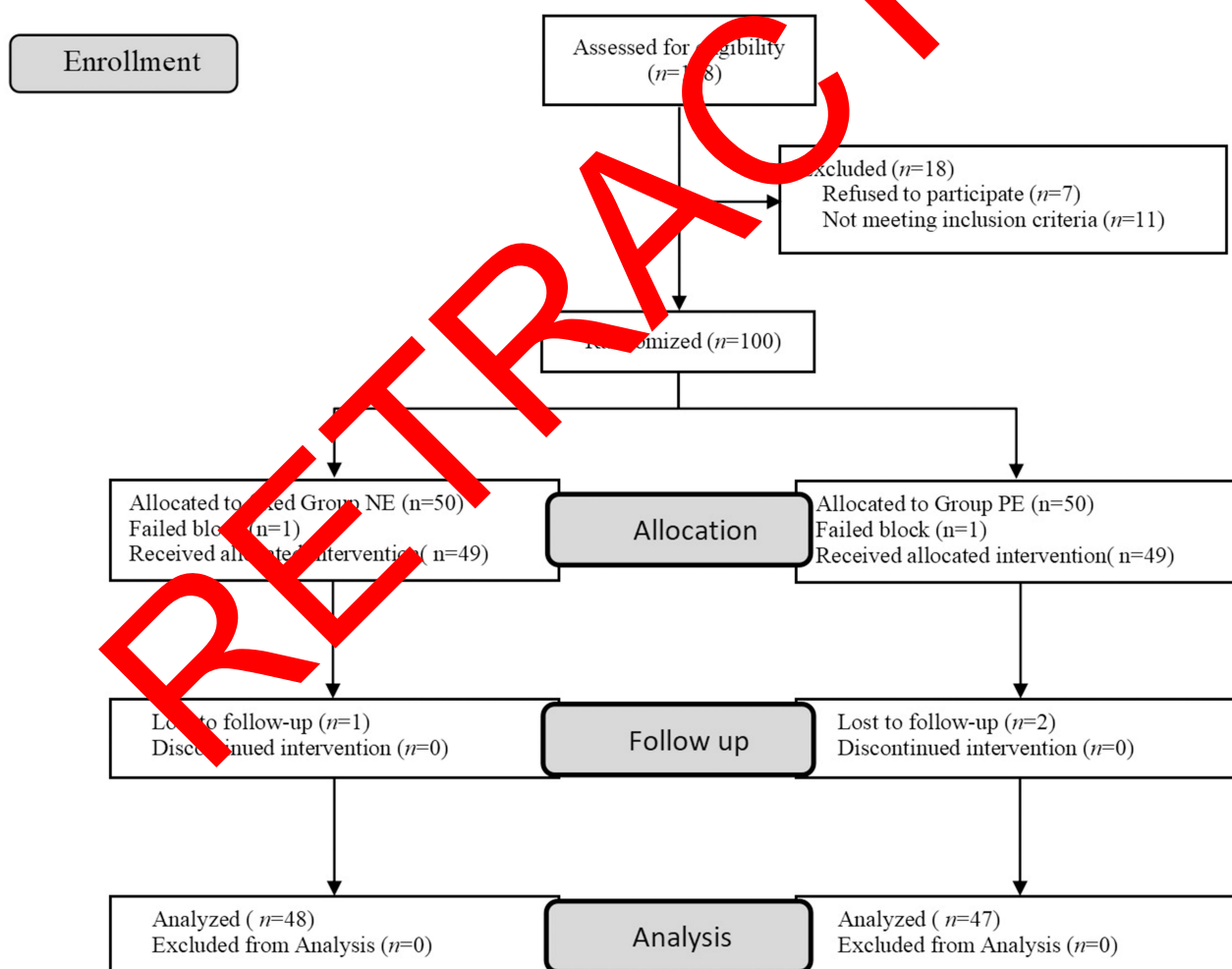


Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

Abbreviations: NE, norepinephrine; PE, phenylephrine.

Table 1 Demographic Data, Sensory Block Level, and Surgical Parameters

	Group NE (n=48)	Group PE (n=47)	P-value
Age (years)	30.4 ± 3.9	29.7 ± 4.8	0.425
Height (cm)	160.7 ± 4.4	159.2 ± 4.7	0.115
Weight (kg)	68.8 ± 9.2	71.4 ± 8.1	0.155
Gestational age (weeks)	38.8 ± 0.8	38.6 ± 1.0	0.342
Gravidity	2 [1–2]	2 [1–3]	0.114
Parity	0 [0–1]	0 [0–1]	0.308
Baseline SBP (mmHg)	120.9 ± 8.2	118.6 ± 8.1	0.173
Baseline HR (bpm)	87.8 ± 11.1	89.0 ± 11.0	0.614
Upper sensory level (T)	T4 [T4–T5]	T4 [T4–T5]	0.289
Spinal anesthesia to delivery interval (min)	13.5 ± 2.7	14.3 ± 2.7	0.151
Intravenous fluid volume given (before delivery) (mL)	601.3 ± 111.6	621.9 ± 107.2	0.371
Total volume of vasopressors administered (before delivery) (mL)	11.2 ± 2.5	11.1 ± 2.7	0.883

Note: Data are presented as mean ± SD, or median [with quartiles].

Abbreviations: Group NE, norepinephrine group; Group PE, phenylephrine group; SBP, systolic blood pressure; HR, heart rate.

Table 2 Hemodynamic Changes, and Side Effects

	Group NE (n=48)	Group PE (n=47)	P-value
Hypotension (before delivery)	4 (8.3)	5 (10.6)	0.701
Hypertension (before delivery)	1 (2.1)	2 (4.3)	0.545
Nausea	1 (2.1)	2 (4.3)	0.545
Vomiting	0 (0)	0 (0)	–
Bradycardia	1 (2.1)	6 (12.8)	0.046*
Incidence of severe hypotension	0 (0)	1 (2.1)	0.310

Notes: Data are presented as number (%). P-value < 0.05 was considered statistically significant.

Abbreviations: Group NE, norepinephrine group; Group PE, phenylephrine group.

surgical parameters are provided in Table 1. The demographic data, level of sensory block, interval from spinal anesthesia to delivery, as well as the total volume of vasopressors administered were comparable between the two groups. Intraoperative hemodynamic parameters and adverse effects are presented in Table 2. The incidences of hypotension (Group NE: 8.3%, Group PE: 10.6%, $P = 0.701$), as well as hypertension, nausea and vomiting were comparable between groups. However, bradycardia incidence was significantly reduced in the Group NE compared to the Group PE (2.1% vs 12.8%, $P = 0.046$). Changes in SBP and HR within the first 15 minutes following subarachnoid block are presented in Figures 2 and 3. SBP showed no significant differences between the groups across time intervals. Only at 7 minutes after spinal anesthesia did we observe that SBP in the Group NE was higher than in the Group PE. Group NE had higher HR than Group PE in most readings.

The values of the primary endpoint UA pH are shown in Table 3, with a mean of 7.296 ± 0.041 in the Group NE and 7.292 ± 0.040 in the Group PE. The mean difference in UA pH among the groups was 0.003 (95% CI, -0.016 to 0.022). Since the CI did not extend beyond the non-inferiority margin of -0.02 , it was demonstrated that norepinephrine is not inferior to phenylephrine (non-inferiority $P = 0.009$) (Figure 4). Birth weight and other measures of neonatal outcome, including the umbilical blood gases and Apgar scores were also similar between the groups (Table 3).

Discussion

Due to the frequent occurrence of reflex maternal bradycardia and the reduction in maternal CO associated with the use of phenylephrine, an increasing number of experts now advocate for norepinephrine as the superior vasopressor in obstetric anesthesia.^{7,21,22} The absence of significant suppression of UA pH values further provides strong evidence supporting the fetal safety of norepinephrine in this clinical setting.²³ Our findings demonstrate that prophylactic norepinephrine infusion is non-inferior to phenylephrine in terms of UA pH outcomes; moreover, the significantly lower incidence of bradycardia in

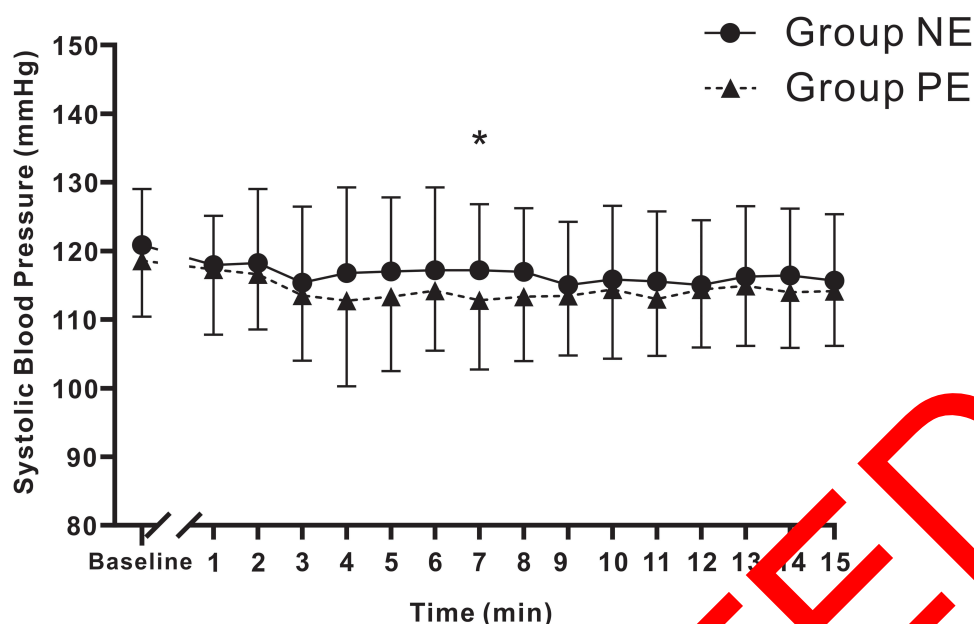


Figure 2 Serial changes in SBP during the first 15 minutes following norepinephrine or phenylephrine infusion. Data are shown as mean and SD. *Statistical significance between the two groups.

Abbreviations: Group NE, norepinephrine; Group PE, phenylephrine.

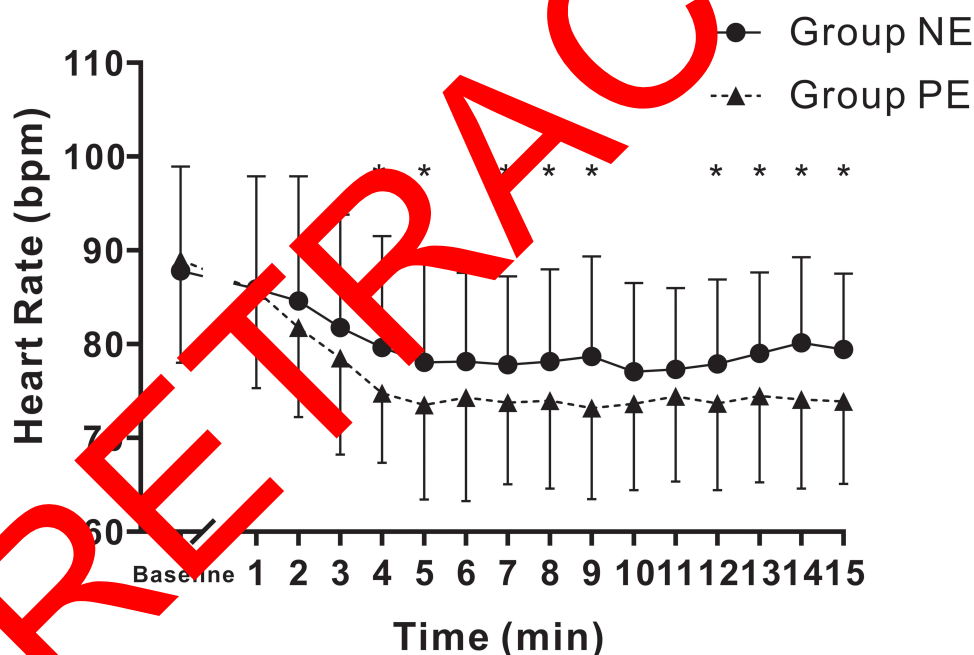


Figure 3 Serial changes in HR during the first 15 minutes following norepinephrine or phenylephrine infusion. Data are shown as mean and SD. *Statistical significance between the two groups.

Abbreviations: Group NE, norepinephrine; Group PE, phenylephrine.

the norepinephrine group compared to the phenylephrine group (2.1% vs 12.8%; $P = 0.046$) highlights its potential clinical advantage. Norepinephrine may serve as a safer alternative for parturients at risk of bradycardia, particularly those with preexisting cardiac conditions, thereby reducing the need for adjunctive interventions such as atropine administration.²²

Since fetal heart rate monitoring is not feasible during the operation, the impact of hypotension on the fetal condition has to be assessed using surrogate markers. UA pH was chosen as the primary endpoint due to its well-recognized role in

Table 3 Neonatal Outcome

	Group NE (n=48)	Group PE (n=47)	P-value
Umbilical arterial blood gases			
pH	7.296 ± 0.041	7.292 ± 0.040	0.731
Base excess (mmol/L)	-1.57 ± 1.7	-1.89 ± 1.1	0.337
PO ₂ (mmHg)	19.1 ± 3.8	19.3 ± 4.1	0.263
PCO ₂ (mmHg)	51.7 ± 5.0	51.3 ± 5.4	0.798
Lactate (mmol/L)	2.17 ± 0.7	2.34 ± 0.6	0.242
Umbilical venous blood gases			
pH	7.356 ± 0.029	7.350 ± 0.023	0.348
Base excess (mmol/L)	-1.70 ± 1.5	-2.16 ± 1.3	0.144
PO ₂ (mmHg)	29.7 ± 5.7	29.0 ± 5.6	0.501
PCO ₂ (mmHg)	42.8 ± 4.0	42.8 ± 5.1	0.961
Lactate (mmol/L)	1.71 ± 0.5	1.84 ± 0.5	0.256
Apgar score <7 at 1 min	1 (2.1)	0 (0)	0.372
Apgar score <7 at 5 min	0 (0)	0 (0)	0.999
Birth weight (g)	3352 ± 416	3367 ± 464	0.866

Note: Data are presented as mean ± SD or number (%).

Abbreviations: PO₂, partial pressure of oxygen; PCO₂, partial pressure of carbon dioxide.

assessing neonatal status at birth, reflecting both the respiratory and metabolic aspects of fetal acidemia.^{12,14} The occurrence of respiratory fetal acidemia is predominantly attributed to carbon dioxide build-up, which results from acute placental hypoperfusion. It is worthy of attention that the use of intraoperative vasopressors and spinal anesthesia are both associated with risk factors for this condition. Base excess (BE) may be considered a more appropriate indicator to reflect the metabolic component of fetal acidosis. However, as a calculated parameter strongly correlated with pH, the added prognostic value of UA BE compared to direct pH measurement remains a subject of debate.²⁴

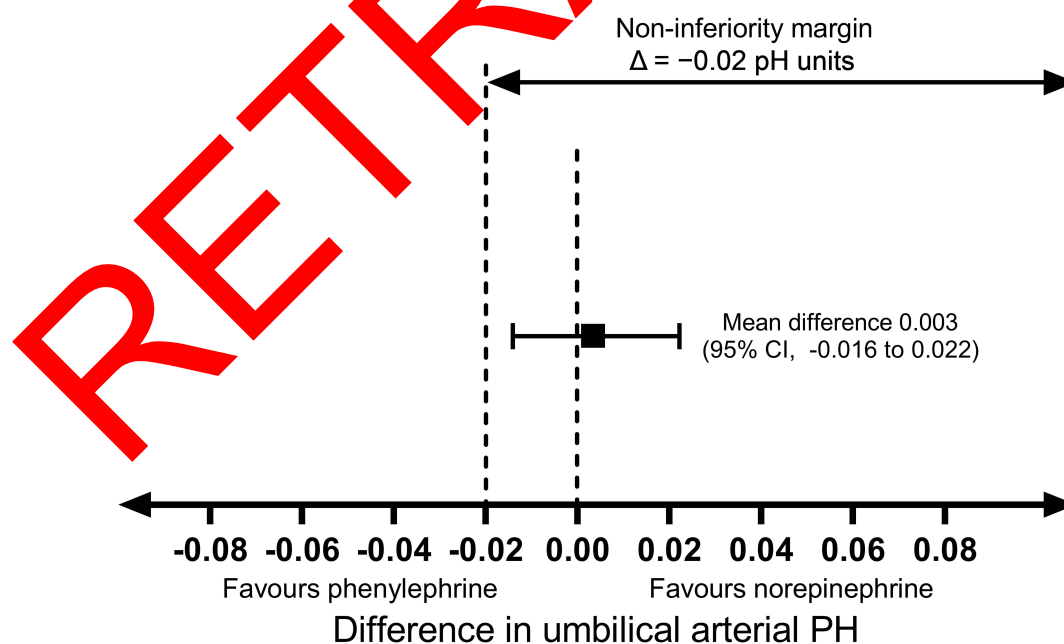


Figure 4 Comparison of differences in umbilical artery pH between norepinephrine and phenylephrine. The confidence interval does not cross the non-inferiority margin (set at -0.02 pH units), it was demonstrated that norepinephrine is non-inferior to phenylephrine.

Prophylactic continuous infusion of vasopressors remains the widely recommended strategy for preventing SAIH in obstetric practice.^{5,6} In this study, the initial infusion doses of norepinephrine (0.10 µg/kg/min) and phenylephrine (0.60 µg/kg/min) were selected based on our previous dose-response study and a study by Fei Xiao et al, which established the ED₉₀ for SAIH prevention during cesarean delivery as 0.097 µg/kg/min for norepinephrine and 0.54 µg/kg/min for phenylephrine.^{17,18} However, these ED₉₀ values were derived from probability regression rather than direct observation of a 10% hypotension incidence at specific infusion rates; moreover, their wide confidence intervals also require further clinical validation. Our results demonstrated that the incidences of hypotension in Group NE and Group PE were 8.3% and 10.6%, respectively, which were remarkably close to the estimated ED₉₀ values. Therefore, we conclude that an initial infusion of norepinephrine at 0.10 µg/kg/min and phenylephrine at 0.60 µg/kg/min is appropriate for clinical practice.

A similar study was conducted by Liu et al,¹⁴ however, their approach differed from ours in that they selected initial infusion doses of 0.08 µg/kg/min for norepinephrine and 0.54 µg/kg/min for phenylephrine based on previous dose-response studies.^{18,25} Although their results indicated no significant difference in UA pH between the two groups, the incidences of hypotension reached 38% for norepinephrine and 12% for phenylephrine. These findings suggest that the previously estimated ED₉₀ values for norepinephrine and phenylephrine may have been underestimated. Several factors may account for these discrepancies. First, different studies utilized varying specific gravities and doses of drugs for spinal anesthesia, which may have influenced the outcomes. Second, the confidence intervals derived from probit regression analyses were relatively wide, potentially leading to deviations in the median ED₉₀ values. Third, differences in fluid co-loading protocols could have contributed to the variation. While most clinical practices adopt a co-loading dose of 10 mL/kg of crystalloid,^{25,26} the study by Fu et al reported a maximum co-loading volume of up to 1.5 liters.²⁷

The results of this study indicated that norepinephrine was non-inferior to phenylephrine regarding its impact on fetal UA pH outcomes, which was consistent with the findings of a recent study.¹² The most plausible explanation is that the combination of prophylactic vasopressor infusion and fluid co-loading effectively prevents SAIH, thereby reducing the fetal adverse effects associated with hypotension. SAIH is known to negatively impact neonatal outcomes, with both the severity and cumulative duration of hypotensive episodes strongly associated with fetal acidemia and lower Apgar scores.^{2,28} Therefore, prompt intervention in respect of the duration and severity of hypotension, rather than merely concentrating on its incidence rate, may hold greater clinical significance. In this study, the occurrence rate of hypotension in both groups was approximately 10%. Moreover, NIBP was measured every minute from the start of spinal anesthesia until delivery, and any detected hypotension was immediately managed with intravenous administration of a 6 µg bolus of norepinephrine or a 100 µg bolus of phenylephrine. Consequently, neither group experienced any adverse neonatal outcomes.

Our study has several limitations. First, the UA pH value can be significantly influenced by various factors, including the timing of sampling, the duration of umbilical cord clamping at both ends, the time of analysis, and the presence of umbilical cord entanglement.²⁹ Therefore, incorporating the cerebroplacental ratio or fetal cardiac output may further aid in the early assessment of fetal hypoxia and the prediction of outcomes. Second, we defined the non-inferiority margin using a small effect size of 0.02 pH units; if a smaller effect size of 0.01 pH units had been used, it might detect even slight potentially detrimental effects of norepinephrine. However, this would have required a larger sample size, significantly increasing the workload. Third, we conducted the trial across two clinical centers, recognizing that factors such as variations in medical resources and patient populations could contribute to inconsistencies in study outcomes, thereby increasing heterogeneity.

Conclusion

In summary, our study demonstrated that prophylactic infusion of norepinephrine (0.10 µg/kg/min) is non-inferior to phenylephrine (0.60 µg/kg/min) for preventing spinal anesthesia-induced hypotension during cesarean delivery in terms of neonatal UA pH, and was associated with a lower risk of bradycardia. Our findings support the use of norepinephrine at an initial infusion rate of 0.10 µg/kg/min in obstetric anesthesia. However, further research is warranted to evaluate the long-term safety of norepinephrine in postpartum maternal hemodynamics and neonatal neurodevelopment.

Abbreviations

SAIH, spinal anesthesia-induced hypotension; ED₉₀, the 90% effective dose; CI, confidence interval; NIBP, noninvasive blood pressure; SBP, systolic blood pressure; HR, heart rate; CO, cardiac output; UA, umbilical artery; ASA, American Society of Anesthesiologist; CONSORT, Consolidated Standards of Reporting Trials.

Data Sharing Statement

The data supporting the findings of this study can be obtained from the corresponding author (Zhimin Sheng) upon legitimate request.

Ethics Approval

This study received approval from the Ethics Committees of Wenling Maternity and Child Health Hospital (No. 2024-IRB-101) and the Affiliated Xiaoshan Hospital of Hangzhou Normal University (No. 2023-IRB-015). This study was conducted in strict accordance with the principles outlined in the Declaration of Helsinki.

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Disclosure

The authors declare no conflicts of interest in this work.

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