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Comparison of phenylephrine bolus and infusion for management of perioperative hypotension in elective caesarean under spinal anaesthesia

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Abstract

Introduction: Phenylephrine bolus and infusion were compared for effectiveness in treating post-spinal hypotension, and observing neonatal outcomes.

Method: This was a prospective, randomized, comparative study conducted in the department of Anaesthesia at Chitwan Medical College, Nepal, from 23 Feb 2022 to 22 Feb 2023 after ethical approval from CMC-IRC. Under inclusion criteria, 84 parturients were randomized into 2 groups with 42 patents in each. Group A received 50 µg bolus phenylephrine after systolic blood pressure fell by 20%, Group B received a prophylactic infusion of 50 µg/min of phenylephrine. Changes in blood pressure and heart rate were noted. Neonatal APGAR score and side effects were compared. Statistical analysis was done with SPSS version 23 using a T-test and frequency table, $p<0.05$ was considered significant.

Result: Systolic blood pressure was significantly greater over time in Group B as compared to Group A. Incidence of maternal hypotension in Group A was 35(83.3%) and 10(23.8%) in Group B. Similarly, the incidence of nausea was high i.e. 10(23.8%) in Group A compared to 1(2.4%) in Group B. At the same time, the incidence of vomiting was higher in Group A as compared to Group B. The APGAR Scores of both groups were similar. Injection of Mephentermine as a rescue drug was needed more times in Group A than in Group B. Injection of Atropine was needed more frequently in Group B.

Conclusion: Phenylephrine infusion is superior to phenylephrine bolus for control of haemodynamics with lesser side effects in elective caesarean under spinal anaesthesia.

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Introduction

Spinal anaesthesia is widely used for caesarean section. However, this is frequently associated with hypotension which has many detrimental effects on the mother and foetus. Spinal anaesthesia in pregnant women is associated with a greater incidence of hypotension in 80% despite the preloaded or coloaded fluid.[1] Various measures are used to prevent hypotension after SA including preload, left lateral tilt and use of vasopressors.[2] Effective drugs to prevent and control hypotension are ephedrine, phenylephrine, adrenaline, metaraminol and dopamine.[3-9] Phenylephrine is the most commonly used vasopressor for prophylaxis against maternal hypotension. Variable intermittent bolus and infusion of phenylephrine have been suggested, however evidence-based evaluation of both regimens is lacking.

Neonates of women with spinal-induced hypotension had significant acidosis[10,11] and hypotension of more than 2 minutes duration was associated with a significant increase in umbilical venous oxypurines and lipid peroxides suggestive of ischemia reperfusion injury.[12] Various studies show hypotension for more than 4 minutes of maternal hypotension was associated with neurobehavioral changes at 4-7 days of life.

A study using infusion and bolus dose of phenylephrine for post-spinal hypotension and neonatal effects during caesarean section under spinal anaesthesia found that BP was under good control in the infusion group than in the bolus group, while the neonatal outcome was similar in both the groups.[13]

Our study aimed to compare the bolus doses of 50 µg of phenylephrine with a fixed infusion rate of 50 µg/min for the management of perioperative maternal hypotension during caesarean section under spinal anaesthesia.

Method

This was a prospective, randomized, comparative study conducted in the department of Anaesthesia at Chitwan Medical College, Nepal from 23 Feb 2022 to 22 Feb 2023. The study was conducted after approval from the institutional ethics committee and written informed consent was obtained from the patients.

We enrolled 84 parturients of the American Society of Anaesthesiologists (ASA) physical status I or II, with uncomplicated singleton pregnancy, without known foetal abnormalities and posted for elective caesarean delivery under spinal anaesthesia. Parturients with complications like the risk of excessive bleeding (placenta previa, prolonged labour, abnormal presentation) pre-existing or pregnancy-induced hypertension, cardiovascular disease, cerebrovascular disease, severe anaemia, known foetal abnormality, contraindication for spinal anaesthesia, known allergy to phenylephrine, maternal systolic blood pressure (SBP) <100 mmHg, and inability or refusal to give informed consent were excluded from the study.

Patients were randomly divided into 2 groups, each group containing 42 patients. Randomization was done using a computer-generated table of random numbers. It was a single-blind study (patients were blinded). Patients were allocated to one of the two groups A and B, therapeutic bolus and prophylactic infusion.

Group A-patients received phenylephrine 50 µg IV bolus after significant hypotension i.e. fall in SBP>20% from baseline and bolus repeated if necessary. Group B patients received prophylactic 50 µg/min infusion through a syringe pump after Spinal anaesthesia. Patients were premedicated with Inj. Ranitidine 50 mg IV one hour before the surgery or as soon as the decision to perform caesarean section.

On arrival to the operation theatre, intravenous line was started using 18-gauge cannula and patients were preloaded with 500 ml of Ringer's lactate over 10 min continued at 7ml/kg/h and monitored with ECG, pulse oximeter and non-invasive blood pressure monitor.

Under strict aseptic conditions subarachnoid space was identified by the return of cerebrospinal fluid through spinal needle and the subarachnoid block was given in a sitting position using a 25G Quincke needle in the L3-L4 or L4-L5 intervertebral space. Inj. fentanyl 10 µg was added to 10 mg of 0.5% heavy Bupivacaine, and the mixture was injected intrathecally. After subarachnoid block, patients were placed in supine position with left uterine displacement.

Group A patient received phenylephrine 50 µg IV bolus after significant hypotension developed, i.e. fall in systolic blood pressure >20% of basal value and bolus was repeated if necessary. Group B patient received prophylactic phenylephrine 50 µg/m infusion through a syringe pump, started immediately after administration of subarachnoid block. The infusion was continued till the delivery of the baby and was stopped if systolic blood pressure raised to >20% baseline.

Loss of sensory block was assessed by checking for the loss of pain sensation to pin prick. Non-invasive blood pressure was measured at 2m intervals till delivery of the baby. The incidence of side effects such as bradycardia, nausea and vomiting were noted.

For persisting hypotension i.e. systolic blood pressure <90, another rescue drug mephentermine 6 mg IV bolus and if heart rate <55 bpm IV bolus of 0.6 mg Atropine was given. Given total doses of rescue medicine were noted.

When spinal anaesthesia failed or the level of block ascended higher than the T4 level, then the procedure was conducted with general anaesthesia, and those parturients were excluded from the study and.

Appearance, pulse, grimace, activity and respiration (APGAR) scores of babies were assumed at 1 and 5 minutes after delivery.

Statistical analysis was done with SPSS version 23 using a T-test and frequency table. The sample size of 84 was calculated with 42 patients in each group with an alpha error of 5% and power of study taken as 80% based on the previous study.[14] Formula used for calculating sample size was:

$$p = \frac{p_1 + rp_2}{1+r}$$

$$n \geq \frac{\left[Z_{1-\alpha/2}\sqrt{(r+1)p(1-p)} + Z_{1-\beta}\sqrt{rp_1(1-p_1)+p_2(1-p_2)}\right]^2}{r(p_2-p_1)^2}$$

Result

The total number of patients was 84, with 42 in each group. Demographic parameters which include age, height, weight and gestational weeks were comparable between Group A and B, Table 1, 2.

The systolic blood pressure was significantly greater over the time in Group B as compared to Group A in 4, 6 minutes ($p<0.05$). There was a significant fall in heart rate in 2, 4 and 6 minutes ($p<0.05$) in Group B as compared to Group A. The heart rates between Groups A and B were comparable, Table 3.

The total number of hypotensive episodes in Group A was more than in Group B at all time intervals from 2 to 16 minutes, and more prominent at 2,6,8,10 minutes, Table 4.

Similarly, the overall incidence of maternal hypotension was higher in Group A as compared to Group B. Incidence of hypotension in Group A was 35(83.3%) and 10(23.8%) in Group B, Figures 1 and 2.

Nausea and vomiting were observed more frequently in Group A than in Group B. The APGAR Score was comparable between both groups, Table 5. There was a more frequent need for rescue drug Inj. Mephentermine to increase SBP in Group A which was 15(35.7%) as compared to Group B. At the same time, bradycardia was more obvious in Group B and there was more frequent use of Inj. Atropine, Table 6.

Table 1. Demographics of patients undergoing elective caesarean under spinal, Group A phenylephrine bolus, Group B infusion, each group n=42

Patient characteristics	Group A Mean±SD	Group B Mean±SD
Age	29.38±4.874	28.88±3.921
Weight	70.26±5.583	69.79±5.698
Height	154.21±4.693	153.48±3.776

Table 2. Gestational weeks of patients undergoing caesarean section, both groups, n=42

Group	50th Percentile (Gestational week)
Group A	38.00
Group B	38.00

Table 3. Systolic blood pressure and heart rate at different time intervals, both groups n=42

Group	Variable	Mean±SD	p-value	Variable	Mean±SD	p-value
Group A	SBP0	130.26±15.539	0.108	HR 0	93.26±15.850	0.874
Group B		125.19±12.922			93.74±11.186	
Group A	SBP2	110.55±20.849	0.353	HR2	91.57±15.991	0.010
Group B		114.86±21.399			82.88±14.139	
Group A	SBP4	110.10±13.391	0.01	HR4	88.86±17.006	0.003
Group B		123.62±19.653			77.86±15.521	
Group A	SBP6	106.67±16.868	0.001	HR6	87.50±17.027	0.001
Group B		128.36±15.653			70.36±11.983	

Table 4. Frequency and percentage of hypotension at different time intervals

Group	2m n(%)	4m n(%)	6m n(%)	8m n(%)	10m n(%)	12m n(%)	14m n(%)	16m n(%)
A	15 (35.7)	10 (23.8)	17 (40.5)	21 (50)	17 (40.5)	8 (19)	4 (9.5)	3 (7.1)
B	8 (19)	4 (9.5)	1 (2.4)	0	0	0	0	0

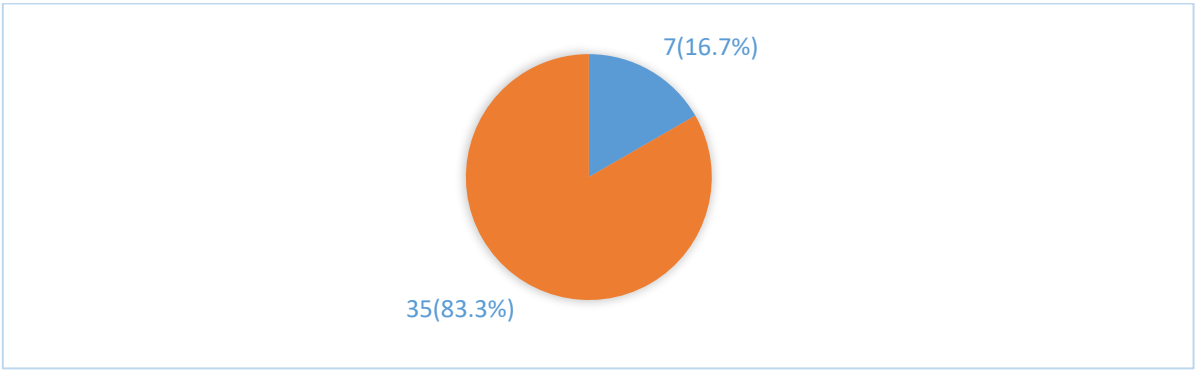

Figure 1. Frequency and percentage of hypotension in Group A, n=42

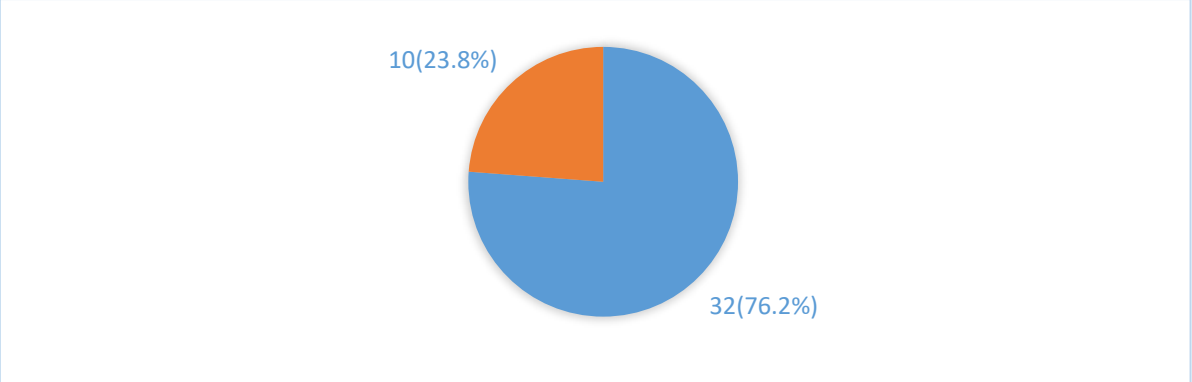

Figure 2. Frequency and percentage of hypotension in Group B, n=42

Discussion

In our study bolus phenylephrine 50 µg was given after an SBP fall of >20% compared to a fixed infusion rate of 50 µg/min of Inj. Phenylephrine prophylactically, we found that the infusion group had fewer episodes of maternal hypotension as compared to bolus**.** Phenylephrine was used in our study because it is considered the first drug of choice, and its efficacy and safety during elective CS have been thoroughly investigated in various studies.[15]

A study describing prophylactic infusion of 100 µg/min IV phenylephrine for the prevention of hypotension during spinal for caesarean delivery conducted in 2004 reported a high incidence of reactive hypertension.[3] The same authors in 2005 showed that hypotension was virtually eliminated by the combination of a high-dose phenylephrine infusion and rapid IV crystalloid cohydration.[16] In our study we didn't notice any reactive hypertension with our infusion dose, and the dose was adequate to control hypotension.

We compared prophylactic infusion because it offers the advantage of reduced incidence of maternal hypotension before delivery of the foetus and thus less uteroplacental insufficiency. Prophylactic variable rate of phenylephrine infusions and rescue phenylephrine boluses,[17] found that in the infusion group SBP was maintained closer to baseline with less nausea and vomiting. A systematic review of 21 randomized trials of prophylactic phenylephrine found that the relative risk of hypotension with a phenylephrine infusion was lower than with an ephedrine infusion and nausea/vomiting was reduced.[18]

Our study demonstrated that starting a prophylactic infusion of phenylephrine immediately after induction of subarachnoid block for elective caesarean section effectively reduced the overall incidence, frequency, and severity of maternal hypotension.

The use of phenylephrine in the infusion group had a similar outcome as the therapeutic bolus group in terms of APGAR score. This finding was similar to the study[14] where the APGAR score of newborns at 1 and 5 minutes were similar in both bolus and infusion groups.

In our study, we noticed episodes of bradycardia were more frequent following the continuous infusion group rather than in the bolus group. However, in another study, there was the absence of reflex bradycardia in both groups with a similar dose of 50 µg in bolus and 50 µg/min in the infusion group.[13]

In our study, the number of hypotensive episodes was higher in bolus group 35(83.3%) compared to infusion 10(23.8%).

Incidence of nausea 10(23.8%) in the bolus group was more compared to only 1(2.4%) in infusion group. Similarly vomiting was 3(7.1%) in bolus group and there was no incidence of vomiting in infusion group. In another study also there was a statistically lesser incidence of nausea and vomiting in the infusion group 10% as compared to the bolus group 23.3%. Similarly, other studies in the literature have also reported

that women who had their SBP maintained near baseline values with a phenylephrine infusion had a reduced incidence of nausea or vomiting and higher umbilical artery pH values (lesser foetal acidosis) compared with patients where SBP was maintained at <100% of baseline values.[3] The effect of post-spinal hypotension on foetal physiology during caesarean section remains poorly characterized in humans, although research shows that a sustained decrease of >60% in uterine blood flow results in bradycardia and acidemia within 10 min in a previously uncompromised foetus.

Similarly, in our study, there was a maximum fall in blood pressure and frequent use of rescue drugs in the bolus group as compared to the infusion group. In the study,[13] they provided a bolus dose of phenylephrine (50 µg) when there was a significant fall in SBP >20% to one group. Continuous fall in SBP was restored with a bolus of phenylephrine and rescue drug. The other group received a prophylactic infusion of phenylephrine (50 µg/min) which was started immediately after the administration of subarachnoid block. There was minimal fall in blood pressure and none of the patients needed a rescue dose in the infusion group.

The primary outcome of our study was that 50 µg/min infusion maintains good control of SBP compared to bolus 50 µg of phenylephrine. The secondary outcome was that the APGAR score was similar in both groups. The side effects such as nausea and vomiting were significantly higher in the therapeutic bolus group. Our findings suggest that prophylactic phenylephrine infusion is superior to therapeutic phenylephrine bolus dose for control of blood pressure after subarachnoid block in elective caesarean section.

The limitation of our study may be a single-centre study, including only ASA I-II healthy parturient undergoing elective caesarean section. Differences in preoperative optimization, and intraoperative management including speed of local anaesthetic injection, level of block, timing of phenylephrine prophylaxis, the doses of vasopressor drugs etc. could affect the outcome of the study.

Conclusion

The results of this study suggest that phenylephrine, when given as a prophylactic infusion, leads to significantly better control of post-spinal hypotension during elective caesarean section. The APGAR scores showed similar results in the bolus and infusion groups. The other maternal adverse effects such as nausea and vomiting were less in the infusion group compared to the bolus group.

Author contribution

Concept design: MG, RB, NKY, RG; Literature search: All; Data collection: MG, PKG; Data analysis: BSR, GPD, JPS, MG, RB, NKY, RG; Draft manuscript: All; Final manuscript and accountability: All

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Conflict of Interest

None

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Supplementary material

The data and supplementary material which support the findings of this study are available from the corresponding author upon reasonable request.

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