Original Research Article

Effectiveness of intravenous boluses of phenylephrine, ephedrine and mephentermine as vasopressors for management of perioperative hypotension in elective lower segment caesarean section under spinal anaesthesia – A prospective comparative study

Garima Sinha1*, Hemalatha S2, Gurudatt C L2

1 Dept. of Anaesthesiology, Institute of Medical Sciences, B.H.U, Varanasi, Uttar Pradesh, India
2 Dept. of Anaesthesiology, J.S.S. Medical College and Hospital, J.S.S. Academy of Higher Education and Research, Mysuru, Karnataka, India

A B S T R A C T

Introduction and Aims: Hypotension after subarachnoid block for caesarean section is the commonest but serious complication encountered by anaesthesiologists. Various vasopressors are used to prevent/treat this complication. This study was done to compare the efficacy of three commonly used vasopressors – phenylephrine, ephedrine, mephentermine for treatment of perioperative hypotension.

Material and Methods: Sixty American Society of Anaesthesiologists (ASA) physical status class II parturients undergoing elective caesarean section under subarachnoid block were randomly allotted three groups (P, E, M) (n = 20) to receive intravenous boluses of phenylephrine 100 mcg, ephedrine 6mg & mephentermine 6mg respectively, following hypotension. Maternal Haemodynamic parameters, complications & neonatal APGAR scores were recorded. P-value < 0.05 was considered significant and P-value < 0.001 considered highly significant.

Results: Demographic values, baseline vital parameters and mean number of vasopressor boluses required were similar in the three groups (P > 0.05). The mean trends of systolic blood pressure (P = 0.06), diastolic blood pressure (P = 0.7) and mean arterial pressure (P = 0.6) were similar in the three groups. Heart rate was raised during periods of hypotension; the mean heart rate was lower in the phenylephrine group after vasopressor administration. The overall trend was similar (P = 0.1) among the three groups. There was (P = 0.003) higher incidence of bradycardia in the phenylephrine group. The neonatal APGAR scores were > 7 in the three groups at the 1st and 5th minute (P = 0.5).

Conclusion: All three vasopressors effectively maintained arterial blood pressure during the subarachnoid block for caesarean section. Phenylephrine caused a significant reduction in heart rate compared to ephedrine or mephentermine.

© 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC-ND license (https://creativecommons.org/licenses/by/4.0/)

1. Introduction

Subarachnoid block (SAB) causes sympathetic blockade and decreased venous return, exacerbated by aortocaval compression leading to hemodynamic sequelae especially hypotension in up to 85% of parturients which is a major concern for both mother & foetus. High incidence and severity of maternal hypotension following subarachnoid block could be attributed to various factors1-

1. Sympathetic blockade leading to vasodilatation causing a decrease in preload and cardiac output accentuated by-
   i. Large amount of blood present in the uterus
   ii. Weight of uterus impairing venous return from extremities, especially in the supine position (Supine

---

*Corresponding author.
E-mail address: rimps16@gmail.com (G. Sinha).
Hypotension Syndrome

iii. “Bearing down” of parturient causes abdominal muscle contraction which further decreases venous return to the heart

iv. Epidural veins engorgement causing reduction in subarachnoid and epidural spaces

2. Parturients usually require a lesser dosage of local anaesthetics for subarachnoid block and the usual dosage might be relative over dosage causing significant hypotension.

Systolic hypotension higher than 20% to 30% of patient’s baseline blood pressure can lead to maternal low perfusion pressure, manifested as nausea, vomiting, dizziness, low level of consciousness & utero-placental hypoperfusion. This can lead to fetal bradycardia & acid-base abnormalities and if prolonged, may lead to neurobehavioral changes later. Newborn APGAR scoring and umbilical artery (UA) acid-base studies are used to evaluate the recent prenatal environment.

Strategies used to minimize/prevent hypotension include proper maternal position with the uterus displaced off the vena cava, intravenous fluid infusion to increase effective blood volume-crystalloids/colloids, physical interventions like leg wrappings minimize venous pooling of blood in the legs, monitoring of blood pressure at frequent intervals after placement of regional anesthetic, vasopressors to cause vasoconstriction of the peripheral circulation, viz., phenylephrine, mephentermine, ephedrine, metaraminol, methoxamine. All these drugs cross the placenta to variable extent and have implications on both mother & fetus. Some studies have shown the superiority of phenylephrine over ephedrine or mephentermine but contradictorily, recent studies show equal efficacy of the 3 drugs in managing perioperative hypotension in the lower segment cesarean section (LSCS).

Hence, we selected this study to assess and compare the efficacy of the three vasopressors.

The hypothesis formed for this study was a null hypothesis with all the three study drugs equally effective in managing perioperative hypotension in elective lower segment cesarean section under subarachnoid block.

2. Materials and Methods

A prospective, double-blinded, randomized controlled study was undertaken at J.S.S. Medical College and Hospital, Mysuru between November 2015 and July 2017. Before commencing the study, approval was obtained from the institutional ethical committee. Participants in this study were explained about the anesthetic procedure and if prolonged, may lead to neurobehavioral changes later.

Strategies used to minimize/prevent hypotension include proper maternal position with the uterus displaced off the vena cava, intravenous fluid infusion to increase effective blood volume-crystalloids/colloids, physical interventions like leg wrappings minimize venous pooling of blood in the legs, monitoring of blood pressure at frequent intervals after placement of regional anesthetic, vasopressors to cause vasoconstriction of the peripheral circulation, viz., phenylephrine, mephentermine, ephedrine, metaraminol, methoxamine. All these drugs cross the placenta to variable extent and have implications on both mother & fetus. Some studies have shown the superiority of phenylephrine over ephedrine or mephentermine but contradictorily, recent studies show equal efficacy of the 3 drugs in managing perioperative hypotension in the lower segment cesarean section (LSCS).

Hence, we selected this study to assess and compare the efficacy of the three vasopressors.

The hypothesis formed for this study was a null hypothesis with all the three study drugs equally effective in managing perioperative hypotension in elective lower segment cesarean section under subarachnoid block.

2.1. Inclusion criteria

1. Full-term parturients undergoing elective cesarean section under subarachnoid block
2. ASA physical status class II
3. Age 20 to 35 years
4. Parturients giving informed written consent

2.2. Exclusion criteria

1. Multiple Pregnancies
2. Parturients having contraindications to subarachnoid block like local infection, coagulation abnormalities or on anti-coagulant medication
3. Parturients with Hypertensive disorders of pregnancy & other high-risk pregnancies, medical comorbidities, hemoglobin <9gm/dl
4. Parturients on drugs which cause interactions with the study drugs, like tricyclic antidepressants, monoamine oxidase inhibitors, etc.
5. Parturients with height < 150cm or > 170cm &/or B.M.I. > 30Kg/m²

Thorough pre-anesthetic evaluation of the parturients including relevant investigations was done, demographic parameters (age, height, weight & BMI) were noted. Data was collected in pretested proforma meeting the objectives of the study. Parturients were premedicated with Tab. Ranitidine 150 mg orally the night before surgery and fasted 6 hours for solid food & 2 hours for clear liquids.

The parturients were randomly divided into 3 groups of 20 each -

Group P – received intravenous 100 mcg Phenylephrine
Group E – received intravenous 6 mg Ephedrine
Group M – received intravenous 6 mg Mephentermine

Participants were randomly allocated to one of the 3 groups using the sealed envelope technique. The intravenous (IV) bolus doses of all the 3 vasopressors were prepared before performing the spinal injection by a separate resident anaesthesiologist who had no involvement with the study.

All solutions were prepared under strict aseptic technique using 0.9% normal saline where reconstitution & dilution were required.

Once prepared, all solutions were labelled with the trial number in a 5 ml syringe. Thus, the anaesthesiologist who managed the case (who is also the observer) and the parturient were blinded to the study drug used.

After securing an 18G intravenous cannula in the non-dominant forearm & administering 10 ml/kg body weight Ringer Lactate over 30 minutes, parturient was shifted to each group). Wherein, we considered the mean number of boluses of the vasopressors with the standard deviations, required for maintaining arterial pressure within 20% of the baseline as per the previous studies done on the subject.
operation theatre in the left lateral position. ASA standard non-invasive monitors (electrocardiography, non-invasive blood pressure, pulse oximeter) were attached. Baseline systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean Arterial Blood Pressure (MAP) & Heart Rate (HR) were measured preoperatively by averaging 3 readings taken 5 minutes apart. Inj. ondansetron 4mg slow IV bolus was given on the table as premedication.

Under strict aseptic precautions, parturients were given SAB in the L3-4 intervertebral space in sitting position using 25G Quincke’s spinal needle with 2 ml of 0.5% hyperbaric bupivacaine after free flow of clear cerebrospinal fluid was observed. The time of SAB was considered time zero. Following this, parturient was put in the supine position and a wedge placed below the right flank. Supplemental oxygen 6litres/minute was given through a simple face mask. Vital parameters (SBP, DBP, HR, MAP) were recorded every 2 minutes till 20 minutes and every 5 minutes thereafter until the surgery was completed. Inj. Oxytocin 10 IU intramuscular and 10 IU as slow IV infusion was given to the parturients after delivery of the baby and clamping of the umbilical cord. The total duration of surgery was recorded.

Hypotension was described as any fall in SBP > 20% of baseline or 90mmHg, whichever was greater. Study drug boluses were administered in parturients who developed hypotension & repeated after 2 minutes if no improvement was observed.

Bradycardia was defined as any fall in heart rate < 60 bpm. Inj. Atropine 0.6 mg IV bolus was given if bradycardia was observed.

Tachycardia was considered as any rise in heart rate > 20% of baseline.

The highest level of sensory block was assessed by the pin-prick method and the level of motor blockade was assessed by Modified Bromage scale. 5 minutes after subarachnoid block. Time of onset of hypotension, time of administration of study drugs & number of study drug boluses required were noted. Any complications, viz., bradycardia, tachycardia, dysrhythmias were noted. Newborn APGAR scores at 1 and 5 min. were obtained from the pediatrician blinded to the study or vasopressor used.

2.3. Statistical analysis

Results were expressed as mean ± standard deviation (SD). Data was entered into Microsoft Excel and statistical analysis was done using SPSS for Windows (Version 22). Baseline summary statistics were calculated using descriptive univariate statistics. Group comparisons between the three vasopressors used and various quantitative variables were conducted by One-way ANOVA (for independent variables) and Two-way Repeated-measure ANOVA (for dependent variables). Post-hoc analyses were carried out.

Qualitative variables were compared using the Chi-square test. P-value < 0.05 was considered significant and P-value < 0.001 was considered highly significant.

3. Results

The demographic values and baseline vital parameters were similar in all the three groups (P > 0.05) (Tables 1 and 2). Indications for elective LSCS were varied, maximum being previous lower segment cesarean section (46.8%) followed by cephalopelvic disproportion (11.7%). The mean number of boluses required in all the groups was similar (P = 0.4) (Table 3). The mean skin incision to delivery time (minutes) (P = 0.9) and mean uterine incision to delivery time (minutes) (P = 0.8) was similar in all the groups. The mean trends of systolic blood pressure (P = 0.06) (Graph 1), diastolic blood pressure (P = 0.7) (Graph 2) and mean arterial pressure (P = 0.6) (Graph 3) were similar in all the three groups. Heart rate was raised in all the three groups during periods of hypotension but the mean heart rate was lower in the phenylephrine group after vasopressor administration but the overall trend was statistically similar among the three groups (P = 0.1) (Graph 4). Bradycardia (Table 4) was reported to be maximum with the Phenylephrine group, occurring in 9/20 (45%) parturients. In the Ephedrine group, 2/20 parturients (10%) developed bradycardia and only 1 parturient (5%) in the Mephentermine group developed bradycardia. This difference was statistically significant (P = 0.003). Tachycardia (Table 4) was noted maximum with Ephedrine group, i.e., in 7/20 parturients (35%) as compared to 2/20 parturients (10%) in Phenylephrine group and 3/20 parturients (15%) in Mephentermine group but this difference was statistically insignificant (P>0.05).

Two events (10%) of Dysrhythmia (transient irregular heart rhythm) (Table 4) were noted in the Mephentermine group and reverted spontaneously but the occurrence was statistically insignificant to assure causal relationship with the vasopressor (P > 0.05). The APGAR Scores (Table 5) at 1 minute & 5 minutes after delivery of baby were similar among the three study groups (P > 0.05). The mean APGAR scores at 1 minute after delivery of babies were 7.8 ± 0.6, 8.0 ± 0.7 and 7.7 ± 0.6 and 8.9 ± 0.4, 9.0 ± 0.6 and 9.1 ± 0.4 at 5 minutes after delivery in Phenylephrine, Ephedrine and Mephentermine groups, respectively. No neonates in the study got admitted to intensive care units.

4. Discussion

Obstetric anaesthetists are faced with the challenge of providing anaesthesia for caesarean sections and care for both the mother and the unborn baby. A team approach is imperative to ensure an optimal outcome. There has been an increasing trend in the caesarean section rate especially after the advent of ultrasonography, with a move towards
more caesarean sections being performed under regional anaesthesia compared to general anaesthesia.\textsuperscript{18} This is also to avoid complications associated with general anaesthesia specially gastric contents aspiration, polypharmacy & its consequences.

Taking into account the exclusion and inclusion criteria, considering ASA physical status class II elective LSCS in our hospital, a power analysis taking 95% confidence interval, $\alpha = 0.05$ and $\beta = 0.2$ brought out the sample size as 20 in each group, i.e., phenylephrine, mephentermine & ephedrine. This was similar to the study done by Das S. et al\textsuperscript{10} and Sahu D. et al\textsuperscript{19} but they included emergency cases as well. The predetermined dose of each vasopressor was given immediately if hypotension developed after SAB to maintain the blood pressure within 20% of the baseline value.

In our study, parturients were randomly divided into 3 groups of 20 patients each - Group P received Inj. Phenylephrine 100 mcg intravenous, Group E received Inj. Ephedrine 6 mg intravenous and Group M received Inj. Mephentermine 6 mg intravenous. Based on previously published data, we chose dosages of vasopressors in our study considered to be approximately equipotent. According to the published data by Thomas D.G. et al,\textsuperscript{6} bolus phenylephrine 100 mcg is as effective as ephedrine 5 mg in restoring maternal blood pressure above 100 mmHg, Saravanan et al\textsuperscript{20} used drug infusions and estimated the relative potency ratio of phenylephrine: ephedrine as 80:1 (phenylephrine 100 mcg = ephedrine 8 mg). Sahu D. et al\textsuperscript{19} carried out studies with phenylephrine, ephedrine and mephentermine boluses and Thomas D.G. et al.\textsuperscript{6} Nazir I. et al\textsuperscript{12} studied phenylephrine and ephedrine boluses with dosages similar to our study.

The demographic data and the baseline vital parameters were similar in all the three groups. Mean Highest level of Sensory Blockade achieved in all the three groups was T4 (T3-6, T2-6 & T2-7 in P, E & M groups; P-value = 0.7) dermatomal level, assessed by pin-prick method. Ngan Kee W.D. et al (2008)\textsuperscript{21} compared phenylephrine & ephedrine IV boluses and ac hieved mean T4 dermatomal level in the parturients. Saravanan S. et al,\textsuperscript{20} Mohta M. et al\textsuperscript{22} did similar studies and achieved T5-6 dermatomal mean sensory block height.

The trend of mean heart rate (HR) (in beats per minute) in the three study groups was similar throughout surgery. Heart rate was raised in all the three study drug groups during periods of hypotension. Though the mean heart rate in the phenylephrine group was lower than the mean baseline value after administering the study drug and remained so until 40 minutes and the mean heart rates in the ephedrine and mephentermine groups were higher than the baseline values throughout surgery after vasopressor administration and came back to near baseline values by 25-40 minutes, these differences were insignificant (P = 0.1) and the overall trend among the three groups remained the same.

Bradycardia (Heart rate<60bpm) requiring treatment with Inj. Atropine 0.6mg IV bolus was reported to be maximum with the Phenylephrine group, occurring in 45% of the parturients as compared to 10% in the Ephedrine group and 5% in the Mephentermine group. This difference was statistically significant (P=0.003).

Phenylephrine is a pure alpha-adrenergic agonist. It causes reflex bradycardia by baroreceptor stimulation due to an increase in the pressure resulting in inhibition of the tonic discharge of the vasoconstrictor nerves and excitation of the vagal innervation (Mary’s Law). Ephedrine and mephentermine stimulate both $\alpha$ and $\beta$ adrenergic receptors and enhance the release of endogenous norepinephrine from sympathetic neurons. Direct $\beta$-action increases heart rate.\textsuperscript{10,19,23}

Thomas D.G. et al,\textsuperscript{6} Sahu D. et al,\textsuperscript{19} Ngan Kee W.D. et al,\textsuperscript{21} Gunda C.P. et al,\textsuperscript{8} Bhattarai B. et al,\textsuperscript{11} Ganeshanavar A. et al,\textsuperscript{8} Natarajan A.K. et al.\textsuperscript{16} Md. Arshad Imam\textsuperscript{23} and Das S. et al\textsuperscript{10} got similar results in similar studies.

The incidence of bradycardia may be due to peritoneal stretching/visceral manipulation if the height of the sensory blockade is not achieved adequately.\textsuperscript{16} Bradycardia could also be caused by cardiac sympathetic denervation/some paralysis of cardiac accelerator nerve associated with high spinal block.\textsuperscript{6,11,19} In parturients receiving phenylephrine, bradycardia may be due to an increase in blood pressure with an $\alpha$-agonist that might lead to reactive bradycardia (baroreceptor reflex).\textsuperscript{16}

The trends of mean Systolic Blood Pressure (SBP) (P=0.06), Diastolic Blood Pressure (DBP) (P=0.7) and Mean Arterial Blood Pressure (MAP) (P=0.6) (in mmHg) intraoperatively in the three study groups were similar throughout with P = 0.06 and hence the differences were statistically insignificant. There was an initial drop in SBP at 2-4 minutes after injecting the drug into subarachnoid space in all the three groups.

Thomas D.G. et al,\textsuperscript{6} Ngan Kee W.D. et al\textsuperscript{21} & Gunda C.P. et al\textsuperscript{8} gave IV boluses of either phenylephrine or ephedrine and observed that phenylephrine is as effective as ephedrine in treating post-spinal hypotension in parturients. Sahu D. et al,\textsuperscript{19} Bhattarai B. et al,\textsuperscript{11} Ganeshanavar A. et al\textsuperscript{8} and Das S. et al\textsuperscript{10} did a clinical study for comparison of IV bolus of phenylephrine, ephedrine or mephentermine and observed that all the three vasopressors effectively maintained arterial pressure within 20% limit of baseline value though, phenylephrine maintained better as compared to ephedrine and mephentermine.

The total number of study drug boluses required to treat post-spinal hypotension/maintain blood pressure as per protocol were 3.3 ± 1.8, 3.2 ± 1.4 and 2.6 ± 1.6 in P, E and M groups, respectively; the mean number of boluses required with phenylephrine and ephedrine compared to mephentermine were more but the difference among groups.
### Table 1: Demographic data of patients among the three study groups

| Group              | Phenylephrine (n=20) | Ephedrine (n=20) | Mephentermine (n=20) | P-Value |
|--------------------|----------------------|------------------|----------------------|---------|
|                    | Mean (years) | Standard Deviation | Mean (years) | Standard Deviation | Mean (years) | Standard Deviation |         |
| AGE (years)   | 26.1        | 3.5               | 25.7        | 5.0               | 26.0        | 3.2               | 0.96     |
| Weight (in kg) | 64.50       | 11.38             | 65.90       | 11.08             | 68.30       | 9.50              | 0.5      |
| Height (in cm) | 157.45      | 5.74              | 156.25      | 6.03              | 155.25      | 3.46              | 0.4      |
| BMI (Kg/m²)   | 26.5        | 3.6               | 26.7        | 4.5               | 28.4        | 4.2               | 0.3      |

### Table 2: The baseline vital parameters among the three study groups - Heart Rate (HR) (in beats per minute), Systolic Blood Pressure (SBP) (in mmHg), Diastolic Blood Pressure (DBP) (in mmHg) and Mean Arterial Pressure (MAP) (in mmHg)

| Group              | Phenylephrine (n=20) | Ephedrine (n=20) | Mephentermine (n=20) | P-value |
|--------------------|----------------------|------------------|----------------------|---------|
|                    | Mean (bpm) | Standard Deviation | Mean (bpm) | Standard Deviation | Mean (bpm) | Standard Deviation |         |
| Baseline HR (bpm) | 96.20      | 13.00             | 94.60       | 11.12             | 101.60     | 9.86              | 0.1      |
| Baseline SBP (mmHg)| 123.90     | 12.46             | 121.35      | 11.23             | 123.35     | 9.57              | 0.4      |
| Baseline DBP (mmHg)| 79.35      | 9.70              | 75.80       | 9.37              | 76.90      | 7.09              | 0.8      |
| Baseline MAP (mmHg)| 94.15      | 9.98              | 91.00       | 8.96              | 92.60      | 7.49              | 0.5      |

### Table 3: Comparison of the three groups on the basis of mean number of study drug boluses required to treat post-spinal hypotension and Skin incision to delivery time (in minutes) and Uterine incision to delivery time (in minutes)

| Group              | Phenylephrine (n=20) | Ephedrine (n=20) | Mephentermine (n=20) | P value |
|--------------------|----------------------|------------------|----------------------|---------|
|                    | Mean                  | Standard Deviation | Mean                  | Standard Deviation | Mean                  | Standard Deviation |         |
| Total Number of Study Drug Boluses | 3.3  | 1.8 | 3.2 | 1.4 | 2.6 | 1.6 | 0.4 |
| Skin Incision To Delivery Time (min.) | 5.3  | 1.6 | 5.3 | 1.4 | 5.1 | 1.6 | 0.9 |
| Uterine Incision To Delivery Time (min.) | 2.25 | 0.85 | 2.40 | 0.82 | 2.20 | 1.40 | 0.8 |

### Table 4: The incidence of complications in each group, intra-operatively

| Complication | Group Phenylephrine (n=20) | Ephedrine (n=20) | Mephentermine (n=20) | P value |
|--------------|---------------------------|------------------|----------------------|---------|
|              | Count | N % | Count | N % | Count | N % |         |
| Bradycardia  | 9  | 45  | 2  | 10  | 1  | 5  | 0.003  |
| Tachycardia  | 2  | 10  | 7  | 35  | 3  | 15 | 0.1    |
| Dysrhythmia  | 0  | 0   | 0  | 0   | 2  | 10 | 0.1    |
Graph 1: Mean trend of Systolic Blood Pressure (SBP) (in mmHg) throughout surgery in the three study groups

Graph 2: Mean trend of Diastolic Blood Pressure (DBP) (in mmHg) throughout surgery in the three study groups

Graph 3: Mean trend of Mean Arterial Blood Pressure (MAP) (in mmHg) throughout surgery in the three study groups

Table 5: Mean Apgar scores in the three study groups at one minute and five minutes after delivery of the baby

| Apgar Score at | Group            | Phenylephrine (n=20) | Ephedrine (n=20) | Mephentermine (n=20) | P Value |
|---------------|------------------|----------------------|------------------|----------------------|---------|
|               |                  | Mean                 | Standard Deviation | Mean                 | Standard Deviation |         |
| 1 min         | Phenylephrine    | 7.8                  | 0.6               | 8.0                  | 0.7               | 7.7      | 0.6     | 0.5     |
| 5 min         | Phenylephrine    | 8.9                  | 0.4               | 9.0                  | 0.6               | 9.1      | 0.4     | 0.5     |
Graph 4: Mean trend of Heart Rate (HR) (in beats per minute) throughout surgery in the three study groups

was statistically insignificant (P > 0.05).

Phenylephrine has a peak effect within one minute, whereas ephedrine and mephentermine take 2-5 minutes. Phenylephrine has quicker control of hypotension (peak onset within 1 minute and short duration of action ~ 10 minutes) and a greater number of bolus doses should be required to manage hypotension than mephentermine and ephedrine.\textsuperscript{11,17}

Ephedrine is an indirect-acting drug and has a slow onset and comparatively long duration of action. Hence, it should require a lesser number of boluses.\textsuperscript{12}

In choosing an appropriate vasopressor in obstetrics, several factors like efficacy for maintaining blood pressure, no cardiovascular maternal effects, ease of use, direct and indirect foetal effects, cost and availability need to be considered. The ideal vasopressor would be one which has a rapid onset, short duration of action, easily titrable, reliable and easy to use prophylactically and lack of any adverse maternal and foetal impact.\textsuperscript{17}

Bhattarai B. et al\textsuperscript{11} gave IV boluses of phenylephrine 25 microgram, ephedrine 5 mg or mephentermine 6 mg and observed that a similar mean number of boluses were required in the groups (P > 0.05). Soxhuku-Isufi A. et al\textsuperscript{15} gave intravenous boluses of either 100 mcg inj. phenylephrine or 5 mg inj. Ephedrine and observed that there was no difference between the groups regarding vasopressor therapy (P = 0.82).

The APGAR Scores at 1 min. & 5 min. after delivery of baby were >7 and similar among the three study groups in our study(P >0.05). Thomas D.G. et al,\textsuperscript{6} Sahu D. et al,\textsuperscript{19} Gunda C.P. et al\textsuperscript{18} & Ngan Kee W.D. et al\textsuperscript{21} did studies similar to ours and observed that the clinical neonatal outcome (APGAR scores) were similar and ≥7 in all neonates. Md. Arshad Imam\textsuperscript{23} gave IV boluses of phenylephrine or ephedrine and observed that APGAR scores at 1 and 5 minutes were >7 for all the neonates in the two groups.

Gambling et al (2010)\textsuperscript{24} said about the use of phenylephrine & ephedrine in caesarean delivery –

1. Phenylephrine can cause bradycardia that requires treatment with atropine, more so with an infusion.

2. The observed differences in neonatal acid-base status observed in many studies aren’t clinically important.

Ephedrine, a mixed agonist of $\alpha$ and $\beta$ adrenoreceptor, maintains blood pressure mainly by activating $\beta_1$ adrenoreceptor and increasing cardiac output and heart rate. However, ephedrine can cross the placental barrier and causes an increase in foetal heart rate and foetal catecholamine levels which increase oxygen consumption and glucose and lactic acid concentrations. Phenylephrine is a pure $\alpha_1$ adrenergic agonist and counteracts the decrease in systemic vascular resistance induced by subarachnoid block.\textsuperscript{13} Although phenylephrine reduces uterine blood flow, studies show that it does not affect foetal outcome and can be used safely during subarachnoid block for caesarean section.\textsuperscript{10}

The percentage decrease in placental perfusion is related to the percentage reduction in maternal arterial pressure and not to the absolute reduction in pressure. Hence, maternal hypotension should be aggressively managed specially for the first 5-10 minutes, when the spinal block is evolving. This minimizes the risk of foetal acidosis.\textsuperscript{14}

5. Conclusion

All three vasopressors in the study, phenylephrine, ephedrine & mephentermine effectively maintained arterial blood pressure during subarachnoid block for caesarean section and can be safely used to treat hypotension. Phenylephrine caused a significant reduction in heart rate compared to ephedrine and mephentermine which may be advantageous in cardiac patients or in whom tachycardia is undesirable. All drugs did not have any statistically significant adverse effects clinically on the mother or the foetus.

5.1. Limitations of this study

1. A higher sample size could have been included in the study groups.
2. Though umbilical cord blood gas analysis is the most sensitive indicator of fetal oxygenation and acid-base condition in the immediate peripartum period, it could not be performed due to financial constraints and ethical issues.

3. Parturients of only ASA physical status class II planned for elective lower segment caesarean section have been included in this study. Further studies are required to evaluate the effects and compare vasopressors for use in ASA physical status class III and IV, cardiac conditions and emergency surgeries.

6. Source of funding

None.

7. Conflict of interest

None.

References

1. Lee A, Kee WDN, Gin T. A quantitative systematic review of randomised controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anaesthesia for caesarean delivery. *Anaesth C*. 2002;94:920–926.

2. Emmett RS, Cyna AM, Andrew M, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. *Cochrane Database Syst Rev*. 2002;(3).

3. Ngankee WD, Khaw KS. Vasopressors in obstetrics: what should we be using? *Curr Opin Anaesthesiol*. 2006;19:238–243.

4. Mercier FJ, Bonnet MP, Dorie ADL, Mouguouki M, Banu F, et al. Spinal anaesthesia for caesarean section. Fluid loading, vasopressors and hypotension. *Ann Fr Anaesth Reanim*. 2007;26:688–693.

5. Mitra JK, Roy J, Bhattacharyya P, Yunus M, Lyngdoh N. Changing trends in the management of hypotension following spinal anaesthesia in caesarean section. *J Postgrad Med*. 2013;59:121–126.

6. Thomas DG, Robson SC, Redfern N, Hughes D, Boys RJ. Randomized trial of bolus phenylephrine or ephedrine for maintenance of arterial pressure during spinal anaesthesia for caesarean section. *Br J Anaesth*. 1996;76:61–65.

7. Mahajan L, Anand LK, Gombar KK. A randomized double-blinded comparison of ephedrine, phenylephrine and mephentermine infusions to maintain blood pressure during spinal anaesthesia for caesarean delivery. The effects on fetal acid-base status and haemodynamic control. *J Anaesthesiol Clin Pharmacol*. 2009;25(4):427–427.

8. Gunda CP, Malinowski J, Tegginmath A, Suryanarayana VG, Chandra SBC. Vasopressor choice for hypotension in elective Caesarean section: Ephedrine or phenylephrine? *Arch Med Sci*. 2010;6:257–263.

9. Ganeshnavar A, Uday SA, Shettar AE, Koppal R, Ravi R. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. *J Clin Diagnostic Res*. 2011;5(5):948–952.

10. Das S, Potli S, Madhusudhana R. A comparative study of phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. 2015;13(5).

11. Bhattarai B, Bhat SY, Upadya M. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. *JNMA J Nepal Med Assoc*. 2010;49:23–28.

12. Nazir I, Bhat MA, Qazi S, Buchh VN, Gurcoo SA. Comparison between phenylephrine and ephedrine in preventing hypotension during spinal anaesthesia for caesarean section. *J Obstet Anesth Crit Care*. 2012;2:92–97.

13. Lin FQ, Qin MT, Ding XXXX, Sh KF, Li Q. Ephedrine versus phenylephrine for the management of hypotension during spinal anaesthesia for caesarean section: An updated meta-analysis. *CNS Neurosci Ther*. 2012;18:591–597.

14. Bhardwaj N, Jain K, Arora S, Bharti N. A comparison of three vasopressors for tight control of maternal blood pressure during caesarean section under spinal anaesthesia: Effect on maternal and fetal outcome. *J Anaesthesiol Clin Pharmacol*. 2013;29(1):26–31.

15. Soxhuku-Isufi A, Shpata V, Sula H. Maternal and neonatal effects of vasopressors used for treating hypotension after spinal anaesthesia for caesarean section: A Randomized Controlled Study. Open Access Maced. J Med Sci. 2016;4(1):54–58.

16. Natarajan AK, Singh NR, Singh LP, Devi RS, Devi NA, Jack A. Comparison of intravenous bolus phenylephrine and intravenous ephedrine during crystalloid coloading in ameliorating hypotension under spinal anaesthesia for caesarean section. *J Med Soc*. 2015;29:155–159.

17. Lonkar SS, Khatavkar SS, Thatte WS, Santhi N. Comparison Between phenylephrine, ephedrine and mephentermine in preventing hypotension during spinal anaesthesia for caesarean section and their effect on fetal outcome. *IOSR J Dent Med Sci* (IOSR-JDMS). 2016;15(9):52–58.

18. Yeoh SB, Sng BL, Sia ATH. Anaesthesia for lower-segment caesarean section: Changing perspectives. *Indian J Anaesth*. 2010;54:409–414.

19. Sahu D, Kothari D, Mehrotra A. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. *Ind J Anaesth*. 2003;47(2):125–128.

20. Saravanan S, Koscarev M, Wilson RC, Watkins E, Cumbol MO, Lyons G. Equivalent dose of ephedrine and phenylephrine in the prevention of post-spinal hypotension in Caesarean section. *Br J Anaes*. 2005;96(1):95–99.

21. Kee N, Khaw WD, Lau KS, Ng TK, Chui FF, et al. Randomised double-blinded comparison of phenylephrine vs ephedrine for maintaining blood pressure during spinal anaesthesia for non-elective Caesarean section. *Anaesth*. 2008;63:1319–1326.

22. Mohta M, Janani SS, Sethi AK, Agarwal D, Tyagi A. Comparison of phenylephrine hydrochloride and mephentermine sulphate for prevention of post spinal hypotension. *Anaesth*. 2010;65:1200–1205.

23. Imam AA. Comparison of vasopressor effects of bolus infusions of phenylephrine and ephedrine for maintenance of maternal arterial pressure during spinal anaesthesia in caesarean section. *J Evol Based Med Healthsc*. 2015;2(18):2439–2444.

24. Gambling DR, McLaughlin KR. Ephedrine and phenylephrine use during caesarean delivery. *Anaesthesiol*. 2010;112:1287–1288.

Author biography

Garima Sinha Senior Resident

Hemalatha S Professor

Gurudatt C L Professor & HOD

Cite this article: Sinha, Hemalatha S, Gurudatt C L. Effectiveness of intravenous boluses of phenylephrine, ephedrine and mephentermine as vasopressors for management of perioperative hypotension in elective lower segment caesarean section under spinal anaesthesia – A prospective comparative study. *Indian J Clin Anaesth* 2020;7(1):46-53.