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Dr. P Savanth Kumar
Associate Professor,
Department of Anaesthesia,
Ayaan Institute of Medical
Sciences, Kanakamamidi (V),
Moinabad (M), Ranagareddy
(D), Telangana, India

Dr. P Lokesh
Assistant Professor,
Department of Anaesthesia,
Modern Government
Maternity Hospital, Osmania
Medical College, Petlaburj,
Hyderabad, Telngana, India

Dr. Balad Karunakar
Senior Resident, Department
of Anaesthesia, King Koti
District Hospital, Hyderabad,
Telangana, India

Corresponding Author:
Dr. P Savanth Kumar
Associate Professor,
Department of Anaesthesia,
Ayaan Institute of Medical
Sciences, Kanakamamidi (V),
Moinabad (M), Ranagareddy
(D), Telangana, India

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

Dr. P Savanth Kumar, Dr. P Lokesh and Dr. Balad Karunakar

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Abstract

Background: Spinal anaesthesia for caesarean section has several advantages over general anaesthesia like decreased risk of failed intubation, decreased risk of pulmonary aspiration of gastric contents, avoidance of the depressant effects of general anaesthetics on neonate etc.

Aim and Objectives: This comparative study was designed to evaluate the efficacy of Mephentermine and Phenylephrine in treating hypotension during spinal anaesthesia for cesarean section. The incidence of undesirable side effects like maternal bradycardia, nausea and vomiting also noted.

Methodology: The study was conducted in the Department of OBG the Maternity Hospital, Osmania Medical College during the year August 2018- November 2019. The study includes 60 patients grouped into two groups.

Results: Both Phenylephrine and Mephentermine maintained the arterial pressure effectively within 20% of baseline values. The mean value of heart rate was high in Mephentermine group compared with Phenylephrine group. The mean values of Systolic BP, Diastolic BP and MAP were higher in Phenylephrine group compared with Mephentermine group throughout the study period. Phenylephrine group required fewer number of bolus doses when compared with Mephentermine. The heart rate generally remained low throughout the study period in Phenylephrine group and the incidence of bradycardia was more in Phenylephrine group when compared with Mephentermine group. The occurrence of nausea and vomiting were similar in both groups.

Conclusion: Thus, it can probably enhance organ blood flow more than mephentermine. Mephentermine increases heart rate and thus may be avoided in population where the effect may be detrimental.

Keywords: Mephentermine, phenylephrine, heart rate, nausea, vomiting.

Introduction

Spinal anaesthesia for caesarean section has several advantages over general anaesthesia like decreased risk of failed intubation, decreased risk of pulmonary aspiration of gastric contents, avoidance of the depressant effects of general anaesthetics on neonate etc. Developments in regional anaesthesia have increased the relative risk of fatality during general anaesthesia for caesarean delivery to more than 16 times ^[1].

Single shot spinal is most commonly performed because it is simple, quicker, has faster onset with superior block and infrequent failure, lesser risk of systemic toxicity due to local anesthetic agent and lesser transfer to fetus as lower doses are used and its cost effectiveness. However, single shot spinal anaesthesia has its own bag of adverse effects. The most common adverse effect is hypotension, primarily because of sympathectomy associated with lumbosacral block. The incidence of hypotension during spinal anaesthesia is as high as 75-85% ^[2].

The clinical question of acceptable level of arterial blood pressure decrease after neuraxial block is acceptable remains to be answered. However, placental perfusion may be reduced in supine parturient even when mean arterial blood pressure is measured normal ^[3]. Hypotension during spinal anaesthesia for cesarean delivery may thus further reduce it and may result in fetal acidosis, hypoxia and neurological injury besides maternal nausea and vomiting, dizziness and severe hypotension may result in loss of consciousness and sudden cardiac arrest ^[4].

Several pharmacologic and non-pharmacologic methods have been used for management of hypotension, with no single method adequate or conclusively superior.

Amongst the vasopressors used (ephedrine, phenylephrine, metaraminol, mephentermine) none is although ephedrine has been used as the agent of choice, but the position has been challenged because of potential to cause supraventricular tachycardia (SVT), tachyphylaxis and fetal acidosis [5-8].

Recent studies favour phenylephrine, an $\alpha 1$ agonist which elevates arterial blood pressure by increasing systemic vascular resistance secondary to vasoconstriction. Since the primary mode of hypotension during spinal anesthesia is vasodilatation, it seems physiologic to use the vasoconstrictor. However, it causes bradycardia and serial dilution for i.v. administration is source of error [9]. It may cause uterine arteriolar constriction and thus diminishing uterine blood flow.

Mephentermine, which has mechanism of action similar to ephedrine, has been used for treatment of hypotension during spinal anesthesia [10, 11]. Mephentermine is direct and indirect sympathomimetic action and probably the increase in arterial blood pressure is chiefly by increased cardiac output. This may be favourable for placental circulation.

The present study has been conducted in Modern Maternity Hospital Petlaburj, Maternity Hospital, Sultan bazaar Maternity Hospital and Niloufer Hospital under Osmania Medical College, Hyderabad from August 2018 to November 2019. It attempts to compare bolus of the two vasopressors: phenylephrine and mephentermine as treatment of hypotension during spinal anaesthesia for cesarean section. Conclusively better over the other [5].

Aims and Objectives

Aim of the study

To compare bolus Phenylephrine and Mephentermine for hypotension during spinal anaesthesia in caesarean section.

Objectives of study

To compare phenylephrine and mephentermine for maintenance of the arterial blood pressure in women undergoing cesarean delivery under spinal anesthesia.

- To compare effect of the two drugs on heart rate.
- To compare incidence of nausea, vomiting.

Materials and Methods

Source of data

This is a prospective comparative study. The study was conducted in maternity hospitals under Osmania medical college, Hyderabad from August 2018 to November 2019.

The study protocol and consent form were reviewed and approved by the Osmania medical college ethical and scientific committee. A written informed consent was taken from the parturients.

Study design

60 parturients, aged between 20 and 40 years, between 34 to 40 weeks of gestational age posted for elective lower segment cesarean section were included. They were divided into two groups:

- In Group P, 30 parturients were included.
- In Group M, 30 parturients were included.

Detailed history was taken from the parturient. Clinical examination and preanesthetic assessment was done.

Inclusion criteria

- ASA grade I and II
- Age 20 to 40 years of age
- Patients who gave written informed consent
- Patients scheduled for elective cesarean delivery under spinal anaesthesia.

Exclusion criteria

- ASA grade III or greater
- Age more than 40 years, less than 20 years
- Base line heart rate less than 60 bpm
- Base line blood pressure less than 100/60 mmHg

Patients with history of hypertension, pre eclampsia/eclampsia, ischemic heart disease, heart block, left ventricular failure, severe renal or hepatic disease, glaucoma, occlusive vascular disorders. Any history of hypersensitivity to local anaesthetic and any contraindications to spinal anaesthesia.

Procedure

Once the patient was shifted to the operating room, standard monitors which included NIBP, pulse oximeter and ECG were connected to the patient. All the resuscitation equipments and the emergency drugs were kept ready. The anesthesia machine was also checked along with the oxygen delivery system.

Intravenous access was secured with 18G IV cannula. All patients were preloaded with lactated Ringer's solution, 15ml/kg body weight, before the anesthesia was administered. The preloading was done with patient in left lateral position and continuous monitoring of heart rate (HR) and blood pressure (BP). Baseline preoperative SBP, DBP, MAP and HR were calculated as mean of 3 consecutive measurements, 2 minutes apart.

Patients were reassured and explained about the technique. Spinal anesthesia was administered, with patient in left lateral position with knees and chin flexed over the abdomen. Under strict aseptic precautions, after skin infiltration with 1ml of 2% lignocaine, lumbar puncture was performed by midline approach by using disposable

Quincke Babcock spinal needle (25G) in L3-L4 intervertebral space. After free flow of CSF, 10 mg (2 ml) of hyperbaric bupivacaine, 0.5% was injected intrathecally and the patient returned to supine position with left uterine displacement. A 10-15 degree head down tilt was used to facilitate upward spread of local anesthetic. O₂ support was given to each patient via Hudson's mask at 4 L/min.

Level of anesthesia was tested with pin prick. With the onset of sensory blockade to T4-T6 level and grade III motor blockade (Bromage scale) surgery was started.

SBP, DBP, MAP and HR recorded 1, 2, 3, 5 mins after sub arachnoid block for first 10 minutes and every 5 min thereafter till the completion of surgery. Spinal hypotension was defined as fall of greater than 20% mean arterial pressure (MAP) from baseline and Intravenous Mephentermine 6 mg or phenylephrine 100 mcg to treat hypotension, the dose was repeated at 5 minutes interval if necessary. Intra operative fluid requirement also was noted.

Bromage scale

1. Full flexion of knees and feet.
2. Inability to raise extended leg, can bend knee.

3. Inability to bend knee, can flex ankle.
4. No movement.

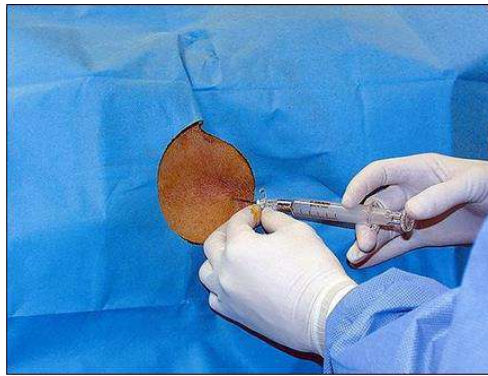


Fig 1: Technique of spinal anesthesia

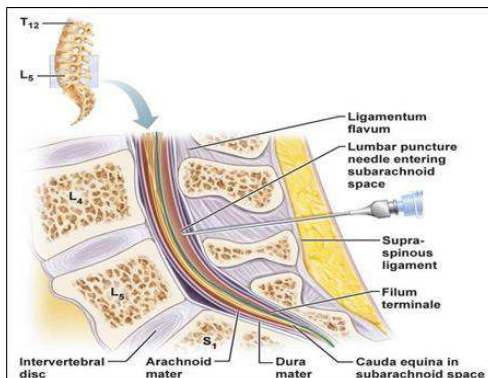


Fig 2: Anatomy of subarachnoid space

Statistical analysis

Appropriate statistical tests were done to compare between qualitative data and quantitative data. The qualitative data were presented in the form of number and percentage and the quantitative data were presented in the form of mean and standard deviation. Statistical analyses were performed using the SPSS version 17.0 program for Windows. Student’s t-test was used for continuous, normal variables. For categorical data, Chi-square test was used to compare the differences in variables between the two groups. A two-sided p value of <0.05 was considered statistically significant

Results

The following observations were made in 60 pregnant women undergoing LSCS. 30 each in group P and group M in maternity hospitals under Osmania general hospital, Hyderabad from January 2018 to June 2019. Demographic data were noted and hemodynamic parameters were compared between the two groups. Data obtained is presented as Mean ± Standard deviation.

Demographic profile

Table 1: Comparison of age

| Age (Years) | Phenylephrine | Mephentermine |
|-------------|---------------|---------------|
| Mean ± S.D. | 26.42±3.50 | 25.63±2.80 |

The women in both groups were between 20 to 40 years the difference in age between the two groups was statistically not significant. In intergroup comparison of age, p value was 0.33, which is statistically not significant.

Table 2: Comparison of height

| Height (cms) | Phenylephrine | Mephentermine |
|--------------|---------------|---------------|
| Mean ± S.D. | 154.3±4.1700 | 156.2±4.62 |

The maximum number of women were in height range of 156 to 160cms. There was no significance in the distribution of women in regard to height.

In intergroup comparison of height, p value was 0.099, which is statistically not significant.

Table 3: Comparison of weight

| Weight (kgs) | Phenylephrine | Mephentermine |
|--------------|---------------|---------------|
| Mean ± S.D. | 63.63±3.5958 | 64.93±4.0593 |

In intergroup comparison of weight, p value was 0.1935, which is statistically not significant.

Table 4: Distribution of average SBP within 5 mins of SAB and 1st minute after giving vasopressor

| Time | Group-P | Group-M | P value |
|------------------------|---------|---------|---------|
| Baseline | 118 | 116 | 0.42 |
| 1min | 125 | 118 | 0.08 |
| 2min | 109 | 108 | 0.95 |
| 3min | 90 | 93 | 0.84 |
| 5min | 85 | 86 | 0.42 |
| 1min after vasopressor | 145 | 109 | 0.0001 |

SBP within 5 mins of SAB & 1st min after vasopressor Table and Figure shows that Within 5 minutes of SAB, 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 ‘P’ group shows very high average SBP compared to Group-M which is statistically highly significant (p<0.0001)

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

| Time | Group-P | Group-M | P value |
|------------------------|---------|---------|---------|
| Baseline | 76 | 75 | 0.78 |
| 1 min | 79 | 76 | 0.26 |
| 2 min | 69 | 71 | 0.56 |
| 3 min | 60 | 55 | 0.87 |
| 5 min | 50 | 52 | 0.58 |
| 1min after vasopressor | 89 | 70 | 0.0001 |

Table and Figure shows that Within 5 minutes of SAB, 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).

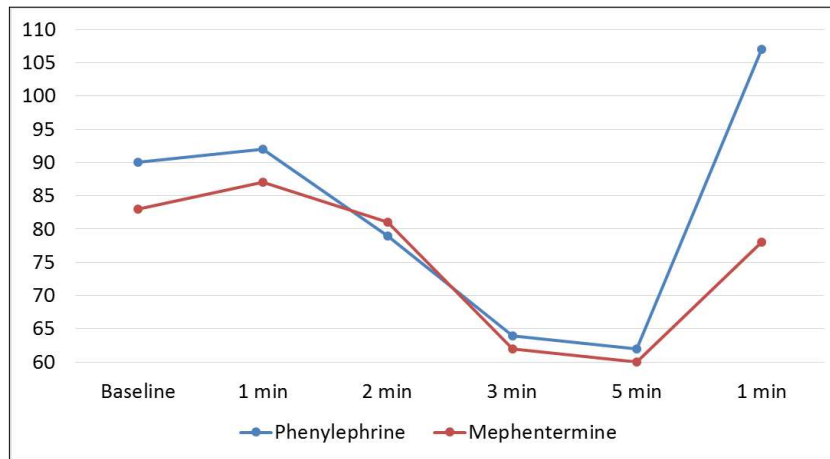


Fig 3: Map within 5 mins of SAB and 1 min after vasopressor

Figure shows that Within 5 minutes of SAB, 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 ($p < 0.0001$).

in the heart rate compared to Group-M which is statistically highly significant ($p < 0.0001$).

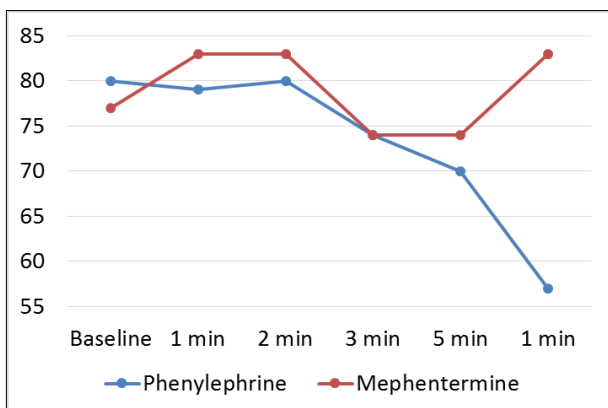


Fig 4: HR within 5 mins of sab and 1 min after vasopressor

Table and Figure 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

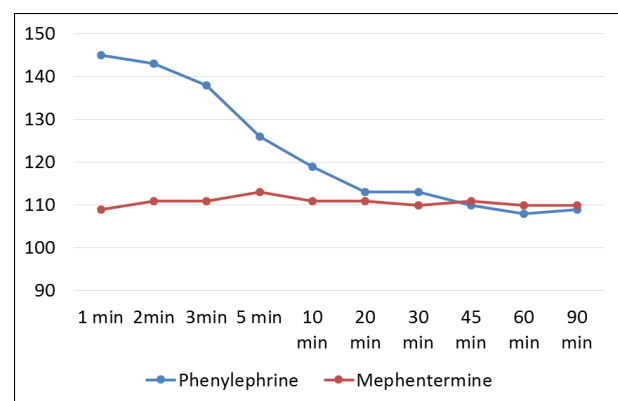


Fig 5: Distribution of SBP after giving vasopressor intraoperatively

Figure reveals that there is significant difference of average SBP between two groups up to 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.

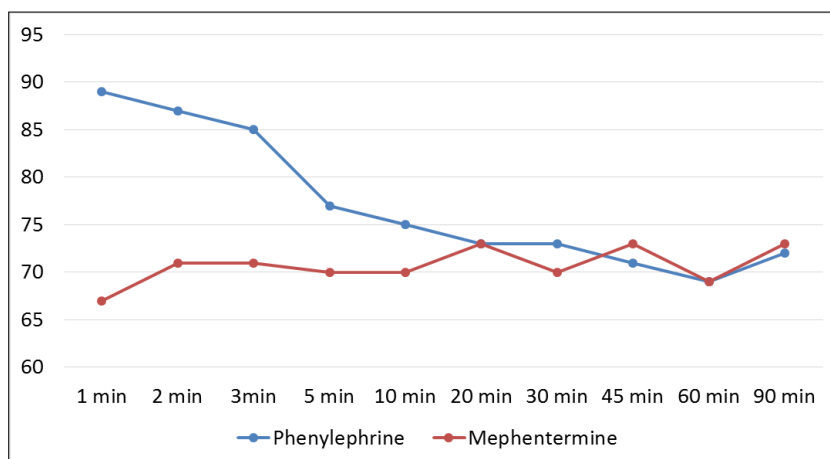


Fig 6: Distribution of DBP after giving vasopressor intraoperatively

Table and figure reveals that there is significant difference of average DBP between two groups

Up to 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.

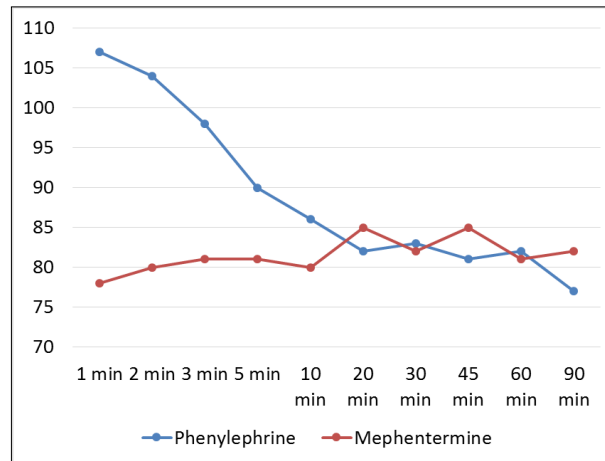


Fig 7: Distribution of MAP after giving vasopressor intraoperatively

Table and figure reveals that there is significant difference of average MAP between two groups up to 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.

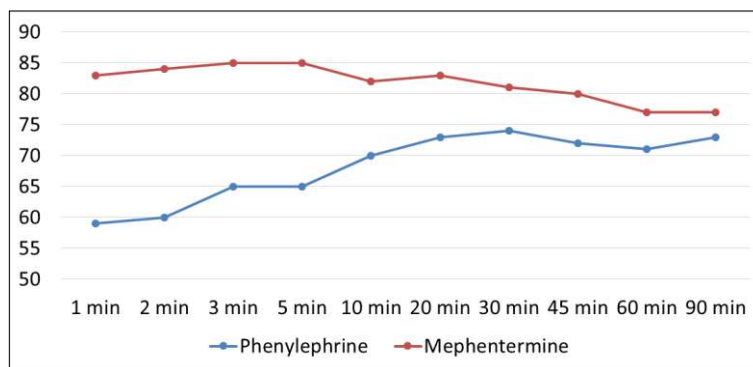


Fig 8: Distribution of HR after giving vasopressor intraoperatively

Table and figure 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 6: Comparison of no of doses of vasopressors

| No of doses | Group-P (n=30) | Group-M (n=30) |
|-------------|----------------|----------------|
| 1 | 23 (77.77%) | 16 (55.55%) |
| 2 | 5 (15.55%) | 7 (22.22%) |
| 3 | 2 (6.66%) | 7 (22.22%) |

No. of repeated doses required is more in Group-M compared to Group-P

Table 7: Comparison of incidence of nausea and vomiting between group-P and group-M

| Severity | Group-P (n=30) | Group-M (n=30) |
|----------|----------------|----------------|
| None | 27 | 24 |
| Nausea | 2 | 3 |
| Retching | 0 | 1 |
| Vomiting | 1 | 2 |

Incidence of nausea and vomiting is almost similar in both groups.

Table 8: Comparison of incidence of other effects between groups

| Event | Group-P (n=30) | Group-M (n=30) |
|-------------------|----------------|----------------|
| Bradycardia | 3 | 0 |
| Shivering | 2 | 4 |
| Dysrhythmia | 0 | 0 |
| Fetal Bradycardia | 0 | 0 |

Incidence of bradycardia is more in Group-P than Group-M

Discussion

After subarachnoid block for caesarean section, hypotension can be minimized by the use of IV fluid preload, avoidance of aortocaval compression and judicious use of vasopressor agent. It has been shown that the percentage decrease in placental perfusion is related to the percentage reduction in maternal arterial pressure and not to the absolute reduction in pressure ⁴¹. For the purpose of this study, hypotension was defined as a decrease in arterial pressure greater than 20% from baseline systolic pressure. Mephentermine has mixed action directly as well as indirectly on α and β receptors, whereas Phenylephrine has pure α receptors activity.

The current study was conducted to compare the two commonly used vasopressors for their efficacy at maintaining the arterial blood pressure. After the selection

of the participants, they were allocated to receive i.v bolus of either phenylephrine 100 mcg. or mephentermine 6 mg on developing hypotension. The method of randomization was allocation by sealed envelope technique. Data was collected and the results were summarized and analyzed statistically by appropriate method.

The demographic data, baseline parameters were comparable in both groups. The hemodynamic parameters at the development of hypotension were also comparable between the groups. The mean time to development of hypotension after administration of spinal anaesthesia was 7.3778 ± 2.20834 (mean \pm SD) minutes in group P and 6.9778 ± 2.47247 (mean \pm SD) minutes in group M. The values were comparable with $p=0.420$.

Haemodynamic variables

Blood pressure: The systolic, diastolic and mean arterial pressure were decreased statistically significant at the onset of hypotension and increased after the bolus dose of drugs. The pressures generally remained high in both. Systolic blood pressure was generally highest in Phenylephrine group immediately after the administration. The diastolic blood pressure was also greater in Phenylephrine group when compared Mephentermine group. Especially after 2nd and 4th minute, after administration of the drug. This finding is consistent with the onset of action and efficacy of the drug that Phenylephrine has quicker onset of action and better maintenance of arterial pressures when compared with the Mephentermine group. The primary mechanism of elevation of arterial blood pressure by phenylephrine is by vasoconstriction due to predominantly α_1 agonist activity whereas mephentermine increases MAP by augmenting cardiac output by increasing heart rate and myocardial contractility due to its α and β agonist activity. The significant differences in diastolic blood pressure in the current study presumably reflect the predominantly α_1 mediated vasoconstriction increased SVR due to phenylephrine.

Dinesh Sahu *et al.*,^[11] studied the effects of bolus Ephedrine, Mephentermine, Phenylephrine for the maintenance of arterial pressure during spinal anaesthesia for LSCS. In their study all the three vasopressor effectively maintained arterial pressure within 20% of baseline value though Phenylephrine maintained better in first 6minutes of bolus dose as compared with Ephedrine and Mephentermine and Phenylephrine has a quicker peak effect. This finding is consistent with present study.

Adrienna Stewart^[12] investigated circulatory effects of single intravenous injections of 0.75 mg/kg Mephentermine in five healthy volunteer subjects. They found that first injection of Mephentermine increased mean arterial pressure, systemic vascular resistance, and left ventricular minute work, with no change in the other variables.

Heart rate: In our study the mean value of heart rate was generally highest in Mephentermine Group compared with Phenylephrine Group. In spinal anaesthesia, since there is decreased venous return, decreased venous pressure and a decreased right heart pressure thus slowing of the heart rate is expected on the basis of the Bain bridge reflex. Bradycardia is also expected in high spinal, probably due to some paralysis of the cardio-accelerator nerves. We found that the maternal heart rate was slower with Phenylephrine group compared with Mephentermine group. This is consistent with the mechanism of action of these drugs that

the decrease in heart rate found in Phenylephrine group was due to pure α receptor activity compared with Mephentermine group, It has mixed action acts directly as well as indirectly on α and β receptors. Similar results were seen in many studies which was consistent with our study.

Dinesh Sahu *et al.*,^[11] Phenylephrine was found to cause significant reduction in heart rate after the bolus dose. Which was similar with present study In the quantitative systematic review done by Critchley LA *et al.*,^[12] they found that maternal bradycardia was more likely to occur with Phenylephrine than with Ephedrine.

In the study done by Brooker RF *et al.*,^[14] they found that Phenylephrine was associated with a decrease in heart rate and in cardiac output.

The time to first repeat dose of vasopressor was comparable in both the groups. However mean number of doses was significantly more in group M. The sample size of the study might not have been large enough to avoid type II error in the comparison of this variable.

Conclusion

The incidence of nausea and vomiting and other effects was comparable between the two groups. In conclusion from the study that both, phenylephrine and mephentermine maintain systolic blood pressure above hypotensive range, though phenylephrine might be better because number of doses needed is less and since phenylephrine increases diastolic blood pressure more than mephentermine and hence mean arterial pressure is increased. Thus, it can probably enhance organ blood flow more than mephentermine. Mephentermine increases heart rate and thus may be avoided in population where the effect may be detrimental.

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