



SPINAL ANESTHESIA; COMPARISON OF EPHEDRINE VERSUS PHENYLEPHRINE FOR PREVENTION OF SPINAL ANESTHESIA INDUCED HYPOTENSION IN PATIENTS.

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ABSTRACT... Objectives: To compare ephedrine versus phenylephrine for prevention of spinal anesthesia induced hypotension in patients undergoing elective caesarean section. **Design:** It was a randomized controlled trial. **Place and Duration of Study:** This study was conducted at the Department of Anesthesia, Allied Hospital Faisalabad from July 2011 to December 2011. **Material and Methods:** 60 women having C-section under spinal anesthesia were included after written informed consent. These patients were randomly allocated into two treatment groups. Group-E received ephedrine 10mg intravenously and group-P received phenylephrine 100µg intravenously just after institution of spinal anesthesia. Outcome variable was frequency of spinal anesthesia induced hypotension which was noted and compared among the groups. A predesigned proforma was used to record patient's demographic details along with other study variables. **Results:** The mean age of the patients was 25.73±3.78 years in Group-P and 26.07±4.32 in Group-E (p=0.37). There was significant difference in the mean heart rate (85.50±2.64 vs. 96.93±9.96 bpm; p=0.001) and mean systolic (100.77±9.77 vs. 94.00±9.28 mmHg; p=0.007) and diastolic (58.53±10.09 vs. 53.03±8.78; p=0.028) blood pressure among the two groups (Group-P vs. Group-E) at 20 minutes after induction. The frequency of spinal anesthesia induced hypotension was significantly lower in patients receiving phenylephrine (30.0% vs. 63.3%; p=0.010) as compared to those receiving ephedrine. Similar significant difference was observed across various age and ASA-Class groups. **Conclusion:** The frequency of hypotension was significantly lower in patients receiving phenylephrine compared to ephedrine which advocate routine use of phenylephrine in such patients to minimize the risk of hypotension with associated morbidity.

Key words: Spinal Anesthesia, Hypotension, Ephedrine, Phenylephrine.

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INTRODUCTION

Regional anesthesia is now used in more than 90% of caesarean sections presently due to its advantages for both the mother and the baby.¹ Spinal anesthesia provides fast, profound and symmetrical sensory and motor block of high quality in patients undergoing caesarean delivery.² Hypotension after spinal anesthesia for caesarean section has an incidence of up to 80% without prophylactic management. Preventive measures include fluid preload, lateral tilt and use of vasopressors.³ Hypotension following spinal anesthesia for caesarean section may result in maternal nausea, vomiting and decreased uteroplacental blood flow with possible fetal acidemia.⁴

The management of choice for this common problem is the use of intravenous vasopressors as required.⁵ However, there is disagreement about the choice of vasopressor and the ideal method of delivery. While choosing a suitable vasopressor in obstetric practice, various factors need to be considered. These include efficacy in preventing hypotension, maternal side effects, ease of use, direct and indirect fetal effects and finally the cost and availability.⁶

Ephedrine is an indirect-acting, non-specific adrenergic agonist.⁶ Although ephedrine has mixed alpha (α) and beta (β) adrenoceptor activity, it maintains arterial pressure mainly by increasing cardiac output through an increase of

heart rate as a result of its predominant activity on β 1-adrenoceptors.⁷ Phenylephrine is a non-catecholamine with predominantly direct α 1-agonist activity (high doses may stimulate α 2 and β -receptors) the primary effect of phenylephrine is peripheral vasoconstriction with a concomitant rise in systemic vascular resistance and arterial blood pressure.⁸

Existing literature contained conflicting evidence regarding the frequency of hypotension after prophylactic use of ephedrine versus phenylephrine making the choice of agent in routine practice difficult.⁹⁻¹⁷ Also there was limited local evidence^{11,12} which necessitated the present study.

MATERIAL AND METHODS

This was a randomized controlled trial conducted at the Department of Anesthesia, Allied Hospital Faisalabad over 6 months from July 2011 to December 2011. Sample size of 60 cases (30 in each group) was calculated with 80% power of test and 95% confidence interval taking expected frequency of spinal anesthesia induced hypotension to be 30% in phenylephrine⁹ and 67.5% in ephedrine groups.¹⁰ Non-probability, consecutive sampling was done and 60 patients undergoing C-section at operation theatres of Allied Hospital Faisalabad were included into this study after taking written informed consent. We only included patients with singleton pregnancy at term (≥ 37 completed weeks of gestation) falling under American Society of Anesthesiologists (ASA) Class I and II. Patients with pregnancy induced hypertension, placenta accreta, placenta previa, diabetes mellitus, cardiovascular or pulmonary disease, coagulopathy, spinal cord abnormalities, previous spinal surgery or pre-existing neurological deficit and those with allergy to local anesthetic drugs were excluded. These patients were randomly allocated into two treatment groups. Patients in Group-E received ephedrine 10mg intravenously while patients in Group-P received phenylephrine 100 μ g intravenously just after institution of spinal anesthesia. Standard monitoring was applied to all the patients including pulse oximetry,

non-invasive blood pressure (NIBP) and ECG monitoring. Every patient was loaded with 500ml Lactated Ringers solution. One baseline reading of blood pressure and heart rate was taken before giving spinal anesthesia with 25G pencil point needle in sitting position with 15mg hyperbaric bupivacaine. All patients were immediately placed in supine position with 15 degree lateral tilt to prevent aortocaval compression. Hypotension (systolic blood pressure lower than 90mmHg) was treated with bolus administration of vasoconstrictor (ephedrine or phenylephrine) at 50% of the initial dose and 200ml of Lactated Ringers solution intravenously. Heart rate, systolic blood pressure, and diastolic blood pressure were measured every two minutes for 1st 2 minutes and then every five minutes for the next 15 minutes. Outcome variable was drop of systolic blood pressure of the patient ≤ 90 mmHg during the first 20 minutes which was labeled as hypotension and was recorded in a predesigned proforma along with demographic details of the patient. All the spinal injections and patients' observation were done by a single consultant who was blinded about the treatment group to eliminate bias.

RESULTS

Demographic details of the patients have been summarized in Table-I. There was significant difference in the mean heart rate (85.50 ± 2.64 vs. 96.93 ± 9.96 bpm; $p=0.001$) and mean systolic (100.77 ± 9.77 vs. 94.00 ± 9.28 mmHg; $p=0.007$) and diastolic (58.53 ± 10.09 vs. 53.03 ± 8.78 ; $p=0.028$) blood pressure among the two groups (Group-P vs. Group-E) at 20 minutes after induction. The frequency of spinal anesthesia induced hypotension was significantly lower in patients receiving phenylephrine (30.0% vs. 63.3%; $p=0.010$) as compared to those receiving ephedrine as shown in Table-II Similar significant difference was observed across various age and ASA-Class groups.

DISCUSSION

Hypotension during spinal anesthesia in patients undergoing caesarean section is secondary to blockade of the sympathetic system and it can cause harm to both the mother and the baby.

Characteristic	Phenylephrine n=30	Ephedrine n=30	P value
Age (years)	25.73±3.78	26.07±4.32	0.37
Age Groups			
20 – 25 years	17 (56.7%)	16 (53.3%)	0.58
26 – 30 years	10 (33.3%)	09 (30.0%)	
31 – 35 years	03 (10.0%)	05 (16.7%)	
ASA Class			
Class-I	22 (73.3%)	24 (80.0%)	0.39
Class-II	08 (26.7%)	06 (20.0%)	

Table-I. Demographic features of study participants
Independent sample t-test and chi-square test, Observed difference was statistically insignificant

Characteristic	Phenylephrine n=30	Ephedrine n=30	P value
Mean Heart Rate (bpm)	85.50±2.64	96.93±9.96	0.001*
Mean Systolic BP (mmHg)	100.77±9.77	94.00±9.28	0.007*
Mean Diastolic BP (mmHg)	58.53±10.09	53.03±8.78	0.028
Hypotension (n %)	09 (30.0%)	19 (63.3%)	0.010*

Table-II. Comparison of different physiological parameters between the two groups
Independent sample t-test and chi-square test, * Observed difference was statistically significant

The harmful effects include but are not limited to decline in placental blood flow, disturbance of fetal oxygen delivery and subsequent fetal acidosis, and maternal symptoms of decreased cardiac output, such as vomiting and altered state of consciousness.¹⁸ In women undergoing C-section, the frequency of hypotension after spinal anesthesia can be as high as 80%.¹⁹ Traditionally, ephedrine has been preferred vasopressor in obstetric practice.²⁰ It was alleged that ephedrine causes an increase in maternal blood pressure, thus maintaining placental blood flow.²¹ However, successive studies demonstrated that it can sometimes precipitate fetal acidosis. A 2004 meta-analysis established that ≥14 mg doses of ephedrine did not reduce the frequency of maternal hypotension, but it triggered reactive hypertension and a small reduction in umbilical cord blood Ph.²² Phenylephrine is a short-acting and potent vasoconstrictor that increases both systolic and diastolic blood pressure. It counteracts the vasodilatation and reestablishes baseline blood pressure. Conventionally, its use was limited to a second line vasoconstrictor in obstetrics because of the fear of vasoconstriction in the uteroplacental circulation. It regained attention in 1988 when Ramanathan and Grant¹⁷ found that it did not produce fetal acidosis while

preventing maternal hypotension. Numerous studies have confirmed these findings and almost all have reported higher umbilical artery (UA) pH values in neonates born to phenylephrine treated mothers.²³ However, there were concerns regarding its efficacy to prevent spinal anesthesia induced hypotension where some studies claimed it to be even better where other reported it to be far less effective compared to conventional practice of ephedrine.⁹⁻¹⁷

In the current study, the frequency of spinal anesthesia induced hypotension was significantly lower in patients receiving phenylephrine (30.0% vs. 63.3%; $p=0.010$) as compared to those receiving ephedrine. Siddiqui et al. (2015) in another local study observed similar significantly lower frequency of hypotension with phenylephrine (8% vs. 22%; $p=0.0009$) as compared to ephedrine in women undergoing C-section at Civil Hospital Karachi.¹¹ Rehman et al. in 2011 also observed similar significant difference (17.1% vs. 65.7%; $p<0.001$) in patients undergoing spinal anesthesia for C-section at Shifa International Hospital, Islamabad.¹² Ngan et al. (2008) also observed similar frequency of hypotension with phenylephrine and ephedrine (4% vs. 32%; $p<0.05$).¹³ However, Magalhães

et al. (2009) conducted a similar study on women undergoing C-section and observed significantly lower frequency of hypotension with ephedrine (70% vs. 93%; $p < 0.05$) as compared to phenylephrine and concluded that ephedrine was superior to phenylephrine.⁹ Nazir et al. (2012) however didn't observe any significant difference in the frequency of hypotension between phenylephrine (70% vs. 66%; $p > 0.05$) and ephedrine in Indian such patients and concluded both the drugs to be equally effective.¹⁴ Alkaissi et al. in 2017 also didn't observe any significant difference in the frequency of hypotension between these two groups (60.7% vs. 66.7%; $p = 0.646$) in Palestinian population.¹⁵ Similar insignificant difference was reported by Cooper et al. (48% vs. 68%; $p = 0.13$) in British population.¹⁶

The results of the present study are in line with those of existing research and thus advocate the routine use of phenylephrine to decrease the occurrence of hypotension in patients undergoing spinal anesthesia. A very strong limitation to the present study was that we didn't compare the side effects of these two drugs particularly the frequency of fetal acidosis which is a very important concern in obstetric anesthesia and should be evaluated in future research.

CONCLUSION

The frequency of spinal hypotension was significantly lower in patients receiving phenylephrine compared to ephedrine which advocate routine use of phenylephrine in such patients to minimize the risk of hypotension with associated morbidity.

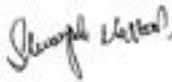
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3	Dr. Beharam Khan	Result interpretation, Statistical evaluation, Technical review	