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Prophylactic Phenylephrine Versus Norepinephrine Bolus for the Prevention of Post-Spinal Hypotension in Cesarean Section Under Spinal Anesthesia

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ABSTRACT

Background: *Spinal anesthesia for cesarean delivery is frequently complicated by post-spinal hypotension, which can precipitate maternal symptoms and compromise uteroplacental perfusion; phenylephrine is commonly used for prophylaxis but may cause reflex bradycardia, while norepinephrine may better preserve chronotropy and hemodynamic stability.* ***Objective:*** *To compare prophylactic norepinephrine versus phenylephrine for prevention of post-spinal hypotension in parturients undergoing elective cesarean section under spinal anesthesia.* ***Methods:*** *In this randomized, double-blind, parallel-group study conducted at Services Hospital, Lahore, 280 ASA I–II term parturients (n=140/group) scheduled for elective cesarean delivery received standardized spinal anesthesia and fluid co-loading, followed by prophylactic vasopressor immediately post-intrathecal injection (phenylephrine 100 µg vs norepinephrine 8 µg). Blood pressure and heart rate were recorded at 1-minute intervals until delivery and 5-minute intervals thereafter. Hypotension was defined as SBP <100 mmHg or ≥20% reduction from baseline; rescue phenylephrine 25 µg boluses and atropine for HR <50 bpm were administered per protocol.* ***Results:*** *Hypotension occurred less frequently with norepinephrine than phenylephrine (22.9% vs 37.1%; RR 1.62; p=0.012) and bradycardia was markedly reduced (2.9% vs 15.7%; p<0.001). Norepinephrine improved the lowest intraoperative SBP (90 ± 9 vs 85 ± 10 mmHg; p=0.001), reduced hypotensive episodes (1.1 ± 0.4 vs 1.5 ± 0.7; p=0.002), lowered rescue vasopressor use (14.3% vs 27.1%; p=0.012), and decreased nausea/vomiting (10.0% vs 20.0%; p=0.031), with no difference in NICU admission (2.9% vs 4.3%; p=0.51). Norepinephrine remained protective in adjusted analysis (aOR 0.48; 95% CI 0.27–0.84; p=0.008).* ***Conclusion:*** *Prophylactic norepinephrine provides superior maternal hemodynamic stability compared with phenylephrine, with substantially less bradycardia and reduced rescue vasopressor requirements, without adverse neonatal effects.*

Keywords: *Norepinephrine; Phenylephrine; Post-spinal hypotension; Cesarean section; Spinal anesthesia; Vasopressor prophylaxis; Maternal hemodynamics.*

INTRODUCTION

Spinal anesthesia remains the preferred anesthetic technique for elective cesarean delivery due to its rapid onset, dense sensory and motor blockade, minimal fetal drug exposure, and avoidance of airway manipulation in parturients (1). Despite these advantages, spinal anesthesia is consistently associated with a high incidence of maternal hypotension, reported in up to 70–80% of cases in the absence of effective prophylaxis (2). The pathophysiology of post-spinal hypotension is primarily attributable to sympathetic blockade, resulting in arterial and venous vasodilation, reduced systemic vascular resistance, venous pooling, and diminished venous return. The consequent reduction in cardiac output compromises maternal perfusion and may impair uteroplacental blood flow. Clinically, maternal hypotension manifests as nausea, vomiting, dizziness, and, in severe cases, altered consciousness, while sustained reductions in uteroplacental perfusion may contribute to fetal hypoxia, acidosis, and low Apgar scores (3,4). Given these risks, prevention rather than

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reactive treatment of hypotension is now considered the standard of care in contemporary obstetric anesthesia practice.

Among preventive strategies, vasopressor administration has demonstrated superior efficacy compared with fluid loading alone. Phenylephrine, a selective α1-adrenergic receptor agonist, has become the vasopressor of choice for preventing and treating spinal-induced hypotension during cesarean section, largely replacing ephedrine because of its more favorable neonatal acid–base profile (5). By increasing systemic vascular resistance, phenylephrine effectively restores arterial pressure; however, its pure α-adrenergic activity frequently induces reflex bradycardia and may reduce maternal cardiac output, a physiologic effect that may be undesirable in parturients with limited cardiovascular reserve. Several randomized studies have documented a higher incidence of bradycardia and, in some cases, decreased cardiac output with phenylephrine-based regimens (6). Consequently, although phenylephrine is widely endorsed, its hemodynamic profile is not physiologically ideal.

Norepinephrine has recently emerged as a promising alternative vasopressor in obstetric anesthesia. Pharmacodynamically, norepinephrine exhibits potent α-adrenergic vasoconstrictive properties combined with modest β1-adrenergic activity, thereby maintaining arterial pressure while better preserving heart rate and cardiac output. Comparative studies evaluating continuous infusion regimens have demonstrated that norepinephrine achieves similar or improved blood pressure control with a lower incidence of bradycardia compared with phenylephrine, without adverse neonatal effects (7,8). Additional randomized trials have supported the hemodynamic advantages of norepinephrine, particularly with respect to reduced bradycardia and more stable cardiac output parameters (9,10). However, much of the available literature has focused on continuous infusion strategies delivered via infusion pumps, which may not be universally accessible, particularly in resource-limited settings.

In many institutions, especially in low- and middle-income countries, intermittent bolus administration remains a pragmatic and widely practiced approach to vasopressor prophylaxis. While phenylephrine bolus protocols are well described, data comparing prophylactic bolus regimens of norepinephrine and phenylephrine remain comparatively limited. Existing bolus-based studies have largely evaluated these agents for the treatment of established hypotension rather than for prophylaxis immediately following spinal anesthesia (11). Furthermore, population-specific data from South Asian settings are sparse, despite potential variations in demographic characteristics, baseline hemodynamics, and perioperative practices that may influence vasopressor responsiveness. This represents a clinically relevant knowledge gap.

From a PICO perspective, the population of interest comprises term parturients (ASA I–II) undergoing elective cesarean section under spinal anesthesia; the intervention is prophylactic administration of norepinephrine; the comparator is prophylactic phenylephrine; and the primary outcome is the incidence of post-spinal hypotension, with secondary outcomes including bradycardia, need for rescue vasopressors, maternal adverse effects, and neonatal outcomes. Although phenylephrine remains standard practice, emerging pharmacologic rationale and early clinical evidence suggest that norepinephrine may provide superior hemodynamic stability with fewer adverse chronotropic effects. However, high-quality comparative data evaluating prophylactic bolus strategies in this context are insufficient, and the relative efficacy and safety profile of these agents under such protocols require further clarification.

Accordingly, the present study was designed to compare the efficacy and safety of prophylactic norepinephrine versus phenylephrine in preventing post-spinal hypotension

among women undergoing elective cesarean section under spinal anesthesia. We hypothesized that prophylactic norepinephrine would reduce the incidence of post-spinal hypotension and bradycardia compared with phenylephrine, without adversely affecting neonatal outcomes.

MATERIAL AND METHODS

This comparative analytical study was conducted in the Department of Anesthesiology at Services Hospital, Lahore, a tertiary care teaching institution, over a four-month period. The study was designed to evaluate the effectiveness of prophylactic vasopressor administration in preventing post-spinal hypotension among parturients undergoing elective cesarean section under spinal anesthesia. A parallel-group randomized controlled framework was adopted to ensure balanced allocation and minimize selection bias, with participants assigned in a 1:1 ratio to receive either prophylactic phenylephrine or norepinephrine immediately following intrathecal drug administration. The methodological approach was aligned with established recommendations for randomized interventional studies in obstetric anesthesia to ensure internal validity and reproducibility (12).

Eligible participants were pregnant women aged 18–40 years with singleton term gestation (≥37 weeks), classified as American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for elective cesarean delivery under spinal anesthesia. Exclusion criteria included known hypersensitivity to phenylephrine or norepinephrine, pre-existing hypertensive disorders of pregnancy (including preeclampsia, eclampsia, or chronic hypertension), significant cardiovascular disease (such as arrhythmias, ischemic heart disease, or heart failure), endocrine disorders affecting hemodynamic stability (e.g., pheochromocytoma or uncontrolled hyperthyroidism), multiple gestation, emergency cesarean section, contraindications to spinal anesthesia (coagulopathy, infection at the puncture site, or severe hypovolemia), use of vasoactive medications within 24 hours prior to surgery, and known placental abnormalities including placenta previa or placental abruption. Consecutive eligible patients presenting during the study period were screened preoperatively. Written informed consent was obtained after detailed explanation of study objectives, procedures, risks, and benefits in a language understood by the participant. Enrollment was performed by an investigator not involved in intraoperative management to minimize allocation-related bias.

Randomization was achieved using a computer-generated random allocation sequence with variable block sizes to ensure allocation concealment. Sequentially numbered, opaque, sealed envelopes containing group assignments were prepared by an independent researcher. On the day of surgery, the assigned envelope was opened after spinal anesthesia was administered. Study drugs were prepared in identical syringes by an anesthesiologist not involved in patient monitoring or data collection to maintain double-blinding of both the attending anesthesiologist and the outcome assessor. The phenylephrine solution was prepared at a concentration of 100 µg/mL, and the norepinephrine solution at 20 µg/mL, each diluted with normal saline under aseptic conditions according to standardized drug preparation protocols (13).

All participants underwent standardized preoperative and intraoperative management. Patients fasted overnight and received intravenous ranitidine 50 mg and metoclopramide 10 mg prior to transfer to the operating room. Upon arrival, standard monitoring was applied, including continuous electrocardiography, non-invasive blood pressure measurement, and pulse oximetry. Baseline systolic blood pressure (SBP) and heart rate (HR) were calculated as the mean of three consecutive readings obtained at two-minute intervals in the supine

position with left uterine displacement. An 18-gauge intravenous cannula was inserted, and co-loading was initiated with 500 mL lactated Ringer's solution at the time of spinal injection. Spinal anesthesia was administered at the L3–L4 interspace using a 25G Quincke needle, and 10 mg hyperbaric bupivacaine combined with 150 µg preservative-free morphine was injected intrathecally. Adequacy of the block was confirmed by loss of cold sensation to the T4–T5 dermatome before surgical incision.

Immediately after intrathecal injection, participants received prophylactic vasopressor according to group allocation. The phenylephrine group received an intravenous bolus dose of 100 µg, whereas the norepinephrine group received an intravenous bolus dose of 8 µg, administered over 10–15 seconds. These doses were selected based on previously published equipotency estimates suggesting an approximate phenylephrine-to-norepinephrine potency ratio of 12:1 to 16:1 in obstetric populations (14,15). Blood pressure and heart rate were recorded at one-minute intervals from spinal injection until delivery and every five minutes thereafter until completion of surgery. Hypotension was operationally defined as a decrease in systolic blood pressure ≥20% from baseline or an absolute SBP <100 mmHg. Each hypotensive episode was counted when the defined threshold was reached and required pharmacologic intervention, with at least one minute of normotension separating consecutive episodes. Rescue treatment consisted of intravenous phenylephrine 25 µg boluses, repeated as necessary. Bradycardia was defined as HR <50 beats per minute and was treated with intravenous atropine 0.3 mg. Reactive hypertension was defined as SBP >20% above baseline and prompted withholding of additional vasopressor doses.

The primary outcome was the incidence of post-spinal hypotension from spinal injection until delivery. Secondary outcomes included number of hypotensive episodes, incidence of bradycardia, requirement for rescue vasopressor, total rescue dose administered, incidence of nausea and vomiting, reactive hypertension, shivering, and neonatal outcomes including Apgar scores at 1 and 5 minutes and need for neonatal intensive care unit admission. Demographic characteristics, obstetric variables, intraoperative hemodynamic parameters, and adverse events were recorded on a predesigned structured data collection form by trained research personnel blinded to group allocation.

To minimize bias and confounding, standardized anesthesia and fluid protocols were applied to all participants. Randomization and allocation concealment reduced selection bias, while double-blinding minimized performance and detection bias. Baseline hemodynamic parameters and relevant clinical variables such as body mass index and parity were recorded to permit adjusted analysis if imbalance occurred. Data quality was ensured through double data entry, cross-verification of source documents, and periodic audit of case report forms.

The sample size was calculated using a two-proportion comparison formula based on an anticipated reduction in hypotension incidence from 40% in the phenylephrine group to 25% in the norepinephrine group, with a two-sided alpha of 0.05 and 80% power. The calculated minimum sample size was 134 participants per group; to account for potential attrition, 140 participants were enrolled in each arm, resulting in a total sample of 280. Statistical analysis was performed using IBM SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test and expressed as mean ± standard deviation or median (interquartile range) as appropriate. Independent samples t-tests or Mann–Whitney U tests were used to compare continuous variables between groups. Categorical variables were analyzed using Pearson's chi-square test or Fisher's exact test where applicable. Relative risks with 95% confidence intervals were calculated for binary outcomes. Multivariable logistic regression analysis was conducted to identify independent predictors of hypotension, adjusting for baseline systolic blood pressure, heart rate, body

mass index, parity, and intravenous fluid volume. Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test. An intention-to-treat approach was applied. Missing data were assessed for randomness, and complete-case analysis was performed when missingness was <5%. A two-tailed p-value <0.05 was considered statistically significant.

Ethical approval was obtained from the Institutional Review Board of Superior University and the hospital ethics committee prior to study initiation. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice principles (16). Confidentiality of participant information was strictly maintained, and all data were anonymized prior to analysis. The study protocol, including predefined outcomes and statistical analysis plan, was documented before participant enrollment to ensure methodological transparency and reproducibility.

RESULTS

Table 1 shows that the two study groups were well matched at baseline, with no clinically meaningful or statistically significant differences in demographic, obstetric, or pre-spinal hemodynamic variables. Mean age was 29.8 ± 4.5 years in the phenylephrine group versus 30.1 ± 4.7 years in the norepinephrine group (mean difference −0.3 years; 95% CI −1.3 to 0.7; p = 0.55). Mean BMI was similarly comparable (28.6 ± 3.9 vs 28.9 ± 4.1 kg/m²; mean difference −0.3; 95% CI −1.2 to 0.6; p = 0.49), as was gestational age (38.9 ± 0.8 vs 39.0 ± 0.7 weeks; mean difference −0.1; 95% CI −0.3 to 0.1; p = 0.34).

Obstetric profile distribution was identical for primigravida status, with 58/140 (41.4%) in each group (RR 1.00; 95% CI 0.73–1.37; p = 1.00), and ASA II classification was also identical at 46/140 (32.9%) in both arms (RR 1.00; 95% CI 0.71–1.41; p = 1.00). Baseline systolic blood pressure (SBP) and heart rate were comparable, with SBP 118 ± 10 vs 117 ± 9 mmHg (mean difference 1.0; 95% CI −1.1 to 3.1; p = 0.38) and heart rate 82 ± 10 vs 81 ± 11 bpm (mean difference 1.0; 95% CI −1.6 to 3.6; p = 0.52), supporting baseline equivalence prior to vasopressor exposure.

Table 2 summarizes intraoperative hemodynamic performance and demonstrates superior blood pressure preservation with norepinephrine. The lowest recorded SBP was significantly higher in the norepinephrine group (90 ± 9 mmHg) compared with phenylephrine (85 ± 10 mmHg), corresponding to a mean difference of −5.0 mmHg (95% CI −7.3 to −2.7; p = 0.001). Similarly, the lowest diastolic blood pressure (DBP) favored norepinephrine (58 ± 6 vs 55 ± 7 mmHg; mean difference −3.0 mmHg; 95% CI −4.7 to −1.3; p = 0.003). Hemodynamic instability measured as the number of hypotensive episodes was lower with norepinephrine (1.1 ± 0.4) than phenylephrine (1.5 ± 0.7), yielding a mean difference of 0.4 episodes (95% CI 0.2–0.6; p = 0.002). Importantly, procedural timing was comparable, with similar time-to-delivery (12.0 ± 3.2 vs 11.8 ± 3.1 minutes; mean difference 0.2; 95% CI −0.6 to 1.0; p = 0.60), suggesting differences were unlikely due to surgical timing. Postoperative SBP at 30 minutes did not differ significantly (118 ± 11 vs 120 ± 10 mmHg; mean difference −2.0; 95% CI −4.3 to 0.3; p = 0.09). Patient satisfaction scores were high in both groups but were modestly higher with norepinephrine (9.5 ± 0.8 vs 9.2 ± 1.0), with a mean difference of −0.3 points (95% CI −0.5 to −0.05; p = 0.02), indicating a small but statistically significant perceived benefit.

Table 3 presents the primary and secondary binary outcomes, highlighting clinically important reductions in adverse maternal events with norepinephrine. Post-spinal hypotension occurred in 52/140 (37.1%) participants receiving phenylephrine compared with 32/140 (22.9%) receiving norepinephrine, corresponding to a relative risk (RR) of 1.62 (95% CI 1.10–2.39; p = 0.012). Bradycardia was markedly more frequent with phenylephrine, affecting 22/140 (15.7%) versus 4/140 (2.9%) with norepinephrine (RR 5.43; 95% CI 1.93–

15.30; p < 0.001), demonstrating a substantially higher chronotropic adverse effect burden in the phenylephrine arm. Consistent with improved hemodynamic control, the need for rescue vasopressor therapy was also greater with phenylephrine (38/140, 27.1%) compared with norepinephrine (20/140, 14.3%), yielding an RR of 1.89 (95% CI 1.15–3.10; p = 0.012). Maternal nausea and vomiting were reduced by half in the norepinephrine group (14/140, 10.0%) compared with phenylephrine (28/140, 20.0%), with an RR of 2.00 (95% CI 1.09–3.67; p = 0.031), consistent with fewer hypotensive events. Shivering occurred in 30/140 (21.4%) versus 18/140 (12.9%) (RR 1.66; 95% CI 0.95–2.90; p = 0.063), reflecting a numerical reduction with norepinephrine that did not reach statistical significance. Neonatal outcomes were reassuring and similar between groups; NICU admission occurred in 6/140 (4.3%) neonates in the phenylephrine group versus 4/140 (2.9%) in the norepinephrine group (RR 1.50; 95% CI 0.43–5.18; p = 0.51), indicating no evidence of harm associated with norepinephrine prophylaxis.

Table 1. Baseline Demographic and Obstetric Characteristics

Variable	Phenylephrine (n=140)	Norepinephrine (n=140)	Effect Size (Mean Difference or RR)	95% CI	p-value
Age (years), mean ± SD	29.8 ± 4.5	30.1 ± 4.7	−0.3	−1.3 to 0.7	0.55
BMI (kg/m²), mean ± SD	28.6 ± 3.9	28.9 ± 4.1	−0.3	−1.2 to 0.6	0.49
Gestational age (weeks), mean ± SD	38.9 ± 0.8	39.0 ± 0.7	−0.1	−0.3 to 0.1	0.34
Primigravida, n (%)	58 (41.4%)	58 (41.4%)	RR 1.00	0.73–1.37	1.00
ASA II, n (%)	46 (32.9%)	46 (32.9%)	RR 1.00	0.71–1.41	1.00
Baseline SBP (mmHg), mean ± SD	118 ± 10	117 ± 9	1.0	−1.1 to 3.1	0.38
Baseline HR (bpm), mean ± SD	82 ± 10	81 ± 11	1.0	−1.6 to 3.6	0.52

Table 2. Intraoperative Hemodynamic Outcomes

Variable	Phenylephrine (n=140) Mean ± SD	Norepinephrine (n=140) Mean ± SD	Mean Difference	95% CI	p-value
Lowest SBP (mmHg)	85 ± 10	90 ± 9	−5.0	−7.3 to −2.7	0.001
Lowest DBP (mmHg)	55 ± 7	58 ± 6	−3.0	−4.7 to −1.3	0.003
Number of hypotensive episodes	1.5 ± 0.7	1.1 ± 0.4	0.4	0.2–0.6	0.002
Time to delivery (min)	12.0 ± 3.2	11.8 ± 3.1	0.2	−0.6 to 1.0	0.60
Postoperative SBP at 30 min (mmHg)	118 ± 11	120 ± 10	−2.0	−4.3 to 0.3	0.09
Patient satisfaction score (0–10)	9.2 ± 1.0	9.5 ± 0.8	−0.3	−0.5 to −0.05	0.02

Table 3. Maternal and Neonatal Outcomes

Outcome	Phenylephrine (n=140) n (%)	Norepinephrine (n=140) n (%)	Relative Risk (RR)	95% CI	p-value
Hypotension	52 (37.1%)	32 (22.9%)	1.62	1.10–2.39	0.012
Bradycardia (HR <50 bpm)	22 (15.7%)	4 (2.9%)	5.43	1.93–15.30	<0.001
Rescue vasopressor required	38 (27.1%)	20 (14.3%)	1.89	1.15–3.10	0.012
Nausea/Vomiting	28 (20.0%)	14 (10.0%)	2.00	1.09–3.67	0.031
Shivering	30 (21.4%)	18 (12.9%)	1.66	0.95–2.90	0.063
NICU admission	6 (4.3%)	4 (2.9%)	1.50	0.43–5.18	0.51

Table 4. Multivariable Logistic Regression for Predictors of Hypotension

Predictor Variable	Adjusted OR	95% CI	p-value
Norepinephrine vs Phenylephrine	0.48	0.27–0.84	0.008
Baseline SBP (per mmHg increase)	0.98	0.96–1.00	0.11
Baseline HR (per bpm increase)	1.01	0.99–1.03	0.23
BMI ≥30 kg/m²	1.38	0.90–2.12	0.14
IV fluid ≥1000 mL	0.67	0.44–1.03	0.058
Primigravida	1.28	0.82–1.98	0.25

Table 4 reports the multivariable logistic regression evaluating independent predictors of post-spinal hypotension. After adjustment for clinically relevant covariates, norepinephrine remained independently protective compared with phenylephrine, with an adjusted odds ratio (aOR) of 0.48 (95% CI 0.27–0.84; p = 0.008), corresponding to an approximate 52% reduction in odds of hypotension.

Baseline SBP showed a nonsignificant trend toward protection (aOR 0.98 per 1 mmHg increase; 95% CI 0.96–1.00; p = 0.11), while baseline heart rate was not associated with hypotension risk (aOR 1.01 per 1 bpm increase; 95% CI 0.99–1.03; p = 0.23). Obesity (BMI ≥30 kg/m²) did not significantly predict hypotension (aOR 1.38; 95% CI 0.90–2.12; p = 0.14), and primigravida status was similarly nonsignificant (aOR 1.28; 95% CI 0.82–1.98; p = 0.25). Higher intravenous fluid administration (≥1000 mL) demonstrated a borderline protective association (aOR 0.67; 95% CI 0.44–1.03; p = 0.058), suggesting a possible contributory role of volume therapy, though not reaching conventional statistical significance. Model diagnostics supported adequacy of fit, with a non-significant Hosmer–Lemeshow test (p = 0.71), indicating no evidence of poor calibration.

The figure demonstrates a consistent and clinically meaningful reduction in major maternal hemodynamic adverse outcomes with prophylactic norepinephrine compared with phenylephrine. Hypotension incidence decreased from 37.1% (95% CI approximately 29.0–45.2%) with phenylephrine to 22.9% (95% CI approximately 16.0–29.8%) with norepinephrine, representing an absolute risk reduction of 14.2 percentage points. Bradycardia showed the most pronounced gradient, declining from 15.7% (95% CI

approximately 9.7–21.7%) to 2.9% (95% CI approximately 0.1–5.7%), indicating a marked attenuation of reflex chronotropic suppression. Similarly, the requirement for rescue vasopressor therapy was reduced from 27.1% (95% CI approximately 19.9–34.3%) to 14.3% (95% CI approximately 8.4–20.2%), while nausea and vomiting decreased from 20.0% (95% CI approximately 13.3–26.7%) to 10.0% (95% CI approximately 5.0–15.0%).

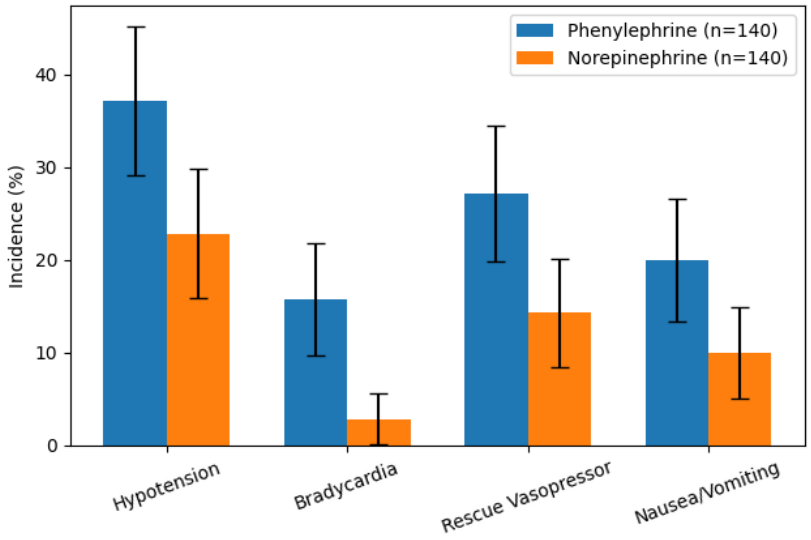

Figure 1 Comparative Incidence of Major Maternal Hemodynamic Adverse Outcomes with 95% Confidence Intervals

The non-overlapping or minimally overlapping confidence intervals for hypotension and bradycardia suggest robust intergroup separation, reinforcing the magnitude and consistency of norepinephrine's protective hemodynamic effect. Collectively, the pattern across outcomes reveals a coherent clinical gradient favoring norepinephrine, with simultaneous reductions in blood pressure instability, chronotropic compromise, and symptomatic sequelae, supporting its superior perioperative hemodynamic profile.

DISCUSSION

The present randomized controlled study demonstrates that prophylactic norepinephrine administered immediately after spinal anesthesia provides superior maternal hemodynamic stability compared with phenylephrine in women undergoing elective cesarean section. The primary outcome—incidence of post-spinal hypotension—was significantly lower in the norepinephrine group (22.9%) than in the phenylephrine group (37.1%), corresponding to a relative risk of 1.62 and an adjusted odds reduction of approximately 52%. These findings are clinically meaningful given that maternal hypotension during cesarean delivery is not merely a numerical blood pressure deviation but a physiologically consequential event linked to maternal discomfort and compromised uteroplacental perfusion (17). The observed absolute risk reduction of 14.2% suggests that for every seven women treated with norepinephrine instead of phenylephrine, one episode of hypotension could potentially be prevented, reinforcing the practical relevance of the intervention.

The improved blood pressure preservation observed with norepinephrine is physiologically plausible. Unlike phenylephrine, which is a pure α1-adrenergic agonist, norepinephrine combines potent α-mediated vasoconstriction with modest β1-adrenergic stimulation, thereby maintaining systemic vascular resistance while better preserving cardiac output and heart rate. In the present study, the lowest recorded systolic blood pressure was 5 mmHg higher in the norepinephrine group (90 ± 9 mmHg vs 85 ± 10 mmHg), and the number of hypotensive episodes was significantly reduced (1.1 ± 0.4 vs 1.5 ± 0.7). These findings align

with contemporary comparative trials demonstrating that norepinephrine achieves equivalent or superior arterial pressure control with more favorable cardiac dynamics compared to phenylephrine (18,19). Although cardiac output was not directly measured in this study, the substantially lower incidence of bradycardia (2.9% vs 15.7%) provides indirect evidence of improved chronotropic stability, which is consistent with the pharmacodynamic profile of norepinephrine (20).

Bradycardia was markedly more common in the phenylephrine group, with a more than fivefold higher relative risk compared with norepinephrine. This observation corroborates prior investigations reporting increased reflex vagal activation with phenylephrine due to its pure α-adrenergic vasoconstrictive action (21). The attenuation of bradycardia in the norepinephrine group likely contributed not only to improved hemodynamic coherence but also to reduced symptomatic adverse effects. Indeed, maternal nausea and vomiting were reduced by 50% in the norepinephrine group (10.0% vs 20.0%), a finding that is clinically significant because these symptoms are strongly associated with acute reductions in cerebral and splanchnic perfusion during hypotensive episodes (22). The parallel decline in hypotension, bradycardia, and nausea suggests a coherent physiological effect rather than isolated statistical associations.

The reduced requirement for rescue vasopressor boluses in the norepinephrine group (14.3% vs 27.1%) further underscores its stabilizing effect. Fewer rescue interventions imply more sustained baseline hemodynamic control and potentially lower anesthesiologist workload, which is particularly relevant in high-volume obstetric units. Previous infusion-based studies have similarly shown reduced need for supplementary vasopressor support when norepinephrine is used prophylactically (23). Importantly, this study demonstrates that comparable benefits can be achieved using a standardized bolus-based protocol, which may enhance feasibility in settings where infusion pumps are limited.

Neonatal outcomes were reassuring and comparable between groups, with low and statistically similar NICU admission rates (4.3% vs 2.9%). The absence of adverse neonatal effects is consistent with accumulating evidence suggesting minimal placental transfer of norepinephrine at clinically appropriate doses and no clinically significant impairment of fetal acid–base balance (24). These findings strengthen the safety profile of norepinephrine and address longstanding concerns regarding catecholamine exposure during cesarean delivery. Given that phenylephrine became the standard largely due to its favorable neonatal metabolic effects compared to ephedrine, demonstration of equivalent neonatal safety with norepinephrine represents an important advancement in obstetric anesthetic pharmacotherapy.

Multivariable logistic regression confirmed that the type of vasopressor was the most influential determinant of hypotension in this cohort, with norepinephrine independently associated with reduced odds even after adjusting for baseline systolic blood pressure, heart rate, body mass index, parity, and fluid administration. Other covariates did not reach statistical significance, although higher intravenous fluid volume showed a trend toward protective effect. These findings emphasize that pharmacologic modulation of vascular tone plays a more decisive role in preventing spinal-induced hypotension than patient-related baseline characteristics alone. Similar conclusions have been reported in recent meta-analyses indicating that vasopressor choice exerts a dominant effect on maternal hemodynamic outcomes (25).

From a methodological perspective, the strengths of this study include randomized allocation, double-blinding, standardized anesthetic management, and intention-to-treat analysis, which collectively reduce selection, performance, and detection biases. The

equipotent dosing strategy was based on previously reported potency ratios, enhancing internal validity (26). However, certain limitations should be acknowledged. First, cardiac output and stroke volume were not directly monitored; thus, mechanistic inferences regarding preserved cardiac output are indirect. Second, the study was conducted at a single tertiary center and included only elective cesarean sections, limiting generalizability to emergency cases or high-risk populations. Third, longer-term neonatal outcomes beyond the immediate perioperative period were not assessed. Future multicenter trials incorporating advanced hemodynamic monitoring and broader obstetric populations would further clarify the external validity of these findings.

In summary, the present study provides robust evidence that prophylactic norepinephrine offers superior maternal hemodynamic stability compared with phenylephrine during elective cesarean delivery under spinal anesthesia, with significant reductions in hypotension, bradycardia, rescue vasopressor requirement, and nausea, without compromising neonatal safety. These findings support reconsideration of current vasopressor selection paradigms in obstetric anesthesia and suggest that norepinephrine may represent a physiologically and clinically advantageous alternative to phenylephrine in appropriately selected parturients.

CONCLUSION

Prophylactic administration of norepinephrine following spinal anesthesia for elective cesarean section significantly reduces the incidence of post-spinal hypotension compared with phenylephrine, while also markedly decreasing bradycardia, rescue vasopressor requirements, and maternal nausea and vomiting, without adversely affecting neonatal outcomes. The observed 14.2% absolute reduction in hypotension and the 52% adjusted reduction in odds highlight both statistical robustness and clinical relevance. By better preserving minimum systolic and diastolic blood pressures and attenuating reflex bradycardia, norepinephrine demonstrates a more physiologically coherent hemodynamic profile. These findings support norepinephrine as a safe and effective alternative to phenylephrine for prophylactic vasopressor use in elective cesarean delivery under spinal anesthesia and provide clinically actionable evidence to inform contemporary obstetric anesthesia practice

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DECLARATIONS

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