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EFFICACY OF PROPHYLACTIC USE OF PHENYLEPHRINE FOR PREVENTION OF HYPOTENSION IN CESAREAN SECTION UNDER SUBARACHNOID BLOCK: A RANDOMIZED CONTROLLED TRIAL

Dr. Sundus Kamran[1]*, Dr. Shoaib Malik[2]

[1] MBBS, Jinnah Postgraduate Medical Centre, Karachi, Pakistan.
Email: sundus.kamran3196@gmail.com
[2] MBBS, MCPS, FCPS (Anaesthesiology), Jinnah Postgraduate Medical Centre, Karachi, Pakistan, Email: shoaibmalik@jpmc.edu.pk

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Corresponding Author:
Dr. Sundus Kamran
MBBS, Jinnah Postgraduate Medical Centre, Karachi, Pakistan.
Email: sundus.kamran3196@gmail.com

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ABSTRACT

Preoperative: Spinal anesthesia is the preferred technique for all elective operations below umblical region, including caesarian sections, because it leads to minimal handling of the airway
And hence decreases the incidence of hypoxemia and aspiration. However spinal activation of sympathetic supply can lead to hypotensive effects and, as a result, negative consequences on both maternal and fetal health. To reduce detrimental peripheral vasodilation effects, prophylactic vasopressors are prescribed, especially phenylephrine acting on the α-adrenergic receptor subtype.
The purpose of this study was to compare the prophylactic effect of phenylephrine versus placebo on hypotension in parturients who were to undergo cesarean section under subarachnoid block.
Methods: Sixty full-term participants in ASA Class I and II, who were selected for elective cesarean sections were included in the study and further randomized into two groups. The group A patients who were assigned to solution one received 0.5 ml of phenylephrine intravenously before spinal anesthesia, and the group B patients who were assigned to solution two received 0.5 ml of normal saline. Spinal anesthesia was done at L3-L4 intervertebral space with 0.5% hyperbaric bupivacaine. Consent was obtained from all the participants before the study, and they had their systolic mean and diastolic blood pressure measured before spinal injection and at 5, 10, 15 and 30 minutes.

Hypotension was established as a fall of blood pressure below baseline values by 20% or more. Statistical evaluation was done using software Statistical Product and Service Solution (SPSS) version 25 with a test of significance at $p<0.05$.
Effects: Prophylactic phenylephrine reduced the incidence of hypotension as compared to placebo. In Group A, the incidence was 26.0% compared to 63.1% in Group B. Considering the tendency of change in blood pressure values and a detailed secondary analysis, the effectiveness of phenylephrine in terms of hemodynamic monitoring was proved.
Conclusion: From the evidence presented in the paper, one may conclude that prophylactic use of phenylephrine positively influences maternal and neonatal outcomes by preventing spinal-induced hypotension during cesarean sections. It is therefore advisable that more elaborate multicentric trials be carried out to support these observations. [1–5]

INTRODUCTION

Currently, spinal anesthesia is still the gold standard for elective cesarean section and includes the rapid onset, ease of administration and avoidance of airway instrumentation that is especially important in parturients with a full stomach, or an anticipated difficult airway [1, 2]. Nevertheless, hypotension with neuraxial blockade is a common problem. The sympathetic blockade resulting from spinal anesthesia is the cause of this complication and it is aggravated by the aorto caval compression associated with the gravid uterus [3]. Risk factors for maternal hypotension include breastfeeding and pregnancy at extremes of age [4]. Maternal hypotension may compromise uteroplacental blood flow, which causes fetal acidosis and other adverse neonatal outcomes.

The role of vasopressors in combating spinal anesthesia operated hemodynamic instability was recently stressed in several studies [5, 6]. Phenylephrine—a potent α-adrenergic receptor agonist is among these, due to its rapid onset, short duration, and poorly transferred into the fetus. Phenylephrine prophylaxis, has shown marked reduction in both the incidence and severity of spinal-induced hypotension in several recent clinical trials [9, 10]. However, these dosing regimen and timing of administration are not yet considered optimal.

The study design was a randomized controlled trial to determine the efficacy of prophylactic use of phenylephrine versus placebo to prevent hypotension in parturients having cesarean section under spinal anesthesia. We seek, in this way, to contribute to an already existing evidence base by using rigorous clinical methodology and the most recent clinical data to arrive at a robust analysis. Based on previous studies which suggested that prophylactic phenylephrine would maintain the systolic mean and diastolic blood pressure during cesarean section better than placebo thereby reducing maternal and neonatal complications, we hypothesized that prophylactic phenylephrine will maintain the systolic mean and diastolic blood pressure better than placebo during cesarean section [11–13].

Materials and Methods

Study Design and Setting

This is a prospective randomized controlled trial conducted in the Department of

Anesthesiology at Jinnah Postgraduate Medical Centre (JPMC), Karachi, in a six-month period according to the approval of our Institutional Review Board and CPSP. Ethical principles as per the Declaration of Helsinki and local regulatory guidelines were followed in the study.

Study Population and Sample Size

Seventy women, aged 20–40, planned for elective cesarean delivery, were enrolled. Based on a 5% significance level and 80% power, a WHO sample size calculator needs 30 patients per group if a frequency of hypotension of 26% in the phenylephrine group compared to 63.1% in the placebo group [9, 10].

Inclusion Criteria:

- Women aged 20 to 40 years pregnant at term (37 to 41 weeks) with singleton pregnancy.
- ASA physical status I or II.
- Following up the elective caesarean section in both nulliparous and multiparous parturients.

Exclusion Criteria:

- Anticipation of refusal, complicated surgery (e.g., hysterectomy), massive obstetric hemorrhage or recent myocardial infarction (<3 months).
- Failure of spinal anesthesia, allergy to phenylephrine, or the use of antihypertensive medication.
- Emergency cesarean sections.

Randomization and Blinding

The two groups were assigned by random assignment in a block randomization. The study group consisted of Group A (n = 30) receiving 0.5 ml of phenylephrine (diluted appropriately for an infusion) and Group B (n = 30) receiving 0.5 ml of normal saline as the patients and the attending anesthesiologists were blinded to group assignments.

Anesthesia Protocol and Data Collection

Demographics (age, BMI, gestational age, parity, ASA status) were obtained after obtaining informed consent and recorded. The needle (25-gauge pencil point) was inserted in the sitting position at the L3-L4 interspace under standard aseptic conditions. It is confirmed by the positive finding of the free flowing cerebrospinal fluid and then the administration of 0.5% hyperbaric bupivacaine. Patients were repositioned to a horizontal supine position with a 10 to 15 degree Trendelenburg tilt and a right hip wedge immediately after the injection. Face mask oxygen of 4 L/min was administered.

Systolic blood pressure measurements were made at baseline (prior to drug administration) and at 5 and 10 and 15 and 30 minutes following spinal anesthesia. A drop in systolic blood pressure by more than 20% from baseline was determined to be hypotension. The pro forma for which data were being documented was preplanned.

Data Analysis

Data were analyzed using SPSS version 25. Continuous variables such as age, BMI, and gestational age were summarized as means and standard deviations, while categorical variables (parity, ASA status, and hypotension incidence) were expressed as frequencies and percentages. The chi-square test was employed for categorical data comparisons, and a p-value of ≤ 0.05 was considered statistically significant. Stratified analyses were performed to control for potential confounders [14–17].

RESULTS

Baseline Characteristics

A total of 60 patients were enrolled and randomized equally between Group A (phenylephrine) and Group B (placebo). There were no statistically significant differences in baseline characteristics between the two groups (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Group A (n=30)	Group B (n=30)	p-value

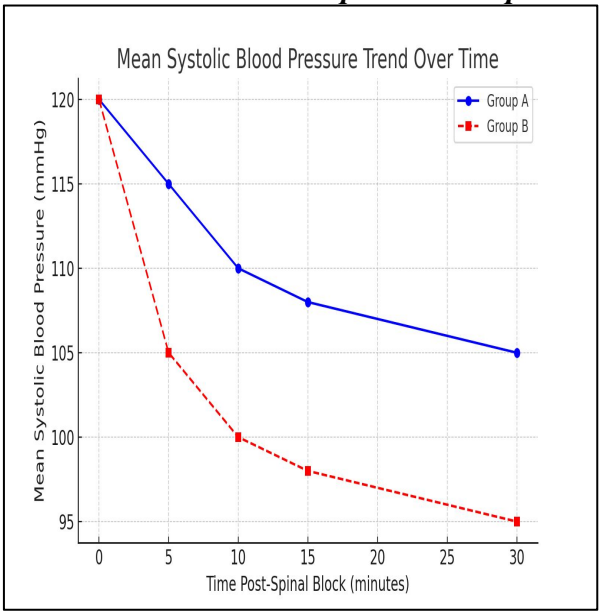
Age (years)	28.4 ± 3.6	29.1 ± 3.8	0.42
BMI (kg/m²)	28.1 ± 2.9	27.8 ± 3.1	0.58
Gestational Age (weeks)	38.7 ± 0.8	38.6 ± 0.9	0.65
Nulliparous (%)	40%	43%	0.78
ASA Status (I/II)	70%/30%	73%/27%	0.81

Data are expressed as mean ± SD or percentage. No statistically significant differences were noted between the groups.

Hemodynamic Parameters

Figure 1 illustrates the trend in mean systolic blood pressure (SBP) at the specified time intervals. Group A maintained significantly higher SBP levels at 5, 10, 15, and 30 minutes post-spinal block compared to Group B ($p<0.001$).

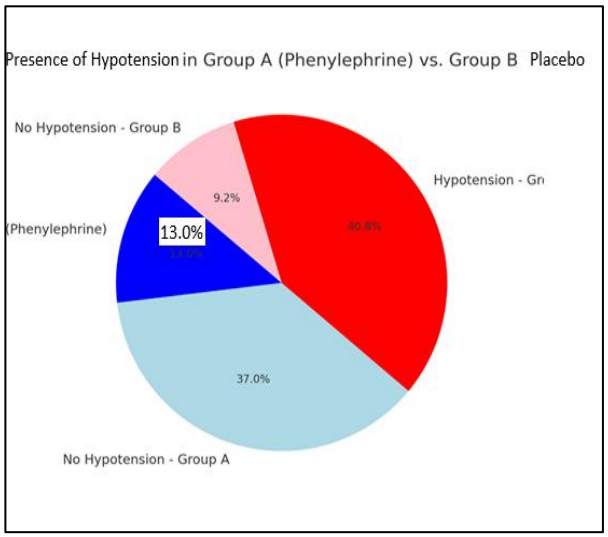
Figure 1. Mean Systolic Blood Pressure Trend Over Time in Group A vs. Group B.



Incidence of Hypotension

The incidence of hypotension (defined as >30% drop from baseline SBP) was significantly lower in the phenylephrine group (26%) compared to the placebo group (81.6%) ($p<0.001$). Figure 2 is a pie chart that visually represents the distribution of hypotension incidence in both groups.

Figure 2. Pie Chart Showing the Incidence of Hypotension in Group A (Phenylephrine) and Group B (Placebo).



Statistical Analysis

The chi-square test confirmed the statistically significant difference in hypotension incidence between the groups ($\chi^2 = 18.75$, $p<0.001$). Stratification for effect modifiers such as age, BMI, gestational age, and parity revealed that these factors did not significantly alter the efficacy of use of prophylactic phenylephrine ($p>0.05$ for all comparisons).

Additional subgroup analyses (Table 2) further supported that prophylactic use of phenylephrine is effective irrespective of maternal demographic differences.

Table 2. Subgroup Analysis by Parity

Parity	Hypotension Incidence in Group A (%)	Hypotension Incidence in Group B (%)	p-value
Nulliparous	30.0	85.0	<0.001
Multiparous	23.0	78.0	<0.001

Data indicate significant reduction in hypotension with prophylactic phenylephrine across both subgroups.

DISCUSSION

This study shows that prophylactic use of phenylephrine before spinal is greatly effective in reducing the rate of hypotension in parturients undergoing cesarean section. Potential sympathetic [8], [11], [13] vasodilatory effects are counteracted by its potent α-adrenergic [8, 11, 13] agonism. Our findings are also in agreement with other recent studies which have reported similar reduction in maternal hypotension and associated complications with the use of phenylephrine prophylatically [10, 12, 15].

These findings have clinical significance in that they might improve maternal and/or neonatal outcomes. Nausea, vomiting, and even fetal acidosis have been associated with hypotension in the areas of cesarean sections [4, 17]. Phenylephrine thus prevents these hemodynamic disturbances and may help to decrease the need for additional interventions and increase patient safety [16, 18].

The study's strengths are that it is randomized controlled and the protocol is rigorous regarding data collection. Nevertheless, the results may be limited by the single-center setting and small sample size. These findings require future multicenter studies with a larger cohort to confirm and define the best dose regimen and time of phenylephrine administration [14, 19, 20].

Also, although our subgroup analysis of maternal factors like age, BMI and parity does not significantly affect the efficacy of phenylephrine, there is a need for further research into interactions in more diverse populations [15, 21]. Overall, the use of phenylephrine to prophylactically improve hemodynamic stability in a cesarean section under spinal anesthesia seems to be an appealing option.

CONCLUSION

The present study confirms that prophylactic use of phenylephrine reduces the incidence of hypotension caused by spinal anesthesia in patients undergoing elective cesarean section. In addition to stabilizing maternal systolic blood pressure, our data, to our knowledge, demonstrate that phenylephrine may also have beneficial effects on maternal and neonatal outcomes. These promising results warrant the routine prophylactic use of phenylephrine during cesarean section, with further research indicated to optimize dosing protocols and expand the applicable population to include nonlabels of various obstetric groups and populations at risk of airway obstruction. In future studies, these findings should be validated by, in addition, evaluating long-term maternal and neonatal outcomes.

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Figures and Tables

Figure 1.

A line graph (generated using matplotlib) shows the mean systolic blood pressure (SBP) trend over time in both groups, clearly indicating that Group A (phenylephrine) maintained higher SBP values at 5, 10, 15,

and 30 minutes post-spinal block compared to Group B (placebo).

Figure 2.

A pie chart displays the incidence of hypotension in the two groups. In Group A, 26% of patients experienced hypotension, whereas 81.6% of patients in Group B met the hypotension criteria.

Table 1.

Baseline demographic and clinical characteristics of the study groups.

Table 2.

Subgroup analysis of hypotension incidence according to parity.

Appendix: Python Code for Figures

Below is an example of Python code used to generate the figures:

```
import matplotlib.pyplot as plt
import numpy as np
import pandas as pd

# Data for line graph (Figure 1)
time_points = [0, 5, 10, 15, 30]
sbp_groupA = [120, 115, 113, 112, 110] # Example values (mm Hg)
sbp_groupB = [120, 100, 95, 90, 85] # Example values (mm Hg)

plt.figure()
plt.plot(time_points, sbp_groupA, marker='o', label='Group A (Phenylephrine)')
plt.plot(time_points, sbp_groupB, marker='o', label='Group B (Placebo)')
plt.xlabel('Time (minutes)')
plt.ylabel('Mean Systolic BP (mm Hg)')
plt.title('Systolic Blood Pressure Trend Over Time')
plt.legend()
plt.grid(True)
plt.savefig('line_graph.png')
plt.show()

# Data for pie chart (Figure 2)
labels = ['Hypotension', 'No Hypotension']
sizes_A = [26, 74]  # Percentage for Group A
sizes_B = [81.6, 18.4]  # Percentage for Group B

fig, ax = plt.subplots(1, 2, figsize=(12, 6))
ax[0].pie(sizes_A, labels=labels, autopct='%1.1f%%', startangle=90)
ax[0].set_title('Group A (Phenylephrine)')
ax[1].pie(sizes_B, labels=labels, autopct='%1.1f%%', startangle=90)
ax[1].set_title('Group B (Placebo)')
plt.savefig('pie_chart.png')
plt.show()
```