

# Effectiveness of Prophylactic Ephedrine versus Fluid Preload in Prevention of Hypotension in Spinal Anesthesia for Cesarean Section

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## ABSTRACT

**Background:** Hypotension following spinal block can be reduced or minimized prophylactically left lateral uterine displacement, volume loading with crystalloid solutions, phenylephrine infusion or ephedrine administration. Fluid pre loading does not negate the hypotension entirely but decreases the risk. This however is time consuming and vasopressors are often required to correct associated hypotension. Prophylactic ephedrine administration lowers the risk of hypotension at the expense of reactive hypertension if spinal block fails and subsequent conversion to general anesthesia.

**Aim:** To compare the efficacy of prophylactic use of ephedrine versus fluid (Hartmann's solution) preload in women undergoing cesarean section under spinal anesthesia at a teaching hospital.

**Study design:** Randomized controlled trial.

**Place and duration of study:** Department of Anesthesiology, Nishtar Hospital Multan, from 1<sup>st</sup> March 2020 to 30<sup>th</sup> September 2020.

**Methodology:** A total of 100 women, twenty to forty years of age undergoing cesarean section were included. Patients with known hypertension, eclampsia, bleeding diathesis, injection site infection, deformity of spinal column or patients having valvular heart diseases were excluded. Group A women were given prophylactic ephedrine while Group B were given fluid (Hartmann's solution) preload. After induction of spinal anesthesia continuous blood pressure monitoring was done for fifteen minutes to diagnose hypotension. Hypotension was noted and recorded by the researcher.

**Results:** The mean age of women in group A was 28.04±6.07 years and in group B was 28.26±6.13 years. Majority of the patients, 56, were between twenty to thirty years of age. The mean BMI in group A was 29.06±3.37kg/m<sup>2</sup> and in group B was 29.38±3.50 kg/m<sup>2</sup>. Efficacy of prophylactic use of ephedrine to prevent hypotension was observed in 37(74%) patients and in 25(50%) patients in fluid preload group undergoing cesarean sections under spinal anesthesia.

**Conclusion:** The frequency of hypotension is lower in parturient undergoing spinal anesthesia with prophylactic use of ephedrine as compared to women having fluid (Hartmann's solution) preload.

**Keywords:** Spinal anesthesia, Hypotension, Ephedrine

## INTRODUCTION

Subarachnoid block is a secure and effective substitute to general anesthesia for the surgeries below the belt including lower limb surgeries, perineal surgeries and lower abdominal wall procedures<sup>1,2</sup>. It has revolutionized the anesthesia practice as it provides a suitable and cost effective technique with preserved airway reflexes, early mobilization, increased patient satisfaction that ensures dense anesthesia and efficient post-operative analgesia.

Spinal anesthesia invariably leads to hypotension due to sympathectomy and loss of sympathetic tone. Subarachnoid blocks variably lowers blood pressure that may be accompanied by bradycardia and negative inotropy which can be minimized either by vasopressors like phenylephrine or ephedrine or by pre-loading the patients<sup>3</sup>. Local anesthetic allergies may pose a challenge but it has been found that real allergy is usually with ester type local anesthetics and not the amide type local anesthetics, so selecting an appropriate local anesthetic is not a big deal<sup>4</sup>. Age, female gender, BMI greater than 30kg/m<sup>2</sup>, diabetes mellitus, low iron levels, PIH history and high spinal levels are the factors that have been associated independently with early hypotension and lowered blood pressure<sup>5</sup>.

In pregnant females undergoing cesarean section, maternal hypotension is the most common complication of subarachnoid block with an estimated incidence that approaches close to 100% without any prophylactic measures. Number of approaches including intravascular compartment volume expansion with fluids and crystalloids, placing a wedge under right hip to displace gravid uterus and using vasopressor drugs like phenylephrine or

ephedrine have been used to decrease prophylactically the severity and occurrence of hypotension following spinal block. Fluid pre loading does not eliminate the risk of hypotension but certainly lowers it. It is however quite time consuming and often times patients still requires ephedrine or phenylephrine to counter the lowered blood pressure effectively. Prophylactic ephedrine reduces the incidence of hypotension but at the expense of reactive hypertension risk if spinal block fails resulting in subsequent conversion to general anesthesia. Chan et al<sup>6</sup> reported lower rates of hypotension in women treated with ephedrine (35%) as compared with fluid group where it was as high as 65% (p=0.04), while a local study reported phenylephrine, a pure alpha agonist is more efficacious than ephedrine for the management of lowered blood pressure due to spinal block during cesarean section surgery<sup>7</sup>.

The purpose of our study was to compare prophylactic ephedrine usage and fluid preload in spinal anesthesia among women undergoing cesarean section. The results of this study will help determine important baseline database in our local population. The results will also help anesthetists to adopt more effective prophylactic therapy for the prevention of hypotension that will decrease the incidence of related morbidities and mortalities.

## MATERIALS AND METHODS

This randomized controlled trial was conducted in the Department of Anesthesiology, Nishtar Medical University Multan after permission from Ethics committee. A total number of 100 patients (50 in each group) by using P1=65% (prevention of hypotension with fluid preload) and P2=35% (prevention of hypotension with ephedrine), with power of 80% and 95% Confidence interval. Patients aged twenty to forty years, both nulliparous and multiparous women of greater than 37 weeks gestational age

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undergoing cesarean section under subarachnoid block were included in this study. While patients with known local anesthetics allergy, hypertensive in shock or patients having bleeding disorders, infection at spinal site injection, deformity of spinal column or women with known valvular heart disease were excluded.

The patients were thoroughly briefed about the procedure and written informed consent was taken from the patients. Baseline data including weight, height, body mass index, age, type of cesarean section and baseline blood pressure was noted. These patients were randomly divided into 2 groups (group A and group B) by draws method. They were given sealed envelopes marked with A and B. The patients were asked to pick any one of the envelopes. Those who pick A were placed in group A (treated with prophylactic ephedrine by intravenous infusion of ephedrine 0.25mg/kg, were administered to the patients immediately after bupivacaine was injected) while those who picked envelope marked with B were placed in group B (treated with prophylactic fluid preload twenty ml/kg of Hartmann's solution over a period of ten to fifteen minutes immediately before institution of spinal anesthesia). Spinal anesthesia was employed by a senior consultant anesthetist, following standard technique after aspiration of free CSF flow from the smallest bore 27G pencil point spinal needle. After induction of spinal anesthesia, continuous blood pressure monitoring was done for 15 minutes to diagnose hypotension (>20% decrease in systolic blood pressure and/or diastolic blood pressure from the baseline). Hypotension was noted and recorded by the researcher. All the relevant information was recorded. The data was entered and analyzed through SPSS-25. Effect modifiers like age, type of cesarean section, and obesity were controlled by making stratification. Post-stratification Chi square test was applied to see their effect on hypotension. P value ≤0.05 was considered statistically significant.

**RESULTS**

The mean age of patients in group A was 28.04±6.07 years and in group B was 28.26±6.13 years. Fifty six patients (56.0%) were between 20 to 30 years of age. The mean BMI in group A was 29.06±3.37 kg/m<sup>2</sup> and in group B was 29.38±3.50 kg/m<sup>2</sup>. Distribution of patients according to residence was fairly distributed between rural and urban. Elective cesarean sections dominated the emergency sections (Table 1). Efficacy of prophylactic use of ephedrine was seen in 37(74%) and in fluid (Hartmann's solution) preload in 25(50%) women undergoing cesarean sections under spinal anesthesia (Table 2). Stratification of efficacy with respect to obesity, age, residence & type of C-section (Table 3).

Table 1: Demographic information of the patients (n=100)

Variable	Group A (n=50)		Group B (n=50)	
	No.	%	No.	%
<b>Age (years)</b>				
20-30	29	56.0	29	56.0
31-40	21	42.0	21	42.0
<b>Body mass index (Kg/m<sup>2</sup>)</b>				
≤27.5	20	40.0	22	44.0
>27.5	30	60.0	28	56.0
<b>Residence</b>				
Rural	23	46.0	25	50.0
Urban	27	54.0	25	50.0
<b>Type of procedure</b>				
Emergency	22	44.0	22	44.0
Elective	28	56.0	28	56.0

Table 2: Comparison of efficacy of prophylactic use of ephedrine versus fluid (Hartmann's solution) preload in women undergoing cesarean sections under spinal anesthesia

Group	Efficacy of ephedrine versus fluid preload				P value
	Yes		No		
	No.	%	No.	%	
A	37	74.0	13	26.0	0.013
B	25	50.0	25	50.0	0.503

Table 3: Stratification of efficacy with respect to age, BMI and type of CS

Variable	Efficacy				P value
	Group A		Group B		
	Yes	No	Yes	No	
<b>Age (years)</b>					
20-30	23	06	16	13	0.050
31-40	14	07	09	12	0.121
<b>Body mass index (kg/m<sup>2</sup>)</b>					
≤27.5	13	07	12	10	0.491
>27.5	24	06	13	15	0.008
<b>Type of CS</b>					
Emergency	14	08	10	12	0.226
Elective	23	05	15	13	0.022

**DISCUSSION**

Subarachnoid block is the most widespread technique of anesthesia for women requiring cesarean section. It offers a lot of advantages including but not limited to early mobility, cost effectiveness and early discharge. Hypotension that accompanies spinal block is the most significant side effect that can negatively impact maternal and fetal well being<sup>8,9</sup>. Pre-loading or co-loading with crystalloids or colloids, left lateral tilt to prevent aortocaval compression and vasopressors are some methods that are frequently employed to treat low blood pressure in mother.<sup>10,11</sup> Fluid preload effects and benefits have been debated and questionable<sup>12-14</sup>. Phenylephrine and ephedrine are usually still needed because the risk of hypotension is minimized by fluid administration but not fully abolished<sup>13,14</sup>. It has been found that a combination of fluids along with vasopressors work much better than either alone to prevent hypotension<sup>15,16</sup>. Conventionally, ephedrine was the drug most commonly employed in obstetric anaesthesia<sup>9</sup>.

In the present study, the patients mean age in group A was 28.04±6.07 years in group A and 28.26±6.13 years in group B. Majority of the parturient 56(56%) were between twenty to thirty years of age. Efficacy of prophylactic use of ephedrine was seen in 37(74%) and in fluid (Hartmann's solution) preload in 25(50%) women undergoing cesarean sections under spinal anesthesia (p-value=0.013). A study conducted by Chan et al<sup>6</sup> from China has reported lower rates of hypotension in women treated with ephedrine (35%) as compared with fluid group where it was as high as 65% (p=0.04), while local study recently found out that vasopressor drug phenylephrine is much more effective than ephedrine to manage lowered blood pressure due to spinal block in women during cesarean delivery.<sup>7</sup>

Desalu et al<sup>17</sup> compared fluid preload of normal saline one liter alone to one liter normal saline mixed with 30mg ephedrine and concluded that systolic blood pressure was higher in the normal saline with ephedrine group than normal saline alone group. After the subarachnoid block, in the preload group, lowered blood pressure was noted most often at 5 minutes. In comparison, in ephedrine group it happened at 10 minutes. Interestingly, the total time duration was fairly brief and often less than 5 minutes. Ephedrine acts primarily on alpha and beta receptors and was the drug of choice for the management of spinal induced lowered blood pressure especially in pregnant females undergoing cesarean section due to its significant ability to keep uteroplacental blood flow in check. A number of researchers have reported hypotension incidence between 50-70% despite ephedrine prophylactic usage either through intramuscular route or intravenous route.<sup>18</sup> As a consequence, it is still debatable the accurate dose and route of ephedrine that should be employed to counter spinal induced lowered blood pressure.<sup>19</sup>

Kamat and colleagues<sup>20</sup> compared ephedrine bolus and infusion with crystalloid preloading for caesarean delivery under subarachnoid block. They concluded that 6mg ephedrine bolus administered to the patient at the onset of spinal block followed by 24mg ephedrine infusion proved to be more effective than crystalloid administration alone in preventing spinal induced hypotension. The findings obtained in our study correlate well with

those reported by Chan et al<sup>6</sup>, Desalu et al<sup>17</sup> and Kamat et al<sup>20</sup> who observed increased incidence of hypotension in the preload group compared to the ephedrine group.

Ephedrine has been in use for about a century to manage spinal induced hypotension. Initially, there were doubts to use vasopressor drugs in obstetric patients because of fear of uterine artery vasoconstriction. Crawford and some other researchers<sup>21, 22</sup> believed that fetal compromise and asphyxia has been related to vasopressor usage to maintain maternal blood pressure. Ralston & Shnider in 1974 measured uteroplacental blood flow and acid base status of fetus in pregnant ewes after giving them equipotent doses of metaraminol, mephentermine and methoxamine and ephedrine. Their findings supported the use of ephedrine in obstetrics anaesthesia<sup>23</sup>.

A survey conducted in United Kingdom of obstetric anaesthetists showed that more than ninety five percent still utilize ephedrine in cesarean deliveries as the preferred vasopressor<sup>24</sup>. Despite other vasopressors gaining popularity in recent times, the concerns still exist over the safety of those agents and potentially deleterious effects on uterine artery and uterine blood flow. Alpha one agonists and ephedrine both tend to maintain normotension in pregnant ladies undergoing cesarean section without having any significant untoward effects on fetal well being. Meta-analysis done however has found out that more significant maternal and fetal acidosis is associated with ephedrine than the alpha receptor agonists phenylephrine and metaraminol during obstetrics anaesthesia. However the evidence is inconclusive regarding fetal asphyxia and more work is needed to prove these findings.

## CONCLUSION

The frequency of hypotension is lower in women undergoing spinal anaesthesia with prophylactic use of ephedrine as compared to women having fluid (Hartmann's solution) preload. So, we recommend that prophylactic use of ephedrine during induction of spinal anaesthesia for caesarean section should be used routinely in general practice for preventing spinal induced hypotension

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