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Hemodynamics following Prophylactic Phenylephrine Infusion in patients undergoing Cesarean Section under Spinal Anesthesia

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ABSTRACT

Introduction

Phenylephrine is considered the vasopressor of choice in hypotension associated with obstetric spinal anesthesia. But the dose and mode of administration that is effective yet safe in mother as well as fetus remains controversial. We studied the hemodynamics of parturients who received prophylactic infusion of phenylephrine 50µg/min following spinal anesthesia.

Methods

Patients posted for elective cesarean section received a prophylactic phenylephrine infusion of 50µg/min immediately after spinal anesthesia for 30 minutes. Parturients were also co-loaded with lactated Ringer's solution 1 litre. Blood pressure and heart rate was monitored at an interval of 3min initially and after the delivery of baby interval was increased to 5min. Episodes of hypotension, reactive hypertension and bradycardia in mother were recorded. Neonatal APGAR score at 1 and 5min was also recorded.

Results

One hundred and forty parturients were included in the study. Twenty patients (14.28%) developed hypotension. Out of 20 patients who developed hypotension, 3 patients (15%) had a single episode, 11 patients (55%) had 2 episodes and 6 patients (30%) had 3 episodes of hypotension. Three patients (2.14%) had reactive hypertension. None of the patients had bradycardia. There was no episode of hypotension induced nausea vomiting. Mean APGAR score at 1min and 5min was 8 and 9 respectively.

Conclusion

The prevalence of hypotension with prophylactic phenylephrine infusion was low. We found minimal episodes of reactive hypertension, no episodes of bradycardia and no adverse effect on fetus. It can be regarded a safe means to minimize hypotension in obstetric spinal anesthesia.

Keywords
Hemodynamics; infusion; phenylephrine; prophylactic; spinal anesthesia

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INTRODUCTION

Spinal anesthesia has become the technique of choice for cesarean section as it is easy to perform, has a rapid onset, provides denser surgical block and has no maternal or fetal risk of toxicity to local anesthetics. However, maternal hypotension is one of the complications of spinal anesthesia. As per a study conducted in a tertiary maternity hospital of our country, the prevalence of post spinal hypotension in obstetric patients when pharmacological prophylaxis is not used has been reported to be 24.8%.[1] Hypotension causes nausea, vomiting and if prolonged can lead to organ ischemia, cardiovascular collapse, utero-placental hypoperfusion, fetal distress and fetal acidosis.[2] Thus, prevention of maternal hypotension is of utmost importance.

Spinal anesthesia causes sympathetic block resulting in arteriolar dilatation and decreased systemic vascular resistance. As vasopressors directly act on the vascular resistance, use of vasopressors has now been emphasized. Phenylephrine is considered vasopressor of choice in obstetric spinal anesthesia.[3,4,5] Maternal bradycardia and reactive hypertension are some of the complications noted with the use of phenylephrine. In our setup, phenylephrine is commonly used for hypotension in obstetric anesthesia. As we do not have a standard protocol for phenylephrine use the dose and mode of phenylephrine is decided by the attending anesthesiologists. Among all the regimens, we studied the hemodynamics of parturients who received continuous infusion of phenylephrine 50µg/min as prophylaxis. Our aim was to determine whether this phenylephrine regime prevents maternal hypotension with minimal risk of reactive hypertension and bradycardia and can be accepted as an optimal regimen in our population.

METHODS

This hospital based cross-sectional study was conducted at Nepal Medical College and Teaching Hospital from March 2022 to November 2022. Ethical approval was obtained from the Nepal Medical College and Teaching Hospital Institutional Review Committee (Reference number: 055-078/079). Among the patients who had singleton pregnancy, who underwent elective cesarean section under spinal anesthesia and received phenylephrine infusion of 50µg/min as prophylaxis, we included only the parturients who were graded as American Society Anesthesiologist physical status II. We included all the non obese patients whose age was in the range of 20-35years, had a height of 145cm – 160cm, a systolic blood pressure of 100-140mmHg and baseline diastolic blood pressure of 70-90mmHg. Parturients with a history of any form of hypertensive disorder, or any disease related to cardiovascular and central nervous system were excluded from the study. Patients in whom Nil per oral duration exceeded 8 hours were also excluded. Informed written consent was obtained from all the participants.

The sample size was calculated using formula $n= z^2pq/d^2$.Prevalence of hypotension in parturients receiving prophylactic phenylephrine infusion in a dose of 50µg/min was found to be 17%.[6] Considering a 7% margin of error and 95% confidence interval minimum sample size required was 111. Assuming a loss of approximately 20%, a minimum of 133 patients were required.

In the preoperative holding area patient's heart rate and blood pressure was recorded with patient in supine position. Baseline systolic arterial blood pressure was calculated from the mean of 3 consecutive systolic arterial blood pressures measured at an interval of 5 minutes. In the operation theatre intravenous cannulation was done with an 18 G cannula. Standard monitors ie ECG electrodes, non- invasive blood pressure monitoring cuff and oxygen saturation probe were attached. Sub arachnoid block was performed with hyperbaric bupivacaine 0.5% 2.2 ml. A left lateral tilt of 15 degree was maintained till the delivery of the baby. Immediately, after spinal anesthesia, Phenylephrine infusion was initiated at the rate of 50 microgram/min and was continued for 30 minutes irrespective of the duration of surgery.

All the patients received lactated Ringer's solution, one liter over 10 minutes as coload followed by a maintenance dose (using Holliday Segar formula, as per kg body weight) until the end of surgery. Patient's hemodynamics (heart rate, systolic blood pressure and diastolic blood pressure) were recorded at an interval of three minutes. The interval was increased to five minutes after the baby was delivered. Any decrease in systolic blood pressure of >20% from the baseline was recorded as hypotension. Reactive hypertension was defined as a rise in systolic blood pressure >20% above baseline. If hypotension occurred, 2ml bolus phenylephrine (100microgram) was administered. In case of hypertension phenylephrine infusion was stopped. Only if the recorded systolic blood pressure was less than the baseline systolic blood pressure infusion was restarted. Episode of bradycardia (heart rate less than 50 bpm) was treated with intravenous atropine 0.6mg.

An intravenous bolus of 3 IU syntocinon was given to the parturient once the baby was delivered and umbilical cord clamped. Infusion of syntocinon was given at a dose as required. APGAR score was recorded at 1min and 5min. Number of episodes of hypotension, reactive hypertension and bradycardia was recorded. Hypotension induced nausea or vomiting was also recorded which was defined

as nausea or vomiting associated with a 20% reduction in maternal SBP. If any of the patients required transfusion within the 30 min study period, she was excluded from the study.

Data was entered and analyzed using IBM SPSS (Statistical package for Social Sciences) software version 16.0. Descriptive statistics was used to summarize and show frequency distribution and percentage of variables.

RESULTS

During the study period, a total 140 parturients receiving prophylactic phenylephrine infusion of 50µg/min were included. The demographic characters of the study population showed an average age of 26.30±3.91 years, average height of 156±3.19cm and an average weight of 68.03±9.12kg.

Serial changes in systolic blood pressure over different time interval are shown in figure 1. A decrease in mean systolic blood pressure was recorded at 3 min till 6 min of subarachnoid block followed by a rise at 9 minutes. Thereafter, the mean systolic blood pressure was within 110 mm Hg to 115mmHg.

Serial changes in heart rate over different time interval is shown in figure 2. In the 30 minute study period, mean heart rate ranged from 65 to 90bpm. There was no episode of bradycardia or tachycardia noted during the study period.

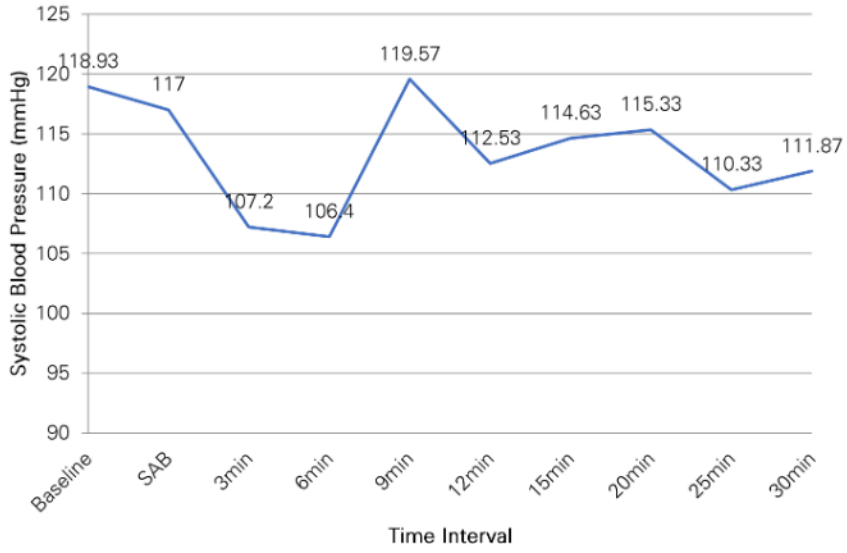

Figure 1. Serial changes in systolic blood pressure

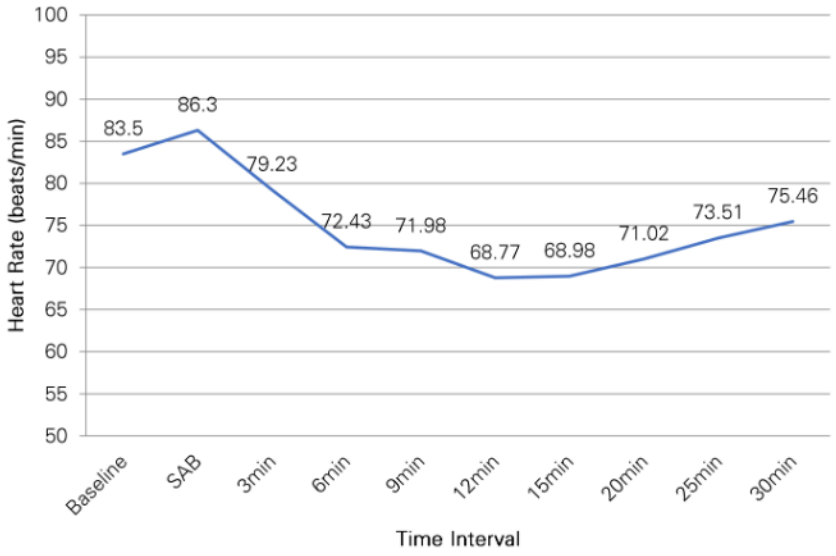

Figure 2. Serial changes in heart rate

Table 1. Intraoperative hemodynamic events

Events	Number (%)
Hypotension	20 (14.28)
Hypertension	3 (2.14)
Bradycardia	0

Intraoperative hemodynamic events are summarized in table 1. Twenty patients (14.28%) developed hypotension. Out of 20 patients who developed hypotension, 3 patients (15%) had a single episode, 11 patients (55%) had 2 episodes and 6 patients (30%) had 3 episodes of hypotension. Three patients (2.14%) had reactive hypertension. None of the patients had bradycardia.

There was no episode of hypotension induced nausea vomiting. Mean APGAR score at 1 min and 5 min was 8 and 9 respectively.

DISCUSSION

The prevalence of hypotension following spinal anesthesia in patients undergoing cesarean section who received prophylactic Phenylephrine infusion of 50µg/min was 14.28%. No episode of bradycardia was noted. Our findings of hypotension and bradycardia are similar to a study comparing different dose of prophylactic phenylephrine in parturients undergoing cesarean section, which reported a predelivery hypotension in 15% and no episode of bradycardia in parturients who received phenylephrine infusion 50µg/min.[7] Phenylephrine has now become the vasopressor of choice in obstetric anesthesia.[3,4,5] It has been studied in different mode and different dose. The optimal dosing regimen and the optimal method of administration for phenylephrine remain controversial.

The use of phenylephrine as intermittent boluses is a simple technique but the incidence, frequency, and severity of hypotension was found to be reduced in parturients when phenylephrine infusion was given as prophylaxis.[8] There was reduction in the incidence of hypotension and fetomaternal side effects with prophylactic administration of phenylephrine when compared with therapeutic administration.[9] Therapeutic administration may also cause a delay in the correction of hypotension.

Prophylactic infusion of phenylephrine when given according to body weight resulted in a fewer episodes of hypotension (18.6%) as compared to fixed rate infusion (35.2%).[10] Infusion adjusted as per kg body weight sounds more appropriate as compared to a fixed dose for all patients irrespective of their body weight. But a fixed dose infusion is a more simple technique that can be adopted easily in a limited resource set up like ours.

The ED 90 for a bolus dose of phenylephrine was reported to be 147 µg (95% confidence interval: 98 to 222 µg).[11] Hence, using phenylephrine in a 100 µg iv bolus dose became a common practice. Among parturients who received prophylactic phenylephrine infusion in the dose of 100µg/min along with rapid crystalloid coload immediately after spinal anesthesia, only one (1.9%) had hypotension.[12] But an intraoperative hypertension was reported in forty seven percent of the parturients.[12] Being an alpha agonist, phenylephrine causes an increase in peripheral vascular resistance that can lead to a reflex maternal bradycardia and decreased cardiac output as well.[13] Hence, there is a concern about the safety of this high dose regimen.

There are studies comparing different doses of phenylephrine. A maximum percentage reductions in cardiac output from baseline values was recorded following spinal anesthesia in patients who were given phenylephrine infusion at the rate of 100µg/min when compared to patients who received phenylephrine infusion at the rate of 50µg/min and 25µg/min.[14] In a comparison of a 4 fixed rate infusion (25µg/min, 50µg/min, 75µg/min and 100µg/min) with placebo, it was concluded that 25µg/min and 50µg/min phenylephrine infusion were associated with greater maternal hemodynamic stability compared with 75µg/min and 100µg/min.[7] An observational study reported 17% prevalence of maternal hypotension with 50µg/min prophylactic phenylephrine infusion.[6] Their study population included ASA PS grade III patients, patients with history of chronic hypertension as well as patients who were obese (BMI>30) whereas only ASA PS II and non obese patients were included in our study. In another similar study, a phenylephrine infusion of 25µg/min given as prophylaxis was compared with a placebo group.[15] The percentage of patients who had hypotension in phenylephrine group (47.4%) though lower when compared to no phenylephrine group (62.1%), it was still high.[15] So, a prophylactic phenylephrine infusion at the dose of 50µg/min can be considered a balance minimizing post spinal hypotension with few episodes of bradycardia and reactive hypertension.

Apart from the physiological effect of spinal anesthesia there are various other factors that can cause hypotension in parturient who are undergoing cesarean section. Dose of bupivacaine is one of the factors. Heavy bupivacaine of 2.2 ml is the most commonly used volume in our practice. To minimize the effect of drug volume on level of block we included patients whose height was in the range of 150-160cm. A study of prophylactic phenylephrine used in the dose of 50µg/min which was done in patients whose height was in the range higher than ours (150-170cm) and had used lower volume of intrathecal bupivaciane reported only a minimal fall in blood pressure with none requiring rescue

vasopressor.[13] In our study maintenance fluid was calculated using Holliday Segar formula, as per kg body weight. To avoid wide variation of intravenous fluid volume we excluded patients whose NPO hour exceeded 8 hours.

Higher block level is another factor that can cause hypotension. Despite choosing patients with height in smaller range and using similar volume of intrathecal drug, height of block can vary. We did not exclude patients based on the level of block. The level of intrathecal injection was also left at the discretion of attending anesthesiologist. We did not take account of the volume of intraoperative blood loss. Patients were excluded only if blood transfusion was required. In our set up all the patients are given intravenous oxytocin 3IU immediately after delivery of baby once the cord is clamped. Thereafter oxytocin infusion is given only if required. Dose of oxytocin given as infusion differs according to the operating surgeon. None of the patients was excluded based on dose of oxytocin administered. These are some of the clinical situations that we commonly encounter in our day to day practice in obstetric anesthesia. We believe, not excluding the factors (types of clinical situation factors) that can cause or aggravate hypotension in obstetric anesthesia, adds to the usefulness of this regime in different types of clinical situation.

Our study has several limitations. We used non invasive blood pressure cuffs to measure intraoperative blood pressure which sometimes fails timely detection of hypotension. Use of direct arterial pressure monitoring would have given an accurate measurement of blood pressure without major fluctuations. Fetal outcome was measured as APGAR score. Fetal blood pH monitoring would have given more accurate assessment. We did not have a comparison group in our study. Comparison with a placebo would have further confirmed the usefulness of prophylactic phenylephrine infusion. Our study was done only in healthy parturients. This limits the generalizability of our study findings to parturient with cardiac or other medical problem.

CONCLUSION

In conclusion, the prevalence of hypotension in parturients who received prophylactic phenylephrine infusion of 50µg/min along with coloading in our setup was 14.28% which is lower as compared to studies conducted in our population without pharmacological prophylaxis. We found minimal episodes of reactive hypertension, no episodes of bradycardia and no adverse effect on fetus as shown by APGAR score. It can be regarded a safe means to minimize hypotension in obstetric spinal anesthesia. Comparative studies using this regime are recommended to confirm the effectiveness.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

SG: Research concept, research design, literature review, data collection, data analysis, statistical analysis, manuscript preparation; CT: Research concept, literature review, data collection, data analysis, manuscript Preparation; SA: Research design, literature review, data collection, data analysis; AK: Research design, literature review, data collection, data analysis.

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