Comparative Study of Intravenous Phenylephrine with Mephenteramine for Maintenance of Arterial Blood Pressure in Caesarean Section

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Abstract
Background: Anaesthesia for caesarean section has been a challenge for anesthesiologists for centuries. Advantages of regional anaesthesia especially, spinal anaesthesia has been documented as early as 1940s by Adrian et al. The advantages being simplicity of administration, reliability of action, faster onset than epidural and minimum effects on foetus. The major drawback was hypotension associated which is a result of sympathetic block. Intravenous vasopressors are the treatment of choice for the quick correction of hypotension. This study was undertaken to compare the effects of phenylephrine and mephenteramine for maintenance of blood pressure during caesarean section.

Aim
1. To compare the hemodynamic effects in the mother caused by phenylephrine and mephenteramine after spinal anaesthesia using 0.5 % Bupivacaine.
2. To assess the requirement of repeated doses of each drug for maintenance of arterial pressure.
3. To assess the effects on neonate by APGAR score.
4. To look for side effects if any, caused by the drugs.

Keywords: Hypotension, Caesarean section, Phenylephrine, Mephenteramine.

Materials and Methods
Approval from ethical committee was obtained. This was a double blind study done at SAT Hospital, Thiruvananthapuram. The study group included 40 patients, age between 20 – 35 years undergoing caesarean section.

Inclusion Criteria
- ASA1 and 2 full term parturients for elective and emergency caesarean section.

Exclusion Criteria
- Uncontrolled PIH
- Uncontrolled GDM
- Height less than 150 cm

- Foetal distress
- Malformed maternal spine
- Heart disease in mother

All patients underwent pre anaesthetic check up. Basal heart rate and blood pressure, both systolic and diastolic were recorded. Parturients were divided by lot method into 2 groups of 20 each.

Group P: Phenylephrine: 100 micrograms
Group M; Mephenteramine: 6 milligram

Premedication
All patients were given Inj. Metoclopramide 10 mg and Inj. Ranitidine 50 mg half an hour before surgery after putting 18 G I/V cannula in the non
dominant hand. Inj. Ringer Lactate 10 ml/kg was given for preloading. Anaesthesia machine, Bain’s circuit, Laryngoscopes, various ET tubes kept ready. All emergency drugs also kept ready.

**Monitors**
Patients were connected to ECG monitor, NIBP, SpO2 monitors. After preloading, pulse rate, systolic blood pressure, diastolic blood pressure were recorded.

**Procedure**
LSAB was given in right lateral decubitus position at L3.4 interspace using 25 G spinal needle. Then 1.6 ml 0.5 % Bupivacaine (heavy) was given. Patient was made supine and a wedge was placed under right buttock. Oxygen at a rate of 4ml/minute was administered through simple face mask. Normal Saline at a rate of 10 -15 ml/ min was given after LSAB. After delivery of baby, Inj. Oxytocin 10 Units was given by slow I/V injection. Once umbilical cord is clamped, Inj. Oxytocin 20 units was given in a separate unit of normal saline as slow infusion.

**Study Method**
Pulse rate Systolic BP, Diastolic BP are meticulously recorded after LSAB. Whenever hypotension (fall in systolic pressure > 20 % from the baseline value) or a value less than 90 mm Hg, study drug was given as intravenous bolus. Pulse rate, systolic BP and diastolic BP are then recorded at every 2 minutes after the drug was given for 30 minutes and thereafter every 5 minutes till the end of surgery. The duration of study was limited to 30 minutes following the initial bolus of the vasopressor. The number of boluses needed were recorded. Bradycardia, (pulse rate of 60/min or less) was treated with Inj. Atropine 0.6 mg I/V. The highest level of sensory block was assessed by pin prick method (1). After the subarachnoid block and delivery (2). Subarachnoid block and occurrence of first episode of hypotension and (3) Uterine incision and delivery were noted.

APGAR scores were assessed 1 and 5 minutes after delivery by attending paediatrician, who was blinded to the patients group. A double clamped segment of umbilical cord was kept for immediate blood gas analysis in case APGAR was less than 7. Blood loss was assessed by volume in the suction bottle and by the number of soaked sponges. Patient was monitored throughout the procedure and for a minimum period of 1 hour in the postoperative recovery room before transferring her from the operating room suite.

**Statistical Analysis**
Data were analysed using computer software, SPSS. Students t test was performed as parametric test to compare different variables. For all statistical evaluations, a two tailed probability value p value ,0.05 was considered significant.

**Observations**

| Variable          | P  | M  | P value |
|-------------------|----|----|---------|
| Age in years      | 28.10, 3.64 | 27.70, 3.31 | 0.718 |
| Height in cm      | 155, 2.08 | 155.50, 2.04 | 0.447 |
| Weight in kg      | 56.30, 1.89 | 56.30, 2.00 | 1.000 |

So, both the groups were comparable with each other.

**2. Level of Sensory Block**

|         | T4 | T5 | T6 |
|---------|----|----|----|
| P       | 5  | 14 | 1  |
| M       | 1  | 15 | 4  |

**3. (a). LSAB – Hypotension interval**

|         | Mean | SD  |
|---------|------|-----|
| P       | 160.85 | 42.21 |
| M       | 185.10 | 42.42 |

P values between M and E is 0.078.

**3. (b) LSAB – Delivery of baby interval**

|         | Mean | SD  |
|---------|------|-----|
| P       | 261.55 | 52.80 |
| M       | 293.60 | 61.25 |

P value between the groups was 0.084
3.(c): Time interval between uterine incision and delivery of baby (UD Interval)

|          | Mean | SD  |
|----------|------|-----|
| P        | 57.75| 10.48|
| M        | 64.00| 17.96|

P value was 0.187.

4 Systolic BP: Comparison between Group P and Group M

|          | T value | df | P value |
|----------|---------|----|---------|
| Basal value | 0.020   | 38 | 0.984   |
| HP-VP     | 0.445   | 38 | 0.659   |
| 2 mts after VP | 5.619 | 38 | 0.000   |
| 4 Mts     | 2.036   | 38 | 0.049   |
| 6 mts     | 2.012   | 38 | 0.047   |
| 8 mts     | 1.995   | 38 | 0.053   |
| 10 mts    | 1.444   | 38 | 0.157   |
| 12 mts    | 1.496   | 38 | 0.143   |
| 14 mts    | 0.333   | 38 | 0.741   |
| 16 mts    | 1.787   | 38 | 0.082   |
| 18 mts    | 1.328   | 38 | 0.192   |
| 20 mts    | 2.068   | 38 | 0.068   |
| 25 mts    | 1.714   | 38 | 0.095   |
| 30 mts    | 1.890   | 38 | 0.066   |

In both groups, systolic BP falls at the onset of hypotension from the basal value and then rises after bolus. Group P showed a rapid restoration of BP in the 2nd, 4th and 6th minute after bolus injection in a statistically significant manner. From 8th to 30th minute, there was a rise in SBP in both groups, but was not significant statistically.

5 Diastolic BP: Intergroup Comparison

|          | t     | df | P value |
|----------|-------|----|---------|
| Basal value | 1.299  | 38 | 0.202   |
| HP-VP     | 0.827 | 38 | 0.413   |
| 2 mts after VP | 5.057 | 38 | 0.000   |
| 4 mts     | 4.357 | 38 | 0.000   |
| 6 mts     | 3.531 | 38 | 0.001   |
| 8 mts     | 1.988 | 38 | 0.054   |
| 10 mts    | 1.822 | 38 | 0.076   |
| 12 mts    | 0.947 | 38 | 0.0349  |
| 14 mts    | 1.822 | 38 | 0.076   |
| 16 mts    | 1.333 | 38 | 0.190   |
| 18 mts    | 1.988 | 38 | 0.054   |
| 20 mts    | 1.333 | 38 | 0.190   |
| 25 mts    | 0.947 | 38 | 0.349   |
| 30 mts    | 1.333 | 38 | 0.190   |

In both groups, diastolic BP also falls at the onset of hypotension from the basal value and then rises after bolus. Group P showed a rapid restoration of BP in the 2nd, 4th and 6th minute after bolus injection in a statistically significant manner. From 8th to 30th minute, there was rise in the diastolic BP, but was not statistically significant between the groups.

6. Changes in Heart Rate: Intergroup Comparison

|          | t     | df | P value |
|----------|-------|----|---------|
| Basal value | 1.691  | 38 | 0.099   |
| HP-VP     | 2.7   | 38 | 0.008   |
| 2 min after VP | 10.465 | 38 | 0.000   |
| 4 min     | 10.804 | 38 | 0.000   |
| 6 min     | 6.224 | 38 | 0.000   |
| 8 min     | 7.288 | 38 | 0.000   |
| 10 min    | 7.649 | 38 | 0.000   |
| 12 min    | 7.587 | 38 | 0.000   |
| 14 min    | 12.524 | 38 | 0.000   |
| 16 min    | 10.136 | 38 | 0.000   |
| 18 min    | 8.686 | 38 | 0.000   |
| 20 min    | 8.805 | 38 | 0.000   |
| 25 min    | 10.62 | 38 | 0.000   |
| 30 min    | 11.122 | 38 | 0.000   |

Heart rate was raised in both groups during hypotension. In group P, heart rate decreased in a significant manner right from the 2nd minute after the vasopressor was given. In most of the cases, the heart rate at the end of the study was less than the basal heart rate. In group M, the heart rate remained almost always elevated than the basal heart rate.

7. Bolus drug needed

|          | P | M |
|----------|---|---|
| 1        | 5 | 11|
| 2        | 9 | 8 |
| 3        | 6 | 1 |

In group P, 25 % required single, 45 % two, 30 % three boluses to maintain blood pressure. Where as in group M, 55 % required single, 40 % two and 5% three doses.

8. APGAR Score

|          | P(mean) | M(mean) | P value |
|----------|---------|---------|---------|
| 1 minute | 8.85    | 8.80    | 0.687   |
| 5 minutes| 9.85    | 9.80    | 0.684   |

APGAR score did not reveal any untoward effect on foetal status since all the newborns of two groups had APGAR > 7.
Discussion
Spinal subarachnoid block has been the mainstay for caesarean sections for decades. The major disadvantage was post spinal headache. Prophylactic use of crystalloids by preloading has been a technique to prevent hypotension. Judicious use of vaspressors has been used to treat hypotension. In our study, all the patients received 10 ml/kg Ringer Lactate as preloading. Vaspressor of individual parturient was selected randomly. Mephenteramine has a mixed alpha and beta action, whereas Phenylephrine is a pure alpha agonist.

Thomas and colleagues reported that bolus Phenylephrine 100 microgram is as effective as Mephenteramine 6mg on restoring maternal arterial pressure above 100 mmHg. Moran et al found a comparable efficacy in comparing 80 microgram phenylephrine and 10 mg mephenteramine boluses. They also concluded when used in small increment bolus injections, phenylephrine has no adverse neonatal effects in normal healthy parturients.

Hall and colleagues compared a prophylactic infusion of phenylephrine 10 microgm/mt with mephenteramine 1 or 2 mg/min supplemented by 20 micro gm or 6 mg boluses respectively, if systolic arterial pressure decreased by 20 % from baseline .Hall et al have remarked that maternal bradycardia in the phenylephrine group corresponded with periods when a number of bolus doses of phenylephrine had been given for maternal hypotension.

In our study, there was an initial fall in both systolic and diastolic blood pressures after spinal anaesthesia.

Phenylephrine showed a rapid restoration of blood pressure. Arterial pressures at 2,4,6 minutes after phenylephrine was greater than that compared to mephenteramine. This may be because phenylephrine has peak effect within one minute whereas mephenteramine within two to five minutes. The number of boluses of drug needed was more in phenylephrine group, suggesting the rapid onset of its action. In the P group, 25 % needed single,45 % needed two ,30 % needed three boluses .In the M group, 55 % needed single,40 % two ,5 % three bolus doses.

On giving phenylephrine, heart rate decreased in some patients. Phenylephrine has the tendency to lower heart rate at 30 minutes than at baseline. Mephenteramine in fact raised the heart rate at 30 minutes than baseline value .In our study ,none of the 40 participants of the study had babies of APGAR less than 8 either at 1 minute or at 5 minutes.

Blood loss was within allowable range for each and every parturient in the study. The crystalloid preloading at the rate of 10 -15 ml/minute have also not confounded the results the height ,weight and other maternal factors were comparable.

Conclusion
Our study shows that vasopressors, Phenylephrine hydrochloride and Mephenteramine hydrochloride used to treat hypotension during spinal anaesthesia for caesarean section when given as intravenous boluses of 100 micro gram and 6 mg are comparable in their efficacy in maintenance of arterial pressure within 20 % limit of baseline.

Regarding maintenance of systolic and diastolic blood pressure, phenylephrine showed a rapid restoration of blood pressure than mephenteramine.

Phenyl ephrine has a heart rate lowering effect, whereas mephenteramine shows a heart rate rising tendency.

The requirement of repeated doses was lower in mephenteramine group compared to phenylephrine due to rapid onset of action of phenylephrine. None of the two vasopresors had any effect on APGAR score or any maternal side effects.

We conclude that Phenylephrine and Mephenteramine are equally efficient in maintaining arterial pressures during spinal anaesthesia in caesarean section.
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