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Comparison of Ephedrine Versus Crystalloid Preload in Prevention of Hypotension after Spinal Anesthesia for Cesarean Section

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ABSTRACT

Background: Spinal anesthesia is commonly used for cesarean delivery because it is simple, quick, and safe for both the mother and fetus compared with other methods like general anesthesia. However, maternal hypotension is the most common side effect experienced by a woman who has undergone spinal anesthesia for a cesarean delivery. Hypotension can cause distress and decreased uteroplacental perfusion. Several methods are used for prevention but their effectiveness is questionable. **Objective:** To compare the efficacy of ephedrine versus crystalloid preload in prevention of hypotension after spinal anesthesia for cesarean section. **Study Design:** Randomized controlled trial. **Duration and Place of Study:** This study was conducted from 10 July 2024 to 10 January 2025 in the Department of Anesthesia, Lady Reading Hospital, Peshawar. **Methodology:** A total of 130 pregnant women aged 20 to 40 years undergoing elective cesarean section were included and randomly divided into two equal groups. One group received crystalloid preload while the other group received prophylactic ephedrine. Maternal blood pressure was monitored at regular intervals after spinal anesthesia. Hypotension was defined as blood pressure less than 100/60 millimeters of mercury. Chi square test were used with p value ≤0.05 considered significant. **Results:** Hypotension occurred in 35.4% patients in crystalloid group and 15.4% patients in ephedrine group showing significant difference with p value of 0.009. **Conclusion:** Ephedrine is more effective than crystalloid preload in preventing hypotension after spinal anesthesia during cesarean section.

INTRODUCTION

Spinal anesthesia is the most commonly used method for cesarean delivery, as it is easy to perform, rapid in action, and offers satisfactory anesthesia with relatively low risks to the mother and the baby compared with general anesthesia.[1] This method allows the mother to be conscious during the time of delivery, reducing the risk of airway problems, aspiration, and neonatal drug exposure.[2] However, the most common problem associated with spinal anesthesia is hypotension in the mother. Hypotension is the reduced pressure in the mother's blood vessels. It is usually caused by sympathetic blockade, which leads to vasodilation.[3] The decrease in venous return causes hypotension. Hypotension may lead to nausea, vomiting, dizziness, or even reduced uteroplacental perfusion. Therefore, the management of hypotension during spinal anesthesia is an important aspect in the care of the mother during cesarean section.[4]

Ephedrine is commonly used as a vasopressor in the prevention and treatment of hypotension in obstetric patients undergoing spinal anesthesia.[5] Its action in the body lies in its ability to increase cardiac output by stimulating alpha and beta-adrenergic receptors, thus increasing blood pressure.[6] Ephedrine has traditionally been the drug of choice in the maintenance of blood pressure during cesarean delivery under spinal anesthesia, as it has been observed that ephedrine preserves uterine blood flow better than any other vasoconstrictor.[7] Prophylactic and therapeutic administration of ephedrine may be effective in reducing the incidence and severity of hypotension in spinal anesthesia.[8] Its administration, however, may also result in certain adverse effects, like tachycardia, hypertension, and fetal acidosis, especially at higher doses, and thus needs to be monitored closely during administration.[9]

The prophylactic technique of crystalloid preload is one of the most frequently adopted methods for the prevention of hypotension due to spinal anesthesia during cesarean delivery.[10] This technique involves the administration of crystalloids prior to the commencement of spinal anesthesia for the purpose of increasing the preload.[11] The technique is effective in the prevention of hypotension. However, the technique has been observed

to be less effective due to the rapid distribution of crystalloids in the body.[12] Despite the limitation of the crystalloid preload technique, it has been frequently adopted for the prevention of hypotension due to spinal anesthesia during cesarean delivery, either alone or in combination with ephedrine.[13] It was found that patients preloaded with crystalloid had 40% hypotension while patients preloaded with ephedrine had 20% hypotension.[14]

There is little information available on how to prevent hypotension effectively in patients undergoing cesarean section under spinal anesthesia from the local community around Peshawar. The patient type, nutritional status, and practices may vary from other areas and may affect the patient's hemodynamics. A comparison of ephedrine and crystalloid preload from the local community may be useful for selecting an appropriate and feasible approach for anesthetic management. The study aims to improve the safety for the mother and fetus and provide standardized practices for anesthesia services in tertiary care centers around Peshawar.

METHODOLOGY

This randomized controlled trial was carried out in the Department of Anesthesia at Lady Reading Hospital, Peshawar, over a period extending from 10 July 2024 to 10 January 2025. Approval for conduction of the study was obtained from the hospital ethical review board prior to initiation of patient enrollment and all study procedures were performed according to institutional ethical standards. The sample size was calculated using the WHO sample size calculator by keeping confidence level at 95%, absolute precision at 10%, and power of study at 80%. The expected proportion of hypotension was taken as 40% in the crystalloid group and 20% in the ephedrine group.[14] Based on these assumptions a total of 130 patients were included with 65 patients allocated to each group. Female patients aged between 20 and 40 years, undergoing elective cesarean section, having full term singleton pregnancy were included in the study. Patients who were on antihypertensive medication, had preterm delivery, multiple gestation, emergency cesarean section or diagnosed with HELLP syndrome were not included. Written informed consent was taken from each patient after explaining the study purpose, possible benefits and risks in understandable language prior to data collection. Demographic variables including age, gestational age, weight, height, BMI, residence and socioeconomic status were recorded on a structured proforma. After enrollment, patients were randomly allocated into two groups using lottery method. In group A, patients received lactated Ringer's solution at a dose of 15 ml/kg intravenously, administered 10 minutes before spinal anesthesia. In group B, prophylactic ephedrine was administered with 5 mg given at first minute and second minute followed by 1 mg every minute up to 15 minutes after spinal anesthesia. Spinal anesthesia was performed in sitting position at L3–L4 interspace using a 22 gauge spinal needle. All patients received the same local anesthetic technique, which was 2 mL of 0.5% bupivacaine with fentanyl 25 µg. Post-procedure positioning included left lateral tilt using a wedge under the right hip, slight head elevation, and supplemental oxygen via nasal cannula at 4 L/min. Non-invasive hemodynamic assessment included the measurement of heart rate and systolic blood pressure at 1 minute after spinal anesthesia, and then at 3-minute intervals for 30 minutes, followed by 5-minute intervals for the subsequent 30 minutes. The main outcome was the incidence of hypotension after spinal anesthesia. Hypotension was defined as when the blood pressure of the mother falls below 100/60 mmHg, measured immediately after spinal anesthesia using a mercury sphygmomanometer.

Data were entered and analyzed using SPSS version 22. Quantitative variables such as age, gestational age, weight, height and BMI were analyzed by calculating mean and standard deviation. Categorical variables including residence, socioeconomic status and hypotension were presented as frequencies and percentages. Comparison of hypotension between the two groups was done using chi square test and Fisher exact test was applied where cell count was ≤5. Stratification was performed for effect modifiers including age, gestational age, BMI, residence, and socioeconomic status and post stratification chi square test was applied. A p value ≤0.05 was taken as statistically significant.

RESULTS

The mean age of participant were 28.86 ± 3.77 years in Group A and 30.49 ± 2.98 years in Group B. Regarding gestational age, Group A patients had mean of 38.02 ± 0.88 weeks while Group B showed 38.40 ± 0.77 weeks. The weight was recorded as 63.96 ± 5.97 kg in crystalloid group and 64.96 ± 5.44 kg in ephedrine group. Height measurements revealed that Group A participants was 158.94 ± 5.71 cm compared to 157.83 ± 6.01 cm in Group B. Body mass index calculations showed 25.85 ± 2.69 in Group A versus 26.27 ± 2.73 in Group B. Distribution of residence showed that majority of participants were from rural areas with 39 (60.0%) in Group A and 43 (66.2%) in Group B, while urban residents comprised 26 (40.0%) in crystalloid group and 22 (33.8%) in ephedrine group. Socioeconomic status distribution revealed that low socioeconomic status was most common category with 35 (53.8%) in Group A and 38 (58.5%) in Group B. Middle socioeconomic status was observed in 23 (35.4%) of Group A participants and 22 (33.8%) of Group B participants, whereas high socioeconomic status were least common with only 7 (10.8%) in crystalloid group and 5 (7.7%) in ephedrine group (Table-I).

Table I

Patients Demographics in both groups

Variables	Group A (Crystalloid)	Group B (Ephedrine)
	n=65	n=65
	Mean ± SD	Mean ± SD
Age (years)	28.86 ± 3.77	30.49 ± 2.98
Gestational Age (weeks)	38.02 ± 0.88	38.40 ± 0.77
Weight (kg)	63.96 ± 5.97	64.96 ± 5.44
Height (cm)	158.94 ± 5.71	157.83 ± 6.01
BMI	25.85 ± 2.69	26.27 ± 2.73
Residence	**n (%)**	**n (%)**
Rural	39 (60.0%)	43 (66.2%)
Urban	26 (40.0%)	22 (33.8%)
Socioeconomic Status	**n (%)**	**n (%)**
Low	35 (53.8%)	38 (58.5%)

Middle	23 (35.4%)	22 (33.8%)
High	7 (10.8%)	5 (7.7%)

The primary outcome of hypotension occurrence demonstrated significant difference between two groups with p-value of 0.009. In Group A, hypotension was developed in 23 (35.4%) participants while 42 (64.6%) did not experience hypotension. In contrast, Group B showed lower incidence with only 10 (15.4%) patients developing hypotension and 55 (84.6%) remaining normotensive (Table-II).

Table II

Comparison of hypotension between the two groups (n=130)

Hypotension	Group A (Crystalloid)	Group B (Ephedrine)	P value
	n (%)	n (%)	
Yes	23 (35.4%)	10 (15.4%)	
No	42 (64.6%)	55 (84.6%)	0.009
Total	65 (100%)	65 (100%)	

Stratified analysis by age categories revealed that among participants aged ≤30 years, hypotension occurred in 17 (37.0%) of Group A and 6 (18.2%) of Group B with p-value of 0.119. For those aged >30 years, 6 (31.6%) in Group A and 4 (12.5%) in Group B experienced hypotension with p-value of 0.196. When stratifying by BMI, participants with BMI ≤25 kg/m^2 showed hypotension in 11 (35.5%) of Group A and 6 (22.2%) of Group B with p-value of 0.414. However, among those with BMI >25 kg/m^2, hypotension was observed in 12 (35.3%) of crystalloid group versus 4 (10.5%) of ephedrine group, which was statistically significant with p-value of 0.025. Residence-based stratification showed that urban residents had hypotension rates of 11 (42.3%) in Group A and 3 (13.6%) in Group B with p-value of 0.063, while rural residents demonstrated 12 (30.8%) in Group A and 7 (16.3%) in Group B with p-value of 0.197. Socioeconomic stratification revealed that among low socioeconomic status participants, hypotension occurred in 12 (34.3%) of Group A compared to 4 (10.5%) of Group B, showing statistically significant difference with p-value of 0.030. Middle socioeconomic status participants showed 10 (43.5%) in Group A and 4 (18.2%) in Group B with p-value of 0.131, whereas high socioeconomic status group had 1 (14.3%) in Group A and 2 (40.0%) in Group B with p-value of 0.523 (Table-III).

Table III

Association of Hypotension with Demographic Variables

Demographic Variables	GROUPS		Hypotension Yes (n, %)	Hypotension No (n, %)	P value
Age (years)	≤30	A	17 (37.0%)	29 (63.0%)	0.119
		B	6 (18.2%)	27 (81.8%)	
	>30	A	6 (31.6%)	13 (68.4%)	0.196
		B	4 (12.5%)	28 (87.5%)	
BMI (kg/m^2)	≤25	A	11 (35.5%)	20 (64.5%)	0.414
		B	6 (22.2%)	21 (77.8%)	
	>25	A	12 (35.3%)	22 (64.7%)	0.025
		B	4 (10.5%)	34 (89.5%)	
Residence	Urban	A	11 (42.3%)	15 (57.7%)	0.063
		B	3 (13.6%)	19 (86.4%)	
	Rural	A	12 (30.8%)	27 (69.2%)	0.197
		B	7 (16.3%)	36 (83.7%)	
Socioeconomic Status	Low	A	12 (34.3%)	23 (65.7%)	0.030
		B	4 (10.5%)	34 (89.5%)	
	Middle	A	10 (43.5%)	13 (56.5%)	0.131
		B	4 (18.2%)	18 (81.8%)	
	High	A	1 (14.3%)	6 (85.7%)	0.523
		B	2 (40.0%)	3 (60.0%)	

DISCUSSION

In the present study, the incidence of hypotension was significantly low in the ephedrine group (10 cases, 15.4%) than in the crystalloid group (23 cases, 35.4%), with a p-value of 0.009. This might be due to the sympathomimetic action of ephedrine, which increases the blood pressure by causing vasoconstriction and an increase in cardiac output. In the present study, the incidence of hypotension was more in obese patients in the crystalloid group than in the ephedrine group, with a significant difference in the incidence of hypotension among obese patients with BMI > 25 kg/m^2 (12 cases, 35.3%) than in the ephedrine group (4 cases, 10.5%), with a p-value of 0.025. This might be due to the increased abdominal pressure in obese patients, who are more likely to develop hypotension following spinal anesthesia and require more stable pressor agent such as ephedrine. In the present study, there was a significant difference in the incidence of hypotension among low socioeconomic populations with 12 cases (34.3%) in Group A than in Group B with 4 cases (10.5%), with a p-value of 0.030. This might be due to nutritional status in low socioeconomic populations, which might contribute to hypotension following spinal anesthesia and render crystalloids less effective in such populations.

Current study findings showed hypotension incidence of 15.4% (10/65) in ephedrine group compared to 35.4% (23/65) in crystalloid group with significant difference (p=0.009). These results are in agreement with multiple studies where ephedrine prophylaxis demonstrated superior efficacy. Andemeskel *et al.* [15] reported hypotension in 0% (0/30) with ephedrine versus 46.7% (14/30) with crystalloid preloading (p<0.0001), showing even more pronounced difference than present study. Similarly, Gunda *et al.* [14] found hypotension in 20% (6/30) with ephedrine versus 40% (12/30) with crystalloid (p=0.01), and Mahmoud Soliman *et al.* [16] reported 24% (6/25) with ephedrine versus 48% (12/25) with fluid preload (p=0.03). Munir *et al.* [17] also demonstrated that 48% (24/50) had no/mild hypotension with ephedrine compared to only 12% (6/50) with crystalloid preload (p=0.001). The consistency across these studies can be attributed to ephedrine's dual mechanism of action through alpha and beta-adrenergic stimulation which

provide sustained vasopressor effect, whereas crystalloid rapidly redistribute to extravascular compartment in pregnant women due to increased capillary permeability and decreased colloid osmotic pressure.

However, Aziz *et al*. [18] compared ephedrine with phenylephrine rather than crystalloid and found hypotension in 28.4% (19/67) with ephedrine versus 34.3% (23/67) with phenylephrine (p=0.288), showing no significant difference between two vasopressors. This suggest that choice of vasopressor is important factor in preventing hypotension. Jawaid *et al*. [19] compared crystalloid versus colloid preloading and reported hypotension in 55.2% (26/48) with crystalloid versus 22.9% (11/48) with colloid, indicating that colloid preloading may be more effective than crystalloid but still inferior to pharmacological prophylaxis.

Present study stratification by BMI >25 kg/m^2 revealed significant difference with hypotension in 12 (35.3%) of crystalloid group versus 4 (10.5%) of ephedrine group (p=0.025). This finding align with physiological understanding that obese parturients have altered hemodynamics and increased sympathetic tone. Gunda *et al*. [14] included patients with similar BMI of 34.5±1.53 versus 35.1±1.64 and found hypotension in 40% versus 20% respectively, supporting present findings. The increased intra-abdominal pressure in obese patients compound the effect of sympathetic blockade during spinal anesthesia, making ephedrine prophylaxis more beneficial.

Socioeconomic stratification in current study showed significant difference among low socioeconomic status participants with hypotension in 12 (34.3%) of crystalloid group versus 4 (10.5%) of ephedrine group (p=0.030). This finding has not been extensively studied in available literature, though it may relate to baseline nutritional status and hemodynamic reserve. Khan *et al*. [20] compared preload versus coload in non-obstetric patients and found hypotension in 70% (21/30) with preload versus 50% (15/30) with coload (p=0.187), suggesting timing of fluid administration also important. Zahid *et al*. [21] further supported this with hypotension in 92.6% (25/27) with preload versus 67% (18/27) with coload (p<0.001) in obstetric population, indicating that coloading technique may offer some advantage over preloading but still not as effective as pharmacological prophylaxis with ephedrine.

This study has several limitations, which are worth mentioning. Firstly, it is conducted in a tertiary care setting, which might restrict the study's application in other settings with different patient populations. Secondly, it has a limited sample size, with 65 in each group, which might restrict the representation of the larger obstetric population. Thirdly, it has not looked at the long-term maternal or neonatal outcomes, only focusing on the perioperative period. Lastly, it has not blinded the healthcare providers, which might result in bias. Moreover, it has not looked at different doses of ephedrine or crystalloid fluids, which might have given us a better understanding.

CONCLUSION

Our study concludes that prophylactic use of ephedrine is more effective than crystalloid preloading in preventing hypotension due to spinal anesthesia during elective cesarean delivery. A lower incidence of hypotension was seen in patients who received prophylactic ephedrine than in patients who received prophylactic crystalloids. This effect was more pronounced in patients with high body mass index and low socioeconomic status.

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