

## Evaluation of Preemptive Intramuscular Phenylephrine vs Ephedrine for Prevention of Hypotension Induced by Spinal Anesthesia in Lower Segment Caesarean Section

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### Abstract

**Background:** Hypotension is the commonest side effect after giving spinal anaesthesia in lower segment caesarean section (LSCS). Various drugs are being used to prevent hypotension due to spinal anaesthesia. **Aim:** The present study was planned to compare role of preemptive (used just after giving spinal anaesthesia) Phenylephrine and Ephedrine intramuscularly (IM) in reducing spinal anaesthesia induced hypotension and other adverse effects in LSCS. **Settings and design:** After approval from ethical committee (Reference No: SGRR/IEC/16/18) a prospective, double blind randomized control clinical study was conducted. **Material and method:** Total 90 pregnant females with single pregnancy, term gestation and aged between 18-45 years and American Society of Anaesthesiologist (ASA) class I, posted for LSCS were selected and randomly divided by using envelope technique into three groups each having 30 patients. In Group A Phenylephrine 4 mg, in Group B Ephedrine 30 mg and in Group C normal saline was given by intramuscular route. **Statistical Analysis:** One way ANOVA test was used to compare means of different groups whereas Chi-square test was used to compare proportions of different group. p value <0.05 was considered statistically significant. **Results:** Mean blood pressure values were found maximum in Phenylephrine group followed by Ephedrine group and least in control group. Incidence of hypotension and nausea/vomiting was seen least in Phenylephrine group in comparison to other groups. **Conclusion:** Phenylephrine and Ephedrine both were effective in maintaining mean blood pressure, lowering incidence of hypotension and associated adverse effects related to spinal anaesthesia however Phenylephrine was found more effective.

**Keywords:** Hypotension; Caesarean; Pre-emptive Phenylephrine; Ephedrine; Spinal Anaesthesia.

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### Introduction

There are many views regarding the ideal anaesthetic technique for Lower segment caesarean section [1]. Subarachnoid block (SAB) is usually

preferred over general anaesthesia in caesarean section to avoid the airway difficulty in pregnant ladies [2]. Hemodynamic changes specially hypotension is the commonest side effect after giving SAB [3]. Hypotension sometimes may be associated with nausea and vomiting, which might

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cause interference in the surgical procedure [4]. Vasopressors are considered as the best way for prevention of hypotension after spinal anaesthesia. The present study was planned to compare the role of preemptive (just after giving spinal anaesthesia) intramuscular Ephedrine, Phenylephrine and normal saline (NS) to prevent hypotension and associated nausea and vomiting.

### Material and Method

A prospective study was conducted after approval from the ethical committee of the institution and 90 patients (pregnant females) were selected. This study was a double blind randomized control clinical trial. Pregnant females belonging to age limits of 18-45 years, with ASA class I physical status, single pregnancy, on term gestation, posted for LSCS were included in the study. Pregnant females with refusal for procedure, any contraindications to spinal anaesthesia, having eclampsia, being known case of diabetes mellitus or gestation diabetes mellitus, having history of any cardiovascular or cerebrovascular diseases, detected with foetal anomalies in antenatal period were excluded from the study. Patients were randomly divided into three groups of 30 patients each; by using sealed envelope technique. In Group A Phenylephrine 4 mg, in Group B Ephedrine 30 mg and in Group C Normal saline was given through intramuscular route.

Firstly all patients were taken in the operation theatre and their vitals were monitored with the help of non-invasive blood pressure monitoring, pulse oximeter and ECG (electrocardiogram) monitor. For preoperative measurement of baseline systolic arterial pressure, average of two readings (taken two minutes apart) was calculated. An 18G cannula was used for intravenous access through non dominant hand and preloading was done at 10 ml/kg body weight with ringer lactate. Afterwards spinal block was given in the left lateral position using 2.2 ml sensoricaine (heavy) in L3-L4 space with the help of a 25G Quincke spinal needle. Just after inducing subarachnoid block, intramuscular injection of the drug to be investigated was administered in the left vastus lateralis muscle. Particular study medication for each group was prepared to a dose of 2 ml with 0.9% normal saline and administered by one anaesthetist, not involved in any data collection or patient care. Another anaesthetist, who was blind to identification of any of the study medication, managed all the patients during whole procedure.

In this study serial measurement of Mean Blood Pressure (MBP), Heart rate (HR), Blood Oxygen saturation (SpO<sub>2</sub>) was done and readings were recorded at the interval of two minutes in initial 20 minutes, then at the interval of five minute till 45 minutes. The frequency, onset, time and duration of hypotension was analyzed. If Mean blood pressure fall was more than 20% of the initial value, rescue dose of intravenous Ephedrine 6 mg was administered. Incidence of hypotension, nausea and vomiting was noted down in all the groups and compared.

### Statistical Analysis

The collected data was entered in SPSS version 23 software and analyzed. Quantitative variables were expressed as mean and standard deviation whereas categorical variables were expressed in terms of percentages and proportions. To compute results, the mean and standard deviation of blood pressure and mean changes of their values over period of time along with standard deviation were calculated statistically. One way ANOVA test was used to compare the mean of different groups whereas Chi-square test was used to compare proportions of different groups. P-value of tests was used to ascertain statistical significance to the tests. p-value <0.05 was considered as significant and p value <0.005 was considered as highly significant. Microsoft Excel software was used for making graphs.

### Results

Total 90 patients (pregnant females) were registered in the study. All the patients (n=30 in each group) completed the study. In Group A patients received Phenylephrine 4 mg, in Group B patients received Ephedrine 30 mg and in Group C which was a control group normal saline was given; via intramuscular route.

While comparing the demographic profile; the age, weight, height and body mass index (BMI) measurements of all the three groups were similar (p value >0.05). [Table 1]

All the patients in each group were in ASA I category with no pre-existing co-morbid condition and got good quality of surgical anaesthesia.

Regarding the mean value of Mean Blood Pressure, all the groups were comparable in base line values. The mean value of Mean Blood Pressure starting from two minutes and up to 45 minutes;

was found highest (less fall) in Phenylephrine group followed by Ephedrine group and least in control group. (p value < 0.05). [Figure 1]

Mean value of Heart Rate was also comparable in base line values in all the three groups, Ephedrine showed statistically significant rise in heart rate throughout caesarian section (from two minutes up to 45 minutes) in comparison to Phenylephrine and control group (p value <0.05). Decrease in heart rate was not observed in any of the group. [Figure 2]

While comparing incidence of hypotension in Phenylephrine group with Control group, it was 23.3% against 70% and this difference was found statistically highly significant (p value=0.000). On comparing Ephedrine group with the Control group, the incidence of hypotension was 43.3% against 70%, this difference was found significant (p=0.037). On comparing Phenylephrine group with Ephedrine group, the incidence of hypotension was

found 23.3% against 43.3% and the difference came to be statistically insignificant (p value= 0.085). [Table 2]

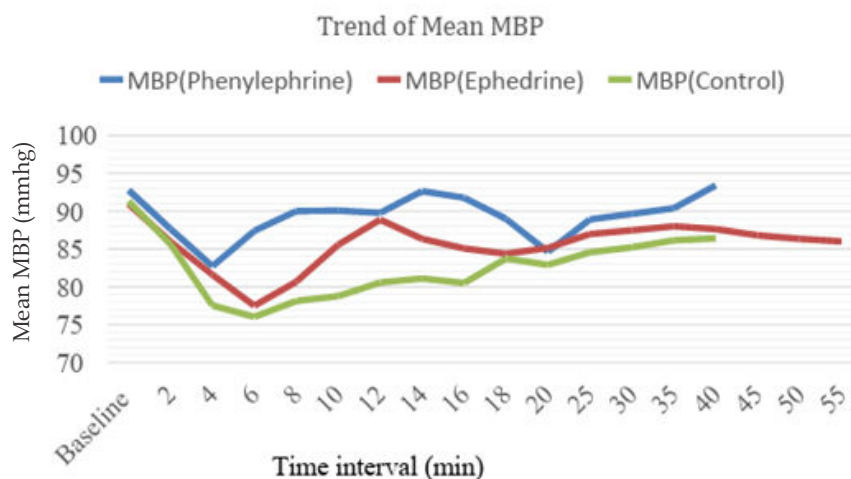
On Comparing Phenylephrine Group with Control group the difference was found statistically significant (p<0.01) in nausea, vomiting. On Comparing Group B (Ephedrine) with Group C (Control) for nausea and vomiting, the difference was found statistically insignificant (p=0.096). When Phenylephrine Group with Ephedrine group were compared the difference was found statistically significant (p value=0.053). [Table 3], [Fig. 3]

The mean value of rescue dose of Ephedrine administered in three groups was found to be 1.6 mg in Phenylephrine group, 3 mg in Ephedrine group and 5.2 mg in control group. The amount was significantly lower in Phenylephrine and Ephedrine group as compared with control group. (p value =0.001). [Table 4], [Fig. 4]

**Table 1:** Demographic Profile of the patients enrolled (n=90)

Group		Age	Wt (Kg)	Ht (Cm)	BMI
Group A	Mean	26.17	59.70	160.13	23.3362
	S D	2.768	7.340	5.993	3.05531
Group B	Mean	26.33	64.90	164.60	24.0211
	S D	3.133	6.116	6.078	2.58280
Group C	Mean	25.17	60.40	162.63	22.9155
	S D	2.755	5.519	5.353	2.65282
p value		0.245	0.886	0.458	0.301

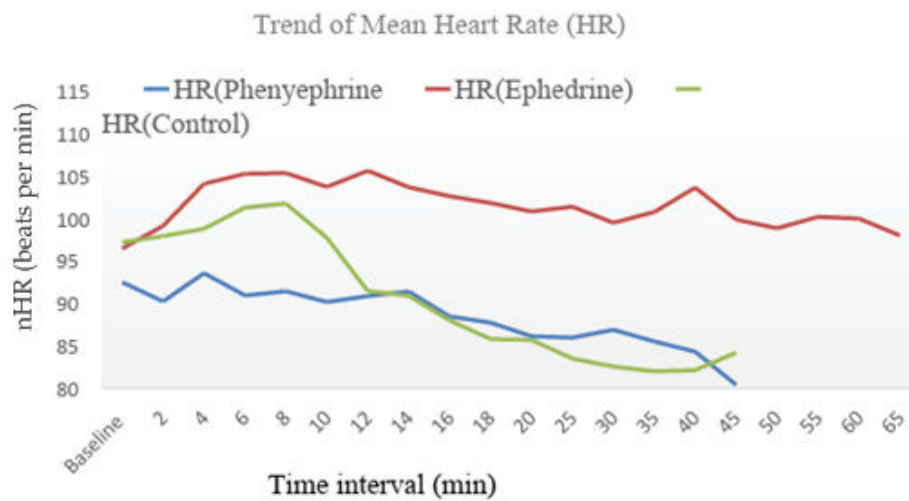
Wt=weight, Ht=height, BMI=body mass index, SD= standard deviation



**Fig. 1:** Line diagram showing trend of mean values of mean blood pressure

**Table 2:** Intergroup comparison of incidence of hypotension

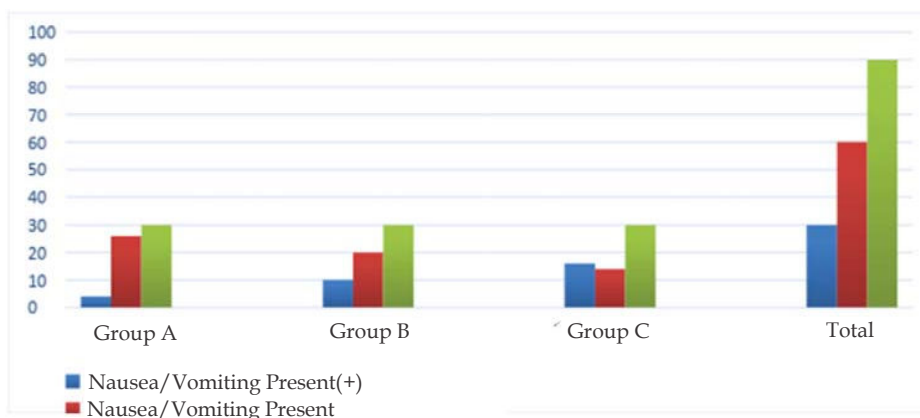
	% of hypotension in each group	% of hypotension within Groups	p value	Significance
Group A	23.3%	Group A vs Group C	0.000	Highly significant
Group C	70%	46.7%		
Group B	43.3%	Group B vs Group C	0.037	Significant
Group C	70%	56.7%		
Group A	23.3%	Group A vs Group B	0.085	Not significant
Group B	43.3%	33.3%		



**Fig. 2:** Line diagram showing trend of mean heart rate

**Table 3:** Intergroup comparison of incidence of nausea/ vomiting

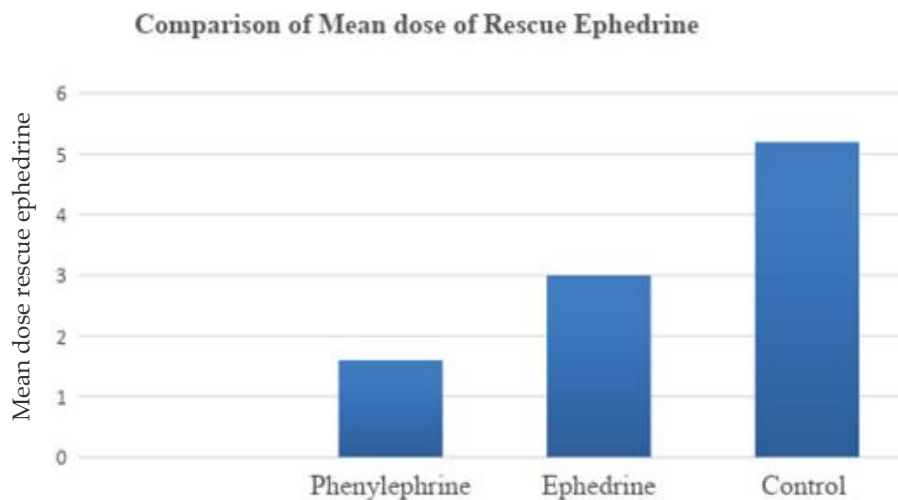
	% nausea/vomiting in each group	% of nausea/vomiting within Groups	p value	Significance
Group A	13.3%	Group A vs Group C	<0.01	Significant
Group C	53.3%	33.3%		
Group B	33.3%	Group B vs Group C	0.096	Not significant
Group C	53.3%	43.3%		
Group A	13.3%	Group A vs Group B	0.053	Significant
Group B	33.3%	23.3%		



**Fig. 3:** Bar diagram showing presence of nausea/vomiting in different groups

**Table 4:** Comparison of mean dose of rescue ephedrine in different groups

Group	Mean dose of Rescue Ephedrine (mg)	Standard Deviation	p-value	Significance
Phenylephrine	1.600	3.1250	0.001	Significant
Ephedrine	3.000	3.7783		
Control	5.200	4.0887		
Total	3.267	3.9371		



**Fig. 4:** Bar diagram showing mean rescue ephedrine dose in different groups

**Discussion**

The incidence of hypotension after spinal anaesthesia is about 70% as reported in many studies. Preloading with crystalloid and keeping left lateral position may be helpful in reducing its incidence but still hypotension is a major side effect [5]. Spinal anaesthesia causes sympathetic blockage which produces vasodilatation and decrease in preload resulting in hypotension. It can further get aggravated by effect of aorto-caval compression in supine position and hypovolemia resulting from loss of blood volume. So to combat this, fluid preloading is being used widely [6].

Dyer and Langesaester colleagues have found that cardiac output and stroke volume increases few minutes after spinal anaesthesia [7,8]. It shows that arteriolar dilatation is the main cause responsible for hypotension after spinal anaesthesia. Thus vasopressor drugs like Ephedrine and Phenylephrine may have a role in reducing incidence of hypotension. Ephedrine is an indirectly acting sympathomimetic amine and commonly used vasopressor in obstetric anaesthesia. Phenylephrine is an  $\alpha_1$  adrenergic agonist, vasoconstrictor which may counteract the vasodilatation caused by spinal anaesthesia. Various studies have highlighted that continuous infusion of intra venous Phenylephrine

(vasopressor) during cesarean section in spinal anaesthesia is preferred for prevention of maternal hypotension and foetal acidosis [9].

In the present study the drugs Phenylephrine, Ephedrine and normal saline were given by intramuscular route just after spinal anaesthesia. It was observed that Phenylephrine and Ephedrine both reduce the incidence of hypotension significantly however Phenylephrine was found more effective than Ephedrine in reducing the episodes of hypotension. These Findings are consistent with a study done by B.T. Ayorinde et al. [10]. in which 4 mg Phenylephrine, 2 mg Phenylephrine and 45 mg Ephedrine (via intramuscular route) were compared, there Phenylephrine 4 mg group showed maximum reduction in episode of hypotension without any rebound hypertension. The findings of lesser consumption of rescue dose of Ephedrine in Phenylephrine group than in Ephedrine group is also consistent with the above study where rescue dose was least required in Phenylephrine 4 mg group.

The lesser incidence of hypotension in Phenylephrine group than Ephedrine group in the present study may be due to the stronger vasoconstrictor action of Phenylephrine, while Ephedrine acts primarily by increasing cardiac

output and heart rate. Yet the incidence of hypotension could not be eliminated completely, this might be because in this study the vasopressor drug was injected after spinal anaesthesia and the onset of peak effect might take time via intramuscular route. It might also be due to lesser amount of vasopressor drug used. Previous studies have shown that effort to eliminate the hypotensive episodes completely might cause increased episodes of hypertension.

In this study it was also found that Ephedrine was more efficacious in reducing hypotension when compared to normal saline group. A previous study done by Webb AA et al. [11] has also shown that intramuscular Ephedrine (37.5 mg) decreases incidence of hypotension significantly than normal saline and that too without causing much side effects. In another study Sternlo and colleagues also found that when Ephedrine was given in a dose of 0.6 mg/kg IM, there was found decreased incidence of hypotension in patients undergoing hip joint surgery [12].

The incidence of nausea, vomiting was highest in control group followed by Ephedrine group and least in the Phenylephrine group. It can be very well explained on the basis of decreased episode of hypotension in Phenylephrine group.

### Conclusion

This study concludes that Phenylephrine and Ephedrine (on preemptive use) both when used via intramuscular route reduce the incidence of hypotension and associated nausea/vomiting which would have been inevitable otherwise as seen in control group. However Phenylephrine was found more efficacious.

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