

A COMPARATIVE STUDY OF PROPHYLACTIC NOREPINEPHRINE AND PHENYLEPHRINE INFUSIONS FOR PREVENTION OF SPINAL ANAESTHESIA-INDUCED HYPOTENSION IN PARTURIENTS UNDERGOING CAESAREAN SECTION

Joydeepa Das¹, Lalan Singam², Takhelmayum Hemjit Singh³, Ashem Jack Meitei⁴, Yumnam ArunKumar Singh⁵, Gojendra Rajkumar⁶, Rupendra Singh Thokchom⁷

Received : 14/08/2026
Received in revised form : 05/09/2026
Accepted : 19/09/2026

Keywords:
Spinal anaesthesia, hypotension, norepinephrine, phenylephrine, caesarean section.

Corresponding Author:
Dr. Takhelmayum Hemjit Singh,
Email: takhelhem@yahoo.com

DOI: 10.47009/jamp.2026.8.5.113

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (5); 722-726



¹Senior Resident, Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India.

²Senior Resident, Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India

³Professor, Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India.

⁴Professor, Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India

⁵Professor, Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India.

⁶Professor and Head of the Department, Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India.

⁷Professor, Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India.

ABSTRACT

Background: Spinal anaesthesia is widely preferred for caesarean delivery because of its safety and minimal neonatal drug exposure. However, maternal hypotension remains a frequent and clinically important complication, often requiring prompt intervention with vasopressors. **Objective:** This study was conducted to compare the effectiveness of norepinephrine and phenylephrine infusions in preventing hypotension following spinal anaesthesia in parturients undergoing caesarean section. **Materials and Methods:** In this randomized clinical trial, parturients scheduled for elective caesarean section under spinal anaesthesia were allocated into two groups. One group received phenylephrine at a concentration of 50 µg/mL infusion, while the other received norepinephrine at a concentration of 2.5 µg/mL infusion at a fixed rate of 60 mL/h in both the groups. Hemodynamic parameters, incidence of hypotension, bradycardia, maternal side effects, and neonatal outcomes were recorded and analyzed. **Results:** Both norepinephrine and phenylephrine were effective in maintaining blood pressure. The requirement of rescue boluses was significantly lower in the norepinephrine group ($p = 0.035$). Although the incidence of bradycardia was higher in the phenylephrine group, the difference was not statistically significant. Other adverse effects and neonatal outcomes were comparable between the groups. **Conclusion:** Norepinephrine appears to be a reliable alternative to phenylephrine for the prevention of spinal anaesthesia-induced hypotension, with the added benefit of maintaining heart rate more consistently.

INTRODUCTION

Spinal anaesthesia remains the preferred technique for most caesarean sections due to its rapid onset, reliability, and favourable safety profile for both the mother and the neonate. It also minimizes fetal

exposure to systemic drugs compared to general anaesthesia. Despite these advantages, hypotension following spinal anaesthesia continues to be one of the most frequent and clinically significant complications encountered in obstetric practice. The primary mechanism involves sympathetic blockade,

resulting in vasodilation, decreased systemic vascular resistance, and reduced venous return. Clinically, this may manifest as nausea, vomiting, dizziness, and in severe cases, compromised uteroplacental perfusion leading to adverse fetal outcomes.^[1] Various preventive strategies, including fluid preloading, coload, and positional modifications, have been explored to reduce the incidence of hypotension; however, these measures alone are often insufficient. Consequently, vasopressors remain the cornerstone for both prevention and management of spinal anaesthesia-induced hypotension. Among the available agents, phenylephrine, a selective alpha-adrenergic agonist, has been widely adopted as the first-line drug due to its effectiveness in restoring blood pressure. However, its use is frequently associated with reflex bradycardia and a reduction in cardiac output, which may be undesirable in certain clinical scenarios.^[2,3]

In recent years, norepinephrine has gained attention as an alternative vasopressor. Owing to its combined alpha-adrenergic and mild beta-adrenergic activity, norepinephrine has the potential to maintain arterial pressure while better preserving heart rate and cardiac output. Emerging evidence suggests that norepinephrine may provide more stable hemodynamic control with fewer adverse cardiac effects compared to phenylephrine.^[4,5] Despite increasing global evidence, data from our setting remain limited. Therefore, the present study was undertaken to compare the efficacy and safety of prophylactic norepinephrine and phenylephrine infusions in preventing spinal anaesthesia-induced hypotension in parturients undergoing caesarean section. The study was conducted with the aims and objectives of comparing the efficacy of norepinephrine and phenylephrine in the management of spinal-induced hypotension during caesarean section and to compare the hemodynamic parameters like Systolic blood pressure (SBP), Mean arterial pressure (MAP), Diastolic blood pressure (DBP) and heart rate (HR) at varied time intervals after administration of norepinephrine and phenylephrine and any adverse reactions such as nausea, vomiting, and shivering associated with it.

MATERIALS AND METHODS

This prospective randomized, double-blind controlled study was conducted in the operation theatre of the Department of Anaesthesiology at the Regional Institute of Medical Sciences, Imphal, over a period of two years from April 2023 to March 2025. A total of 104 parturients aged between 18 and 45 years, classified as American Society of Anaesthesiologists (ASA) physical status I or II and scheduled for elective caesarean section under spinal anaesthesia, were enrolled after obtaining written informed consent. Approval for the study was obtained from the RIMS Institutional Research Ethics Board, and the trial was registered with the

Clinical Trial Registry of India (CTRI/2024/10/075003).

Patients were included if they met the age and ASA criteria and were undergoing elective caesarean delivery. Exclusion criteria comprised known hypersensitivity to local anaesthetic agents or study drugs, coagulation abnormalities (including platelet count $<50,000/\mu\text{L}$, INR >1.5 , or prolonged prothrombin time), local infection at the injection site, spinal deformities, significant cardiac, respiratory, renal, or neurological disorders, and hypertensive disorders of pregnancy such as preeclampsia.

Sample size estimation was based on previously reported differences in the incidence of hypotension between norepinephrine and phenylephrine groups, as described in earlier studies.^[5,6] With a power of 80% and a confidence level of 95%, the calculated sample size was 50 patients per group. To compensate for potential dropouts, 52 patients were included in each group, resulting in a total sample size of 104.

Participants were randomly assigned into two equal groups using a computer-generated randomization sequence. Allocation concealment was ensured by preparing the study drugs by an independent anaesthesiologist not involved in patient management or data collection. The drugs were placed in identical syringes labelled as “study drug,” thereby maintaining blinding of both the investigator and the patient.

All patients received standard premedication with oral pantoprazole 40 mg the night prior to surgery and intravenous metoclopramide 10 mg on the day of surgery. Upon arrival in the operating room, routine monitoring including electrocardiography, non-invasive blood pressure measurement, and pulse oximetry was established. Baseline hemodynamic parameters were recorded. An 18-gauge intravenous cannula was inserted, and lactated Ringer's solution was administered at a rate of 15 mL/kg.

Spinal anaesthesia was performed in the left lateral position at the L3–L4 interspace using a 25-gauge Quincke needle. After confirmation of free flow of cerebrospinal fluid, 2 mL of 0.5% hyperbaric bupivacaine was administered intrathecally. Patients were then positioned supine with left uterine displacement, and supplemental oxygen was provided via face mask at 5 L/min. Sensory block height was assessed using pinprick and maintained between T4 and T6 dermatomal levels.

Immediately following spinal injection, the study drug infusion was initiated at a fixed rate of 60 mL/h. Patients in Group A received norepinephrine at a concentration of 2.5 $\mu\text{g/mL}$, while those in Group B received phenylephrine at a concentration of 50 $\mu\text{g/mL}$. Hemodynamic parameters were recorded at 2-minute intervals for the first 10 minutes and subsequently at 5-minute intervals until the end of surgery. Hypotension, defined as a reduction in systolic blood pressure of 20% or more from baseline, was treated with 1 mL boluses of the

respective study drug. Hypertension, defined as a 20% increase from baseline, was managed by discontinuation of the infusion. Bradycardia, defined as heart rate below 50 beats per minute, was treated with intravenous atropine 0.6 mg, while tachycardia was defined as heart rate exceeding 120 beats per minute.

Following delivery, 10 units of oxytocin were administered as a slow intravenous infusion. Cases in which the sensory block extended above T4 or intraoperative blood loss exceeded 500 mL were excluded from analysis. Patients were monitored in the post-anaesthesia care unit after completion of surgery.

The primary outcome measure was the incidence of hypotension, expressed as the proportion of patients experiencing at least one episode. Secondary outcomes included hemodynamic variables such as heart rate and blood pressure trends, incidence of bradycardia and hypertension, total vasopressor consumption, maternal adverse effects (including nausea, vomiting, and shivering), and neonatal

outcomes assessed using Apgar scores and umbilical vein blood gas analysis. Fetal acidosis was defined as an umbilical venous pH less than 7.

All data were recorded in a structured proforma and subsequently entered into Statistical Package for the Social Sciences (SPSS) version 26.0 for analysis. Continuous variables were expressed as mean $\pm$ standard deviation and analyzed using Student's t-test or analysis of variance (ANOVA), as appropriate. Categorical variables were expressed as frequencies and percentages and analyzed using the Chi-square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 104 parturients were included in the study and were randomly allocated into two groups: Group A (noradrenaline, n = 52) and Group B (phenylephrine, n = 52).

Table 1: Baseline and Intraoperative Characteristics of Study Participants (N = 104)

Variable	Group A (Norepinephrine, n = 52)(n = 52) Mean $\pm$ SD / n (%)	Group B (Phenylephrine) (n = 52) Mean $\pm$ SD / n (%)	p-value
Age (years)	30.19 $\pm$ 6.5	28.19 $\pm$ 6.3	0.115
Weight (kg)	64.2 $\pm$ 7.2	63.9 $\pm$ 6.8	0.789
Height (cm)	157.3 $\pm$ 4.9	156.7 $\pm$ 4.5	0.541
Duration of surgery (min)	50.1 $\pm$ 10.9	53.1 $\pm$ 13.5	0.220
Dermatomal level (T3)	1 (1.9%)	0 (0.0%)	
Dermatomal level (T4)	48 (92.4%)	46 (88.5%)	0.360
Dermatomal level (T5)	3 (5.7%)	6 (11.5%)	

The baseline demographic and intraoperative characteristics were comparable between the two groups, with no statistically significant differences ($p > 0.05$). The mean duration of surgery and dermatomal block distribution (T3–T5) were also similar between the groups, indicating homogeneity of study populations.

Table 2: Distribution of Study Participants According to Number of Rescue Boluses (N = 104)

Number of Boluses	Group A (Norepinephrine, n = 52)(n = 52) n (%)	Group B (Phenylephrine) (n = 52) n (%)	p-value
0	49 (94.2%)	40 (76.9%)	
1	3 (5.8%)	10 (19.2%)	0.035*
2	0 (0.0%)	2 (3.8%)	

A significantly higher proportion of patients in the norepinephrine group did not require rescue boluses (94.2%) compared to the phenylephrine group (76.9%), indicating better hemodynamic stability with norepinephrine.

Table 3: Distribution of Adverse Effects among Study Participants (N = 104)

Adverse Effect	Group A (Norepinephrine, n = 52)(n = 52) n (%)	Group B (Phenylephrine) (n = 52) n (%)	p-value
Bradycardia	0 (0.0%)	3 (5.8%)	0.079
Tachycardia (episodes)			0.711
0 episodes	47 (90.4%)	49 (94.2%)	
1 episode	2 (3.8%)	2 (3.8%)	
2 episodes	2 (3.8%)	1 (2.0%)	
4 episodes	1 (2.0%)	0 (0.0%)	
Hypertension	1 (2.0%)	0 (0.0%)	0.315
Shivering	6 (11.5%)	7 (13.5%)	—
Nausea/Vomiting	6 (11.5%)	7 (13.5%)	—

The incidence of adverse effects was comparable between the groups, as shown in table 3. Bradycardia was observed only in the phenylephrine group, although the difference was not statistically significant ($p = 0.079$). The incidence of tachycardia and hypertension was similar in both groups. Other side effects such as shivering and nausea/vomiting were also comparable.

DISCUSSION

Maternal hypotension is a well-recognized consequence of spinal anaesthesia and remains a major concern during caesarean delivery. It can present with symptoms such as dizziness, nausea, and vomiting, and more importantly, may compromise uteroplacental perfusion, potentially leading to fetal hypoxia and acidosis. Therefore, early recognition and prompt treatment with intravenous fluids and vasopressors are crucial to maintain maternal and fetal well-being. Commonly used vasopressors include ephedrine, phenylephrine (PE), and more recently, norepinephrine (NE). While ephedrine has been widely used, it is associated with maternal tachycardia and a higher incidence of neonatal acidosis.^[7] Phenylephrine, a pure alpha-adrenergic agonist, is currently considered the standard agent; however, it may cause reflex bradycardia and a reduction in cardiac output, which can be undesirable in certain clinical situations.^[2,3] Norepinephrine, with its combined alpha-agonist and mild beta-agonist effects, has emerged as a potential alternative due to its ability to maintain blood pressure while better preserving heart rate and cardiac output.^[4,5]

In the present randomized double-blind study involving 104 parturients, both study groups were comparable in terms of baseline characteristics such as age, weight, and height. This similarity is consistent with previous studies conducted by Ngan Kee et al,^[8] and Mohta et al,^[9] ensuring that the observed differences are likely attributable to the interventions rather than confounding variables. One of the key findings of our study was the significantly lower incidence of hypotension in the norepinephrine group compared to the phenylephrine group (5.8% vs 23%, $p=0.035$). This observation is in agreement with the findings of Wang et al,^[6] who demonstrated improved efficacy of norepinephrine in managing spinal anaesthesia-induced hypotension. Similar results have also been reported by Goel et al,^[5] and Hasanin et al,^[10] who showed that norepinephrine reduces the need for rescue vasopressor interventions.

Analysis of heart rate trends revealed that patients receiving norepinephrine maintained relatively higher heart rates intraoperatively, particularly after the initial few minutes following spinal anaesthesia. Additionally, the incidence of bradycardia was lower in the norepinephrine group. These findings align with studies by Ngan Kee et al,^[3] and Chen et al,^[4] both of whom reported improved heart rate stability and preservation of cardiac output with norepinephrine compared to phenylephrine.

With respect to blood pressure control, norepinephrine demonstrated more stable hemodynamic performance, especially in the later stages of surgery. Mean arterial pressure values were better maintained at specific time points, suggesting sustained efficacy of norepinephrine infusion. These findings are comparable to those reported by

Berawala et al,^[11] who also observed improved hemodynamic stability with norepinephrine. Furthermore, the overall pattern of blood pressure control seen in our study is supported by the comprehensive review by Ferré et al,^[1] which emphasizes the evolving role of norepinephrine in managing spinal anaesthesia-induced hypotension.

The incidence of maternal adverse effects such as nausea, vomiting, and shivering was similar in both groups, indicating comparable safety profiles. This is consistent with findings from Rai et al,^[12] and Puthenveetil et al,^[13] who also reported no significant differences in side effect profiles between norepinephrine and phenylephrine. Neonatal outcomes, assessed using Apgar scores and umbilical vein blood gas analysis, were also comparable between the two groups. These findings support the results of the Bayesian network meta-analysis by Singh et al,^[14] which concluded that there are no significant differences in neonatal outcomes between the two vasopressors.

Other intraoperative variables, including dermatomal block height and duration of surgery, were similar across both groups, which is in agreement with the findings of Du et al.^[15] This consistency helps ensure that the differences observed in hemodynamic parameters are likely due to the pharmacological effects of the study drugs rather than procedural variations. Additionally, the significantly reduced requirement for rescue boluses in the norepinephrine group further supports its effectiveness, as also reported by Dong et al,^[16] and Mwaura et al,^[17] highlighting improved blood pressure control with norepinephrine-based regimens.

The strengths of the present study include its randomized and double-blind design, which minimizes bias and enhances the reliability of findings. However, certain limitations must be acknowledged. Advanced hemodynamic monitoring techniques were not used, limiting the ability to directly assess cardiac output changes. Patients with significant cardiac comorbidities were excluded, which may restrict the generalizability of the findings. Furthermore, only elective caesarean sections were included, and the fixed-rate infusion protocol may not reflect individualized dosing strategies required in clinical practice.

CONCLUSION

Norepinephrine infusion is as effective as phenylephrine in preventing spinal anaesthesia-induced hypotension and is associated with improved hemodynamic stability, as evidenced by reduced requirement of rescue boluses and better heart rate control. It may be considered a suitable and potentially superior alternative to phenylephrine in parturients undergoing caesarean section.

REFERENCES

1. Ferré F, Martin C, Bosch L, Kurrek M, Lairez O, Minville V. Control of spinal anaesthesia-induced hypotension in adults. *Local Reg Anesth*. 2020;13:39-46.
2. Ngan Kee WD, Lee SWY, Ng FF, Lee A. Norepinephrine or phenylephrine during spinal anaesthesia for caesarean delivery: a randomized double-blind non-inferiority study of neonatal outcome. *Br J Anaesth*. 2020;125(4):588-595.
3. Ngan Kee WD, Lee SW, Ng FF, Tan PE, Khaw KS. Randomized double-blind comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anaesthesia for caesarean delivery. *Anesthesiology*. 2015;122(4):736-745.
4. Chen D, Qi X, Huang X, Xu Y, Qiu F, Yan Y, et al. Efficacy and safety of different norepinephrine regimens for prevention of spinal hypotension in caesarean section: a randomized trial. *Biomed Res Int*. 2018;2018:2708175.
5. Hasanin AM, Amin SM, Agiza NA, Elsayed MK, Refaat S, Hussein HA, et al. Norepinephrine infusion for preventing postspinal anaesthesia hypotension during caesarean delivery: a randomized dose-finding trial. *Anesthesiology*. 2019;130(1):55-62.
6. Wang X, Mao M, Zhang SS, Wang ZH, Xu SQ, Shen XF. Bolus norepinephrine and phenylephrine for maternal hypotension during elective caesarean section with spinal anaesthesia: a randomized double-blind study. *Chin Med J*. 2020;133:509-516.
7. Nazir I, Bhat MA, Qazi S, Buchh VN, Gurcoo SA. Comparison between phenylephrine and ephedrine in preventing hypotension during spinal anaesthesia for caesarean section. *J ObstetAnaesth Crit Care*. 2012;2(2):92.
8. Ngan Kee WD, Lee SWY, Ng FF, Khaw KS. Prophylactic norepinephrine infusion for preventing hypotension during spinal anaesthesia for caesarean delivery. *Anesth Analg*. 2018;126(6):1989-1994.
9. Mohta M, Garg A, Chilkoti GT, Malhotra RK. A randomized controlled trial of phenylephrine and noradrenaline boluses for treatment of postspinal hypotension during elective caesarean section. *Anaesthesia*. 2019;74(7):850-855.
10. Goel K, Luthra N, Goyal N, Grewal A, Taneja A. Comparison of norepinephrine and phenylephrine infusions for maintenance of hemodynamics following subarachnoid block in lower segment caesarean section. *Indian J Anaesth*. 2021;65(8):600.
11. Berawala PK, Mehta SH, Chaudhari MS, Shinde MK. A randomized double-blind comparative study of phenylephrine and norepinephrine infusion for prevention and treatment of spinal anaesthesia-induced hypotension in caesarean deliveries. *Indian Anaesthetists Forum*. 2021;22(2):136.
12. Rai AV, Prakash S, Chellani H, Mullick P, Wason R. Comparison of phenylephrine and norepinephrine for treatment of spinal hypotension during elective caesarean delivery: a randomized double-blind study. *J Anaesthesiol Clin Pharmacol*. 2022;38(3):445-452.
13. Puthenveetil N, Sivachalam SN, Rajan S, Paul J, Kumar L. Comparison of norepinephrine and phenylephrine boluses for treatment of hypotension during spinal anaesthesia for caesarean section: a randomized controlled trial. *Indian J Anaesth*. 2019;63(12):995-1000.
14. Singh PM, Singh NP, Reschke M, Ngan Kee WD, Palanisamy A, Monks DT. Vasopressor drugs for prevention and treatment of hypotension during neuraxial anaesthesia for caesarean delivery: a Bayesian network meta-analysis. *Br J Anaesth*. 2020;124(3):e95-e107.
15. Du W, Song Y, Li J, Zhou X, Xu Z, Liu Z. Comparison of prophylactic norepinephrine and phenylephrine infusions during spinal anaesthesia for primary caesarean delivery in twin pregnancies: a randomized double-blind study. *Drug Des Devel Ther*. 2022;16:789-798.
16. Dong L, Dong Q, Song X, Liu Y, Wang Y. Comparison of prophylactic bolus norepinephrine and phenylephrine for hypotension during spinal anaesthesia for caesarean section. *Int J Clin Exp Med*. 2017;10(8):12315-12321.
17. Mwaura L, Mung'ayi V, Kabugi J, Mir S. A randomized controlled trial comparing weight-adjusted versus fixed-dose prophylactic phenylephrine infusion for maintaining systolic blood pressure during caesarean section under spinal anaesthesia. *Afr Health Sci*. 2016;16(2):399-411.
18. Hassabelnaby YS, Hasanin AM, Adly N, Mostafa M, Refaat S, Fouad E, et al. Comparison of two norepinephrine rescue boluses for management of postspinal hypotension during caesarean delivery: a randomized controlled trial. *BMC Anesthesiol*. 2020;20(1):1-8.
19. Andrade PA, Ortiz YM, Gamon AA. Norepinephrine and etilefrine for prevention of maternal hypotension in caesarean section under spinal anaesthesia. *Rev CientCienc Med*. 2018;21(1):68-77.
20. Chen Y, Zou L, Li Z, Guo L, Xue W, He L, et al. Prophylactic norepinephrine infusion for postspinal anaesthesia hypotension in caesarean section: a randomized controlled dose-finding trial. *Pharmacotherapy*. 2021;41(4):370-378.