

# A Comparative Study Of Bolus Phenylephrine, Ephedrine And Mephentermine For Maintenance Of Arterial Pressure During Spinal Anaesthesia In Caesarean Section

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## **Abstract:**

**Introduction:** *Obstetric anaesthesia and analgesia are associated with many unique and different problems for the anaesthesiologists. Arterial hypotension in pregnant women following spinal anaesthesia continue to be a matter of concern to the anaesthetist.*

**Objective:** *The study was carried out to compare the efficacy of IV bolus Phenylephrine, Ephedrine and Mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. To monitor and record side effects, if any.*

**Subjects and methods:** *The present study was undertaken on 90 subjects with American society of anaesthesiologist (ASA) type I and II who underwent lower segment caesarean sections under spinal anaesthesia and developed hypotension were selected. Cases were drawn from obstetrics and gynaecology department of NSCB Medical college and Hospital, in whom the decision was taken to perform caesarean section. The subjects are divided into 3 groups of 30 each to receive Group I - Phenylephrine 100ug, Group II - Ephedrine 6mg and Group III - Mephentermine 6mg IV bolus.*

**Results:** *The ANOVA test was used to compare the group among the study groups. In group I (Phenylephrine) it was observed that the peak effect was seen between 1-2 minutes, in group II (Ephedrine) between 3-5 minutes. and in group III (Mephentermine) it was seen between 5-6 minutes .*

**Conclusion-** *It was concluded that Phenylephrine, Ephedrine and Mephentermine all could be used for maintenance of arterial pressure during spinal anaesthesia for caesarean section. Phenylephrine had an immediate peak, so it may be beneficial for initial control of hypotension. It also shows some advantage over others with regard to reduction in heart rate.*

**Keywords:** *Arterial pressure, spinal anaesthesia,*

**Study Design:** *Observational Study.*

## 1. INTRODUCTION

Obstetric anaesthesia and analgesia are associated with many unique and different problems for the anaesthesiologists. Sub arachnoid blocks, epidural blocks and general anaesthesia are only techniques commonly employed. Sub-arachnoid block is the preferred anaesthetic for elective caesarean section. The advantages are simplicity, rapid onset, reliability, dense motor block and avoidance of the potential airway complications associated with general anaesthesia. In recent decades regional anaesthesia as the method of choice for caesarean delivery in terms of safety, conduct evidence and advantages for the neonate.

Arterial hypotension in pregnant women during spinal anaesthesia is due to paralysis of sympathetic nerve fibres with consequent decrease venous return and cardiac output. Venacaval compression by gravid uterus accentuates these responses. However, hypotension occurs following spinal block despite the use of standard preventive measures such as pre hydration and left uterine displacement. This is distressing to mother who often develops nausea and vomiting and may also endanger the fetus as change in maternal arterial pressure affects uteroplacental blood flow. Fetal bradycardia develops shortly after maternal systolic BP falls below 80 mm of Hg.

Various measures for prevention and treatment of Hypotension include preloading, left uterine displacement, Trendelenburg position, Leg wrapping, prophylactic and therapeutic use of vasopressors.

Use of vasopressor as it is the only quick and effective means of correcting severe hypotension. Various vasopressors such as phenylephrine, ephedrine, mephentermine, metaraminol etc. IV bolus phenylephrine, an  $\alpha_1$ -adrenergic agonist counteracts the decrease in systemic vascular resistance induced by spinal anaesthesia. It can raise maternal blood pressure without restoring uterine blood flow and improving the intrauterine status of the foetus. Ephedrine an indirectly acting sympathomimetic is probably the vasopressor of choice in obstetric anaesthesia. It has mixed  $\alpha$  and  $\beta$  adrenoceptor activity and it maintains arterial pressure mainly by increases in cardiac output and heart rate due to predominant  $\beta_1$  adrenoceptors activity. Ephedrine thought earlier to have a deleterious effect on foetal blood gas status was proved to arrest and correct foetal acidosis during spinal hypotension. Mephentermine is a sympathomimetic with both  $\alpha$  and  $\beta$  adrenoceptor activity, used for same purpose.

In our institution spinal anaesthesia is most commonly used technique for caesarean section. Mephentermine is most commonly used vasopressor to treat hypotension during spinal anaesthesia. Other vasopressor like phenylephrine and ephedrine also used.

It was therefore decided to carry out study "Comparison between bolus Phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section".

## 2. MATERIAL AND METHOD

This comparative study was carried on parturient coming for lower segment caesarean section conducted under spinal anaesthesia in Department of Anaesthesiology, NSCB medical college and hospital, Jabalpur (MP).

Approval from institutional ethics committee was taken. 90 parturients with ASA class I and II; aged between 20-35 years; weight <70kg; baseline systolic blood pressure 100-140 mmHg and diastolic blood pressure between 70-89 mmHg scheduled for lower segment caesarean section who were considered fit for spinal anaesthesia and developed hypotension after subarachnoid block (SAB) included in this study. The aim was not to allow hypotension of magnitude more than 20% baseline or 90 mm of Hg systolic blood pressure.

Patients with medical complications like severe anaemia, cardio and cerebrovascular diseases, diabetes mellitus; weight <70kg; patient with obstetrical complications; foetal malformation and mal presentations etc.

After taking informed consent, patients were divided into 3 groups of 30 each;

Group I; Phenylephrine 100µg iv bolus

Group II: Ephedrine 6mg iv bolus

Group III: Mephentermine 6mg iv bolus

Standard monitoring with NIBP, ECG, pulseoximetry was done. Three recordings of BP were done and mean value was taken as baseline blood pressure and pulse rate was also recorded.

AN iv cannula of 18G was inserted into one of veins of right forearm. All patients were given Ringer's Lactate solution 10ml/kg body weight within 15 minutes before performing sub-arachnoid block.

Lumbar puncture was performed using 23G Quincke's spinal needle (Tops Corporation, Japan) by midline approach. In all the cases Lignocaine (heavy) 5% (Lox) 1.2 ml was injected. After the injection of lignocaine patients were placed supine. Trendelenburg tilt of 5 degree was given to achieve the height of analgesia at least upto T6. The wedge was placed under right buttock for left uterine displacement in all patients. All patients breathed oxygen 4L/min given through facemask.

Throughout the surgery the systolic blood pressure and pulse rate was recorded. The recordings were done at every 1 minute for 10 min then every 2 min for next 10 min and every 5 min thereafter. Oxytocin 10U in 5% dextrose was given after clamping the cord. SAB-delivery interval, SAB-hypotension time and uterine incision-delivery interval were recorded. The status of neonate was assessed by Apgar scores at 1min and 5 min.

Results were analysed statistically for significance applying of Variance (ANOVA) test.

### 3. OBSERVATION

In this study the same local anaesthetic and dose Lignocaine heavy (5%) 1.2 ml was used to control the variables so that the spread of the drug was same in all patients. The maximum number of patients in group I, II, and III were in age group 20-25 yrs i.e., 83.3% in group I, 66.7% in group II and 60% in group III. The mean weight of patients was in group I, II, and III were 52.8kg, 53.4kg and 51.7kg respectively. The maximum percentage of patients had their height in range of 56-60 inches. Thus regarding the age, weight, height, nature of surgery and spinal technique all three groups were comparable. The level of analgesia T4-T6, fluid preload 10ml/kg and had a same wedge under right hip in all three groups. In this way many variables were kept constant and only choice of vasopressor different in each group.

The mean systolic pressure was  $128 \pm 10.5\%$ ,  $130.931 \pm 0.85$  and  $133.53 \pm 11.05$  mmHg in group I, II and III respectively. Similarly the diastolic pressure was  $83.73 \pm 6.9$ ,  $86.67 \pm 10.11$  and  $88.53 \pm 7.35$  mmHg in group I, II and III respectively. Pulse rate was  $88.93 \pm 11.5$ ,  $86.4 \pm 9.4$  and  $92.73 \pm 13.49$ /min in group I, II and III respectively. These baseline parameters were also comparable.

The mean SAB-HTN time in group I was  $3.8 \pm 1$ min, in group II  $4.13 \pm 1.5$ min and  $4.27 \pm 1.34$ min in group III. All three groups had first hypotensive episode at about 4min and this was the time when study drug was administered.

It was observed that whenever hypotension developed in group I at 2,3,4,5 and 6 min, phenylephrine 100µg was given; it was seen that there was an increase in SBP in all the cases and the peak effect of the drug was reached in 1-2 min. Applying Analysis of Variance (ANOVA) test the rise in SBP was highly significant ( $p < 0.01$ ,  $p < 0.025$ ,  $p < 0.005$ ) 1 min after administration of the drug. The peak effect of ephedrine was seen at 2-3 min and mephentermine at 5-6 min. The rise was significant ( $p < 0.05$ ) 5min after the drug was given at

4 min(SAB-HTN time) showing that the rise in SBP was more than group I and II at 5<sup>th</sup> min. Thus mephentermine showed peak at 5-6 min after producing a gradual rise in BP after its administration.

Pulse rate was decreased after phenylephrine (group I) administration with peak at 1-2 min. Applying ANOVA it was seen that change in pulse rate in between the groups were highly significant ( $p < 0.0001$ ) at all time when drug was given at 3,4,5 and 6 min (SAB-HTN time). In group II and III pulse rate was also increased with peak between 3-6min and 4-6min respectively. All the value were highly significant ( $p < 0.0001$ ).

Diastolic BP increased in all the three groups but increase was significant only at 1<sup>st</sup> min after the bolus vasopressor was given, showing that phenylephrine produced immediate effect ( $p < 0.025$ ,  $p < 0.0006$ ,  $p < 0.004$ ). increase in diastolic BP was not significant in between the groups (ANOVA test).

In our study we found that maternal heart rate was slower with phenylephrine (a agonist action) than with ephedrine and mephentermine because of lacks of action on:  $\beta$ -receptors.

No patient in our study develop nausea and vomiting. It was found that bolus injection 1,2, and 3 were required in 70%, 26.7% and one patient (group I), 63.3%, 30% and two patient (group II) and 76.7%, 20% and One patient (group III) respectively. The mean drug dose was 133.34ug in group I; 8.6mg in group II and 7.6mg in group III.

Apgar score at 1 and 5 min were recorded and found that all neonates had  $>7$  apgar score.

#### 4. RESULT

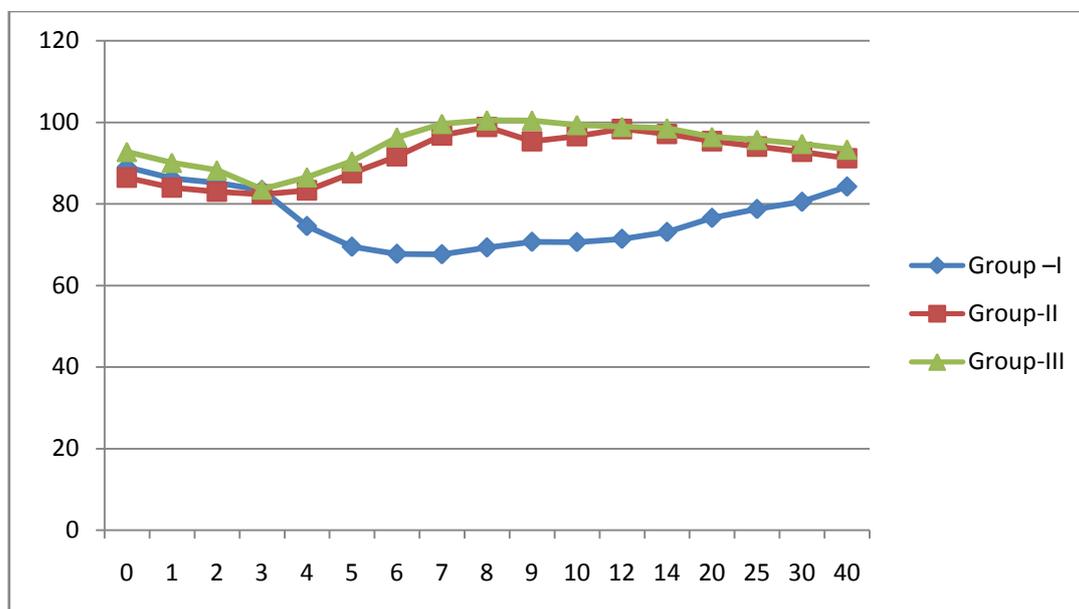
After administration of the study Group drug as IV bolus, it was observed that there was an increase in systolic and diastolic BP. In group I it was observed that the peak effect of phenylephrine was seen between 1-2 mins The peak effect of ephedrine was seen between 3-5 min .the peak effect of mephentermine was seen between 5-6 mins .As far as pulse rate was concerned, there was a decline in pulse rate after administration of phenylephrine which was due to reflex bradycardia due to its @ agonist action. There was in increase in pulse rate in group II and group III .All the data was recorded and analyzed using analysis of variance [ANOVA TEST] . Neonatal Apgar Score were recorded at 1min and 5 min and it was found that the neonatal outcome was similar in all the three groups.

Mean Pulse Rate  
(Duration Wise)

Table- 1

Pulse Rate	Group -I	Group-II	Group-III
0	88.93	86.4	92.73
1	86.2	83.93	90.07
2	85.13	82.93	88.2
3	83.33	82.3	83.53
4	74.53	83.27	86.53
5	69.47	87.47	90.4
6	67.73	91.6	96.27
7	67.63	96.73	99.6
8	69.3	98.8	100.47
9	70.67	95.3	100.4
10	70.6	96.53	99.33
12	71.4	98.3	98.87
14	73.07	97.07	98.5

20	76.53	95.33	96.4
25	78.7	94	95.7
30	80.47	92.7	94.7
40	84.2	91.13	93.3

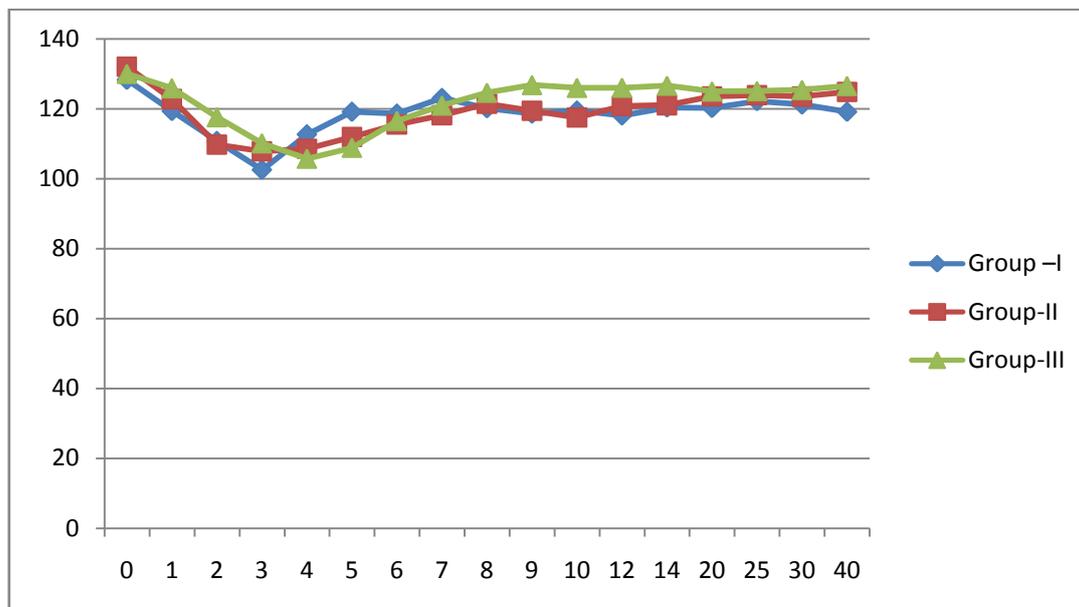


The above table and graph shows duration wise mean pulse rate for all three groups. The overall trend depicts that there is a rise in pulse rate in group II and III after administration of bolus drug while there is a decrease in pulse rate in group I.

Mean Systolic Blood Pressure  
 (Duration Wise)

Table- 2

Systolic BP	Group -I	Group-II	Group-III
0	128.27	132	130
1	119.33	122.73	125.87
2	110.77	109.73	117.6
3	102.53	107.8	110.13
4	112.67	108.5	105.73
5	119.13	111.87	108.87
6	118.6	115.47	116.53
7	123.07	118.1	120.93
8	120.13	121.43	124.6
9	118.6	119.4	126.8
10	119.47	117.47	126
12	118.07	120.77	126.03
14	120.37	121	126.6
20	120.2	123.53	124.97
25	122.17	123.87	125.07
30	121.2	123.47	125.4
40	119.13	124.77	126.53

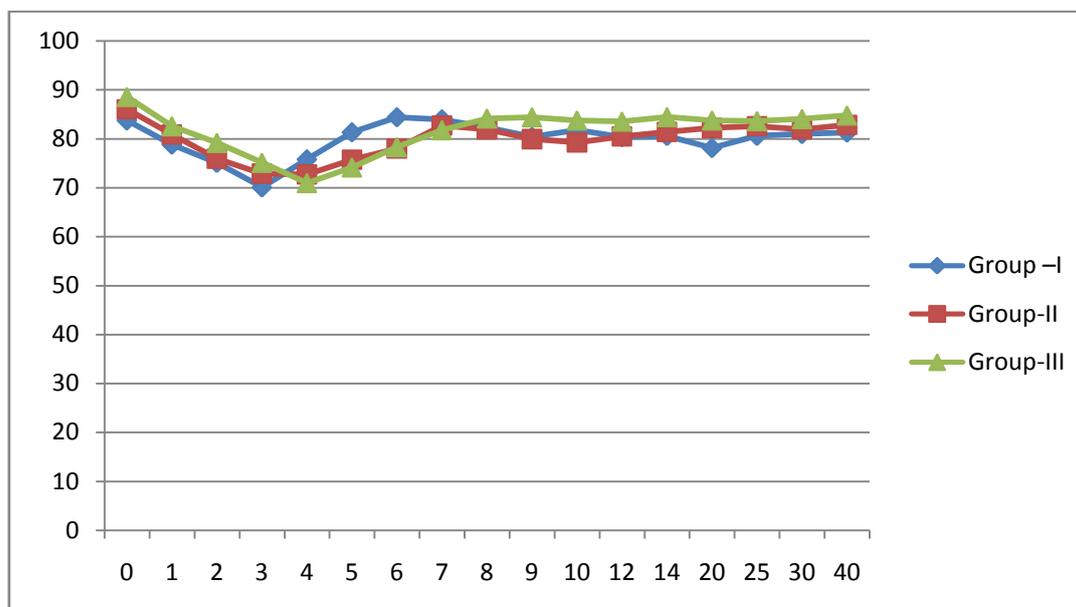


The above table and graph shows duration wise mean systolic blood pressure for all three groups. The overall trend depicts that there is a rise in systolic blood pressure in all three groups after administration of bolus drug.

Mean Diastolic Blood Pressure  
 (Duration Wise)

Table- 3

Diastolic BP	Group -I	Group-II	Group-III
0	83.73	86	88.53
1	78.8	80.87	82.53
2	75.07	75.9	79.13
3	70.07	72.87	75.07
4	75.8	72.73	70.93
5	81.33	75.73	74.13
6	84.4	78	78.27
7	83.97	82.67	81.73
8	82.33	81.93	84.13
9	80.4	79.93	84.37
10	81.77	79.23	83.73
12	80.33	80.47	83.5
14	80.57	81.37	84.4
20	78.1	82.2	83.73
25	80.6	82.57	83.6
30	80.97	81.93	84
40	81.27	82.83	84.73



The above table and graph shows duration wise mean diastolic blood pressure for all three groups. The overall trend depicts that there is a rise in diastolic blood pressure in all three groups after administration of bolus drug.

## 5. DISCUSSION

The study was conducted on 90 parturients aged 20 to 35 yrs belonging to ASA I and II, scheduled to undergo lower segment caesarean section.

Hypotension frequently occurs in LSCS under SAB. Symptomatic blocked leading to the pooling of blood, diminished cardiac output is the main factor but it is aggravated by inferior vena cava occlusion by gravid uterus. Marx et al (1968) demonstrated that hypotension could be dominated by using

Apgar score at 1 min and 5 min were recorded for each neonate and it was found that all neonate had apgar score was more than 7, reflects no significant difference in neonatal outcome irrespective of vasopressor given. Hall et al (1994) also showed similarity in Apgar score on blood-gas status of the neonate. Thomas DG at al (1996) showed significantly higher umbilical artery pH in phenylephrin group. Ann le et al(2002) showed that use of phenylephrine was associated with better fetal acid-base status. Ngankee et al (2004) showed no difference in Apgar score and fetal acid-base status. No infant had Apgar score of less than 7 at 1 and 5 min, in our study.

Caesarean section is one of the oldest operations in recorded history, however anaesthesia for Caesarean section is just a century old and is not bereft of controversies. Over time, regional anaesthesia especially spinal anaesthesia proved to be the most preferred technique for Caesarean section [5, 6]. The reason being, the unique potential of spinal technique to provide anaesthesia with a blend of low degree of physiologic trespass and with profound degrees of sensory denervation and muscle relaxation. Thus, the safety of spinal anaesthesia is of dual nature; pharmacological as well as physiologic. However one main hurdle with this technique is the troublesome and persistent incidence of hypotension especially in gravid parturients. Hypotension is the commonest serious problem endangering both the mother and the child [5, 7]. Dinesh Sahu et al [8] found that maternal hypotension during spinal anaesthesia for Caesarean delivery was a persistent problem in approximately 85% of cases [8]. This high incidence and severity of maternal hypotension following spinal anaesthesia could be attributed to various factors like the amount of local anaesthetic injected,

sympathetic blockade, uterus impairing venous return from extremities in supine position etc [6].

When a drug is used to treat the same many questions arise in mind of the anaesthetist. What level of hypotension should they treat?, what will be effects of hypotension on mother and unborn baby and if treated what effects will the drug have on the duo. Also the degree of hypotension that requires treatment itself is controversial with various authors using different cutoffs [9,10,11]. In this study three drugs were evaluated. Each having its own pharmacological properties. Phenylephrine being a synthetic noncatecholamine primarily stimulating  $\alpha_1$  – adrenergic receptors by a direct action. Ephedrine being a indirectly acting synthetic noncatecholamine, that stimulates  $\alpha$  and  $\beta$  adrenergic receptors. Mephentermine is an indirect acting synthetic non-catecholamine that stimulates alpha and beta adrenergic receptors.

All the three vasopressor effectively maintained arterial pressure within 20% limit of baseline value though phenylephrine maintained better in first 6 minutes of bolus dose as compared to ephedrine and mephentermine. This may be due to that, phenylephrine has peak effect within one minute, whereas ephedrine has 2-5 minutes and mephentermine has 5 minutes. After this time all three drugs were comparable in their control of blood pressure.

Thomas et al reported that bolus phenylephrine is as effective as ephedrine in restoring maternal arterial pressure above 100 mmHg [12]. Similarly, Moran et al reached the same conclusion and further concluded that the drug appears to have no adverse neonatal effects [13]. Current study also did not find any significant effect of vasopressor on foetus in terms of Apgar score at 1 and 5 minutes.

In our study cardiovascular stability was better with phenylephrine. It caused significant reduction in heart rate after the bolus dose, which is a consistent effect in phenylephrine treated women in their studies also [13,14,15]. In ephedrine and mephentermine group the heart rate increased compared to pre-operative values. This was alike to an earlier Indian study by Dinesh Sahu [8]. This is probably due to:  $\beta$  adrenergic effect of ephedrine and mephentermine which the phenylephrine lacks

Thomas D.G. et al [12] reported a high (58%) incidence of bradycardia (heart rate less than 60 beats /min) when phenylephrine was given as IV bolus after induction of spinal anaesthesia, but in our study the incidence for such extreme hypotension was nil. Selection of patients and different criteria of treating hypotension could have caused the difference. In the current study the only side effects noticed were nausea and vomiting. No extreme hypertension and headache was noticed as found in two cases in the study by Taylor JC et al [16].

## 6. CONCLUSION

It was concluded that phenylephrine ,ephedrine,and mephentermine all could be used for maintenance of arterial pressure during spinal anaesthesia for caesarean section. Phenylephrine had an immediate peak,so it may be beneficial for initial control of hypotension.Because phenylephrine caused reflexbradycardia it may be desirable in patients with cardiac disease and also whenever tachycardia is undesirable.There was no difference in neonatal outcomes in all three groups as no neonate had Apgar score less than 7 in any of the three groups.

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