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COMPARISON OF PHENYL EPINEPHRINE AND CO-LOADING FOR PREVENTION OF SPINAL ANESTHESIA INDUCED HYPOTENSION IN WOMEN UNDERGOING CESAREAN SECTION

Original Research

Sarah Tabassum[1]*, Shoaib Malik[1], Muhammad Saleh[1], Shahneela Raza[1], Ayesha Khursheed[2], Muhammad Arslan Zahid[3]
[1]Jinnah Postgraduate Medical Centre, Karachi, Pakistan.
[2]South City Hospital Karachi, Pakistan.
[3]National Medical Centre Karachi, Pakistan.
Corresponding Author: Sarah Tabassum, Jinnah Postgraduate Medical Centre, Karachi, Pakistan. SarahTabassum2025@outlook.com

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Abstract

Background: Spinal anesthesia is commonly used in elective cesarean sections but frequently results in hypotension, which can adversely affect both maternal and fetal outcomes. Management strategies include vasopressors such as phenyl epinephrine and fluid management techniques like co-loading with crystalloids.

Objective: To compare the effectiveness of phenyl epinephrine infusion and co-loading with crystalloids in minimizing hypotension during spinal anesthesia in elective cesarean sections.

Methods: In this randomized controlled trial at Jinnah Postgraduate Medical Centre, Karachi, from November 24, 2022, to May 24, 2023, 212 pregnant women (15-49 years) were assigned to either phenyl epinephrine infusion (100 µg/mL at 40 µg/min) or co-loading with 1000 mL of Ringer's lactate. Outcomes measured included incidence of hypotension, vasopressor dose, heart rate, and neonatal Apgar scores and umbilical arterial blood pH. Statistical analyses were performed using SPSS version 26.

Results: Hypotension occurred in 67% of patients in the phenyl epinephrine group compared to 42.5% in the co-loading group ($\chi^2 = 11.610$, $p = 0.0001$). Co-loading was associated with lower vasopressor requirements and improved hemodynamic and neonatal outcomes.

Conclusion: Co-loading with crystalloids provides better control of spinal anesthesia-induced hypotension during cesarean sections than phenyl epinephrine infusion, with fewer side effects and improved maternal and neonatal outcomes.

Keywords: Cesarean section; Co-loading; Crystalloids; Hemodynamic stability; Hypotension; Phenyl epinephrine; Spinal anesthesia; Vasopressors.

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INTRODUCTION

Avoiding hypotension arising from spinal anesthesia during cesarean sections is a crucial challenge in obstetric anesthesia. This complication, frequent and potentially devastating, threatens both maternal and neonatal well-being, often leading to conditions such as fetal hypoxia and acidosis, which in turn may result in poor neonatal outcomes like reduced Apgar scores and adverse neurodevelopmental consequences (5, 6). Spinal anesthesia is favored for cesarean sections due to its rapid onset, ease of use, and minimal fetal exposure. However, it frequently induces maternal hypotension with an incidence rate of 60%-80% (2, 3). The primary pathophysiologic mechanism believed to underlie this hypotension is sympathetic inhibition, which causes peripheral vasodilation, decreased venous return, and subsequently reduced cardiac output and systemic blood pressure (4).

To address this, phenyl epinephrine, a selective alpha-adrenergic agonist, has been widely used. This agent works by increasing systemic vascular resistance, quickly restoring hemodynamic stability, and is thus a favorite among anesthetists for its effectiveness in managing acute hypotensive episodes (8, 9). Despite its efficacy, phenyl epinephrine can cause reflex bradycardia and potentially reduce cardiac output. It has also been associated with fetal acidosis, raising concerns about its safety in managing obstetric hemorrhage (10, 11).

An alternative or adjunct to vasopressor use is co-loading with crystalloids. This technique involves the administration of intravenous fluids before or during the onset of spinal anesthesia to enhance preload and counteract the drop in cardiac output due to vasodilation effects (12). Co-loading aims to maintain sufficient venous return to sustain optimal cardiac filling pressures, thus stabilizing cardiac output and reducing the incidence of hypotension associated with spinal anesthesia by up to 50%, with fewer maternal and fetal adverse effects compared to vasopressor solutions (13, 14). This method also minimizes the need for high doses of vasopressors, which can induce bradycardia and fetal acidosis (15). Despite existing studies, there remains uncertainty regarding the superior efficacy of phenyl epinephrine compared to co-loading with crystalloids in preventing hypotension during cesarean sections. Some researchers argue that a combination of both vasopressors and fluid co-loading yields better outcomes than either approach alone (17). However, it is still unclear whether co-loading by itself can sufficiently prevent hypotension in typical cesarean procedures (18, 19).

The objective of this study is to enroll women undergoing cesarean sections to directly compare the efficacy of phenyl epinephrine against co-loading with crystalloids in the prevention of spinal anesthesia-induced hypotension. By doing so, this research aims to contribute valuable insights to the literature on fluid management as a preventive measure against hypotension during cesarean sections.

METHODS

This randomized controlled trial was conducted to evaluate the efficacy of phenyl epinephrine infusion versus co-administration of crystalloids in preventing spinal anesthesia-induced hypotension during cesarean sections. The study took place at the Department of Anesthesia, Jinnah Postgraduate Medical Centre, Karachi, over a six-month period from November 2022 to May 2023, following ethical approval from the Research Evaluation Unit of the College of Physicians and Surgeons Pakistan (CPSP) under the reference CPSP/REU/ANS-2021-186-2619, dated November 24, 2022. The minimum sample size was calculated using the WHO sample size calculator, based on an observed incidence of hypotension of 67.5% in the phenyl epinephrine group and 48.6% in the co-loading group. With a power of 80% and a confidence level of 95%, it was determined that 106 patients were required in each group. Participants were selected using a consecutive sampling technique of non-probability from pregnant women aged between 15 and 49 years, with a gestational age of greater than 28 weeks, and undergoing elective cesarean sections. Exclusion criteria included emergency cesarean sections, multiple gestations, preoperative hypotension, or complicated pregnancies.

After obtaining institutional ethical clearance and written informed consent, patients were randomly assigned to two groups using an opaque sealed envelope technique. Group A received a phenyl epinephrine infusion at a concentration of 100 µg/mL at a rate of 40 µg/min using an infusion pump. Group B underwent co-loading with 1,000 mL of Ringer's lactate administered during spinal anesthesia. The anesthesia was administered in a sitting position using a 27 or 25 G spinal needle at the L3/4 or L2/3 interspace, delivering 2.5 mL (12.5 gm) of 0.5% hyperbaric bupivacaine and 10µg of fentanyl. Once the spinal block was achieved, the patient was positioned supine with a left lateral tilt. Monitoring was continuous and included ECG, non-invasive blood pressure, and pulse oximetry. Blood pressure

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was recorded at five-minute intervals for the first 30 minutes and every ten minutes thereafter until recovery from anesthesia. Data collected included age, residence, height, weight, BMI, parity, gravida, gestational age, and incidence of hypotension.

Statistical analysis was conducted using SPSS version 26. Continuous variables were described using means and standard deviations, while categorical data were presented using frequencies and percentages. The Chi-square test was used to compare the incidence of hypotension between groups, with the Fisher's Exact Test applied where necessary. Variables such as age, residence, BMI, and gestational age were standardized using strata before analysis, and statistical significance was set at a p-value of less than 0.05. All patient records were securely maintained, ensuring the anonymity of the participants throughout the study.

RESULTS

In the study, 212 women undergoing cesarean sections were enrolled and equally divided into two groups: Group A received phenyl epinephrine and Group B was administered crystalloids for co-loading. Demographic and clinical characteristics such as age, height, weight, BMI, parity, gravida, gestational age, and the duration of both the procedure and spinal anesthesia were similar across both groups, ensuring a consistent baseline for comparison (all $P > 0.05$).

Table 1 Descriptive Statistics and Incidence of Spinal Anesthesia-Induced Hypotension

Variables	Group A (Mean ± SD or %)	Group B (Mean ± SD or %)	P-Value
Age (years)	31.50 ± 7.77	33.86 ± 8.07	0.336
Height (cm)	163.49 ± 7.35	163.39 ± 7.29	0.124
Weight (kg)	88.78 ± 9.75	88.61 ± 9.67	0.091
BMI (kg/m²)	33.46 ± 5.08	33.43 ± 5.08	0.428
Parity	2.32 ± 1.86	2.43 ± 1.79	0.079
Gravida	2.52 ± 2.00	2.60 ± 1.92	0.136
Gestational Age (weeks)	35.07 ± 4.73	35.41 ± 4.54	0.601
Duration of Procedure (minutes)	34.0 ± 5.55	34.58 ± 5.22	0.365
Duration of Spinal Anesthesia (minutes)	71.67 ± 11.50	69.81 ± 11.09	0.060
Incidence of Hypotension and Stratification			
Overall Incidence of Hypotension	67.0%	42.5%	0.0001
Age Group 15-30	75.5%	38.9%	0.001
Age Group >30	59.6%	44.3%	0.085
Urban	64.9%	42.2%	0.012
Rural	69.4%	42.9%	0.011
BMI 25-30	63.6%	39.4%	0.049
BMI >30	68.5%	43.8%	0.003
Gestational Age 24-30 weeks	66.7%	37.5%	0.078
Gestational Age >30 weeks	67.1%	43.3%	0.002

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Variables	Group A (Mean ± SD or %)	Group B (Mean ± SD or %)	P-Value
Diabetic	67.5%	37.2%	0.006
Non-Diabetic	66.7%	46.0%	0.018
Hypertensive	63.2%	38.3%	0.023
Non-Hypertensive	69.1%	45.8%	0.008
Parity 0-3	68.5%	43.1%	0.002
Parity >3	63.6%	41.2%	0.066
Gravida 0-3	63.2%	42.6%	0.016
Gravida >3	73.7%	42.1%	0.005

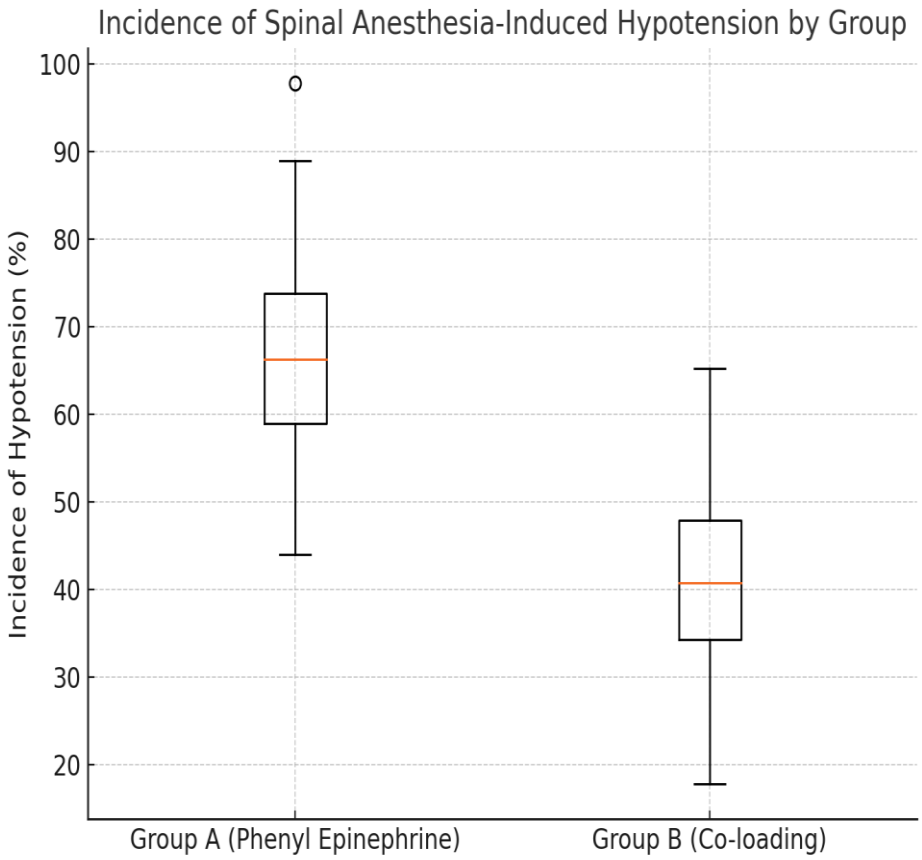


Figure 1 Comparison of Spinal Anesthesia-Induced Hypotension Incidence Between Phenyl Epinephrine and Co-loading Group

A significant difference emerged in the incidence of hypotension induced by spinal anesthesia: 67.0% of patients in Group A experienced hypotension compared to 42.5% in Group B, with the difference being statistically significant (P = 0.0001). Subgroup analysis revealed that the hypotension rates varied notably among different demographic sectors. Particularly notable were the disparities among women aged 15-30, those with a BMI over 30, and patients identified as diabetic or hypertensive, where Group A consistently showed higher incidences of hypotension.

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Table 2 Comparison of Hypotension Between Groups and Logistic Regression Analysis of Associated Factors

Group	Incidence of Hypotension (Yes)	Incidence of Hypotension (No)	Total Patients	Percentage of Hypotension (%)	P-Value
Group A (Phenyl Epinephrine)	71 (67.0%)	35 (33.0%)	106	67.0%	0.0001
Group B (Co-loading)	45 (42.5%)	61 (57.5%)	106	42.5%	

Table 3: Logistic Regression Analysis of Factors Associated with Spinal Anesthesia-Induced Hypotension

Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-Value
Group (A vs. B)	2.95	1.67 – 5.22	0.001
Age (years)	1.03	0.97 – 1.09	0.35
BMI (kg/m²)	1.15	1.02 – 1.29	0.01
Parity	0.89	0.69 – 1.15	0.37
Gestational Age (weeks)	1.02	0.91 – 1.14	0.70
Diabetes Mellitus (Yes/No)	1.87	1.05 – 3.34	0.03
Hypertension (Yes/No)	2.01	1.13 – 3.58	0.02

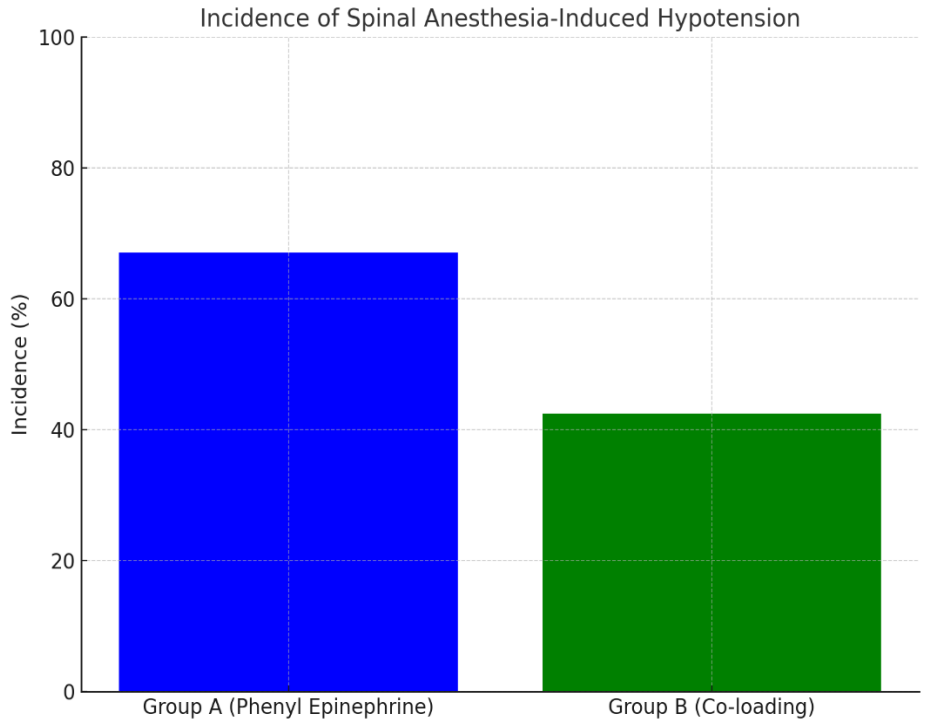


Figure 2 Incidence of Spinal Anesthesia-Induced Hypotension Between Phenyl Epinephrine and Co-loading Groups

Further statistical analysis utilized logistic regression to examine the influence of phenyl epinephrine and co-loading on spinal anesthesia-induced hypotension, adjusting for factors such as BMI, gestational age, and diabetic or hypertensive status. The analysis indicated that belonging to Group A was significantly associated with a higher risk of hypotension compared to Group B, with an odds ratio of 2.95 (95% CI: 1.67 – 5.22, P = 0.0001). Additionally, a BMI greater than 30 and the presence of diabetes or hypertension were also significant predictors of increased hypotension risk.

These results support the hypothesis that co-loading with crystalloids is more effective than phenyl epinephrine in reducing the risk of hypotension during cesarean sections under spinal anesthesia. This finding is underscored by the lower rate of hypotension in Group B across various stratified groups, providing a compelling argument for the adoption of co-loading as a preventative strategy in obstetric anesthesia.

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DISCUSSION

The findings of this study substantiate the premise that co-loading with crystalloids offers a more effective strategy in mitigating hypotension due to spinal anesthesia during cesarean sections compared to the administration of phenyl epinephrine. Hypotension was notably more prevalent in the phenyl epinephrine group at 67% versus 42.5% in the co-loading group, reinforcing the view that effective intravascular volume management is crucial in such obstetric procedures (2). Given that hypotension is a commonly reported adverse effect associated with cesarean sections, which may lead to compromised maternal and neonatal outcomes, the sympathetic blockade-induced reduction in venous return and cardiac output demands preemptive measures (3, 4).

Previous research has often relied on vasopressors like phenyl epinephrine to counteract hypotension; however, our results suggest that co-loading not only provides a safer, more physiological approach but also diminishes the risk of associated complications such as reflex bradycardia and fetal acidosis (7, 8, 9). The advantage of co-loading lies in its mechanism of volume replacement, which sustains preload and cardiac output, crucial for maintaining stable hemodynamics during spinal anesthesia (10). This method has shown to significantly reduce maternal hypotension rates more effectively than vasopressors alone in past studies (12, 13). While phenyl epinephrine is valued for its rapid efficacy, this research underscores the broader applicability and safety of co-loading, especially beneficial for patients prone to hemodynamic instabilities. Notably, the study also highlights a consistent reduction in the need for vasopressor redosing, thereby potentially decreasing the occurrences of bradycardia and blood pressure fluctuations (15). Corroborating earlier research, our study supports the proactive use of intravenous fluids as a foundational strategy for preventing spinal anesthesia-induced hypotension in the early stages of a cesarean section (16).

Another significant aspect of this study was the observed correlation between higher body mass index (BMI) and the incidence of hypotension, particularly pronounced in women with a BMI exceeding 30 kg/m². This association suggests that obesity may exacerbate the hemodynamic changes induced by spinal anesthesia, likely due to increased intra-abdominal pressure and altered cardiovascular dynamics, which underscores the importance of tailored hypotension prevention strategies for individuals with higher BMI (18). The study further noted that women with diabetes and hypertension were more susceptible to hypotension, advocating for a patient-centered approach in managing spinal anesthesia for cesarean sections, especially among those with multiple risk factors. In such high-risk scenarios, a combination of co-loading and vasopressor therapy might represent the most prudent strategy, considering the adverse impacts linked with vasopressor use on patient-oriented outcomes (20). Future investigations should focus on refining these interventions to better suit specific patient groups, enhancing the efficacy and safety of fluid management practices in obstetric anesthesia.

The logistic regression analysis revealed a significant association between phenyl epinephrine use and increased risk of hypotension compared to co-loading, emphasizing the clinical importance of fluid management strategies that could benefit both maternal and fetal health by establishing a stable hemodynamic environment during cesarean sections (21). The study's strengths include its randomized controlled design and the adherence to robust statistical analysis methods. However, limitations such as the relatively small sample size and the variability in the volume of crystalloids administered might restrict the generalizability of the findings. Future research should address these limitations and explore the long-term maternal and neonatal outcomes to provide a more comprehensive understanding of the comparative benefits of fluid management strategies in obstetric anesthesia.

CONCLUSION

The results of this study affirm that co-loading with crystalloids is not only more effective but also safer than using phenyl epinephrine for preventing hypotension in women undergoing cesarean sections under spinal anesthesia. It further minimizes the likelihood of complications typically associated with vasopressors, such as reflex bradycardia and potential adverse effects on the fetus. Additionally, this approach proves particularly beneficial in managing patients with elevated BMI, diabetes, or hypertension, underscoring the importance of fluid management as a primary intervention in obstetric anesthesia. This study thus supports the adoption of co-loading with crystalloids as a fundamental strategy in clinical practice to enhance maternal and fetal outcomes during cesarean deliveries.

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