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Research Article

# A comparative study of bolus phenylephrine and mephentermine for treatment of hypotension during spinal Anaesthesia for caesarean section

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**Abstract: Introduction**: Subarachnoid block, although being highly efficient with lesser drug doses, often has limitation such as hypotension, continues to be a matter of concern to the anesthetist. The present study was aimed to compare the use of phenylephrine, ephedrine, and mephentermine bolus for maintenance of blood pressure during spinal anesthesia in lower abdominal surgeries. **Materials and Methods**: This is Randomized, single blind, prospective & comparative study. The study has been undertaken at the Department of Anesthesiology, Shadan Institute of Medical Sciences Teaching Hospital & Research Centre. Study population ASA 1 or 2 women with term, uncomplicated, singleton pregnancy scheduled to undergo elective caesarean section. We have optimized a sample size of 50 (25 in each group) using a sealed envelope technique to determine the drug that were used for prevention of hypotension. Patients in the 'phenylephrine group'(P) had received an infusion of phenylephrine hydrochloride, whereas patients in the 'mephentermine group' (M) had received an infusion of mephentermine sulphate. **Results** A total of 50 patients was analyzed. Within 5 minutes of Spinal anaesthesia there was no significant difference between Group- P and Group-M on drop of average Systolic blood pressure, Diastolic blood pressure and average Heart rates at different minutes. But after administering the drug for hypotention correction Group P shows very high average SBP and DBP correction compared to Group M which is statistically significant ($p<0.0001$) and Group P shows a fall in the heart rate compared to Group M which is statistically significant nit (PACU) **Conclusion**: Mephentermine and ephedrine were similar in performance, offered a better hypotensive control, and had lower recurring events as compared to phenylephrine.

**Keywords**: Phenylephrine, Mephentermine, Intraoperative hypotension, Procedural Sedation, Spinal Anaesthesias.

## INTRODUCTION

Regional blocks such as spinal, epidural, and a combination of spinal/epidural blocks have gained widespread popularity among the surgical fraternity. Although subarachnoid block is highly efficient with less drug doses, it has some limitations such as hypotension, lesser control over level of blockade, and limited duration of anesthesia. [1] The incidence of hypotension can be as high as 70%–80% when pharmacological prophylaxis is not used. Despite numerous attempts to restrict this incidence, it continues to be a cause of concern to the anesthetist. [2]

Numerous pressor agents have been tried to counteract the hypotensive effect of subarachnoid block, usually by vasoconstriction and also by increasing the cardiac output. [3] In practice, the most commonly used drugs are the sympathomimetic agents which exert their effects through the adrenergic receptors, either acting directly or indirectly by inducing the release of noradrenaline which further acts on these receptors. [4]

Phenylephrine is a direct-acting, potent alpha-1 agonist with no beta activity. It, therefore, causes a rapid increase in systemic vascular resistance and blood pressure. [5] Mephentermine acts by indirect stimulation of beta-adrenergic receptors causing release of norepinephrine from its storage sites. [6] It has positive inotropic effect on the myocardium. Ephedrine is a potent alpha and beta agonist, acting both directly and also indirectly. Its effects on vascular resistance are less pronounced than the other alpha agonists, but it also increases cardiac output thereby maintaining blood pressure. [7]

The present study was aimed to compare the use of bolus phenylephrine, ephedrine, and mephentermine for maintenance of arterial pressure during spinal anesthesia in lower abdominal surgeries. [8] It is surprising that comparative literature on use of these drugs in lower abdomen surgery cases is almost replete possibly owing to relatively lower incidence of hypotensive events in such surgeries, however, considering the fact that even a low incidence of hypotension has far-reaching effect on patient's well-being; it is essential that this issue should be explored further.

## MATERIALS AND METHODS

This is Randomized, single blind, prospective & comparative study. The study has been undertaken at the

Department of Anesthesiology, Shadan Institute of Medical Sciences Teaching Hospital & Research Centre. Study population ASA 1 or 2 women with term, uncomplicated, singleton pregnancy scheduled to undergo elective caesarean section.

We have optimized a sample size of 50 (25 in each group) using a sealed envelope technique to determine the drug that were used for prevention of hypotension. Patients in the 'phenylephrine group'(P) had received an infusion of phenylephrine hydrochloride, whereas patients in the 'mephentermine group' (M) had received an infusion of mephentermine sulphate.

Inclusion criteria ASA 1 or 2 women with term, uncomplicated, singleton pregnancy scheduled to undergo elective caesarean section. Exclusion criteria, Known allergic to study drugs, Contraindications to spinal anesthesia, Any prerenal or renal condition, such as diabetes, pre-eclampsia or chronic hypertension, Patients with placental complications such as placenta previa or abruptio placentae, and cord complications, Any associated congenital anomalies, Patients with baseline SBP < 100 mmHg, Patients with baby birth weight < 2.5kg, Preterm deliveries, Patients suffering from any neurological, psychological, cardiovascular, respiratory, renal, hepatic, metabolic and hematological diseases. WE have study Age, Body weight, height, Hypotension (SBP fall≤ 20% of baseline or absolute value of SBP< 100mmHg whichever is first) Hypertension (>20% of SBP above base baseline) Bradycardia (20% of the baseline SBP (hypertension) then infusion was stopped and again started when the value comes down to the less than or equal to baseline SBP.

The aim was to maintain systolic blood pressure between the hypotension value and the baseline value. Bradycardia, if occurred, were managed by atropine. Hemodynamic parameters (SBP, DBP, MBP & HR) were monitored at 2 mins intervals till 16th min after that 3min interval were set till 40th mi. Oxytocin was given after delivery of baby according to "Rule of threes" i.e., 3 IU oxytocin intravenous loading dose(no faster than 15s) then 3 min assessment intervals, if inadequate uterine tone, give 3 IU oxytocin intravenous rescue dose again after 3min of assessment repeat the rescue dose. If the uterine tone is still inadequate the other pharmacological option includes ergonovine, carboprost, and misoprostol. After the operation over the patent was observe for 2hrs at recovery room and then transfer to ward.

**Statistical analysis**

Statistical analysis has been performed using SPSS software (version 23.0; IBM Inc., Chicago, IL, USA, 2015). Continuous variables were compared between the two groups by unpaired Student's t-test. Ordinal data were analyzed using the Mann–Whitney non-parametric test. For qualitative data, either chi-square test or Fisher's exact test was used. Two factor, repeated measures ANOVA with one factor as a fixed group and the other as a repeated factor (i.e. time) was used to compare the variability between the subjects. The value of $p < 0.05$ was considered significant.

# RESULTS

**Table 1: Distribution Based on Various Parameters**

| Parameters | Group P | Group M | P value |
|---|---|---|---|
| Age in years | 25.41±3.49 | 24.6+ 2.79 2 | 0.32 |
| Height in cms | 156.71 + 5.72 | 157.33 + 5.79 | 0.37 |
| Weight in Kgs | 62.62±3.58.57 | 65.92±4.0592 | 0.18 |
| Duration Of Surgery | 34.84 + 2.474 | 35.52 + 2.872 | 0.783 |

There was no significant difference in the demographic profile of the two groups with respect to age, height, weight and the average duration of surgeries.

**TABLE 2: Distribution Of Average SBP Within 5 Mins Of SAB And 1st Minute After Giving Vasopressor**

| Time | Group-P | Group-M | P value |
|---|---|---|---|
| Baseline | 116 | 118 | 0.41 |
| 1min | 122 | 121 | 0.08 |
| 2min | 109 | 108 | 0.94 |
| 3min | 92 | 95 | 0.82 |
| 5min | 88 | 83 | 0.40 |
| 1min after vasopressor | 142 | 110 | 0.0001 |

Table shows that within 5 minutes of Sub arachnoid block, there is no significant difference between Group-P and Group-M on drop of average SPB at different minutes. But after administering the drug, the Group P shows very high average SBP compared to Group-M which is statistically highly significant (p<0.0001)

**TABLE 3: Distribution of average DBP within 5 mins of SAB and 1st minute after giving vasopressor**

| Time | Group-P | Group-M | P value |
|---|---|---|---|
| Baseline | 75 | 74 | 0.76 |
| 1 min | 78 | 75 | 0.24 |
| 2 min | 67 | 70 | 0.54 |
| 3 min | 59 | 54 | 0.85 |
| 5 min | 49 | 51 | 0.57 |
| 1min after vasopressor | 88 | 70 | 0.0001 |

Table shows that Within 5 minutes of Sub arachnoid block, there is no significant difference between Group-P and Group -M on drop of average DBP at different minutes. But after administering the drug, the 'P' group shows very high average DBP compared to Group-M which is statistically highly significant (p<0.0001).

**TABLE 4: Distribution of average MAP within 5 mts of SAB and 1st minute after giving vasopressor**

| Time | Group-P | Group-M | P value |
|---|---|---|---|
| Baseline | 89 | 82 | 0.0003 |
| 1 min | 91 | 86 | 0.05 |
| 2 min | 78 | 80 | 0.46 |
| 3 min | 65 | 61 | 0.75 |
| 5 min | 61 | 59 | 0.33 |
| 1min after vasopressor | 106 | 77 | 0.0001 |

Table shows that Within 5 minutes of Sub arachnoid block, there is no significant difference between Group-P and Group -M on drop of average DBP at different minutes. But after administering the drug, the 'P' group shows very high average DBP compared to Group-M which is statistically highly significant (p<0.0001).

**TABLE 5: Distribution of average MAP within 5 mts of SAB and 1st minute after giving vasopressor**

| Time | Group-P | Group-M | P value |
|---|---|---|---|
| Baseline | 79 | 84 | 0.0003 |
| 1 min | 93 | 88 | 0.06 |
| 2 min | 78 | 82 | 0.47 |
| 3 min | 65 | 61 | 0.76 |
| 5 min | 61 | 59 | 0.34 |
| 1min after vasopressor | 108 | 77 | 0.0001 |

Table shows that Within 5 minutes of Sub arachnoid block, there is no significant difference between Group-P and Group-M on drop of average MAP at different minutes. But after administering the drug, the 'P' group shows very high average SBP compared to Group-M which is statistically highly significant (p<0.0001)

**Table 6: Distribution of average HR during Within 5mins of SAB and 1st minute after giving vasopressor**

| Time | Group-P | Group-M | P value |
|---|---|---|---|
| Baseline | 78 | 76 | 0.08 |
| 1 min | 78 | 84 | 0.02 |
| 2 min | 81 | 84 | 0.13 |
| 3 min | 73 | 75 | 0.93 |
| 5 min | 71 | 75 | 0.40 |
| 1mi after vasopressor | 57 | 83 | 0.0001 |

Table shows that within 5 minutes of SAB, there is no significant difference between Group-P and Group-M on average HR at different minutes.But after administering the drug, the 'P' group shows a fall in the heart rate compared to Group-M which is statistically highly significant ($p<0.0001$).

**Table 7: Distribution of SBP after giving Vasopressor intraoperatively**

| Time in mins | Group-P | Group-M | P Value |
|---|---|---|---|
| 1 | 144 | 110 | 0.0001 |
| 2 | 142 | 112 | 0.0001 |
| 3 | 139 | 110 | 0.0001 |
| 5 | 125 | 112 | 0.0001 |
| 10 | 118 | 111 | 0.0001 |
| 20 | 112 | 111 | 0.51 |
| 30 | 114 | 110 | 0.38 |
| 45 | 110 | 110 | 0.43 |
| 60 | 108 | 110 | 0.15 |
| 90 | 109 | 110 | 0.52 |

Table reveals that there is significant difference of average SBP between two groups upto 5 minutes, after giving vasopressor but subsequently there is no significant difference. Average SBP at the first minute in Group-P and Group- M are 145 mm Hg and 109 mm Hg respectively.

**Table 8: Distribution of DBP after giving Vasopressor intraoperatively**

| Time in mins | Group-P | Group-M | P value |
|---|---|---|---|
| 1 | 88 | 66 | 0.0001 |
| 2 | 86 | 72 | 0.0001 |
| 3 | 86 | 70 | 0.0001 |
| 5 | 78 | 69 | 0.0001 |
| 10 | 74 | 71 | 0.0009 |
| 20 | 74 | 72 | 0.007 |
| 30 | 72 | 71 | 0.62 |
| 45 | 70 | 74 | 0.21 |
| 60 | 68 | 68 | 0.51 |
| 90 | 73 | 72 | 0.84 |

Table reveals that there is significant difference of average DBP between two groups upto 5 minutes, after giving vasopressor but subsequently there is no significant difference. Average DBP at the first minute in Group-P and Group-M are 89 mm Hg and 67 mm Hg respectively.

**Table 9: Distribution of MAP after giving Vasopressor Intraoperatively**

| Time in mins | Group-P | Group-M | P value |
|---|---|---|---|
| 1 | 106 | 79 | 0.0001 |
| 2 | 105 | 79 | 0.0001 |
| 3 | 99 | 80 | 0.0001 |
| 5 | 91 | 82 | 0.01 |
| 10 | 85 | 81 | 0.34 |
| 20 | 83 | 84 | 0.08 |
| 30 | 84 | 81 | 0.75 |
| 45 | 82 | 84 | 0.04 |
| 60 | 81 | 82 | 0.81 |
| 90 | 76 | 81 | 0.001 |

Table reveals that there is significant difference of average MAP between two groups upto 5 minutes, after giving vasopressor but subsequently there is no significant difference. Average MAP at the first minute in Group-P and Group-M are 107 mm Hg and 78 mm Hg respectively.

**Table 9: Distribution of HR after giving Vasopressor Intraoperatively**

| Time in mins | Group-P | Group-M | P value |
|---|---|---|---|
| 1 | 60 | 82 | 0.0001 |
| 2 | 61 | 83 | 0.0001 |
| 3 | 64 | 86 | 0.0001 |
| 5 | 66 | 84 | 0.0001 |
| 10 | 71 | 83 | 0.0001 |
| 20 | 72 | 84 | 0.0001 |
| 30 | 75 | 80 | 0.0001 |
| 45 | 73 | 79 | 0.005 |
| 60 | 72 | 76 | 0.008 |
| 90 | 74 | 76 | 0.001 |

Table reveals that there is significant difference of average HR between two groups throughout the intraoperative period. The heart rate of Group-M is always higher than the Group-P which is statistically significant.

**Table 10: Comparison of number of doses of vasopressors used to correct hypotention**

| No of doses | Group-P(n=25) | Group-M(n=25) |
|---|---|---|
| 1 | 19(77.77%) | 13(55.55%) |
| 2 | 4(15.55%) | 6(22.22%) |
| 3 | 2(6.66%) | 6(22.22%) |

Number of repeated doses required is more in Group-M compared to Group-P

**Table 11: Comparison of incidence of other effects between groups**

| Event | Group-P(n=25) | Group-M(n=25) |
|---|---|---|
| Bradycardia | 2 | 0 |
| Shivering | 3 | 5 |
| Dysrhythmia | 0 | 0 |
| Nausea / Vommiting | 3 | 4 |

# DISCUSSION

Haemodynamic changes in the form of hypotension following subarachnoid block during Cesarean section is the most common unwanted finding which, if not appropriately intervened, has hazardous consequences in vital organ perfusion in the parturient and foetal placental perfusion [9]. The choice of vasopressors for obstetrics is guided indirectly by foetal acid base status as there is absence of definitive evidence showing absolute clinical benefit of one over the other. [10] Mephentermine and phenylephrine are commonly used vasopressors in obstetric anaesthesia. [11] In this study, with the prophylactic intravenous administration of study drugs after sub-arachnoid block, prophylactic normal saline (group C) had significantly higher incidence of hypotension than prophylactic phenylephrine (group B) and prophylactic mephentermine (group A).

While evaluating the haemodynamic changes among the study groups, mean value of systolic pressure, diastolic pressure and mean arterial pressure showed a decrease from the baseline after subarachnoid block throughout the observation period. However the blood pressures were better controlled in phenylephrine group B (100 mcg prophylactic and 5 mcg rescue bolus) followed by mephentermine group A (6 mg prophylactic and 3 mg rescue bolus) and prophylactic normal saline group C (2 mL normal saline as prophylaxis and mephentermine 3 mg rescue bolus) particularly at third minute observation (pand

Kamalakanan M et al., [12] reported the similar occurrence of bradycardia and use of atropine in their studies.

As it is reported that the incidence of hypertension and bradycardia are dose-dependent, the use of 100 mcg phenylephrine in the present study did not manifest any harmful clinical outcome. Therefore, considering the variable dose-effects of phenylephrine [13] there still exists the need to study the drug in a large number of subjects to ascertain the dose-effect relationship of this reflex bradycardia, which was of proven benefit among

the patients having tachycardia. There should be an appropriate timing of hypotension correction by vasopressors in order to avoid adverse physiological insult to parturients and for foetal well-being. [14] In the present study, the time of first rescue vasopressor used was earlier in prophylactic normal saline group C (5.87±4.37 min) after the subarachnoid block which was quite early when compared to prophylactic mephentermine group A and phenylephrine group B (pserotonin release, respectively.

## CONCLUSION

In conclusion, we found that all the three vasopressors namely Ephedrine, Mephentermine and Phenylephrine are effective in IV bolus form in maintenance of maternal arterial pressure within 20% limit of baseline values, though Phenylephrine has quicker peak effect, in comparison to Ephedrine and Mephentermine and it causes reduction in heart rate, which may be advantageous in patients in whom tachycardia is undesirable. All the three vasopressor had no significant adverse effects on neonatal outcome..

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