A Comparative Study of the Efficacy of Intravenous Bolus of Mephentermine and Phenylephrine in Maintaining Arterial Blood Pressure During Spinal Anaesthesia in Caesarean Section

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**ABSTRACT**

**BACKGROUND**
Spinal anaesthesia is the most popular and elegant approach for obstetric patients undergoing caesarean section due to its several advantages. Hypotension resulting from sympathectomy due to subarachnoid block can have detrimental effects on the foetus as well as the mother, so needs to be prevented and treated adequately. Vasopressors for the treatment of hypotension have a well-established role as vasodilatation is the primary cause of the reduction in arterial blood pressure. The primary objective of the study was to compare mephentermine and phenylephrine with respect to their clinical efficacy in maintaining arterial blood pressure during spinal anaesthesia in caesarean section and the secondary objective was to determine any untoward effects of the study drugs on the mother and foetus.

**METHODS**
This prospective, randomized, comparative, double-blind study was conducted among 90 pregnant women of ASA-I physical status having singleton pregnancies in the age group of 18-30 years undergoing elective as well as emergency caesarean section and were randomly allocated in to two groups. Group M (n=45), received 6 mg of mephentermine as an intravenous bolus (volume made up to 1 ml) and Group P (n=45), received 100\(\mu\)g of phenylephrine as intravenous bolus (volume made up to 1 ml) whenever hypotension occurred after spinal anaesthesia. A comparison of the mean values among the two groups was done using a student t-test. To compare more than two variables, ANOVA test was used. The p-values of less than 0.05 were considered statistically significant.

**RESULTS**
The systolic blood pressure, diastolic blood pressure and mean arterial pressure remained significantly high (P < 0.05) in the phenylephrine group as compared to the mephentermine group. The phenylephrine group also showed a significant fall (P < 0.05) in heart rate as compared to the mephentermine group.

**CONCLUSIONS**
Both the drugs were effective in treating the hypotension caused by spinal anaesthesia without any adverse effects on the mother as well as on neonatal outcome but phenylephrine had a quicker onset, better maintenance of blood pressure and can be preferred in patients in whom tachycardia is undesirable.

**KEY WORDS**
Subarachnoid Block, Hypotension, Mephentermine, Phenylephrine.
The obstetric patient for caesarean section usually presents more challenges to the anaesthesiologist than the other patients. Spinal anaesthesia is perhaps the most elegant approach to these challenges.[1,2] Its popularity is due to the relative simplicity, rapidity, certainty, duration, postoperative analgesia and minimal side effects. But like any other anaesthetic technique, it is not devoid of complications, the most common being hypotension.[3] For the mothers, hypotension is especially associated with nausea and vomiting and in extreme cases, there is a risk of decreased consciousness, respiratory depression and cardiac arrest. Hypotension can also have detrimental effects on the foetus which include a decrease in uteroplacental blood flow, impaired foetal oxygenation with asphyxia and foetal acidosis.[4] The place of vasopressors for the treatment of hypotension during spinal anaesthesia in the caesarean section is well established because vasodilatation is the primary cause of arterial pressure reduction.[5] Mephentermine is a non-catecholamine sympathomimetic amine which acts both directly and indirectly via an action on α and β adrenergic receptors. It has both cardiac and peripheral action.[6] Phenylephrine is another drug which is a direct-acting, selective α adrenergic agonist. It increases blood pressure by increasing systemic vascular resistance.[7] As these drugs have a similar clinical profile and the experience in comparing these two drugs is limited, so we decided to compare these two drugs in relation to their clinical effects during spinal anaesthesia.

Aim
The primary aim of the present study was to compare the efficacy of intravenous bolus of mephentermine and phenylephrine in maintaining arterial blood pressure during spinal anaesthesia in caesarean section.

Objectives
To determine the efficacy of intravenous bolus of mephentermine and phenylephrine in maintaining arterial blood pressure during spinal anaesthesia in caesarean section, to assess the difference in systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate across both groups and evaluate the incidence of any undesirable side effects on mothers as well as the neonates.

METHODS
The present study was conducted for 18 months at the Department of Anaesthesiology and critical care, Bokaro General Hospital, Bokaro steel city, Jharkhand, after obtaining approval from the hospital’s ethical and scientific committee. The study was conducted on 90 pregnant women of ASA-I physical status having singleton pregnancies in the age group of 18-30 years undergoing elective as well as emergency caesarean section after obtaining informed written consent. The patients were allocated into the mephentermine group (Group-M) and phenylephrine group (Group-P) randomly by research randomizer software in a double-blinded fashion, in which both the study subjects and investigators were blinded. The sample size of 90 patients was calculated using 80% power of the study and an expected standard deviation of 2.25 in the population. The exclusion criteria were medical complications like diabetes mellitus, hypertension, cardiovascular diseases, severe anaemia, obstetric complications like antepartum haemorrhage, cord complications, foetal malformations and other contraindications to regional anaesthesia. A methodical pre-anaesthetic check-up and assessment were performed which included a detailed history of chronic medical illness, general and systemic examination, routine investigations and enquiry about previous anaesthetic exposure if any. In the recovery room, an intravenous line was secured preferably with 18G-Cannula and pre-loading was done with 15 ml/kg Ringer lactate solution. Injection ranitidine 50 mg was given intravenously 30 minutes before the surgery. In the operation theatre, patients were made to lie in a supine position with left uterine displacement with a standard size wedge under the right hip. Standard monitors like pulse oximeter, non-invasive blood pressure and ECG were attached. Then after placing the patient in a left lateral position, a subarachnoid block was administered using 0.5% heavy bupivacaine. The patient was again placed in the supine position and the highest level of sensory block was assessed by pin-prick method 5 minutes after subarachnoid block. Systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, and SPO₂ were recorded every 2 minutes for 20 minutes and thereafter every 5 minutes for 1 hour. Hypotension was defined as a fall in systolic BP> 20% from the baseline or systolic BP< 90 mmHg. Whenever hypotension occurred, Group M (n=45) – received 6 mg mephentermine as I/v bolus (volume made up to 1ml) and Group P (n=45) – received 100μg phenylephrine as I/v bolus (volume made up to 1ml) and the drug was repeated if required. The number of boluses and total dose of vasopressors used to recover from hypotension was recorded. Bradycardia (Heart rate <50 b/m) was treated with an injection of atropine 0.6mg intravenously when required. Occurrences of adverse effects in the perioperative period were noted particularly in relation to respiratory and cardiovascular problems, nausea, vomiting and headache. Neonatal outcome was assessed by using the APGAR score at the 1st and 5th minute.

Statistical Analysis
All the data had been selected randomly, then tabulated and analyzed with appropriate statistical tools ‘MedCalc’. The statistical significance tests applied were the student unpaired T-test, Chi-Square test and test of significance for difference of proportions. A P-value of >0.05 was considered to be non-significant and significant if the P value was <0.05.
**RESULTS**

Data from 90 patients were analyzed and the baseline demographic parameters like mean age, height and weight distribution were comparable in both the groups as depicted in table 1.

| Parameters       | Group-M | Group-P | p-value |
|------------------|---------|---------|---------|
| Age (in years)   | 22.49 ± 2.83 | 22.76 ± 2.60 | 0.831   |
| Height (in cms)  | 150.87 ± 1.82 | 150.98 ± 1.91 | 0.712   |
| Weight (in kgs)  | 62.04 ± 4.51 | 63.29 ± 4.08 | 0.315   |

Table 1: Demographic data

There was no statistically significant difference in relation to the baseline Systolic BP, Diastolic BP, Mean arterial pressure and heart rate between the two groups. The duration between subarachnoid block and time to hypotension among group M (3.31 ± 1.20) and group P (3.33 ± 1.28) was also comparable.

Figure 1 shows changes in systolic blood pressure (SBP); SBP in group M at 2 min after I/v bolus was 97.38 mm of Hg and in the group P was 101.69 mmHg. SBP remained significantly high with a P value < 0.05 in group P (117.71 mmHg) till 50 min as compared to group M (112.07 mmHg).

Figure 2 shows changes in diastolic blood pressure (DBP); DBP in group M at 2 min was 56.31 mm of Hg and in the group P was 59.80 mm of Hg, which significantly remained high with P value < 0.05 till 60 minutes in group P (75.73 mmHg) as compared to group M (72.33 mmHg).

Figure 3 depicts changes in mean arterial pressure (MAP); MAP in group M at 2 min was 70.00 mm of Hg and in the group P was 73.73 mm of Hg. MAP remained significantly high with a P value <0.05 in group P (89.60 mm Hg) till 60 minutes as compared to group M (86.71 mm of Hg). Group M required a statistically significantly higher number of boluses with a p-value = 0.0117 (P<0.005) than group P. Also, the mean number of boluses required was more in group M as compared to group P with a p-value = 0.0073 (P<0.05).
Results. It causes a number of boluses of mephentermine, there was a significant (P<0.05) fall in heart rate while with mephentermine there was a significant (P<0.05) rise in heart rate. This result was consistent with the mechanism of action of these drugs that the decrease in heart rate found in the phenylephrine group was due to its pure α receptor activity as compared with mephentermine which had got mixed action directly as well as indirectly on α and β receptors. Similar results were seen in studies done by Sahu et al. and Rajanaleni et al.[8,9] Anusorntanawat R et al studied the safety of phenylephrine.[10] and Choudhary M et al compared phenylephrine bolus and infusion and found it as a safe and efficacious drug for the treatment of maternal hypotension during caesarean section.[11] The mean number of boluses required for maintaining arterial blood pressure was more in the mephentermine group as compared to the phenylephrine group; this shows that phenylephrine is more effective in maintaining arterial blood pressure. Singh PM et al and Nag DS et al found in their respective studies that all the three vasopressors namely, ephedrine, mephentermine and phenylephrine were effective in intravenous bolus form in the maintenance of maternal arterial pressure, though phenylephrine has a quicker peak effect, and it causes a reduction in heart rate which may be advantageous to patients in whom tachycardia is undesirable as found in our study.[12,13] Also, the three vasopressors had no adverse effects on the neonatal outcome as was also cited in the study done by Bhattacharjee B et al and Cooper et al.[14,15] Kaur et al in their study also found no untoward effect on the neonates that coincides with our results.[16] However, Mohta M et al concluded in their study that both phenylephrine and mephentermine infusions were equally effective in preventing post-spinal hypotension in patients undergoing caesarean section with the similar neonatal outcome and with no advantage of one drug over the other.[17]

**DISCUSSION**

In the present study, both vasopressors, mephentermine and phenylephrine were found to be effective in maintaining arterial blood pressure following spinal anaesthesia but phenylephrine had quicker onset of action and better maintenance of systolic blood pressure when compared with mephentermine. Also with phenylephrine, there was a significant (P<0.05) fall in heart rate while with mephentermine there was a significant (P<0.05) rise in heart rate. Further studies can be done on a larger group of patients for better verification of the effectiveness of both the drugs and their effects on neonatal outcomes. The main limitation of the present study is that it supports the use of both vasopressors while considering the influence on feto-maternal physiology. However, we have included patients undergoing both elective as well as emergency caesarean sections, but the same principle cannot be extrapolated in both cases.

**Limitations**

Table no. 02 and table no. 03 show the comparison of APGAR scores at 01 min and 05 min between two groups. There was statistically no significant difference between the two groups in accordance with their Apgar scores at 1 min with p-value = 0.833 (P>0.05) and at 5 min with p-value = 0.0720 (P<0.05). Adverse effects like nausea and vomiting were seen in two patients both in group M and group P. No other adverse effect like headache, respiratory or cardiovascular problem was seen in both the groups and was statistically non-significant (P>0.05).

**CONCLUSIONS**

Both vasopressors, mephentermine and phenylephrine are effective in the management of hypotension following spinal anaesthesia in caesarean section and can be safely used.
without any adverse effect on mothers as well as on neonatal outcomes. But phenylephrine has a quicker peak effect and causes better maintenance of blood pressure. It also causes a significant reduction in heart rate and thus can be advantageous in cardiac patients and patients for whom tachycardia is undesirable.

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