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Original Article

Effect of Prophylactic Phenylephrine Infusion versus Norepinephrine Infusion on Maternal Hemodynamics during Spinal Anaesthesia

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ABSTRACT

Background: Spinal anaesthesia-induced hypotension is a common complication during caesarean delivery. Phenylephrine is widely used for prophylaxis; however, its association with reflex bradycardia has increased interest in norepinephrine as an alternative vasopressor. This study compared the effect of prophylactic phenylephrine and norepinephrine infusion on maternal haemodynamics during spinal anaesthesia for caesarean delivery.
Methods: This prospective randomized comparative study included 90 parturients undergoing elective caesarean section under spinal anaesthesia. Patients were allocated into two groups: Group P received prophylactic phenylephrine infusion (n=45), and Group N received prophylactic norepinephrine infusion (n=45). Maternal blood pressure, heart rate, incidence of hypotension, bradycardia, vasopressor requirement, maternal adverse effects, and neonatal outcomes were assessed.
Results: Baseline characteristics were comparable between both groups. Both vasopressors effectively maintained maternal blood pressure. The incidence of hypotension was lower in the norepinephrine group compared with the phenylephrine group (22.2% vs 31.1%, p=0.324). Mean systolic blood pressure at 10 minutes after spinal anaesthesia was significantly higher with norepinephrine (109.9 ± 9.8 vs 105.7 ± 10.4 mmHg, p=0.048). Bradycardia occurred significantly more frequently in the phenylephrine group (24.4% vs 6.7%, p=0.018), with better preservation of heart rate in the norepinephrine group. Maternal adverse effects and neonatal outcomes were comparable between groups.
Conclusion: Prophylactic norepinephrine infusion provided effective prevention of spinal anaesthesia-induced hypotension with better maintenance of maternal heart rate and reduced bradycardia compared with phenylephrine. Norepinephrine may be considered a suitable alternative vasopressor for obstetric spinal anaesthesia.

Keywords: Caesarean delivery; spinal anaesthesia; hypotension; phenylephrine; norepinephrine; maternal haemodynamics; vasopressor.

INTRODUCTION

Caesarean delivery is one of the most commonly performed obstetric surgical procedures worldwide, and spinal anaesthesia is the preferred anaesthetic technique for most elective caesarean sections due to its rapid onset, effective surgical anaesthesia, minimal neonatal drug exposure, and avoidance of airway-related complications associated with general anaesthesia. [1] However, spinal anaesthesia is frequently complicated by maternal hypotension, which remains the most common haemodynamic adverse event during caesarean delivery. The incidence of spinal anaesthesia-induced hypotension is particularly high in parturients because of sympathetic blockade-induced vasodilatation, reduced systemic vascular resistance, decreased venous return, and additional aortocaval compression by the gravid uterus. [2]Maternal hypotension during caesarean delivery is associated with significant maternal and fetal consequences. Clinically, it may result in nausea, vomiting, dizziness, discomfort, and reduced maternal satisfaction. Severe or prolonged hypotension may compromise

uteroplacental perfusion, leading to decreased fetal oxygen delivery, fetal acidosis, and adverse neonatal outcomes. Therefore, prevention and prompt management of hypotension are essential components of obstetric anaesthetic care to maintain maternal cardiovascular stability and ensure adequate fetal well-being. [3,4]Various preventive strategies, including fluid preloading, co-loading, positioning techniques, and pharmacological interventions, have been explored to reduce the incidence of spinal anaesthesia-related hypotension. Among these approaches, prophylactic vasopressor infusion has emerged as the most effective method for maintaining maternal blood pressure during caesarean delivery. [5] Phenylephrine, a selective α1-adrenergic receptor agonist, has traditionally been considered the first-line vasopressor because of its rapid and predictable ability to increase systemic vascular resistance and restore arterial pressure. Continuous phenylephrine infusion has demonstrated efficacy in reducing the frequency and severity of spinal anaesthesia-induced hypotension and is widely incorporated into current obstetric anaesthesia protocols. [6]

Despite its effectiveness, phenylephrine has certain limitations related to its pharmacological profile. As a pure α-adrenergic agonist with minimal β-adrenergic activity, phenylephrine increases vascular tone primarily through arterial vasoconstriction. This increase in systemic vascular resistance may trigger reflex bradycardia and reduce cardiac output, which may potentially affect maternal haemodynamic balance. Although these effects are usually well tolerated, concerns remain regarding the optimal vasopressor strategy, particularly in situations where preservation of cardiac output and uteroplacental circulation is important. [3–5]Norepinephrine, a potent sympathomimetic vasopressor with predominant α1-adrenergic activity and mild β1-adrenergic effects, has recently gained attention as a potential alternative to phenylephrine in obstetric anaesthesia. The additional β1 activity of norepinephrine may provide better maintenance of maternal heart rate and cardiac output while effectively preventing hypotension. [7] Recent randomized controlled trials have suggested that prophylactic norepinephrine infusion provides comparable blood pressure control to phenylephrine, with a lower incidence of maternal bradycardia and improved preservation of haemodynamic parameters. [8,9]Several studies have compared norepinephrine and phenylephrine for prevention of spinal anaesthesia-induced hypotension during caesarean delivery. Ngan Kee et al. demonstrated that norepinephrine was effective for maintaining blood pressure during spinal anaesthesia and was associated with better preservation of maternal heart rate compared with phenylephrine. [7] Similarly, Vallejo et al. reported that continuous norepinephrine infusion provided comparable prevention of spinal hypotension compared with phenylephrine, with favourable maternal haemodynamic effects. [10] Available evidence from randomized trials and systematic reviews indicates that both agents are effective in maintaining maternal blood pressure; however, norepinephrine may offer potential advantages because of its more balanced adrenergic profile. [7,10]Nevertheless, variations in infusion doses, timing of administration, patient characteristics, and outcome assessment methods have resulted in ongoing uncertainty regarding the optimal vasopressor agent for routine clinical practice. Although phenylephrine remains widely accepted as the standard vasopressor for obstetric spinal anaesthesia, increasing evidence supports norepinephrine as a promising alternative with potential advantages in maintaining cardiac output and reducing maternal bradycardia. [6–10]Maintaining stable maternal haemodynamics during spinal anaesthesia is essential for improving maternal comfort, reducing anaesthesia-related complications, and optimizing neonatal outcomes. A direct comparison of prophylactic phenylephrine and norepinephrine infusions provides important information regarding their relative efficacy, safety, and haemodynamic effects in obstetric patients.Therefore, the present study was undertaken to compare the effect of prophylactic phenylephrine infusion versus norepinephrine infusion on maternal haemodynamics during spinal anaesthesia for caesarean delivery.

MATERIALS AND METHODS

Study Design and Participants

This prospective, randomized comparative study was conducted in the Department of Anaesthesiology after approval from the Institutional Ethics Committee.The study was done at Gandhi medical College ,Bhopal, Madhya Pradesh for 7 month duration. A total of 90 parturient undergoing elective caesarean delivery under spinal anaesthesia were enrolled and randomly allocated into two groups:

- **Group P (Phenylephrine group, n=45):** Received prophylactic phenylephrine infusion.
- **Group N (Norepinephrine group, n=45):** Received prophylactic norepinephrine infusion.

Written informed consent was obtained from all participants.

Inclusion Criteria

Pregnant women aged 18–40 years, ASA physical status I–II, singleton term pregnancy (≥37 weeks), and scheduled for elective caesarean section under spinal anaesthesia were included.

Exclusion Criteria

Patients with emergency caesarean delivery, contraindications to spinal anaesthesia, cardiovascular disease, pregnancy-induced hypertension/preeclampsia, significant systemic illness, drug allergy, or baseline haemodynamic instability were excluded.

Anaesthetic Technique and Intervention

Baseline haemodynamic parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO_2) were recorded. Spinal anaesthesia was performed

using standard institutional protocol with hyperbaric bupivacaine. Patients received intravenous crystalloid co-loading and left uterine displacement.

After spinal anaesthesia, patients received prophylactic vasopressor infusion according to group allocation. Phenylephrine and norepinephrine infusions were titrated to maintain maternal blood pressure within 20% of baseline values. Rescue vasopressor was administered if significant hypotension occurred.

Haemodynamic Monitoring and Outcomes

Maternal haemodynamic parameters were recorded at baseline and at regular intervals after spinal anaesthesia until completion of surgery. The primary outcome was comparison of maternal haemodynamic stability between the two groups. Secondary outcomes included:

- Incidence of hypotension and bradycardia
- Changes in SBP, MAP, and HR
- Total vasopressor requirement
- Maternal adverse effects (nausea, vomiting, shivering, dizziness)
- Neonatal outcomes including Apgar scores at 1 and 5 minutes and birth weight

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentage. Independent t-test/Mann–Whitney U test was used for continuous variables, and Chi-square/Fisher's exact test was used for categorical variables. Repeated haemodynamic measurements were analysed using repeated-measures ANOVA. A p-value <0.05 was considered statistically significant.It was done by SPSS.25

RESULTS

A total of 90 parturients undergoing elective caesarean delivery under spinal anaesthesia were enrolled and randomly allocated to the phenylephrine group (Group P, *n*=45) and the norepinephrine group (Group N, *n*=45). All participants completed the study protocol and were included in the final analysis, with no protocol deviations or exclusions.

The baseline demographic and obstetric characteristics were comparable between the two study groups (Table 1). The mean maternal age was 28.4 ± 3.6 years in Group P and 28.1 ± 3.9 years in Group N (*p*=0.712). Similarly, the mean body mass index was 26.1 ± 2.8 kg/m² and 25.8 ± 3.1 kg/m², respectively (*p*=0.648). Mean gestational age at delivery was 38.2 ± 1.1 weeks in Group P and 38.3 ± 1.0 weeks in Group N (*p*=0.654). There were no statistically significant differences in parity, ASA physical status, or duration of surgery between the two groups (all *p*>0.05), indicating that both groups were well matched at baseline.

Baseline systolic blood pressure (SBP) was comparable between Group P and Group N (124.6 ± 9.8 mmHg vs 125.2 ± 10.1 mmHg; p=0.781) (Table 2, Figure 1). Following spinal anaesthesia, SBP decreased in both groups; however, patients receiving norepinephrine maintained higher SBP values throughout the intraoperative period. A statistically significant difference was observed at 10 minutes, with Group N demonstrating a higher mean SBP than Group P (109.9 ± 9.8 mmHg vs 105.7 ± 10.4 mmHg; p=0.048). Although SBP remained consistently higher in the norepinephrine group at subsequent time points, the differences were not statistically significant.

The baseline heart rate (HR) was similar between the two groups (88.6 ± 8.4 beats/min vs 89.1 ± 8.7 beats/min; p=0.784) (Table 3, Figure 2). Following spinal anaesthesia, HR decreased significantly in both groups, with a more pronounced reduction in the phenylephrine group. Mean HR was significantly lower in Group P at 5 minutes (74.8 ± 7.2 vs 80.1 ± 7.6 beats/min; p=0.002), 10 minutes (75.6 ± 6.8 vs 81.2 ± 7.4 beats/min; p=0.001), and 20 minutes (77.4 ± 7.1 vs 82.0 ± 7.5 beats/min; p=0.004). By the end of surgery, HR values became comparable between the groups (82.1 ± 7.4 vs 84.6 ± 7.8 beats/min; p=0.124).

The incidence of spinal anaesthesia-induced hypotension was lower in the norepinephrine group (22.2%) than in the phenylephrine group (31.1%), although the difference was not statistically significant (*p*=0.324) (Table 4). Bradycardia occurred significantly more frequently in Group P than in Group N (24.4% vs 6.7%; p=0.018). Rescue vasopressor administration was required in 26.7% of patients receiving phenylephrine compared with 17.8% receiving norepinephrine (*p*=0.287). The mean total vasopressor dose was 168.4 ± 42.6 µg in Group P and 154.7 ± 39.8 µg in Group N (*p*=0.118). Atropine administration was significantly more frequent in the phenylephrine group (13.3% vs 2.2%; p=0.048).

Maternal adverse effects were comparable between the two groups (Table 5). Nausea and vomiting occurred in 20.0% of patients in Group P and 11.1% in Group N (*p*=0.247). Shivering (13.3% vs 8.9%; p=0.505) and dizziness (8.9% vs 4.4%; p=0.396) were also similar between the groups.

Neonatal outcomes were comparable in both groups. The mean Apgar score at 1 minute was 7.8 ± 0.8 in Group P and 7.9 ± 0.7 in Group N (p=0.532), while the corresponding 5-minute Apgar scores were 8.9 ± 0.5 and 9.0 ± 0.4, respectively (p=0.318). Mean birth weight (2.91 ± 0.34 kg vs 2.94 ± 0.36 kg; p=0.684) and NICU admission rates (4.4% vs 2.2%; p=0.556) were likewise comparable.

Pearson correlation analysis demonstrated a significant positive correlation between vasopressor dose and reduction in systolic blood pressure in both groups (Table 6, Figure 3). The correlation was stronger in the phenylephrine group (r=0.62, p<0.001) than in the norepinephrine group (r=0.48, p=0.001). A significant negative correlation between vasopressor dose and heart rate change was observed in Group P (r=−0.54, p<0.001), whereas the corresponding relationship in Group N was weaker and not statistically significant (r=−0.28, p=0.061). Similarly, vasopressor dose showed a significant positive correlation with changes in mean arterial pressure in both Group P (r=0.59, p<0.001) and Group N (r=0.45, p=0.002).

Table 1. Baseline Demographic and Obstetric Characteristics of Study Participants (n=90)

Variable	Group P (Phenylephrine) (n=45)	Group N (Norepinephrine) (n=45)	p-value
Maternal age (years), Mean ± SD	28.4 ± 3.6	28.1 ± 3.9	0.712
BMI (kg/m²), Mean ± SD	26.1 ± 2.8	25.8 ± 3.1	0.648
Gestational age (weeks), Mean ± SD	38.2 ± 1.1	38.3 ± 1.0	0.654
Primigravida, n (%)	26 (57.8)	25 (55.6)	0.829
Multigravida, n (%)	19 (42.2)	20 (44.4)	
ASA Grade I, n (%)	31 (68.9)	32 (71.1)	0.819
ASA Grade II, n (%)	14 (31.1)	13 (28.9)	
Duration of surgery (min), Mean ± SD	52.6 ± 8.7	51.9 ± 9.2	0.711

Statistical test: Independent sample t-test, Chi-square test/Fisher's exact test

Table 2. Comparison of Maternal Systolic Blood Pressure at Different Time Intervals

Time interval	SBP (mmHg) Group P	SBP (mmHg) Group N	p-value
Baseline	124.6 ± 9.8	125.2 ± 10.1	0.781
After spinal anaesthesia (5 min)	108.4 ± 11.2	111.8 ± 10.6	0.142
10 min	105.7 ± 10.4	109.9 ± 9.8	0.048
20 min	108.9 ± 9.7	111.7 ± 9.4	0.167
30 min	112.6 ± 8.9	114.3 ± 8.7	0.356
End of surgery	116.8 ± 9.1	118.4 ± 8.6	0.394

Statistical test: Independent sample t-test, Repeated Measures ANOVA

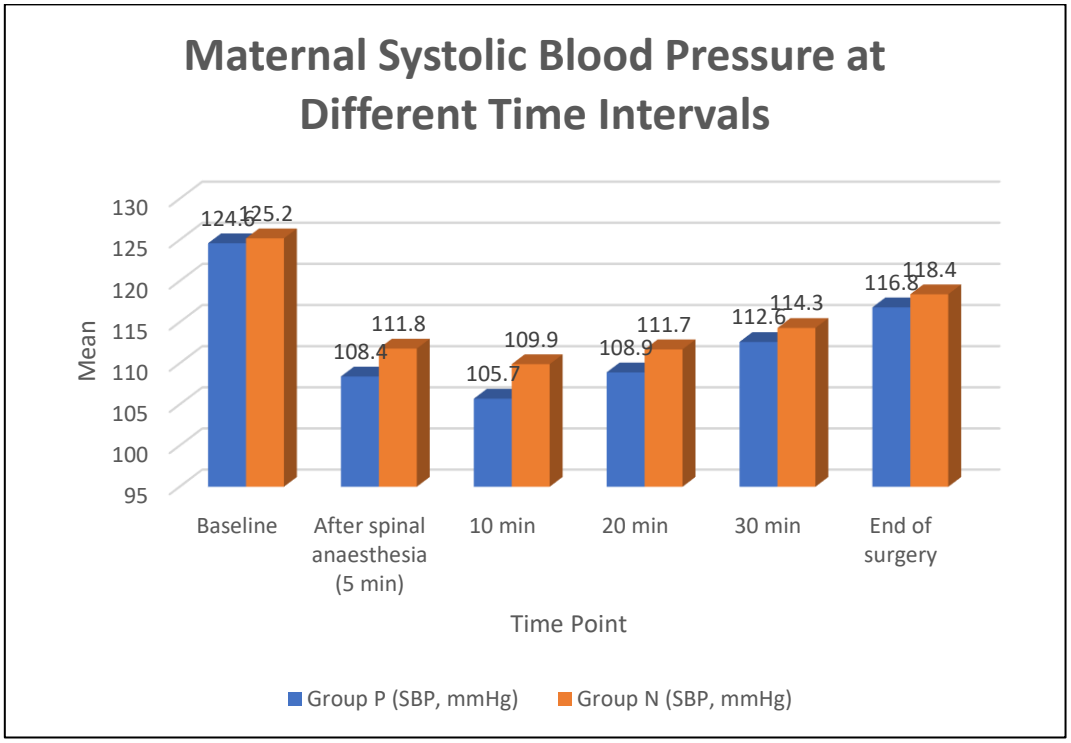

Figure 1. Comparison of Maternal Systolic Blood Pressure at Different Time Intervals

Table 3. Comparison of Heart Rate Changes During Surgery

Time interval	HR (beats/min) Group P	HR (beats/min) Group N	p-value
Baseline	88.6 ± 8.4	89.1 ± 8.7	0.784
5 min after spinal anaesthesia	74.8 ± 7.2	80.1 ± 7.6	0.002
10 min	75.6 ± 6.8	81.2 ± 7.4	0.001
20 min	77.4 ± 7.1	82.0 ± 7.5	0.004
End of surgery	82.1 ± 7.4	84.6 ± 7.8	0.124

Statistical test: Independent sample t-test

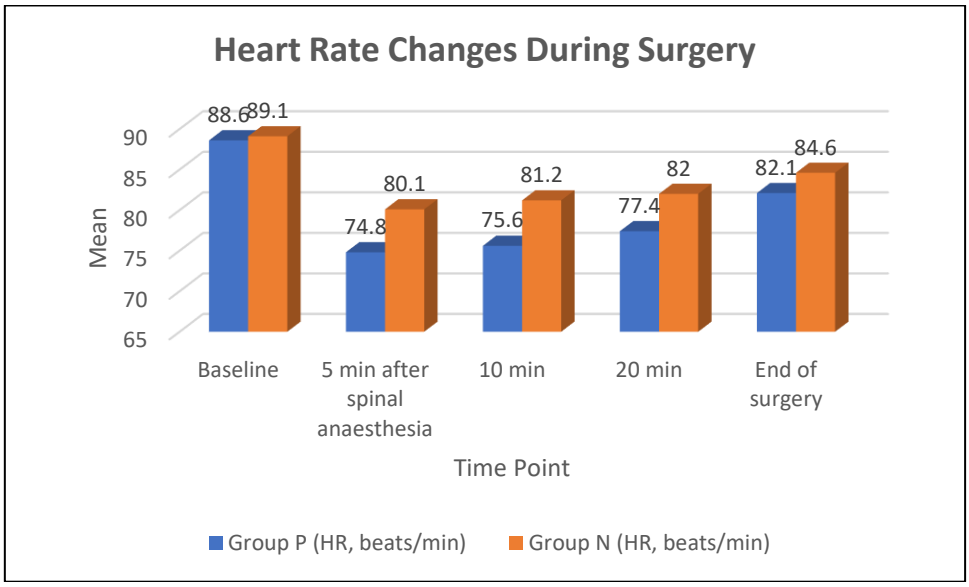

Figure 2. Comparison of Heart Rate Changes During Surgery

Table 4. Incidence of Hypotension, Bradycardia and Vasopressor Requirement

Outcome	Group P (n=45)	Group N (n=45)	p-value
Hypotension, n (%)	14 (31.1%)	10 (22.2%)	0.324
Bradycardia, n (%)	11 (24.4%)	3 (6.7%)	0.018
Rescue vasopressor required, n (%)	12 (26.7%)	8 (17.8%)	0.287
Total vasopressor dose (µg), Mean ± SD	168.4 ± 42.6	154.7 ± 39.8	0.118
Atropine requirement, n (%)	6 (13.3%)	1 (2.2%)	0.048

Statistical test: Chi-square test/Fisher's exact test, Continuous variables (vasopressor dose): **Independent sample t-test**

Table 5. Comparison of Maternal Adverse Effects and Neonatal Outcomes

Outcome	Group P (n=45)	Group N (n=45)	p-value
Nausea/vomiting, n (%)	9 (20.0%)	5 (11.1%)	0.247
Shivering, n (%)	6 (13.3%)	4 (8.9%)	0.505
Dizziness, n (%)	4 (8.9%)	2 (4.4%)	0.396
Apgar score at 1 min	7.8 ± 0.8	7.9 ± 0.7	0.532
Apgar score at 5 min	8.9 ± 0.5	9.0 ± 0.4	0.318
Birth weight (kg)	2.91 ± 0.34	2.94 ± 0.36	0.684
NICU admission, n (%)	2 (4.4%)	1 (2.2%)	0.556

Statistical test: Independent sample t-test, Chi-square test/Fisher's exact test

Table 6. Correlation Between Vasopressor Dose and Maternal Haemodynamic Changes

Parameter	Group P (Phenylephrine)	Group N (Norepinephrine)
Correlation between vasopressor dose and fall in SBP	r = 0.62, p<0.001	r = 0.48, p=0.001
Correlation between vasopressor dose and HR change	r = −0.54, p<0.001	r = −0.28, p=0.061
Correlation between vasopressor dose and MAP change	r = 0.59, p<0.001	r = 0.45, p=0.002

Statistical test: Pearson's correlation coefficient

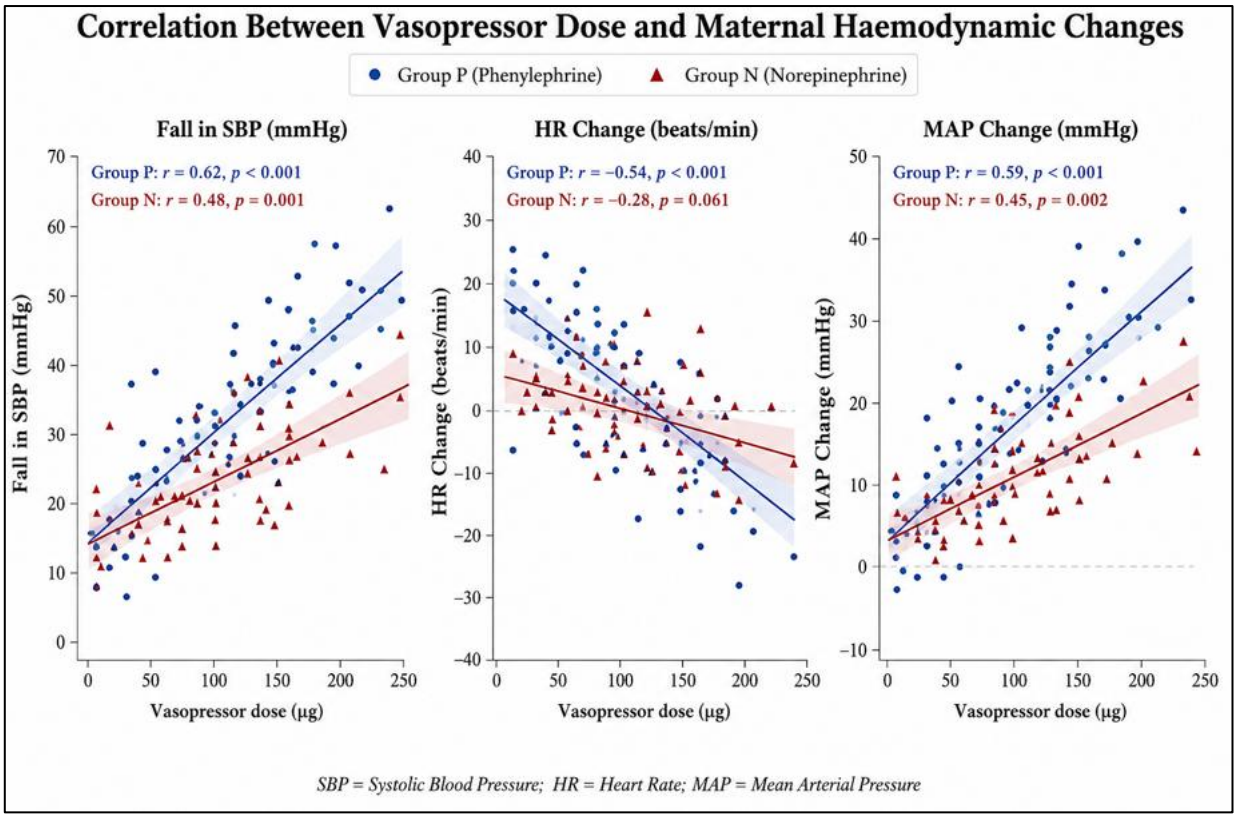

Figure 3. Correlation Between Vasopressor Dose and Maternal Haemodynamic Changes

DISCUSSION

The present randomized comparative study evaluated the effect of prophylactic phenylephrine versus norepinephrine infusion on maternal haemodynamics during spinal anaesthesia for caesarean delivery. Among 90 parturients (45 in each group), both vasopressors effectively maintained maternal blood pressure; however, norepinephrine demonstrated a more favourable haemodynamic profile with better preservation of maternal heart rate and reduced incidence of bradycardia.

Spinal anaesthesia-induced hypotension is a common complication during caesarean delivery due to sympathetic blockade, reduced systemic vascular resistance, and aortocaval compression. In the present study, hypotension occurred in 31.1% of patients in the phenylephrine group and 22.2% in the norepinephrine group (p=0.324), indicating comparable efficacy of both vasopressors. Norepinephrine showed a trend toward better maintenance of blood pressure, with significantly higher SBP at 10 minutes after spinal anaesthesia (109.9 ± 9.8 vs 105.7 ± 10.4 mmHg, p=0.048).

Ngan Kee et al. [11] compared a closed-loop computer-controlled infusion system of norepinephrine and phenylephrine during spinal anaesthesia for caesarean delivery and reported effective blood pressure control with both agents, while norepinephrine provided improved haemodynamic stability. Similarly, Ngan Kee et al. [12] demonstrated that prophylactic norepinephrine infusion effectively prevented spinal hypotension without adverse maternal or neonatal outcomes, supporting its use as an alternative vasopressor.

The major difference observed in the present study was the effect on maternal heart rate. Bradycardia occurred significantly more frequently in the phenylephrine group compared with the norepinephrine group (24.4% vs 6.7%, p=0.018). Mean heart rate at 5 minutes after spinal anaesthesia was also significantly lower with phenylephrine (74.8 ± 7.2 vs 80.1 ± 7.6 beats/min, p=0.002).

This finding is explained by the pharmacological properties of phenylephrine, which acts as a pure α1-adrenergic agonist and may cause reflex bradycardia due to increased vascular resistance. Norepinephrine, due to its additional β1 activity, may better preserve heart rate and cardiac output.

Sharkey et al. [13] compared intermittent boluses of phenylephrine and norepinephrine during caesarean delivery and reported that norepinephrine provided effective blood pressure control with reduced maternal bradycardia. Carvalho and Dyer [14] suggested that norepinephrine may represent a paradigm shift in obstetric vasopressor therapy because of its ability to maintain arterial pressure while minimizing reductions in cardiac output.

In the present study, rescue vasopressor requirement was lower in the norepinephrine group (17.8% vs 26.7%), although statistically non-significant. The mean total vasopressor dose was also lower with norepinephrine (154.7 ± 39.8 µg vs 168.4 ± 42.6 µg).

Similar findings were reported by Sharkey et al. [13], who demonstrated fewer rescue interventions with norepinephrine compared with phenylephrine during caesarean delivery. Ngan Kee et al. [11] also reported that norepinephrine infusion maintained blood pressure effectively with reduced need for additional interventions.

Maternal adverse effects were comparable between groups in the present study. Nausea and vomiting occurred in 20.0% of phenylephrine patients and 11.1% of norepinephrine patients (p=0.247), with no significant differences in shivering or dizziness.

Smiley [15] emphasized that the ideal vasopressor in obstetric anaesthesia should maintain blood pressure while minimizing effects on cardiac output and maternal comfort. The present findings support this concept, with norepinephrine demonstrating haemodynamic advantages without increasing adverse effects.

Neonatal outcomes were similar between groups, with comparable Apgar scores at 1 minute (7.8 ± 0.8 vs 7.9 ± 0.7; p=0.532) and 5 minutes (8.9 ± 0.5 vs 9.0 ± 0.4; p=0.318). Ngan Kee et al. [12] and Ngan Kee et al. [11] also reported comparable neonatal outcomes between norepinephrine and phenylephrine groups, confirming the safety of norepinephrine in obstetric anaesthesia.

In the present study, vasopressor dose showed a significant negative correlation with heart rate changes in the phenylephrine group ($r=-0.54$, $p<0.001$), whereas the correlation was weaker and non-significant with norepinephrine ($r=-0.28$, $p=0.061$). This suggests a greater tendency for phenylephrine to produce dose-related reductions in heart rate.
Sharwood-Smith and Drummond [16] highlighted the importance of maintaining cardiovascular compensation during obstetric spinal anaesthesia, particularly in preventing compromised maternal and fetal perfusion.

CONCLUSION

Prophylactic norepinephrine infusion provided effective prevention of spinal anaesthesia-induced hypotension during caesarean delivery, with comparable blood pressure control to phenylephrine.

Norepinephrine demonstrated a more favourable haemodynamic profile by reducing maternal bradycardia and better preserving heart rate. Norepinephrine may be considered a suitable alternative to phenylephrine for maintaining maternal haemodynamic stability during obstetric spinal anaesthesia.

Limitations

The study was conducted with a relatively small sample size from a single centre, which may limit the generalizability of the findings. Cardiac output monitoring and long-term neonatal follow-up were not performed, limiting assessment of detailed cardiovascular effects and outcomes.

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