

Comparison of Phenylephrine, Ephedrine and Mephentermine for Control of Hypotension following Spinal Anaesthesia for Infra-Umbilical Surgeries

Dr. Shweta Naresh Satia¹, Dr. Sameer Kulkarni², Dr. Jyoti Kale³

Abstract: *Background:* Neuraxial anaesthesia remains the preferred choice for infra-umbilical surgeries. Three vasopressors phenylephrine, ephedrine and mephentermine in intravenous bolus form, are effective in maintenance of blood pressure (BP). Absolute supremacy of one vasopressor over the others is not yet established. The current study was undertaken to compare the three vasopressors for maintenance of BP during spinal anaesthesia. *Material and Methods:* Clinical observational study over a period of one year was conducted in a tertiary medical center and teaching hospital in Maharashtra. Ninety patients of American Society of Anaesthesiologist classification: class I and II were distributed into three groups of thirty patients each. Following hypotension, group A received ephedrine 10 mg, group B received mephentermine 10 mg and group C received phenylephrine 100µg as intravenous bolus in 1 ml of 0.9% sodium chloride solution. Blood pressure, heart rate and oxygen saturation were recorded every 2 minutes for first 10 minutes and then every 15 minutes for one hour. *Results:* In ephedrine group 9 (30%) patients required second dose and 8 (26%) patients developed tachycardia. In mephentermine group, 33% patients developed tachycardia and 4 (13%) developed hypertension. In phenylephrine group 8 (26%) developed bradycardia and 3 (10%) developed severe bradycardia pulse rate dropped to 42 /min corrected by giving injection atropine and in all patients BP was maintained within 6-8 minutes after giving vasopressors and only in ephedrine group i.e. 9 patients required two doses of ephedrine. *Conclusions:* All the three vasopressors were equally effective in maintaining blood pressure after spinal anaesthesia induced hypotension. Elevation of systolic pressure in phenylephrine group was significantly high for first 6 min of bolus dose as compared to other two and bradycardia in these patients was a significant finding.

Keywords: hypotension, surgery, tachycardia, bradycardia

1. Introduction

Regional anaesthesia is the preferred choice for infraumbilical surgeries like vaginal or abdominal hysterectomies and surgeries like fractures of lower-limbs across the world.¹ It has established itself as one of the most popular techniques for lower limb and lower abdominal procedures as it has many advantages like adequate relaxation of the muscles and is easy to administer. It offers a fast, profound and high quality sensory and motor block in patients undergoing infra-umbilical surgeries.¹ Hypotension usually occurs after spinal anaesthesia and should be treated with prompt action and aggressive management to stabilise the patient so that the risk of cardiac arrest is minimised. The simplicity of the technique, reliable effect and lack of all those complications that are associated with general anaesthesia has made it a safe alternative.² The fatality rate directly attributed to anaesthesia, is approximately 17-fold more frequent with GA as compared to regional anaesthesia.³ Careful positioning volume preloading with crystalloids or colloids has been used to prevent it, but these are not complete measures⁴ and vasopressors are required to correct hypotension quickly, these agents have been tried to counteract the hypotensive effect of subarachnoid block, and their main action being vasoconstriction and increase in the cardiac output.⁵ In practice, the most commonly used drugs are the sympathomimetic agents which exert their effects through the adrenergic receptors, either acting directly or indirectly. Also it has been found that the three vasopressors phenylephrine, ephedrine and mephentermine in intravenous bolus form, are effective in maintenance of arterial pressure within 20% limit of baseline, although action of phenylephrine is faster as compared to ephedrine and

mephentermine⁵. Thus it is clear that which drug among the three is superior to the other is not yet concluded and hence we decided to conduct the present study.

Objective

The objective of this study was to compare the control of blood pressure and assess safety profile of three vasopressors phenylephrine, ephedrine and mephentermine during spinal anaesthesia in lower abdominal surgeries.

2. Material and Methods

A clinical observational study over a period of one year from June 2018 to June 2019 was conducted in the Department of Anaesthesiology at a tertiary care medical center and teaching hospital. All patients undergoing infra-umbilical surgeries with American Association of Anaesthesiology Classification (ASA) grade 1 and 2 were included those with ASA grade 3 and 4, pregnant women, and patients not giving consent were excluded. Enrolled patients were divided into Group A where ephedrine was given and Group B where mephentermine was used and Group C where phenylephrine was used. Following hypotension, defined as blood pressure less than 90mm of Hg systolic and less than 60 mm Hg diastolic. Group A received ephedrine 10 mg, group B received mephentermine 10 mg and group C received phenylephrine 100µg as intravenous bolus in 1 ml of 0.9% sodium chloride solution. Vital parameters like blood pressure (systolic, diastolic and mean), heart rate and oxygen saturation were recorded preoperatively as well as intra-operatively every 2 minutes for the first 10 minutes and then every 15 minutes for one hour. First assessment of the patient was done during the pre-

anaesthesia workup to rule out any conditions listed in the exclusion criteria. A second assessment was done immediately prior to the SA after confirming that there are no contraindications. BP was checked immediately after SA and also every 2 minutes for first 10 minutes. If hypotension was detected i.e. when systolic BP was less than 90 mm of Hg then vasopressors were given. Any side effects observed were recorded. Patients were counselled during the routine pre-anaesthesia check-up and also prior to anaesthesia.

Anaesthesia procedure

Patients were kept nil by mouth for 6-8 hours prior to surgery. On the day of surgery, patients received pre-medications with a single injection of metoclopramide 10 mg and a single injection of pantoprazole 40 mg intravenous one hour prior to surgery. After securing intravenous access and attaching monitors patients in all three groups were pre-loaded with Ringer Lactate 10 ml/kg 20 min before spinal anaesthesia. The operating table was kept flat. Using aseptic precautions, lumbar puncture performed at L3-4 using midline approach with 26 Gauge sterile Quinke's needle with the patient in sitting position. After visualization of clear and free flow of cerebrospinal fluid bupivacaine 0.5% heavy, 2.2 ml bolus was injected into L3-4 subarachnoid space patients then turned to supine position with a wedge under the right buttock. Thereafter oxygen through facemask at the rate of 4L/min was administered.

Antiemetic injection ondansetron 0.08-0.1mg/kg and anxiolytic injection midazolam 0.02-0.05mg/kg was given. Intra-operative fluids were given as necessary depending on the blood loss and hemodynamic parameters. After recording basal heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial

pressure (MAP), and SPO₂ patients were monitored according to the protocol as indicated in the study design section. If hypotension occurred, one of the vasopressors was given by the anaesthesiologist. Time of vasopressor administration, duration of surgery, and time of hypotension was recorded as minutes after start of surgery. All incidences of bradycardia (heart rate less than 60 bpm) were treated with intravenous atropine 0.6 mg; any tachycardia (HR > 30% above the basal HR) was noted. Intra-operative nausea and vomiting were recorded. Patients were monitored postoperatively in the recovery room for 2 hours.

Statistical analysis

Descriptive analysis is presented in the result section. Categorical data are presented as number and percentages. Group wise comparison of efficacy and side effects is presented.

3. Results

A total of 90 patients were enrolled in the study. Out of these, 40 (44%) were male patients posted for lower limb surgeries and 50 (55%) were females posted for vaginal/abdominal hysterectomies. A total of 22 (24.4%), 34 (37.8%) and 34 (37.8%) patients received ephedrine, mephentermine and phenylephrine respectively. Ephedrine, mephentermine and phenylephrine groups comprised of 10 (45.45%), 16 (47.06%) and 14 (41.18%) male patients respectively. The corresponding number of female patients were 12 (54.55%), 18 (52.94%) and 20 (58.82%) respectively (Figure 1).

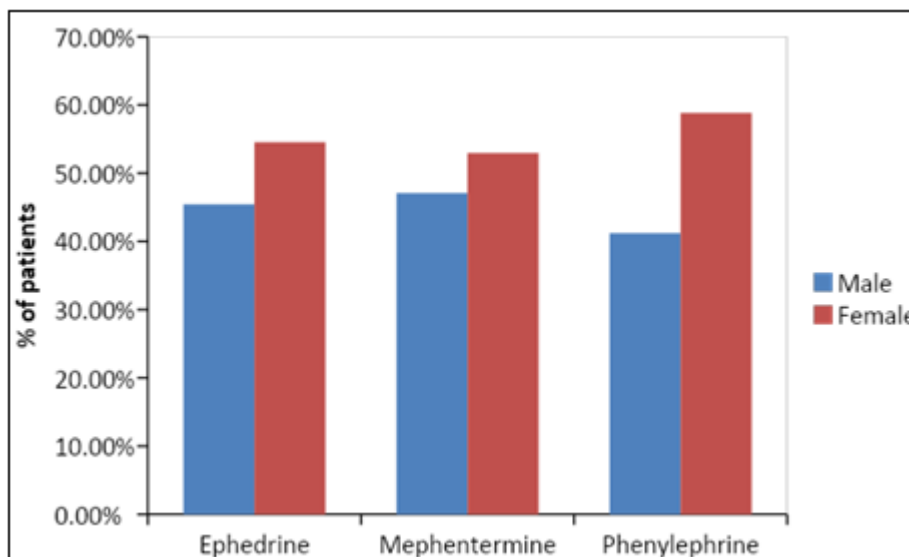


Figure 1: Gender distribution of patients in the study

In a total of 9 (30%) patients from ephedrine group hypotension persisted. The mean arterial pressure after 2 minutes of intravenous bolus was 65 mm Hg, hence these patients required second dose (Figure 2). In all patients BP was controlled after an initial hypotension which developed within 6 to 8 minutes after patient was made to lie down after spinal anaesthesia.

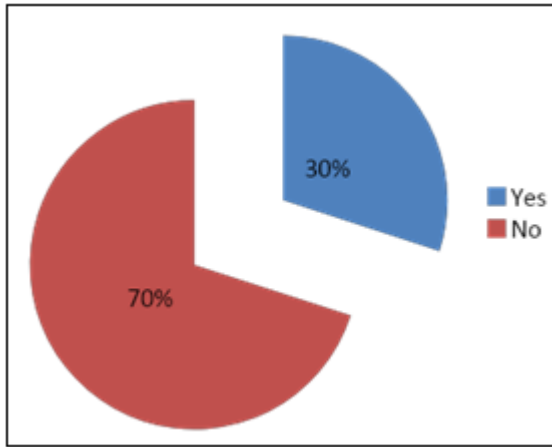


Figure 2: Percentage of patients requiring second dose of ephedrine

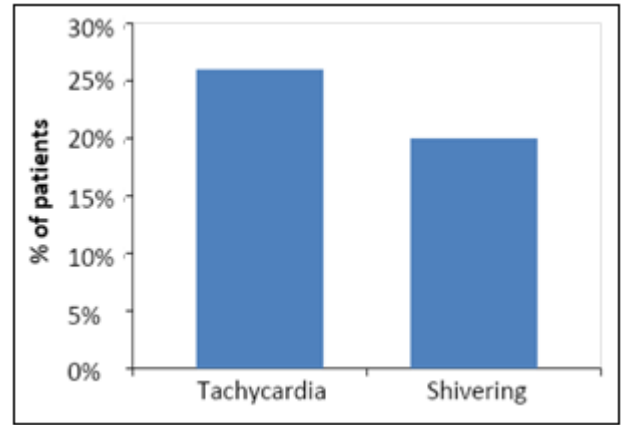


Figure 3: Side effects in patients receiving ephedrine

A total of 8 (26%) patients had tachycardia and 20% of patients had shivering (Figure 3).

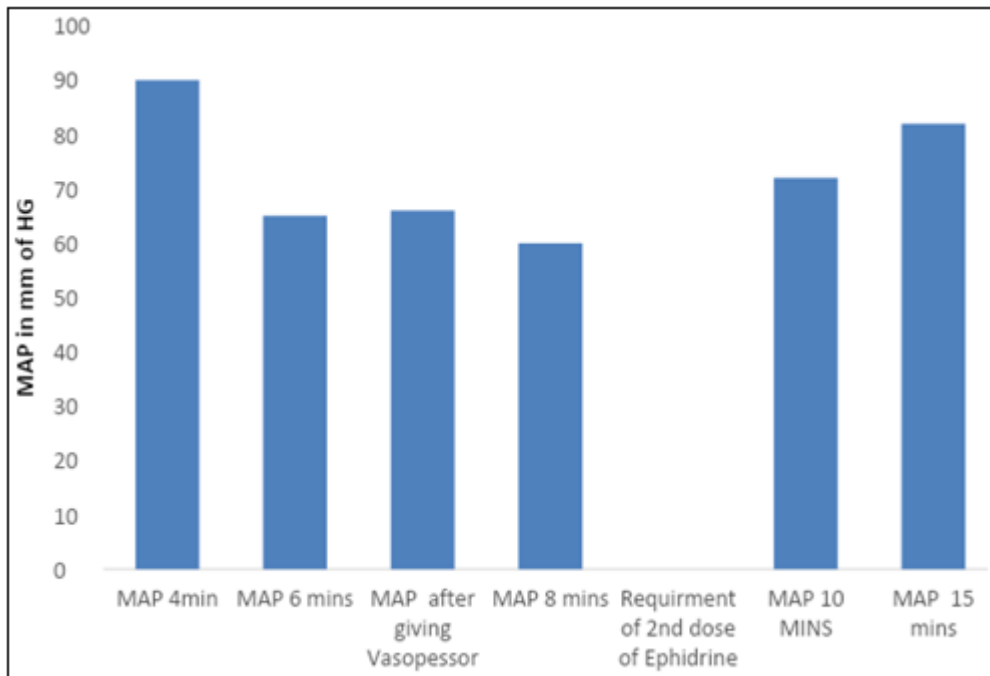


Figure 4: Mean arterial pressure in Group A

A total of 10 (33%) patients in mephentramine developed tachycardia and 4 (13%) developed hypertension because of its inotropic action (Figure 5). In patients receiving mephentermine, MAP increased to 90 mm Hg after an initial drop to 65 mm Hg within 3 minutes after vasopressor bolus and BP was well under control in all patients

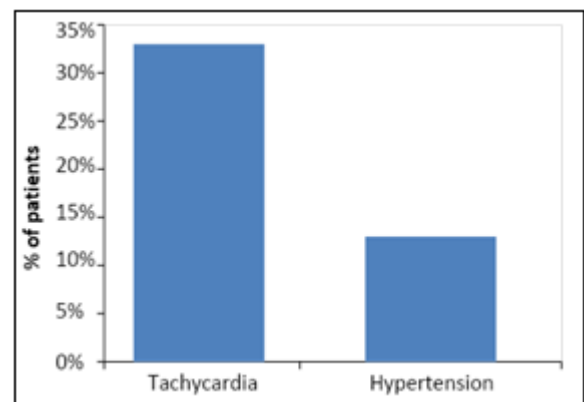


Figure 5: Side effects in patients receiving mephentermine

In phenylephrine group, 8 (26%) developed bradycardia. Pulse rate dropped to 50 beats per minute and only 3 (10%) patients developed severe bradycardia pulse rate ranging

between 42 to 45 beats per minute which was corrected by giving injection atropine so total 11/30 ie 36% had bradycardia and 26% of patients developed headache. Shivering was seen in 28% patients (Figure 6). Its action being quick and short and mean arterial pressure which had dropped to 55 increased to 80 within 1 minute after intravenous bolus.

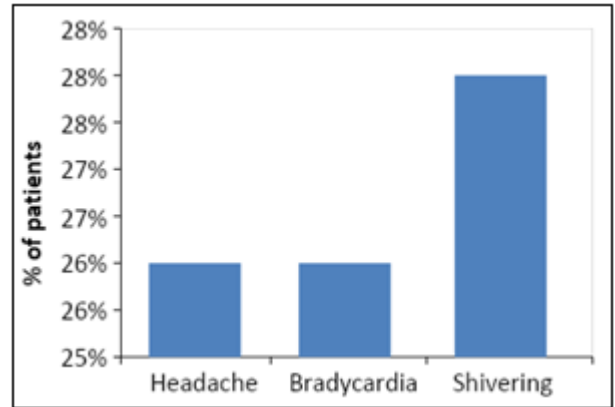


Figure 6: Side effects in patients receiving phenylephrine

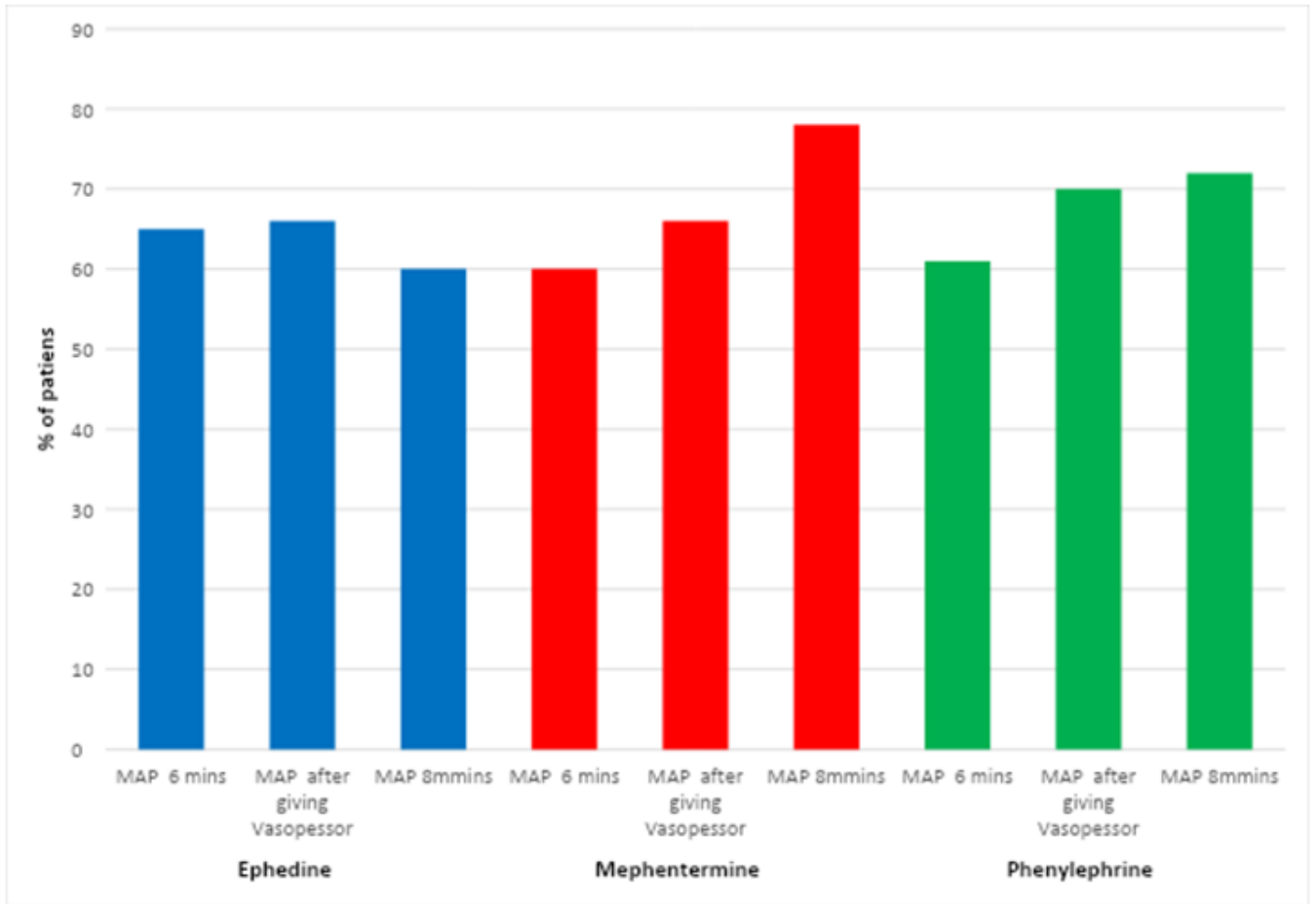


Figure 8: Comparison of three groups i.e. ephedrine, mephentermine and phenylephrine

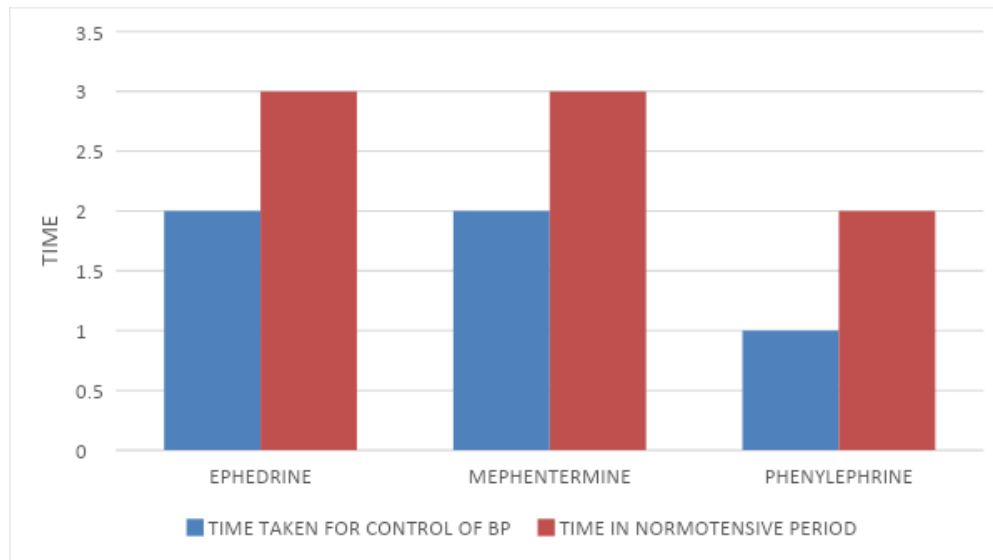


Figure 9: Onset and duration of response in three group

4. Discussion

Hypotensive effects of spinal anesthesia are widely studied in Ceasarean Sections which occur due to the compounding effects of aortocaval compression and various physiological changes of pregnancy. Despite being the subject of research since decades with numerous attempts to restrict the incidence it still remains an important cause for concern⁶. It has been realized that hypotension can be a major limiting factor for a more widespread use of spinal anaesthesia. Vasopressors with different pharmacological actions are used for counteracting spinal hypotension. Intravenous bolus or infusion of vasopressors with side by side monitoring of patients response has a greater margin of safety and better flexibility. The aim of the present study was to compare the use of Phenylephrine, Ephedrine, and Mephentermine for control of Blood pressure for spinal induced hypotension in below umbilical surgeries The commonest procedure in each type of surgery performed was Total abdominal hysterectomy with salpingo- oophorectomy or Vaginal hysterectomies as 55% of patients in the study group were females from Gynaec operation theatre and 44 % of patients were from Orthopedic operation theatre undergoing lower limb surgeries. In Group C as compared to Group A and Group B Bradycardia was an important finding and similar observation was also made by Bhattarai *et al.*⁷ Tachycardia was noted in patients who received Ephedrine or Mephentrimine while bradycardia was noted with Phenylephrine which was corrected with injection Atropine

0.6mg as reported by Mohta *et al*⁸ was also seen in the present study . All the three vasopressor agents were equally effective in maintaining the vital parameters like heart rate and blood pressure as was also found in the study done by Mahajan *et al.*⁹. Nausea and Vomiting occurred in all the groups but was more associated with hypotension¹⁰ Mean arterial pressure was found to be higher in group C as compared to the other two groups as was seen in a study done by Sahu *et al.*¹¹. Action of Ephedrine and mephentermine is on both alpha and beta receptors, whereas phenylephrine has pure alpha receptors' activity.^{12, 13, 14} A study done by Ganeshnavar *et al.*¹⁵ had findings which were in consonance with the present study. Similar results have been obtained in the present study as the in studies mentioned above except hypertension in 13 % of patients in who received Mephentramine because of its inotropic action and headache in 26% of cases in phenylephrine group . The results of the present study are directly related to the the pharmacological actions of the vasopressor agents Mephenteramine with positive inotropic and chronotropic effect increases the force of contraction of heart. It also produces a positive effect at the sinoatrial node but this effect is usually overcome by increased vagal activity occurring as a reflex to increased blood pressure. Phenylephrine, on the other hand, is a direct-acting synthetic noncatecholamine that principally stimulates the alpha1-adrenergic receptors with minimal effect on the beta-adrenergic receptors

Comparison of our study with similar studies by various authors

Authors	Group A	Group B	Group C
Shifaat et al. ¹	Equally effective in correcting hypotension	Equally effective in correcting hypotension	Equally effective in correcting hypotension
Kamalakannan and Anandha Lakshmi. ⁴	maintenance of maternal arterial pressure within 20% limit of baseline values,	maintenance of maternal arterial pressure within 20% limit of baseline values,	Quicker peak in BP and bradycardia
Kaur D, et al ⁶	Tachycardia	Tachycardia	Bradycardia
Bhattarai et al ⁷	Tachycardia	Tachycardia	Bradycardia
Mohta et al ⁸	Tachycardia	Tachycardia	Bradycardia (23%)
Mahajan et al ⁹	Tachycardia	Tachycardia	Bradycardia
Present Study	Tachycardia	Tachycardia	Bradycardia (26%)

5. Limitations of the Study

Small number of patients and single centre study are the limitations of our work. Larger studies are required to confirm our observations.

6. Conclusion

Effectiveness of ephedrine, mephentramine and phenylephrine was almost equal in controlling the blood pressure for spinal induced hypotension for below umbilical surgeries without any detrimental effects on outcome. Elevation of systolic arterial pressure in phenylephrine was significantly high for first 6 minutes of bolus dose as compared to other two drugs. Significant bradycardia was noted in phenylephrine group.

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