

ORIGINAL RESEARCH

A Comparative Study Between Ephedrine and Phenylephrine in Control of Spinal Anaesthesia Induced Hypotension in Elective LSCS

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ABSTRACT

Introduction: The number of caesarean sections has increased over the last two decades. Maternal hypotension is an undesirable and the most frequent consequence of spinal anesthesia for cesarean delivery as it causes detrimental maternal and fetal effects. The present study is planned to study the efficacy of ephedrine and phenylephrine to prevent the occurrence of hypotension after spinal anaesthesia before delivery.

Material and Method: Sixty pregnant women of age between 18 and 35 years falling in ASA grade I or II are being selected and randomly allocated into two groups v.i., group 'P' for phenylephrine (n=30) and group 'E' for ephedrine (n=30).

Results: Ephedrine in dose of 3mg/ml/min infusion effectively maintains maternal blood pressure after spinal anaesthesia in majority of patients. Its use is associated with a stable or slight increase in heart rate with good neonatal outcome. Phenylephrine in the dose of 100 microgram/ml/min raises the blood pressure in majority of patients. Its use is associated with a stable or reduction in heart rate, with good neonatal outcome. Incidence of nausea, vomiting and tachycardia are slightly higher with ephedrine than phenylephrine at the present rate of infusion.

Conclusion: It can be concluded that both ephedrine and phenylephrine intravenous infusion of 3mg/ml/min and 100 microgram/ml/min respectively can safely be employed to control hypotension in patients undergoing elective lower segment cesarean section under spinal anaesthesia. Neonatal outcome is also good with both the drugs.

Keywords: Caesarean Section, Obstetrics, Regional Anaesthesia, Vasopressors

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INTRODUCTION

Maternal hypotension induced by spinal anesthesia for cesarean delivery is detrimental.¹ Obstetric anaesthesia requires special attention for the fact that it involves caring of two lives as there is a little margin for error in practice of obstetric anaesthesia. In earlier studies, the vasopressor was withheld until after maternal systolic blood pressure (SBP) started to decrease and therefore there were initial periods of uncorrected hypotension resulting in placental hypoperfusion.^{2,3} The anesthesiologist does not allow hypotension to persist and the treatment often requires the use of vasopressors to maintain blood pressure.^{4,5} Recent studies have shown that any reduction in maternal blood pressure following spinal anesthesia is undesirable and the best strategy is to maximize the use of vasoconstrictors to maintain SBP at 100% of baseline.⁶ This strategy gives the best outcome for the baby (highest umbilical artery pH) and the mother (less nausea).^{6,7,9} Ephedrine has been the drug of choice for prophylaxis and treatment of post spinal hypotension for many years. It is considered to maintain uteroplacental blood flow but has been shown to cause fatal acidosis.^{4,5} Recent clinical trials have shown that α -agonist phenylephrine produces better fatal acid base status than ephedrine in healthy term cesarean deliveries.^{6,7,8} We hypothesized that regardless of the vasopressor chosen, maintaining SBP at 100% baseline by early administration of a vasopressor would be more beneficial for the mother and baby. By keeping a tight control of maternal blood pressure, using ephedrine or phenylephrine, we planned to study their fetal and maternal effects.

MATERIAL AND METHOD

The present clinical study was performed on sixty female patients who underwent elective lower segment cesarean section at hospital during December 2013 – July 2014. Informed and written consent, institutional ethical committee approval has been taken. The cases were selected between the age of 18 to 35 yrs of ASA I and II. The study population was randomly divided into 2 groups with 30 patients in each group. Group E – Ephedrine group (number-30)

Group P – Phenylephrine (number- 30).

Inclusion Criteria

1) Aged between 18 to 35 yrs. 2) ASA grade I and II, having uncomplicated singleton pregnancy beyond 36 weeks, scheduled to have elective cesarean section under spinal anaesthesia, 3) Weight between 40 and 70 kg. 3) Height between 140 and 170cm.

Exclusion Criteria

1) Patients with coagulation disorders, cardiovascular abnormalities, patient's refusal, spinal abnormalities. 2) PIH ,renal disease, DM, placenta praevia, abruptio placenta. 3) Patients posted for cesarean section for fetal abnormalities.

Pre-Anaesthetic Assessment

Pre anaesthetic assessment of each patient including detailed medical history such as diabetes mellitus, hypertension, pulmonary tuberculosis, allergy to drugs, bronchial asthma, epilepsy and bleeding disorders were taken. History of pregnancy induced hypertension, Gestational diabetes were also elicited. Symptoms and signs suggestive of antepartum haemorrhage like placenta praevia and abruptio placenta were ruled out.

Clinical examination included general physical examination and recording of vital data as well as systemic examination of cardiovascular system, respiratory system, gastrointestinal tract, central nervous system and also airway and spine assessment.

All the patients were advised overnight fasting . Haemoglobin , Blood cell count RBCs, WBCs & Platelets , Bleeding time and clotting time, Blood urea, Serum creatinine , Serum electrolytes, Blood grouping and Rh typing , Complete urine examination. Patients were premedicated with injection Ondansetron 4mg and inj. Ranitidine 50mg IV 1 hr before surgery. Both the groups (E and P) were preloaded with RL 10 ml/kg over 20 minutes before anaesthetic procedure.

Technique

Patients pulse rate, Blood pressure were recorded on the operative table. Patients were positioned in left lateral position with the flexion of thigh and legs, hip and knees and flexion at the head. The operating table was kept flat. Under strict aseptic precautions, lumbar puncture was performed at L₃₋₄ using midline approach with 26G sterile Quinckie needle. After the clear and free flow of CSF Bupivacaine 0.5% heavy, 2ml was injected into L₃₋₄ subarachnoid space over 10-15 sec. Then patient was turned to supine posture using a wedge under the right buttock for a tilt of 15°. Immediately after the patient is given spinal drug and turned supine, the vasopressor infusion was started which was done with the help of an infusion pump. Group 'E' received infusion of a solution containing 3mg/ml of ephedrine in normal saline at a rate of 60ml/hour. Group 'P' received infusion of a solution containing 100mcg/ml of phenylephrine in normal saline at a rate of 60ml/hour. The in-

fusion was stopped in both the groups immediately after baby delivery(umbilical cord clamping). Any patient who attained sensory level greater than T₄ or lesser than T₆ are excluded from the study.

Non-invasive blood pressure, pulse rate, respiratory rate and oxygen saturation were monitored every 2 minutes till baby delivery. If there was hypotension 1ml of the test drug ephedrine (3mg/ml) or phenylephrine (100microgram/ml) with normal saline was given. The anaesthesiologist monitoring the patient and administering the drug were blinded about the drug in the syringe. Hypotension is defined as a fall of systolic blood pressure < 90 mmHg or 20% less than the basal systolic BP or both.

The effectiveness of maintenance of blood pressure and any side effects if present by the administration of test drug were noted .Heart rate was monitored and any bradycardia (HR less than 60bpm) was treated with atropine 0.6 mg IV. Any tachycardia (HR > 30% above the basal HR) was noted. Intra operative nausea and vomiting was recorded. Neonatal well being was assessed at 1 minute and 5 minutes using APGAR score by the attending neonatologist. Postoperatively the patient was monitored in the postoperative ward for 24 hours for any adverse events.

Statistical Analysis-

All data were entered into an excel sheet and descriptively analysed statistically with software SPSS 20 version.

RESULTS

Sixty patients posted for elective cesarean section under spinal anaesthesia were enrolled in the present study. Group 'E' received 3mg/min of intravenous infusion and group 'P' received 100mcg/min of phenylephrine intravenous infusion for the prevention of post spinal hypotension. The results of the study are as follows.

The mean heart rates at 2 minutes interval in ephedrine group increased transiently but later reached to the base line values, in phenylephrine group it was maintained around baseline throughout the procedure.

The mean systolic blood pressures at 2 minutes interval in ephedrine group decreased initially but later reached to the base line values, in phenylephrine group it was maintained around baseline throughout the procedure. The mean diastolic blood pressures at 2 minutes interval in ephedrine group decreased initially but later reached to the base line values, in phenylephrine group it was maintained around baseline throughout the procedure.

The mean arterial blood pressures at 2 minutes interval in ephedrine group decreased initially but later reached to the base line values, in phenylephrine group it was maintained around baseline throughout the procedure. The mean values of Apgar scores in both the groups are similar at 1min and 5 min. The incidence of hypotension is less both the groups but it is

Parameter	Ephedrine	Phenylephrine
Age (yr)	23.43	23.70
Height(cm)	152.57	151.90
Weight(kg)	56.20	56.97

Table-1: Comparison of mean age, height and weight in both ephedrine and phenylephrine groups

	Ephedrine	Phenylephrine	'p' value
SBP at time in min			
0 (basal)	118.70±10.40	121.73±7.07	0.01*
2	111.30±9.64	123.80±8.15	0.124
4	107.30±11.89	122.00±11.42	0.579
6	117.43±10.57	125.80±11.93	0.423
8	124.93±9.80	131.33±12.57	0.209
10	134.57±4.86	127.73±12.59	0.004*
12	131.00	118.00±14.14	-
DBP at time in min			
0 (basal)	75.37±7.26	78.00±7.31	0.850
2	69.97±7.74	78.70±8.15	0.749
4	67.57±9.71	76.70±9.16	0.686
6	73.77±10.00	79.93±9.23	0.920
8	79.31±9.76	81.97±10.28	0.665
10	84.57±5.50	76.64±8.89	0.167
12	86.00	78.50±3.53	-

Table-2: Mean changes in Systolic and Diastolic blood pressure in both the groups at 2minutesinterval

	Ephedrine	Phenylephrine	'p' value
Hypotension	2	1	0.554
Nausea	4	1	0.161
Vomiting	2	1	0.554
Bradycardia	1	3	0.301
Tachycardia	5	1	0.085

Table-3: Incidence of side effects in both the group

much lesser in phenylephrine group than ephedrine. The incidence of both nausea and vomiting are higher in ephedrine group than phenylephrine group. Tachycardia is more common in ephedrine group while bradycardia is more common in phenylephrine group.

DISCUSSION

Although a number of regional anaesthesia techniques are available, spinal anaesthesia is particularly popular because it is fast, easy to perform and provides excellent post operative analgesia¹⁰. Spinal anaesthesia has all the benefits, its administration is invariably associated with hypotension. Apart from affecting the mother, it can also have deleterious effects on fetus. On the maternal side, it causes hypoperfusion of the vital organs leading to hypoxia. By decreasing the uteroplacental blood flow it can induce hypoxia in fetus also. Various methods have been employed in the management of hypotension including foot end elevation, use of leg compression, prophylactic

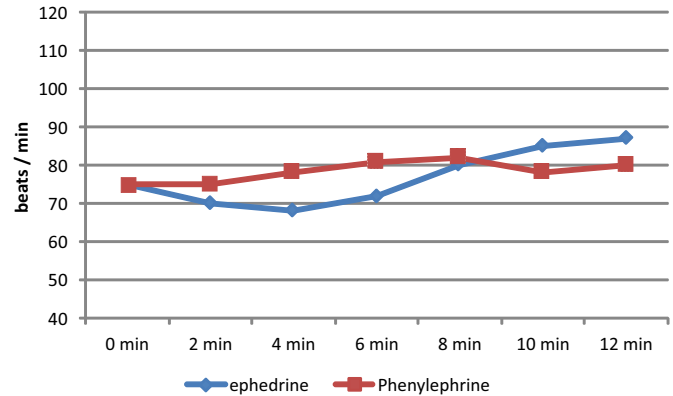


Figure-1: Comparison of Heart rate in the groups

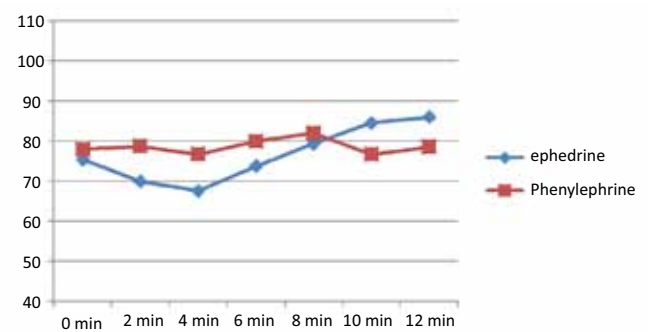


Figure-2: Comparison of mean arterial blood pressures at 2 minutes interval

lactic preloading with crystalloids¹. However none of them have shown to produce consistent results.¹¹ Vasopressors remain the mainstay of drugs used in management of spinal induced hypotension. A desirable property for use in obstetric practice is that it should not cause uterine vasoconstriction. Many vasopressors like mephentermine, methoxamine, noradrenaline, dopamine, dobutamine, metaraminol, ephedrine and phenylephrine have been tried.¹² Various studies have repeatedly established the efficacy of the ephedrine as vasopressor of choice in obstetric practice which increases the blood pressure by increasing the cardiac output and also has favourable effect on uteroplacental circulation. But few studies pose question about its effect on neonatal Apgar scores and umbilical artery blood pH values.^{13,14} Phenylephrine has also been reported to be efficient in management of hypotension due to spinal anaesthesia for caesarean section without having any effect on fetal outcome¹. Hence this study was undertaken to compare the efficacy of ephedrine and phenylephrine for management of hypotension. Various studies were mentioning different ratios of ephedrine and phenylephrine ranging from 1:11 to 1:250 respectively (like 1:30, 1:40, 1:80, 1:125). We have chosen the dose of 3mg/min infusion for ephedrine and 100mcg/min of phenylephrine as mentioned in majority of studies.¹⁵⁻¹⁸ David W Cooper et al.¹⁹ observed that ephedrine and phenylephrine given alone or in combination maintained SAP effec-

tively during spinal anaesthesia. Incidence of hypotension was less with phenylephrine group (48%) compared to ephedrine group (68%). The incidence of hypotension is much lower in the present study than that mentioned by David W Cooper et al.¹⁹ because the concentrations of the vasopressors given in the present study are higher.

Although there is difference in the incidence of hypotension between the two groups, the 'p' value (0.554) in the present study shows that there is no statistical difference between the two groups. Anna Lee MPH et al.⁸ studied and observed that there was no difference between phenylephrine and ephedrine in the management of maternal hypotension. Hence it can be said that the efficacy of ephedrine and phenylephrine is similar and the present study is concurrent with the conclusion given by Anna Lee MPH et al.⁸

NganKee WD et al. studied and concluded that phenylephrine is more efficient in maintaining maternal blood pressures and there is no added advantage of combining ephedrine and phenylephrine.¹⁰ The results in the present study show that phenylephrine has lower incidence (1 case) of hypotension than ephedrine (2 cases) and is concurrent with the conclusion given by NganKee WD et al.¹⁰

Sabyasachi Das et al.²⁰ observed that incidence of hypotension was 4 out of 29 in ephedrine group while in the phenylephrine group it is 1 out of 31 patients.²⁰ They concluded that Prophylactic phenylephrine infusion is superior to ephedrine infusion or combination of phenylephrine and ephedrine in the management of predelivery maternal hypotension during spinal anaesthesia for cesarean delivery. In the present study the incidence of hypotension is also 4 in ephedrine group and 1 in phenylephrine group of each 30 patients and is very much similar to those mentioned by Sabyasachi Das et al.²⁰

Bradycardia is common accompanying manifestation apart from hypotension in a subarachnoid block. Bradycardia in lower segment caesarean section is more frequent than in other surgeries. Higher spread of local anaesthetics in pregnancy due to engorgement of epidural veins (leading to cardioaccelerator nerve fibre paralysis), increased neuronal sensitivity for local anaesthetics due to progesterone effect, exaggerated activation of Bain bridge reflex due to aortocaval compression and peritoneal traction have been implicated as the causes of bradycardia. Treatment of bradycardia is important as it can significantly affect the cardiac output there by affecting mother and fetus.

Ephedrine due to its intrinsic sympathomimetic effects through beta receptors increases the heart rate during spinal anaesthesia. Phenylephrine is said to produce significant bradycardia. Thomas DG et al.²¹ postulated that this bradycardia could be caused by cardiac sympathetic denervation or secondary baroreflex response to phenylephrine induced hypertension.²¹

In the present study, there was an increase in heart rate in 5 patients (15.66%) of the ephedrine group and only 1 (3.33%) patient went into bradycardia that had to be given atropine

0.6mg intravenously to correct. In the phenylephrine group 3(10%) patients had bradycardia for a short duration of time which got corrected spontaneously but in 1 patient atropine had to be given to correct bradycardia reflecting the probable baroreceptor reflex. This effect was transient lasting for 2 to 5 min, but in 1(3.33%) heart rate persistently decreased to bradycardiac levels, this promptly responded to intravenous atropine 0.6 mg. However, in studies of Thomas DG et al.²¹ the incidence of bradycardia was higher with 11 out of 19 patients developing heart rate less than 60/min requiring atropine for treatment. This may probably be due to higher level block achieved in their study (T2-T4).

Neonatal well being has been assessed using various techniques ranging from simple APGAR score to sophisticated techniques such as umbilical cord blood gas assessment and pH measurement. Thomas DG et al.²¹ noted that umbilical artery pH was significantly higher in phenylephrine and also a small reduction in the heart rate in phenylephrine group.²¹ However, in their study, there was no clinical effect in neonatal outcome as suggested by absence of APGAR score <7 in any of the neonates of either groups.

Maternal nausea & vomiting is an important problem in obstetric anaesthesia, and majority of the times it heralds the onset of hypotension well before the change in numerical values of blood pressure.²² In the present study 2(6.67%) patients had both nausea and vomiting while another 2(6.67%) patients had only nausea. Only 1(3.33%) patient had both nausea and vomiting in phenylephrine group. Saravanan et al.²² noted that incidence of vomiting was higher in ephedrine group compared to phenylephrine group (1 v/s 9 patients). David Cooper et al. also noted increased incidence of nausea and vomiting in ephedrine group compared to phenylephrine group. It concurs with the studies of Saravanan et al.²² and David Cooper et al.¹⁸ The possible explanation for this difference cited by Cooper et al seems to be due to increased vagal tone following reduction of preload more likely, in the presence of beta stimulation (ephedrine stimulation), but phenylephrine is a pure alpha agonist provides better vasoconstriction reducing the decrease in the cardiac preload and diminishing the vagal reflex. This may explain the high incidence of vomiting after the ephedrine where the dose is ineffective.¹⁸

CONCLUSION

Ephedrine in dose of 3mg/ml/min infusion effectively maintains maternal blood pressure after spinal anaesthesia in majority of patients. Its use is associated with a stable or slight increase in heart rate with good neonatal outcome. Phenylephrine in the dose of 100 microgram/ml/min raises the blood pressure in majority of patients. Its use is associated with a stable or reduction in heart rate, with good neonatal outcome. Incidence of nausea, vomiting and tachycardia are slightly higher with ephedrine than phenylephrine at the present rate

of infusion.

Hence it can be concluded that both ephedrine and phenylephrine intravenous infusion of 3mg/ml/min and 100 microgram/ml/min respectively can safely be employed to control hypotension in patients undergoing elective lower segment cesarean section under spinal anaesthesia. Neonatal outcome is also good with both the drugs.

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