



## Original Research Article

# COMPARISON OF THE EFFECT OF EPHEDRINE AND PHENYLEPHRINE IN THE TREATMENT OF HYPOTENSION AFTER SPINAL ANESTHESIA DURING CAESAREAN SECTION AND THEIR EFFECT ON FETAL OUTCOME

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## ABSTRACT

**Background:** Neuraxial anesthesia remains the preferred choice for Caesarean deliveries across the world. Hypotension is the physiologic consequence and perhaps the most common complication of neuraxial anesthesia in obstetric patients. In this study, we compared the effectiveness of vasopressors, ephedrine versus phenylephrine in the treatment of hypotension after spinal anesthesia and also the fetal outcome.

**Materials and Methods:** Patients aged group between 18-and 35 years posted for elective cesarean section with term pregnancy were allocated randomly to the two groups, Group-1 (E) Ephedrine and Group-II (P) Phenylephrine. Changes in maternal blood pressure, heart rate, and saturation were monitored and noted till the end of the surgery. The total dose of vasopressor and number of boluses used, total volume of fluids infused, the time of spinal anesthesia given, the delivery of the fetus, and the duration of the procedure were documented. Umbilical artery cord blood for determination of the acid-base status of the fetus. APGAR scores 1 min and 5 min of delivery of all newborns were noted and a score of <8 was considered low.

**Results:** In our study, all patients in the two groups were comparable concerning age, height, weight, gestational age, and ASA status. The differences observed in baseline values of mean arterial blood pressure and saturation between the two groups were statistically insignificant. Also, there was a statistically insignificant difference between the duration of surgery, the total volume of fluid used intra-operatively, and the time of spinal to the delivery of the fetus in both groups. Further in my study, it was observed that there was a statistically significant difference in mean arterial blood pressure between the two groups up to 20 minutes post spinal anesthesia, but beyond the 25th minute, there was no statistical difference in mean arterial blood pressure between the two groups till the end of the surgery.

**Conclusion:** The use of phenylephrine or ephedrine to correct maternal hemodynamic changes during spinal block for cesarean section does not show any marked difference in the outcome. The effect on fetal pH fetal acid-base status is comparable with both groups. The results of my study show that phenylephrine and ephedrine are both efficient and suitable vasopressors for the treatment of hypotension following spinal block in patients undergoing cesarean section.

**Keywords:** Cesarean deliveries, hypotension, spinal anesthesia, vasopressors.

## INTRODUCTION

During most of the 19th century, physicians performed very few Caesarean sections because the mortality rate was so high and the procedure was reserved for desperate situations. Only in the past four decades, there have been incentives to develop better anesthetic techniques for cesarean section. Anaesthesiologists have placed better emphasis on the well-being of the neonate and hence have developed better anaesthesia techniques that protect the mother and also have the least possible effects on the child.

Neuraxial anesthesia remains the preferred choice for Caesarean deliveries across the world. Hypotension is the physiologic consequence of spinal anesthesia and is perhaps the most common complication of neuraxial anesthesia in obstetric patients.<sup>[1]</sup> Hypotension can have a potentially deleterious maternal and fetal impact. Maternal hypotension produces unpleasant symptoms such as nausea, vomiting, and lightheadedness. More importantly, when severe and sustained, hypotension can impair uterine and intervillous blood flow and ultimately result in fetal acidosis and neonatal depression.<sup>[2]</sup> Many interventions, such as prehydration, vasopressor drugs (ephedrine, phenylephrine), left lateral tilt, and lower leg compression, have been used to prevent hypotension.<sup>[3]</sup>

Both epinephrine and phenylephrine have a long history of use as adjuvants in the administration of local anesthesia. As a result, both drugs will increase the intensity and prolong the duration of sensory and motor anesthesia, allowing for the administration of lower dosages of local anesthetic in a dose-dependent manner (0.1–0.6 mg).<sup>[4]</sup> Traditionally, ephedrine “which has strong  $\beta$ -adrenergic and weaker  $\alpha$ -adrenergic effects” has been recommended in this situation, but its position has been challenged because of potential complications such as supraventricular tachycardia, tachyphylaxis and most importantly fetal acidosis. Phenylephrine, an  $\alpha$ -adrenergic agonist, can be used for the prevention and treatment of maternal hypotension. Moreover, phenylephrine reduces the incidence of nausea and vomiting as well as fetal acidosis, but it may cause maternal bradycardia [8]. Kang et al in 1982 assessed whether prophylactic intravenous infusion of ephedrine can effectively maintain maternal blood pressure without adversely affecting the mother or fetus.<sup>[5]</sup> T. Ayorinde, P. Buczkowski, J. Brown, J. Shah D. J. Buggy in 2001 conducted an evaluation of preemptive intramuscular phenylephrine and ephedrine for reduction of spinal anesthesia-induced hypotension during cesarean section.<sup>[6]</sup> They concluded that preemptive intramuscular phenylephrine 4 mg and ephedrine 45 mg reduce the severity of hypotension and the total dose of rescue intravenous ephedrine during spinal anesthesia for cesarean section.

Cooper and colleagues in their studies and Lee et al in a quantitative and systematic review have reported that managing maternal hypotension with phenylephrine has fewer propensities to depress fetal pH than ephedrine.<sup>[1,7]</sup> Although recent studies have confirmed the beneficial fetal effects of phenylephrine, there are several controversies in this concept.

In this study, we compared the effectiveness of ephedrine versus phenylephrine in the treatment of hypotension after spinal anesthesia and also the fetal outcome.

## MATERIALS AND METHODS

### Study Design

The study was approved by the hospital's ethical committee. Informed consent was obtained from all the patients to take part in this study. The study is a prospective, randomized, controlled study. This study population consisted of a hundred American Society of Anaesthesiologists (ASA) I patients and ASA II patients.

### Selection

This study population consisted of a hundred American Society of Anaesthesiologists (ASA) I patients and ASA II patients. The inclusion criteria were patients belonging to ASA physical status I and II, age group between 18-35 years, posted for elective cesarean section with term pregnancy, and giving informed, written, and valid consent. Patients with obstetric complications, pregnancy-induced hypertension, obesity, preexisting hypertension, asthma, and heart disease, evidence of fetal anomalies and fetal compromise, having contraindications for regional anesthesia, any allergies to the local anesthetic or the study drugs, ASA III and ASA IV and patients on drugs which will cause interactions with the study drugs like tricyclic antidepressants and MAO inhibitors because phenylephrine is contraindicated in these cases.

### Study assessments and outcome measures

Parturients were assigned to receive one of the two vasopressor solutions, whenever maternal systolic pressure was reduced to 20% of baseline or less. Group E received a bolus of 6 mg increments of ephedrine if there was a decrease in HR (20% lower than baseline values) with systolic pressure more than 20% from the baseline. Group P received a bolus of phenylephrine in 20 mcg increments whenever there was an increased heart rate (rate > 20%) higher than baseline values, with a decrease in systolic blood pressure more than 20% from the baseline.

Changes in maternal Blood pressure (SBP, DBP, MAP), Heart Rate, and Saturation were monitored and noted till the end of the surgery. The total dose of the vasopressors, the number of boluses used, and the total volume of fluids infused were also recorded

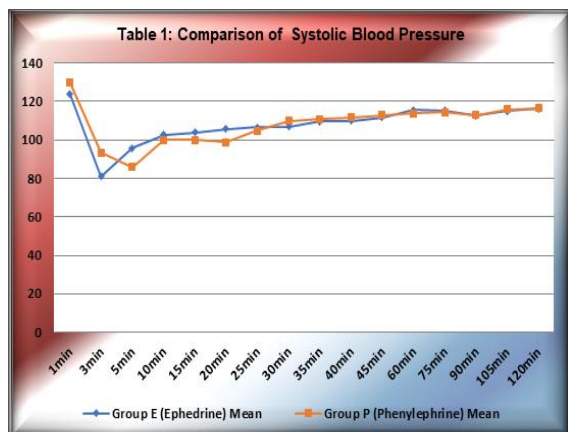
along with the time of spinal anesthesia given to the delivery of the fetus and the duration of the procedure were also documented. Umbilical artery cord blood was sampled for determination of acid-base status of the fetus. APGAR scores 1 min and 5 min of delivery of all newborns were noted and a score of <8 was considered low.

### Statistical Analysis

Descriptive statistical data was presented as mean ± standard deviation and percentages. Student t-test was used to compare mean differences between different groups. A chi-square test was performed to assess the association among different categorical variables. Power analysis was done with a beta error of 0.8 and alpha error of 0.05 and the sample size was calculated 50 in each group. For all statistical analyses,  $p < 0.05$  was considered statistically significant.

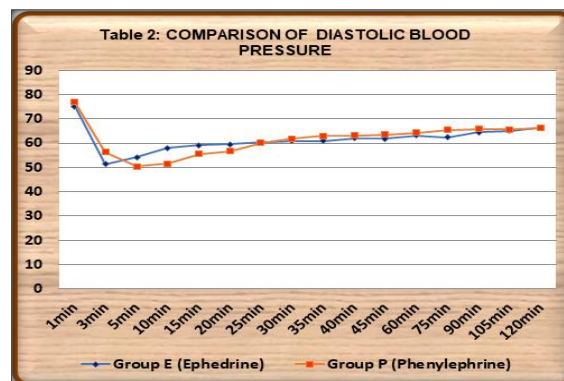
## RESULTS

In our study, statistically, there was no mean significant difference in physical characteristics of the two parturient groups. The difference in the mean values of age, height, and weight are insignificant ( $P$  value  $> 0.05$ ). [Table 1] Drug doses administered between the two groups were statistically significant ( $p < 0.05$ ).



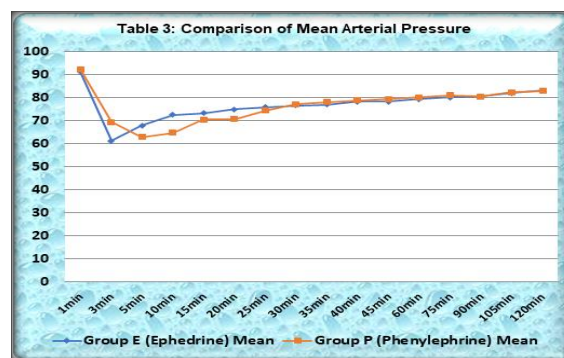
**Table 1: Comparison of Systolic Blood Pressure**

The mean baseline systolic arterial blood pressure in Group E was 124 mm of Hg fell to a minimum of 95 mm of Hg at the end of five minutes and reached a peak of 116 mm of Hg at 120 minutes. [Table 1] The mean baseline systolic arterial blood pressure in Group P was 130 mm of Hg fell to a minimum of 85 mm of Hg at the end of 5 minutes and reached a value of 116 mm of Hg at 120 minutes.



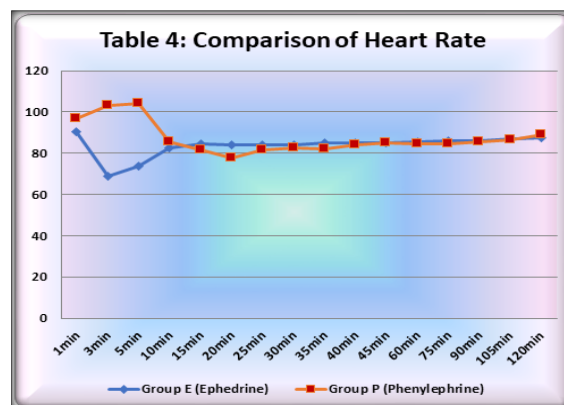
**Table 2: Comparison of Diastolic Blood Pressure**

The mean baseline diastolic arterial blood pressure in Group E was 75 mm of Hg fell to a minimum of 51 mm of Hg at the end of 3 minutes and reached a peak of 66 mm of Hg at 120 minutes. [Table 2] The mean baseline diastolic arterial blood pressure in Group P was 76 mm of Hg fell to a minimum of 50 mm of Hg at the end of 5 minutes and reached a value of 66 mm of Hg at 120 minutes.



**Table 3: Comparison of Mean Arterial Pressure**

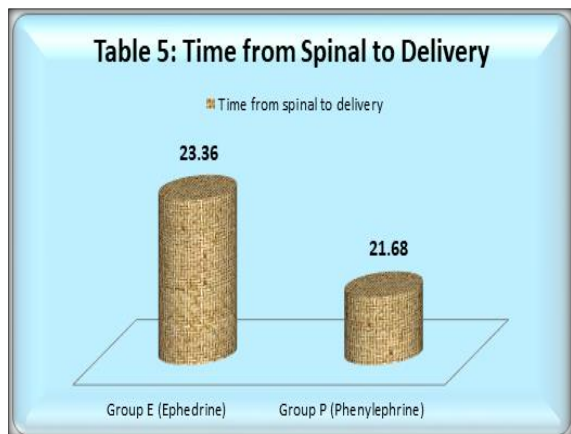
The mean baseline arterial blood pressure in group E was 92 mm of Hg, fell to a minimum of 68 mm of Hg at the end of 5 minutes, and reached a value of 83 mm of Hg at 120 minutes. [Table 3] The mean baseline arterial blood pressure in group P was 92 mm of Hg, fell to a minimum of 62 mm of Hg at the end of 5 minutes, and reached a value of 82 mm of Hg at 120 minutes.



**Table 4: Comparison of Heart Rate**

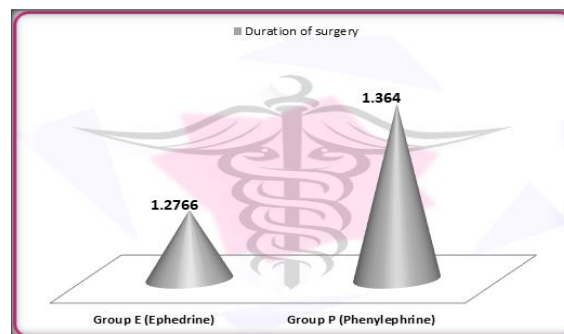
The mean baseline heart rate in group E was 90 per minute, fell to a minimum of 68 per minute at the end of 3 minutes, and reached a value of 88 per minute at 120 minutes. [Table 4]

The mean baseline heart rate in group P was 96 per min, fell to a minimum of 81 per min at the end of 15 minutes, and reached a value of 88 per min at 120 minutes.



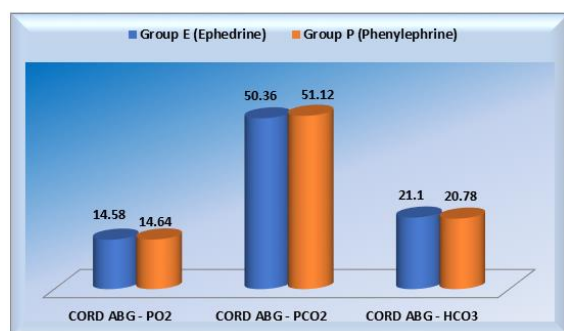
**Table 5: Time from Spinal to Delivery**

In the present study, statistically, there was no mean significant difference in time from spinal to delivery among the two parturient groups (P value >0.05). [Table 5]



**Table 6: Duration of Surgery**

In the present study, statistically, there was no mean significant difference between the duration of surgery among the two parturient groups (P value >0.05). [Table 6]



**Table 7: Statistical comparison of CORD ABG – PO2; PCO2; HCO3**

In the present study, statistically there was no mean significant difference in cord ABG - pO2, pCO2, HCO3 among the two parturient groups (P value >0.05). [Table 7]

**Table 1**

Parameter	Group E (Ephedrine)		Group P (Phenylephrine)		p value
	Mean	Std Dev	Mean	Std Dev	
Drug dose / Volume given (ml)	2.2	0	2.24	0.08	0.02

## DISCUSSION

Spinal anesthesia is the most commonly administered anesthesia for cesarean sections. It allows the mother to be awake, minimizes (or completely avoids) the problems of maternal aspiration and difficult tracheal intubation, and avoids neonatal depression from general anesthetics. It has also been suggested that operative blood loss is less with regional anesthesia than with general anesthesia.

The common and serious problem with spinal anesthesia for cesarean section remains the rapid onset of profound hypotension caused by sympathetic blockade which persists for a few hours. If prophylactic measures were not taken, the incidence of hypotension increases to more than 80% of the population.<sup>[8]</sup> During this period, there is

an increase in the capacity of intravascular space due to vasodilation. This causes relative hypovolemia and hypotension which are frequent adverse effects of spinal anaesthesia, often exaggerated by aorto-caval compression.

Hypotension is associated with a comparable fall in uterine blood flow and placental perfusion leading to fetal hypoxemia and acidosis if not promptly treated.<sup>[2]</sup> Abnormal APGAR and neuro-behavioral scores were noted when systolic blood pressure dropped by more than 30% baseline (or) stayed less than 80 mmHg for more than 4 minutes.

On evaluating the control of hypotension, several studies have demonstrated similar efficacy of ephedrine and phenylephrine on preventing and treating this complication, both when used in bolus or continuous infusion. In the present study, for

practical purposes, it was decided to administer the medication as a bolus. Even though the use of epinephrine is not associated with an elevated risk of TNS, it has been linked to a case of cauda equina syndrome in one study.<sup>[9,10]</sup> The usage of phenylephrine has been associated with an increased risk of TNS (10-fold increase).<sup>[11]</sup>

In the present study, parameters associated with post-spinal block hypotension were controlled to evaluate which drug would be more effective in the prevention of hypotension with fewer deleterious consequences to the fetus. Prior studies have presented different methodologies and questionable results regarding the ideal vasopressor, dose, and administration regimen, as well as the use of other techniques to control maternal blood pressure with minimal deleterious effects on the fetus.

In my study, all patients in the two groups were comparable concerning age, height, weight, gestational age, and ASA status. The differences observed in baseline values of mean arterial blood pressure and saturation between the two groups were statistically insignificant. Also, there was a statistically insignificant difference between the duration of surgery, the total volume of fluid used intra-operatively, and the time of spinal to the delivery of the fetus in both groups. Further in my study, it was observed that there was a statistically significant difference in mean arterial blood pressure between the two groups up to 20 minutes post-spinal anesthesia, but beyond the 25th minute, there was no statistical difference in mean arterial blood pressure between the two groups till the end of the surgery. Thus it is confirmed that there is no difference between ephedrine and phenylephrine in their efficacy for the management of hypotension in healthy parturients undergoing cesarean section.

- The results of my study are by the studies of Adigun et al. They observed that both vasopressors effectively restored the blood pressure.<sup>[12]</sup> They also concluded that phenylephrine is safe and can be used as effectively as ephedrine. Atashkhoyi Simin et al compared the effectiveness of ephedrine and phenylephrine in the treatment of hypotension post-spinal anesthesia in cesarean section and concluded that ephedrine and phenylephrine are both effective vasopressors for the treatment of hypotension.<sup>[13]</sup> Ngan Kee WD, et al. in 2008 conducted a randomized double-blinded comparison of phenylephrine and ephedrine infusion combinations to maintain blood pressure during spinal anesthesia for cesarean delivery, the effects on fetal acid-base status, and hemodynamic control.<sup>[14]</sup> Combinations of phenylephrine and ephedrine appear to have no advantage compared with phenylephrine alone when administered by infusion for the prevention of hypotension.
- Saravanan. S (2006) compared equivalent doses of ephedrine and phenylephrine in the

prevention of post-spinal hypotension in cesarean section and concluded that the potency ratio was equal between ephedrine and phenylephrine in the prevention of hypotension.<sup>[15]</sup>

## CONCLUSION

The use of phenylephrine or ephedrine to correct maternal hemodynamic changes during the spinal block in patients undergoing cesarean section does not show any marked difference in the outcome. Both drugs are comparable in their effects in correcting hemodynamic changes. The effect on fetal pH is comparable with both the groups and there is no difference in fetal acid-base status which shows that strict control of blood pressure is an important condition for maternal and fetal well-being. The results of my study, show that phenylephrine and ephedrine (concerning maternal hemodynamic changes) are both efficient and suitable vasopressors for treatment (not prophylaxis) of hypotension following spinal block in patients undergoing cesarean section. Both drugs have similar efficacy on neonates. APGAR score is the most applied and easily interpretable clinical method of neonatal wellbeing. Mean APGAR scores of the neonates at 1 and 5 min were comparable between the two groups.

### Additional Information

#### Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study.

**Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue.

**Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following:

**Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work.

**Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

**Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## REFERENCES

1. Collins V.J., Complication during spinal anaesthesia "Principles of anaesthesiology 3 rd ed Philadelphia, Lea and Febiger 1993:1540 -1554
2. Miller, R.D. (2015) Millers anaesthesia; 8th Edition, Churchill Livingstone, Philadelphia.
3. Amy H, Cockerham R. Managing hypotension during anaesthesia for caesarean section. *Anaesthesia Intensive Care Med* 2013;14(7): 280.
4. Kito K, Kato H, Shibata M, Adachi T, Nakao S. The effect of varied doses of epinephrine on duration of lidocaine spinal anaesthesia in the thoracic and lumbosacral dermatomes. *Anesth Analg* 1998; 86:1018.

5. Kang YC, Abouleish E, Carirtis S. Prophylactic intravenous ephedrine infusion during spinal anesthesia for Cesarean section. *Anesth Analg* 1982; 61: 839–42
6. Ayorinde, B.T., Buczkowski, P., Brown, J., Shah, J. and Buggy, DJ. (2001) Evaluation of pre-emptive intra- muscular phenylephrine and ephedrine for reduction of spinal anaesthesia-induced hypotension during caesarean section. *British Journal of Anaesthesia*, 86, 372-376.
7. Lee, A., Ngan Kee, W.D. and Gin, T. (2002) A Quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean deli- very. *Anesthesia & Analgesia*, 94, 920-926.
8. NganKee WD. Prevention of maternal hypotension after regional anaesthesia for caesarean section. *Curr Opin Anesthesiol* 2010; 23:304-9.
9. Koo CH, Shin HJ, Han SH, Ryu JH, Koo CH, et al. Lidocaine vs other local anesthetics in the development of transient neurologic symptoms (TNS) following spinal anesthesia: a meta-analysis of randomized controlled trials. *J Clin Med* 2020;9(2):493
10. Shields LBE, Iyer VG, Zhang YP, Shields CB. Shields LBE, et al. Acute cauda equina syndrome following orthopedic procedures as a result of epidural anesthesia. *Surg Neurol Int* 2018; 9:81.
11. Park YH, Ryu T, Hong SW, Kwak KH, Kim SO. Park YH, et al. The effect of the intravenous phenylephrine on the level of spinal anesthesia. *Korean J Anesthesiol* 2011;61(5): 372-6.
12. Adigun TA, Amanor-Boadu SD, Soyannwo SD. Comparison of intravenous ephedrine with phenylephrine for the maintenance of arterial blood pressure during elective caesarean section under spinal anaesthesia. *Afr J Med Sci* 2010; 39:13-20.
13. Atashkhoyi Simin, Fardiazar Zahra, Hatami Marandi Pouya, Torab Reza et al, in 2012 compared the effectiveness of ephedrine and/or phenylephrine, in treatment of hypotension secondary to spinal anesthesia for cesarean section and their effects on fetal/neonatal outcome. *Open Journal of Obstetrics and Gynecology*, 2012, 2,192-196
14. Ngan Kee, W.D., Khaw, K.S., Lau, T.K., Ng, F.F., Chui, K. and Ng, K.L. (2008) Randomised double-blinded comparison of phenylephrine vs ephedrine for maintaining blood pressure anaesthesia for non-elective caesarean section. *Anaesthesia*, 63, 1319-1326,365-2044,2008.
15. Saravanan, S., Kocarev, M., Wilson, R.C., Watkins, E., Columb, M.O. and Lyons, G. (2006) Equivalent dose of ephedrine and phenylephrine in the prevention of post- spinal hypotension in caesarean section. *British Journal of Anaesthesia*, 96, 95-99.