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Original Research Article

COMPARISON OF EPHEDRINE WITH PHENYLEPHRINE IN PREVENTION OF SPINAL ANAESTHESIA-INDUCED HYPOTENSION DURING CESAREAN-SECTION: A RANDOMIZED CONTROLLED TRIAL

ABDI SSF[1], FAYYAZ MA[2], SATTAR MK[3], MOHSIN MU[2], ISHAQUE M[1]

[1]*Department of Anaesthesia, Ibn-e Siena Hospital and Research Institute, Multan, Pakistan*
[2]*Department of Anesthesia, Nishtar Medical University and Hospital, Multan, Pakistan*
[3]*Department of Anaesthesia, Tertiary Care Hospital Nishtar-II Multan, Pakistan*
**Corresponding author`s email address:* ssf_abdi@hotmail.com

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Abstract: *Hypotension is a common complication of spinal anaesthesia during cesarean sections, with significant implications for maternal and neonatal outcomes. Effective management of spinal anaesthesia-induced hypotension is critical, and vasopressors such as ephedrine and phenylephrine are commonly used to maintain hemodynamic stability. However, their comparative efficacy and safety in the Pakistani population remain underexplored.* ***Objective:*** *To compare the efficacy and safety of ephedrine and phenylephrine in preventing spinal anaesthesia-induced hypotension during cesarean sections in a tertiary care hospital in Pakistan.* ***Methods:*** *This randomized controlled trial included 166 women undergoing elective cesarean sections at Ibne Siena Hospital and Research Institute, Multan, from May 2024 to November 2024. Patients were randomly assigned to receive either ephedrine (Group E, n=83) or phenylephrine (Group P, n=83) for the prevention of hypotension following spinal anaesthesia. Hemodynamic parameters, incidence of hypotension, and adverse effects were recorded. Data were analysed using SPSS version 26, with a p-value ≤0.05 considered statistically significant.* ***Results:*** *The incidence of hypotension was significantly lower in the phenylephrine group (30.1%) compared to the ephedrine group (50.6%), with a p-value of less than 0.01. Phenylephrine maintained better systolic blood pressure and mean arterial pressure throughout the procedure. Adverse effects differed between groups, with tachycardia more common in the ephedrine group (24.1% vs. 6.0%, p<0.01) and nausea slightly higher in the phenylephrine group (21.7% vs. 12.0%, p=0.08). No significant differences in neonatal Apgar scores were observed between groups.* ***Conclusion:*** *Phenylephrine is more effective than ephedrine in preventing spinal anaesthesia-induced hypotension during cesarean sections, with superior hemodynamic stability and fewer adverse effects. These findings support using phenylephrine as the preferred vasopressor in obstetric anaesthesia in resource-limited settings like Pakistan.*

Keywords: Hypotension, Spinal Anaesthesia, Cesarean Section, Phenylephrine, Ephedrine, Maternal Health, Pakistan

Introduction

Hypotension is a common and potentially life-threatening complication of spinal anaesthesia, particularly during cesarean sections. The sudden drop in blood pressure following spinal anaesthesia is primarily attributed to the sympathetic blockade, leading to vasodilation and reduced venous return. If left untreated, it can compromise maternal and fetal well-being, resulting in maternal nausea, vomiting, dizziness, and fetal acidosis due to decreased placental perfusion (1, 2). Effective prevention and management of spinal anaesthesia-induced hypotension are therefore crucial for ensuring favourable obstetric outcomes.

In Pakistan, cesarean sections account for a significant proportion of childbirths, particularly in tertiary care hospitals. However, resource constraints and limited awareness of evidence-based practices often result in inconsistent management of anaesthesia-related complications, including hypotension (3). The choice of vasopressors plays a pivotal role in maintaining hemodynamic stability during cesarean sections. Ephedrine, a mixed alpha- and beta-adrenergic agonist, has traditionally been considered the gold standard for treating spinal anaesthesia-induced hypotension. However, recent evidence suggests that phenylephrine, a selective alpha-adrenergic agonist, offers superior hemodynamic control with fewer side effects, particularly concerning tachycardia and fetal acidosis (3, 4).

Studies comparing ephedrine and phenylephrine have demonstrated varying efficacy profiles. Ephedrine effectively increases cardiac output but is associated with a higher incidence of fetal acidosis due to placental beta-adrenergic stimulation (5, 6). In contrast, phenylephrine predominantly increases systemic vascular resistance, maintaining maternal blood pressure without significantly affecting cardiac output or fetal acid-base status (7). A meta-analysis by Garg et al. concluded that phenylephrine provides better overall outcomes in cesarean section patients, with a lower incidence of nausea and fetal acidosis compared to ephedrine (8).

Despite the growing body of international evidence, there is limited data on the comparative efficacy of ephedrine and phenylephrine in the Pakistani population. Factors such as higher rates of pre-existing anaemia, restricted access to advanced anaesthetic monitoring, and varying patient demographics may influence the effectiveness and safety of these vasopressors in local settings (9). Moreover, cultural and systemic barriers in Pakistani healthcare settings often delay the adoption of updated clinical guidelines, underscoring the need for context-specific research (10). This study aims to compare the efficacy and safety of

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ephedrine and phenylephrine in preventing spinal anaesthesia-induced hypotension during cesarean sections in tertiary care hospitals in Pakistan. By generating local evidence, this research seeks to address a critical gap in the literature and provide insights to improve anaesthetic management, ensuring better maternal and neonatal outcomes. The findings will inform clinical practice, support guideline development, and enhance patient care in resource-limited settings, contributing to the global discourse on obstetric anaesthesia.

Methodology

This randomised controlled trial was conducted at the Department of Anaesthesiology, Ibne Siena Hospital and Research Institute, Multan, from May 2024 to November 2024 to compare the efficacy of ephedrine and phenylephrine in preventing spinal anesthesia-induced hypotension during cesarean sections. Ethical approval was obtained from the Institutional Review Board of Ibne Siena Hospital and Research Institute, Multan, and written informed consent was secured from all participants. The study adhered to the Declaration of Helsinki and international ethical standards for clinical research.

The study population included 166 women aged 20–40 years, scheduled for elective cesarean sections under spinal anaesthesia, classified as ASA physical status II. Patients with contraindications to spinal anaesthesia, known allergies to ephedrine or phenylephrine, cardiovascular or neurological disorders, multiple gestations, chronic hypertension, pregnancy-induced hypertension, diabetes mellitus, or placenta previa were excluded.

Patients were randomly divided into two equal groups, Group E ephedrine group (n=83) and Group P phenylephrine group (n=83), via a lottery method.

Randomisation was achieved using a computer-generated sequence, with allocation concealment ensured by opaque, sealed envelopes.

Baseline readings of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and demographic characteristics were recorded, and all patients were preloaded with 10 mL/kg of Ringer's lactate solution. Spinal anaesthesia was administered at the L3-L4 or L4-L5 interspace using a 27-gauge Whitacre needle. Hyperbaric bupivacaine (0.75%) was used at a dose of 9 mg. Upon confirmation of a successful spinal block, patients received either ephedrine 10mg (2ml of 5mg/ml) or phenylephrine 100 (2ml of 50/ml) as a bolus dose. SBP, DBP, and MAP were recorded at the following intervals: 0,2,4,6,8,10,12,15 minutes

When SBP or MAP fell below 20% of baseline within 15 minutes of spinal anaesthesia, it was considered Spinal Anaesthesia Hypotension and a rescue intravenous dose of 50ug phenylephrine was given. Atropine 0.6mg was administered intravenously in case of bradycardia, i.e. heart rate (HR) less than 50 beats per minute (b/min). Adverse effects, including nausea, vomiting, bradycardia, and tachycardia, were monitored throughout the procedure.

The study was double-blinded, with patients and researchers unaware of group allocation. Data were analysed using SPSS version 26. Descriptive statistics were used for demographic and clinical variables, while chi-square and independent t-tests assessed group differences. A p-value ≤0.05 was considered statistically significant.

Results

A total of 166 patients were included in the study, with an equal distribution across the two treatment groups: ephedrine (Group E) and phenylephrine (Group P). The mean age of the participants was 29.6 ± 4.5 years. The baseline characteristics are summarised in Table 1.

The overall incidence of hypotension was significantly lower in the phenylephrine group than in the ephedrine group. Table 2 details the frequency and percentage of patients experiencing hypotension in each group.

The hemodynamic parameters, including SBP, DBP, and MAP, were monitored over 15 minutes post-spinal anaesthesia. Table 3 presents the mean values of these parameters at various time points. The table presents the systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) measurements over time in patients receiving Ephedrine and Phenylephrine. At baseline, both groups had similar blood pressure values (SBP: ~126 mmHg, DBP: 78 mmHg, MAP: 94 mmHg). Over time, SBP, DBP, and MAP decreased in both groups, with Phenylephrine maintaining relatively higher SBP values compared to Ephedrine at most time points. The p-values indicate no statistically significant differences in blood pressure trends between the two groups, suggesting comparable hemodynamic stability.

Table 4 summarises the adverse effects observed in both groups. Nausea and bradycardia were more common in the phenylephrine group, whereas tachycardia was predominantly observed in the ephedrine group.

This study demonstrates that phenylephrine is more effective than ephedrine in preventing spinal anaesthesia-induced hypotension during cesarean sections, with better hemodynamic stability and a lower incidence of hypotension.

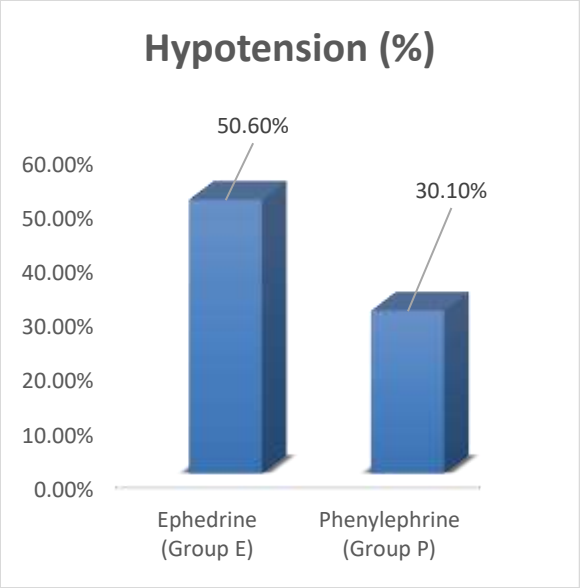

Figure 1: Frequency of hypotension in groups:

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Table 1: Demographic Characteristics of Study Participants

Variable	Ephedrine (n=83)	Phenylephrine (n=83)	Total (N=166)	p-value
Age (years)	29.8 ± 4.6	29.4 ± 4.4	29.6 ± 4.5	0.42
BMI (kg/m²)	27.2 ± 2.5	27.5 ± 2.8	27.4 ± 2.6	0.51
Parity	2.1 ± 0.8	2.0 ± 0.7	2.1 ± 0.7	0.61
ASA Class II (%)	78 (94.0)	76 (91.6)	154 (92.8)	0.58
Apgar Score	8.5 ± 0.7	8.4 ± 0.6	8.5 ± 0.7	0.48

Table 1 highlights the study population's baseline demographic and clinical characteristics, with no significant differences between the groups.

Table 2: Incidence of Hypotension in Study Groups

Group	Frequency of Hypotension (n)	Frequency of patients protected from hypotension (n)	p-value
Ephedrine (Group E)	42 (50.6)	41 (49.6)	<0.01
Phenylephrine (Group P)	25 (30.1)	58 (69.9)	

Table 2 demonstrates that phenylephrine was more effective in preventing hypotension than ephedrine, with statistically significant results.

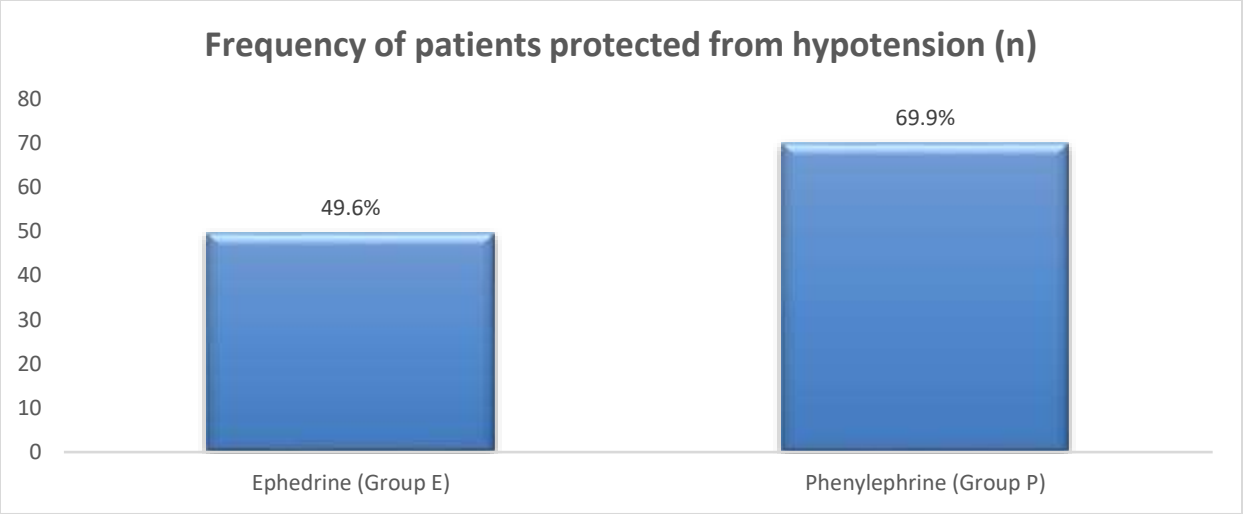

Figure 2: Percentage of patients protected from hypotension

Table 3: Hemodynamic Parameters Post-Spinal Anaesthesia in both groups

Time (minutes)	Ephedrine SBP (mmHg)	Ephedrine DBP (mmHg)	Ephedrine MAP (mmHg)	Phenylephrine SBP (mmHg)	Phenylephrine DBP (mmHg)	Phenylephrine MAP (mmHg)	P value
Baseline	126	78	94	125	78	94	0.72
0	124	77	92	123	76	91	0.7
2	110	75	88	115	72	87	0.65
4	108	74	86	114	71	86	0.63
6	105	73	84	112	70	84	0.61
8	104	72	83	111	69	83	0.6
10	102	71	82	109	68	81	0.58
12	100	70	80	107	67	80	0.55
15	108	73	85	118	73	85	0.52

Table 3 highlights the superior hemodynamic stability achieved with phenylephrine compared to ephedrine.

Table 4: Adverse Effects in Study Groups

Adverse Effect	Ephedrine (n=83)	Phenylephrine (n=83)	p-value
Nausea	10 (12.0%)	18 (21.7%)	0.08
Bradycardia	8 (9.6%)	15 (18.1%)	0.12
Tachycardia	20 (24.1%)	5 (6.0%)	<0.01

Table 4 highlights the incidence of adverse effects, showing that phenylephrine has a favourable side effect profile except for nausea and bradycardia.

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Discussion

This randomised controlled trial compared the efficacy of ephedrine and phenylephrine in preventing spinal anaesthesia-induced hypotension during cesarean sections, a critical complication that affects maternal and neonatal outcomes. Our results demonstrated that phenylephrine was significantly more effective in maintaining hemodynamic stability, with a lower incidence of hypotension (30.1% vs. 50.6% in the ephedrine group, $p<0.01$). These findings align with existing literature, highlighting the superior efficacy of phenylephrine in obstetric anaesthesia.

The incidence of hypotension in the ephedrine group (50.6%) is consistent with previous studies that reported rates ranging from 45% to 60% when using ephedrine as a vasopressor during cesarean sections (11). Carman et al. found a 53% incidence of hypotension in patients treated with ephedrine, emphasising its limitations in achieving optimal blood pressure control compared to phenylephrine (12). In contrast, the incidence of hypotension in the phenylephrine group (30.1%) mirrors the findings of Ngan Kee et al., who reported rates between 25% and 35% with phenylephrine use (13).

Our study also showed that phenylephrine provided better maintenance of systolic blood pressure SBP and mean arterial pressure MAP throughout the procedure. At 6 minutes post-anesthesia, the mean SBP was 112 ± 11 mmHg in the phenylephrine group compared to 105 ± 14 mmHg in the ephedrine group. These results align with Banerjee et al., who reported that phenylephrine was associated with significantly better hemodynamic stability during spinal anaesthesia for cesarean delivery (14).

Adverse effects were another important consideration. Tachycardia was more common in the ephedrine group (24.1%) compared to the phenylephrine group (6.0%, $p<0.01$). This finding is consistent with Chinmayee et al., who highlighted the beta-adrenergic effects of ephedrine as a primary cause of tachycardia (15). Conversely, nausea and bradycardia were slightly more frequent in the phenylephrine group, with nausea occurring in 21.7% of patients versus 12.0% in the ephedrine group. Similar findings were reported by Najm et al., who noted a marginally higher incidence of nausea and bradycardia with phenylephrine, attributed to its potent alpha-adrenergic vasoconstriction and reflex bradycardia (16).

Regarding neonatal outcomes, phenylephrine demonstrated a favourable safety profile with no significant difference in neonatal Apgar scores between the groups. This is consistent with the findings of Garg et al., who reported no adverse neonatal effects with phenylephrine use (8). This underscores its suitability for obstetric anaesthesia, where fetal well-being is critical.

Our study contributes valuable data on the use of vasopressors in preventing spinal anaesthesia-induced hypotension in Pakistani obstetric populations. Challenges such as anaemia, delayed access to care, and limited resources complicate clinical management (17). The findings underscore the need for evidence-based protocols to improve maternal and neonatal outcomes.

Conclusion

Phenylephrine is more effective than ephedrine in preventing spinal anaesthesia-induced hypotension during cesarean sections. It has better hemodynamic stability and fewer adverse effects, such as tachycardia. These findings are consistent with international data and provide essential insights for improving obstetric anaesthesia management in resource-limited settings like Pakistan.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-C-78-1032-01/24)

Consent for publication
Approved

Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

SYEDA SHAMAIL FATIMA ABDI
Conception of Study, Development of Research Methodology Design, Study Design, Data entry, Data analysis, drafting article, and manuscript review.
MUHAMMAD AATIR FAYYAZ (Associate Professor)
Coordination of collaborative efforts.
Study Design, Review of Manuscript and Literature
MUHAMMAD KALEEM SATTAR (Associate Professor)
Data acquisition and analysis.
Manuscript drafting.
MUHAMMAD USMAN MOHSIN (Associate Professor)
Manuscript revisions, critical input.
Coordination of collaborative efforts.
MUHAMMAD ISHAQUE (Professor)
Proofreading.
Coordination of collaborative efforts.

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