Original Article
DOI: https://doi.org/10.70749/ijbr.v4i1.2852

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

Prophylactic Ephedrine versus Phenylephrine for Prevention of Maternal Hypotension Following Spinal Anesthesia for Elective Cesarean Section: A Prospective Randomized Comparative Study

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ARTICLE INFO

Keywords: Ephedrine; Phenylephrine; Spinal anesthesia; Cesarean section; Maternal hypotension

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Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History
Received: 01-08-2025 Revised: 28-11-2025
Accepted: 21-12-2025 Published: 30-01-2026

ABSTRACT

Objective: To compare the efficacy of prophylactic intravenous bolus ephedrine and phenylephrine in preventing maternal hypotension following spinal anesthesia for elective cesarean section. **Study Design:** Prospective randomized comparative study. **Place and Duration of Study:** Department of Anesthesiology, Dow University of Health Sciences and Civil Hospital Karachi, from June to December 2023. **Methodology:** One hundred and sixty-six ASA physical status I–II parturients undergoing elective cesarean section under spinal anesthesia were randomly allocated to receive either ephedrine 10 mg IV (Group E, n=83) or phenylephrine 100 µg IV (Group P, n=83) as a prophylactic bolus administered three minutes prior to spinal anesthesia. Maternal hypotension was defined as a >20% reduction in mean arterial pressure (MAP) from baseline at any intraoperative time point. Data were analyzed using SPSS version 11. **Results:** Maternal hypotension occurred in 56 (67.5%) patients in Group E and 74 (89.2%) patients in Group P (p=0.001). **Conclusion:** In a bolus-based vasopressor protocol, prophylactic ephedrine was more effective than phenylephrine in preventing maternal hypotension following spinal anesthesia for elective cesarean section.

INTRODUCTION

Spinal anesthesia is the anesthetic technique of choice for elective cesarean delivery owing to its rapid onset, reliability, dense sensory blockade, and reduced maternal morbidity compared with general anesthesia. Despite these advantages, spinal anesthesia is frequently associated with maternal hypotension resulting from sympathetic blockade, with reported incidences ranging from 60% to 80%.

Maternal hypotension is clinically significant as it may lead to maternal symptoms such as nausea, vomiting, dizziness, and decreased level of consciousness. More importantly, a reduction in maternal blood pressure can compromise uteroplacental blood flow, potentially resulting in fetal hypoxia and metabolic acidosis. Consequently, prevention of spinal anesthesia–induced hypotension remains a fundamental objective in obstetric anesthesia practice.

Several strategies have been proposed to mitigate hypotension, including intravenous fluid loading, left uterine displacement, modification of intrathecal local anesthetic dose, and the administration of vasopressor agents. Among these, vasopressors represent the cornerstone of both prevention and treatment. Ephedrine, a mixed α- and β-adrenergic agonist, has traditionally been favored in obstetric anesthesia due to its ability to maintain cardiac output and uterine blood flow. In contrast, phenylephrine, a selective α-adrenergic agonist, has gained popularity in recent years, particularly in infusion-based protocols, owing to reports of improved fetal acid–base status.

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However, most evidence supporting phenylephrine is derived from infusion-based regimens in well-resourced healthcare settings. In many low- and middle-income countries, including Pakistan, bolus administration of vasopressors remains the most feasible and commonly practiced approach due to limited availability of infusion pumps and advanced hemodynamic monitoring. There is a paucity of local data comparing bolus ephedrine and phenylephrine in this pragmatic clinical context. This study therefore aimed to compare the efficacy of prophylactic intravenous bolus ephedrine and phenylephrine in preventing maternal hypotension following spinal anesthesia for elective cesarean section.

METHODOLOGY

This prospective randomized comparative study was conducted in the Department of Anesthesiology, Dow University of Health Sciences and Civil Hospital Karachi, after obtaining approval from the institutional ethical review committee. Written informed consent was obtained from all participants.

A total of 166 ASA physical status I–II parturients aged 20–40 years with singleton term pregnancies scheduled for elective cesarean section under spinal anesthesia were enrolled. Patients with hypertension, pre-eclampsia or eclampsia, cardiovascular disease, contraindications to spinal anesthesia, or known hypersensitivity to the study drugs were excluded.

Sample size was calculated using OpenEpi (version 2) based on previously reported incidences of hypotension of 70% in the ephedrine group and 93% in the phenylephrine group, with a study power of 90% and a confidence level of 99%. This yielded a required sample size of 166 patients, with 83 patients allocated to each group.

Participants were randomized into two groups using a lottery method. Group E received ephedrine 10 mg IV, while Group P received phenylephrine 100 µg IV as a prophylactic bolus administered three minutes prior to spinal anesthesia. All patients were preloaded with Ringer's lactate solution at a dose of 15 ml/kg.

Spinal anesthesia was administered in the sitting position at the L3–4 or L4–5 interspace using a 25-gauge Quincke spinal needle. A dose of 1.5 ml of 0.75% hyperbaric bupivacaine was injected after confirmation of free flow of cerebrospinal fluid. Patients were subsequently positioned supine with left uterine displacement.

Maternal heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were recorded at baseline and every three minutes intraoperatively. Maternal hypotension was defined as a greater than 20% decrease in mean arterial pressure from baseline at any point during surgery.

Data were analyzed using SPSS version 11. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The chi-square test was used to compare categorical outcomes. A p-value ≤0.05 was considered statistically significant. Stratified analysis was performed for age, ASA physical status, and body weight to control for potential confounding factors.

RESULTS

A total of 166 patients were included in the final analysis, with 83 patients in each group. Baseline demographic and clinical characteristics were comparable between the two groups (Table 1).

Table 1

Baseline Demographic and Clinical Characteristics

Variable	Group E (Ephedrine)	Group P (Phenylephrine)
Age (years)	28.5 ± 5.3	29.3 ± 5.3
Weight (kg)	72.2 ± 12.4	71.5 ± 12.4
Height (cm)	151.8 ± 5.9	150.1 ± 6.7
ASA I / II	66 / 17	70 / 13
Baseline MAP (mmHg)	92.4 ± 6.8	91.9 ± 7.1

Table 2

Comparison of Maternal Hypotension between Groups

Outcome	Group E (n=83)	Group P (n=83)	p-value
Maternal hypotension	56 (67.5%)	74 (89.2%)	0.001

Table 3

Stratified Analysis of Maternal Hypotension

Stratum	Group E (%)	Group P (%)	p-value
Age ≤30 years	65.2	88.6	0.01
Age >30 years	70.1	89.7	0.02
ASA I	66.0	88.5	0.001
ASA II	70.6	92.3	0.04
Weight ≤75 kg	64.8	87.9	0.01
Weight >75 kg	71.4	90.2	0.03

DISCUSSION

This prospective randomized comparative study demonstrates that prophylactic intravenous bolus ephedrine is more effective than phenylephrine bolus in preventing maternal hypotension following spinal anesthesia for elective cesarean section. These findings are clinically relevant and must be interpreted in the context of bolus-based vasopressor administration. Although contemporary international guidelines increasingly recommend phenylephrine as the first-line vasopressor for the management of spinal anesthesia–induced hypotension, this recommendation is predominantly derived from studies utilizing continuous infusion protocols rather than intermittent bolus dosing [1,2,5].

Phenylephrine is a selective α-adrenergic agonist that increases systemic vascular resistance primarily through arterial vasoconstriction. When administered as an intravenous bolus, the sudden increase in afterload may provoke baroreceptor-mediated reflex bradycardia, which can lead to a reduction in cardiac output and, paradoxically, contribute to hypotension [3,7,9]. Several studies have demonstrated that while phenylephrine infusions provide stable blood pressure control, bolus administration may be associated with greater hemodynamic variability, particularly in parturients who already experience reduced venous return due to aortocaval compression [4,10].

In contrast, ephedrine exerts its vasopressor effects through combined α- and β-adrenergic stimulation, resulting in both peripheral vasoconstriction and augmentation of cardiac output. This pharmacodynamic profile supports maintenance of venous return and cardiac output, which may explain the lower incidence of maternal

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hypotension observed in the ephedrine group in the present study. Previous investigations evaluating bolus ephedrine have similarly reported more stable maternal hemodynamics when compared with bolus phenylephrine, particularly in settings where continuous infusion techniques are not employed [4,12,14].

Concerns regarding ephedrine-induced fetal acidosis have contributed to the gradual shift toward phenylephrine in modern obstetric anesthesia practice. However, available evidence suggests that although ephedrine may be associated with lower umbilical artery pH values, these changes are generally mild and are not consistently associated with adverse neonatal outcomes, especially when ephedrine is used in prophylactic bolus doses rather than repeated rescue dosing [8,11,15]. It is important to acknowledge that neonatal acid–base status was not assessed in the present study, and therefore definitive conclusions regarding fetal outcomes cannot be drawn.

The findings of this study are particularly relevant to resource-limited healthcare settings, where infusion pumps, invasive monitoring, and automated vasopressor delivery systems may not be routinely available. In such environments, bolus administration of vasopressors remains the most practical and widely used strategy. Under these circumstances, ephedrine continues to represent a reliable and effective option for the prevention of spinal anesthesia–induced hypotension during cesarean delivery.

This study has several limitations. It was conducted at a single center, which may limit the generalizability of the results. Neonatal outcomes, including umbilical cord blood gas analysis, were not evaluated. Additionally, the study assessed only bolus vasopressor protocols and did not include infusion-based comparisons. Future multicenter studies incorporating neonatal outcome measures and direct comparisons between bolus and infusion strategies are warranted to further refine vasopressor selection in obstetric anesthesia.

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