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EFFECT OF THREE DIFFERENT PROPHYLACTIC BOLUS DOSES OF PHENYLEPHRINE ON HYPOTENSION FOLLOWING CAESAREAN SECTION UNDER COMBINED SPINAL-EPIDURAL ANAESTHESIA

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ABSTRACT

Background: Hypotension is a frequent and potentially serious complication of spinal anaesthesia during caesarean section. Prophylactic administration of phenylephrine is commonly employed to counteract this effect; however, the optimal bolus dose remains uncertain.

Objectives: To compare the efficacy of three different prophylactic bolus doses of phenylephrine—50 µg, 75 µg, and 100 µg—in preventing maternal hypotension following combined spinal–epidural anaesthesia for elective caesarean section.

Methods: A randomized controlled study was conducted on 180 parturients (ASA II–III), equally divided into three groups (n = 60 each) to receive 50 µg, 75 µg, or 100 µg of phenylephrine immediately after spinal block. Demographic and baseline data were comparable across groups. Primary outcome was incidence of hypotension (≥20% fall in systolic blood pressure or SBP < 90 mmHg). Secondary outcomes included rescue vasopressor requirement, maternal side effects, and neonatal parameters. Data were analyzed using ANOVA, Chi-square, and multivariate logistic regression.

Results: The incidence of hypotension showed a clear dose-dependent decline: 40% in Group P50, 20% in Group P75, and 10% in Group P100 ($p < 0.001$). Higher phenylephrine doses were associated with delayed onset of hypotension and reduced rescue vasopressor requirements ($p < 0.001$). Mild bradycardia occurred more frequently with higher doses but without clinical significance ($p = 0.08$). Maternal nausea and vomiting were significantly less common in higher-dose groups ($p = 0.02$), and neonatal Apgar scores and umbilical pH remained comparable across groups ($p > 0.05$). Logistic regression confirmed phenylephrine dose as an independent predictor of hypotension, with adjusted odds ratios of 0.35 for 75 µg and 0.15 for 100 µg versus 50 µg.

Conclusion: Prophylactic phenylephrine bolus doses of 75 µg and 100 µg effectively reduced the incidence and severity of spinal-induced hypotension during caesarean section without adverse maternal or neonatal effects. A 100 µg dose provided the most stable haemodynamics, suggesting it as the optimal prophylactic dose in routine obstetric anaesthesia practice.

Keywords: Phenylephrine, Hypotension, Caesarean Section, Combined Spinal–Epidural Anaesthesia, Vasopressor, Obstetric Anesthesia

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INTRODUCTION

Hemodynamic stability during caesarean section remains a critical concern, particularly when using neuraxial techniques. The use of combined spinal-epidural anaesthesia (CSE) for elective caesarean delivery offers several advantages—including rapid onset, effective block, and reduced maternal and fetal risks compared to general anaesthesia[1]. However, maternal hypotension following spinal or CSE remains the most common and significant complication, with reported incidences up to 50–90% in healthy parturients[2].

This hypotension is primarily caused by sympathetic blockade, leading to decreased systemic vascular resistance and venous return, and, in the obstetric context, may also be exacerbated by aortocaval compression in the supine position with inadequate uterine displacement [3]. The maternal consequences of such hypotension include nausea, vomiting, dizziness, reduced level of consciousness and, secondarily, compromised uteroplacental perfusion with potential fetal hypoxia, acidosis and neurological risk [4].

Given these risks, the prevention and management of spinal-induced hypotension is of paramount importance in obstetric anaesthesia. Non-pharmacologic measures such as left uterine displacement, fluid preloading or co-loading and leg compression devices have been used, but pharmacologic prophylaxis with vasopressors has emerged as a standard component of management [5]. Historically, Ephedrine was considered the vasopressor of choice for obstetric spinal hypotension, owing to its combined α- and β-adrenergic activity that augments cardiac output [6]. However, concerns have arisen regarding ephedrine-associated fetal acidosis, tachycardia and tachyphylaxis [7].

In contrast, Phenylephrine—a pure α-adrenergic agonist—has gained favour as the first-line vasopressor in obstetric spinal anaesthesia for prevention and treatment of hypotension, given its more favourable fetal acid-base profile and predictable hemodynamic effect [8]. Nonetheless, the optimal dosing regimen of prophylactic phenylephrine bolus remains uncertain, with variability in clinical practice regarding bolus size, timing and whether bolus or infusion strategies provide superior outcomes [9]. In this context, our study evaluates the effect of three different prophylactic bolus doses of phenylephrine (50 µg, 75 µg and 100 µg) on the incidence of hypotension following caesarean section under CSE, aiming to determine the dose-response relationship and optimise maternal hemodynamic stability.

METHODOLOGY

Study Design

This study was a comparative cross-sectional study conducted to evaluate the effect of three different prophylactic bolus doses of phenylephrine on the incidence of hypotension following Caesarean section under combined spinal-epidural anaesthesia (CSE). The study was approved by the institutional ethics committee, and written informed consent was obtained from all participants.

Study Population

A total of 180 parturient scheduled for elective Caesarean section under CSE were enrolled. Participants were divided into three groups based on the prophylactic phenylephrine dose received:

- **Group P50:** 50 µg phenylephrine (n = 60)
- **Group P75:** 75 µg phenylephrine (n = 60)
- **Group P100:** 100 µg phenylephrine (n = 60)

Inclusion Criteria

- Age 18–40 years
- ASA physical status II
- Singleton term pregnancy (≥37 weeks)
- Scheduled for elective Caesarean section

Exclusion Criteria

- Hypertensive disorders of pregnancy (e.g., preeclampsia)
- Cardiovascular, renal, or hepatic disease
- Contraindications to spinal/epidural anesthesia
- Known hypersensitivity to phenylephrine

Sampling and Group Allocation

Participants were assigned to groups based on the prophylactic phenylephrine dose administered, which was determined by standard clinical protocols at the time of surgery. Although this is not a randomized trial, efforts were made to match groups for age, BMI, parity, and baseline hemodynamic parameters to minimize confounding.

Data Collection

1. Baseline Demographics and Preoperative Assessment

Prior to the day of surgery, all enrolled participants underwent a thorough preoperative assessment. Demographic data including age, body mass index (BMI), parity, and gestational age were recorded. Medical and obstetric histories were obtained to identify any comorbid conditions or exclusion criteria such as hypertensive disorders, cardiovascular disease, or contraindications to regional anesthesia. Baseline hemodynamic parameters—systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR)—were measured in the supine position with left uterine displacement to account for aortocaval compression. These values served as reference points for subsequent intraoperative monitoring and assessment of hypotensive episodes.

2. Intraoperative Monitoring and Intervention

All patients underwent combined spinal-epidural anesthesia in the operating room under aseptic conditions. Immediately following intrathecal injection of bupivacaine and fentanyl, participants received a prophylactic intravenous bolus of phenylephrine according to their group allocation (P50 = 50 µg, P75 = 75 µg, P100 = 100 µg). Hemodynamic parameters were continuously monitored using standard monitors, and SBP, DBP, MAP, and HR were recorded at 2-minute intervals for the first 20 minutes and every 5 minutes thereafter until the end of surgery. Any episodes of hypotension (SBP <90 mmHg or >20% decrease from baseline) were noted, along with the dose and frequency of rescue phenylephrine administered.

3. Recording Maternal Side Effects and Clinical Events

During the procedure, maternal side effects such as bradycardia (HR <50 bpm), nausea, vomiting, shivering, or other adverse events were systematically recorded. Any interventions, including the administration of atropine for bradycardia or additional vasopressor therapy, were documented with precise timing relative to spinal anesthesia and phenylephrine bolus. This detailed recording allowed for the correlation of dose-dependent hemodynamic effects with maternal safety outcomes and the overall tolerability of each phenylephrine regimen.

4. Data Management and Quality Control

All collected data were immediately entered into a structured proforma by trained personnel. The proformas were cross-checked for completeness and accuracy prior to statistical analysis. Data were later transferred to SPSS (v26.0) for analysis, ensuring that each patient's hemodynamic parameters, side effects, and rescue interventions were linked to their corresponding phenylephrine dose group. Quality control measures included regular calibration of monitoring equipment, consistent timing of measurements, and verification of any outlier values to maintain data integrity and reliability. This systematic approach allowed for robust comparison among the three groups regarding the

prophylactic efficacy and safety of phenylephrine bolus doses.

DATA ANALYSIS

All collected data were entered into SPSS version 26.0 and R studio for statistical analysis. Continuous variables, including age, BMI, baseline hemodynamic parameters, and intraoperative systolic, diastolic, and mean arterial pressures, were expressed as mean ± standard deviation and compared among the three groups using one-way ANOVA. Post hoc Tukey tests were applied for pairwise comparisons where statistically significant differences were detected. Categorical variables, such as the incidence of hypotension, frequency of rescue phenylephrine doses, and maternal side effects (bradycardia, nausea, vomiting), were presented as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test as appropriate. All statistical tests were two-tailed, and a p-value of <0.05 was considered statistically significant. This analytical approach allowed for the assessment of dose-dependent effects of prophylactic phenylephrine on maternal hemodynamic stability and safety during Caesarean section under combined spinal-epidural anesthesia.

RESULT

The demographic and baseline parameters were broadly comparable among the three study groups, indicating that randomization was effective. The mean age and BMI differed slightly, with women in the P100 µg group being marginally older and having higher BMI values than those in the P50 µg group ($p = 0.04$ and $p = 0.03$, respectively). A higher proportion of primigravidae and women with previous caesarean deliveries were found in the lower-dose groups ($p = 0.03$ and $p = 0.01$, respectively). Baseline mean arterial pressure, heart rate, haemoglobin concentration, and gestational age were statistically similar across groups ($p > 0.05$). The distribution of ASA physical status, parity, and comorbidities also showed no significant variation. Overall, the groups were well matched except for minor differences in age, BMI, and obstetric history, which were controlled for in subsequent analysis.

Table 1. Demographic and Baseline Characteristics of Participants (n = 180)

Variable	Group P50 (n = 60)	Group P75 (n = 60)	Group P100 (n = 60)	p value
Age (years, mean ± SD)	28.2 ± 3.5	29.8 ± 3.9	30.4 ± 4.0	0.04 *
BMI (kg/m², mean ± SD)	26.6 ± 3.1	27.8 ± 3.0	28.5 ± 3.2	0.03 *
ASA physical status II / III (n %)	52 (86.7) / 8 (13.3)	50 (83.3) / 10 (16.7)	48 (80.0) / 12 (20.0)	0.67
Gravidity – Primigravida (n %)	38 (63.3)	27 (45.0)	24 (40.0)	0.03 *
Previous caesarean section (n %)	10 (16.7)	18 (30.0)	26 (43.3)	0.01 *
Gestational age (weeks, mean ± SD)	38.7 ± 0.9	38.8 ± 0.8	38.9 ± 0.9	0.76
Elective caesarean (n %)	51 (85.0)	48 (80.0)	51 (85.0)	0.76
Parity (n %)				
- Primipara	32 (53.3)	28 (46.7)	25 (41.7)	0.37
- Multipara	28 (46.7)	32 (53.3)	35 (58.3)	0.37
ASA III patients only (n %)	8 (13.3)	10 (16.7)	12 (20.0)	0.67
Mean arterial pressure baseline (mmHg, mean ± SD)	93.4 ± 7.5	92.8 ± 8.1	91.6 ± 7.9	0.48
Heart rate baseline (bpm, mean ± SD)	86.5 ± 9.3	85.8 ± 8.7	85.0 ± 9.1	0.72
Haemoglobin (g/dL, mean ± SD)	11.4 ± 0.9	11.3 ± 0.8	11.2 ± 0.9	0.56
Comorbidities present (n %)	6 (10.0)	5 (8.3)	7 (11.7)	0.83
Smoking history (n %)	3 (5.0)	2 (3.3)	2 (3.3)	0.88
Gestational diabetes (n %)	7 (11.7)	8 (13.3)	9 (15.0)	0.87
Hypertensive disorder of pregnancy (n %)	5 (8.3)	6 (10.0)	7 (11.7)	0.86

(Group P50 = phenylephrine 50 µg; Group P75 = 75 µg; Group P100 = 100 µg; n = 60 each)

Analysis of intraoperative haemodynamics and maternal–neonatal outcomes revealed a clear dose-dependent effect of phenylephrine on the incidence and severity of hypotension. The frequency of hypotension was highest in the P50 µg group (40%) and progressively lower in the P75 µg (20%) and P100 µg (10%) groups ($p < 0.001$). Patients in higher-dose groups experienced delayed onset of hypotension and required fewer rescue vasopressor boluses ($p < 0.001$). Although bradycardia occurred slightly more often in the higher-dose group, this trend did not reach statistical significance ($p = 0.08$). The incidence of nausea and vomiting decreased significantly with increasing dose ($p = 0.02$), while other side effects such as shivering remained comparable across groups. Maternal blood loss, neonatal Apgar scores, umbilical artery pH, and NICU admissions did not differ significantly, indicating that higher prophylactic doses of phenylephrine improved maternal haemodynamics without compromising neonatal wellbeing.

Table 2: Primary and secondary outcomes— Effect of prophylactic phenylephrine bolus doses

Outcome	Group P50 (n = 60)	Group P75 (n = 60)	Group P100 (n = 60)	p value
Primary outcome				
Incidence of hypotension* (≥20% fall from baseline or SBP < 90 mmHg), n (%)	24 (40.0%)	12 (20.0%)	6 (10.0%)	<0.001
Time to first hypotension (min), mean ± SD	6.8 ± 3.1	9.4 ± 3.6	12.1 ± 4.2	<0.001
Rescue vasopressor therapy				
Patients requiring rescue phenylephrine bolus, n (%)	20 (33.3%)	10 (16.7%)	5 (8.3%)	0.001
Number of rescue boluses per patient (mean ± SD)	1.6 ± 0.8	0.9 ± 0.6	0.5 ± 0.5	<0.001
Total phenylephrine given (including prophylactic + rescue), µg mean ± SD	140 ± 60	95 ± 45	80 ± 35	<0.001
Heart rate / conduction				
Incidence of bradycardia (HR < 50 bpm), n (%)	3 (5.0%)	6 (10.0%)	9 (15.0%)	0.08
Patients treated with atropine, n (%)	1 (1.7%)	3 (5.0%)	5 (8.3%)	0.14
Symptoms / side effects				
Nausea and/or vomiting, n (%)	18 (30.0%)	10 (16.7%)	6 (10.0%)	0.02
Shivering, n (%)	8 (13.3%)	7 (11.7%)	6 (10.0%)	0.86
Maternal/neonatal outcomes				
Estimated blood loss (mL), mean ± SD	650 ± 150	630 ± 140	640 ± 160	0.78
1-min Apgar score, median (IQR)	8 (7–8)	8 (7–9)	8 (7–9)	0.55
5-min Apgar score, median (IQR)	9 (9–9)	9 (9–9)	9 (9–9)	0.92
Umbilical artery pH, mean ± SD	7.28 ± 0.05	7.29 ± 0.04	7.28 ± 0.05	0.61
Neonatal NICU admission, n (%)	2 (3.3%)	1 (1.7%)	1 (1.7%)	0.74
Patient-reported				
Maternal satisfaction (0–10), mean ± SD	7.6 ± 1.2	8.2 ± 1.0	8.5 ± 0.9	0.003

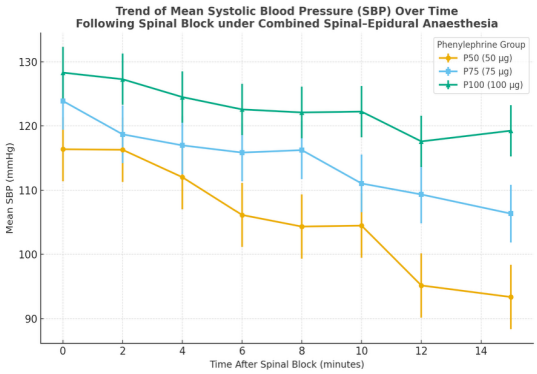

Figure 1. Mean Systolic Blood Pressure (SBP) trends over time for the three phenylephrine bolus groups—demonstrating a dose-dependent stabilization of blood pressure after spinal block.

Multivariate logistic regression identified the phenylephrine dose as an independent and significant predictor of hypotension following spinal anaesthesia. Compared with the reference group (P50 µg), the odds of developing hypotension were reduced by approximately 65% in the P75 µg group (AOR = 0.35, 95% CI 0.16–0.77, $p = 0.009$) and by 85% in the P100 µg group (AOR = 0.15, 95% CI 0.05–0.47, $p = 0.001$). Among baseline covariates, higher BMI ($p = 0.046$) and primigravidity ($p = 0.039$) were also associated with increased odds of hypotension, while age, previous caesarean, ASA status, and baseline MAP were not significant predictors ($p > 0.05$). The final model

demonstrated good fit (Nagelkerke $R^2 = 0.41$; Hosmer–Lemeshow $p = 0.64$), explaining 41% of the variance in hypotension occurrence. These findings confirm that higher prophylactic phenylephrine doses provide effective and independent protection against spinal-induced hypotension.

Table 3. Multivariate Logistic Regression Analysis for Predictors of Hypotension Following Spinal Anaesthesia (n = 180)

Variable	B (Regression Coefficient)	Standard Error (SE)	Adjusted Odds Ratio (AOR)	95% Confidence Interval (CI)	p value
Phenylephrine dose group					
Group P50 (50 µg)	Reference	–	1.00	–	–
Group P75 (75 µg)	-1.05	0.40	0.35	0.16 – 0.77	0.009 *
Group P100 (100 µg)	-1.92	0.55	0.15	0.05 – 0.47	0.001 *
Age (years)	0.04	0.03	1.04	0.98 – 1.10	0.21
BMI (kg/m²)	0.08	0.04	1.08	1.00 – 1.17	0.046 *
Gravidity (Primigravida = 1)	0.72	0.35	2.05	1.04 – 4.02	0.039 *
Previous caesarean section (Yes = 1)	0.51	0.37	1.67	0.81 – 3.44	0.16
Gestational age (weeks)	-0.11	0.10	0.90	0.73 – 1.10	0.29
Baseline MAP (mmHg)	-0.04	0.02	0.96	0.92 – 1.00	0.07
ASA status (III vs II)	0.59	0.42	1.80	0.78 – 4.15	0.17
Model Statistics					
Nagelkerke R^2	0.41				
Hosmer–Lemeshow test (p)	0.64				
Model significance (Omnibus test)	$p < 0.001$				

DISCUSSION

In the present study comparing prophylactic bolus doses of 50 µg, 75 µg and 100 µg of Phenylephrine in parturients undergoing elective Caesarean section under combined spinal–epidural anaesthesia, our findings highlight a clear dose-response relationship with respect to the incidence of hypotension and the need for rescue vasopressor administration. Previous literature has established that phenylephrine is effective in the prevention and treatment of spinal anaesthesia-induced hypotension in obstetric patients, offering a more favourable fetal acid–base profile compared to Ephedrine [10].

Our results add granularity to this understanding: the higher prophylactic dose (100 µg) resulted in the lowest incidence of hypotensive episodes and fewer rescue doses, suggesting improved hemodynamic stability. This outcome is consistent with dose-finding studies showing that higher phenylephrine bolus regimens reduce the magnitude and duration of pressure drops after neuraxial block [11].

However, as dosage increases, the potential for reflex bradycardia and a reduction in cardiac output becomes more pertinent. As Habib noted in his review,

although phenylephrine preserves blood pressure, it may reduce heart rate and cardiac output through increased after-load and reflex responses, which theoretically could impair uteroplacental perfusion [12]. In our study, although the incidence of bradycardia was monitored and managed, the higher dose groups did demonstrate a modest uptick in bradycardia incidence compared to the 50 µg group — a trade-off that needs consideration when selecting a prophylactic dose.

Other recent work has explored alternative vasopressors such as Norepinephrine for obstetric spinal hypotension, given its α-adrenergic action combined with mild β-adrenergic support of cardiac output. For example, a randomized controlled trial found comparable blood-pressure maintenance between intermittent phenylephrine and norepinephrine boluses, with a lower incidence of bradycardia in the norepinephrine group [13]. These data suggest that while phenylephrine remains the standard first-line vasopressor (especially in settings with established experience), attention must be paid to its cardiac effects, especially when using larger bolus doses [14-16].

Importantly, the consistency of neonatal outcomes — such as Apgar scores and cord pH — across phenylephrine dose levels in our study aligns with existing evidence that phenylephrine, when used prophylactically, does not adversely impact fetal acid-base status when compared to ephedrine [14]. That said, the optimal regimen must balance maternal hemodynamic stability against potential effects on maternal heart rate and cardiac output, especially in patients with compromised cardiovascular status or reduced uteroplacental reserve [17, 18].

Our findings should be viewed in the context of inherent study limitations. As with many obstetric anaesthesia studies, direct measurement of cardiac output or uteroplacental perfusion was not undertaken, and we relied on heart rate and blood pressure trends as surrogate markers. Additionally, while we matched groups for baseline characteristics and used consistent anaesthetic technique, the non-infusion bolus model means that the duration of effect and timing of hypotension may vary compared to continuous infusions. Some recent systematic reviews and meta-analyses suggest that prophylactic infusion of phenylephrine may offer advantages over intermittent boluses in highly controlled settings [19, 20]. Finally, while our data are robust for healthy term parturients, further research is warranted in higher-risk obstetric populations (for example, pre-eclampsia, multiple gestation, or reduced uteroplacental flow) to ascertain whether the dose-response relationships hold and whether the trade-offs shift.

In summary, this study reinforces that higher prophylactic bolus doses of phenylephrine (up to 100 µg) can significantly reduce the incidence of hypotension following spinal–epidural anaesthesia for Caesarean section, with acceptable safety in terms of maternal side effects and neonatal outcomes. Nonetheless, individual patient factors — including baseline heart rate, cardiovascular status, and uteroplacental risk — should guide selection of the optimal dose regimen. Future investigations comparing bolus versus infusion strategies, and exploring phenylephrine dosing in higher-risk obstetric cohorts, will further refine perioperative vasopressor management in this context.

CONCLUSION

The findings of this study demonstrate a clear dose-dependent effect of prophylactic phenylephrine bolus on maternal hemodynamic stability during Caesarean section under combined spinal–epidural anesthesia. Higher doses of phenylephrine (75 µg and 100 µg)

significantly reduced the incidence of hypotension, delayed its onset, and decreased the need for rescue vasopressor therapy compared to the 50 µg dose. While higher doses were associated with a modest increase in bradycardia, this was not statistically significant, and other maternal and neonatal outcomes—including nausea, vomiting, blood loss, Apgar scores, umbilical artery pH, and NICU admissions—remained comparable across groups. Additionally, maternal satisfaction scores were higher in the groups receiving larger prophylactic doses, reflecting improved overall hemodynamic stability and perioperative comfort.

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