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Original Research Article

Comparative evaluation of two prophylactic intravenous bolus doses of phenylephrine for prevention of spinal-induced hypotension in elective cesarean sections: a prospective and randomized study

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ABSTRACT

Background: Hypotension is a common and clinically significant complication associated with spinal anesthesia during cesarean section, often persisting despite standard preventive strategies such as fluid preloading and left uterine displacement. Vasopressors like phenylephrine are routinely employed to counteract the hemodynamic instability, yet limited data exist comparing different fixed bolus doses of phenylephrine for prophylaxis against spinal-induced hypotension in obstetric anesthesia. This study aimed to evaluate and compare the efficacy and safety of two intravenous bolus doses of phenylephrine-150 micrograms and 200 micrograms-administered immediately following spinal anesthesia, in preventing maternal hypotension during cesarean delivery.
Methods: A prospective, randomized, double-blind study was conducted at Adichunchanagiri Institute of Medical Sciences, Karnataka, India involving 60 parturients scheduled for elective cesarean section. Group A received 150 µg and group B received 200 µg phenylephrine IV bolus immediately after spinal anesthesia. Hemodynamic parameters, incidence of hypotension and bradycardia, requirement of rescue boluses, and Apgar scores were recorded.
Results: The incidence of hypotension was 16.6% in both groups. Group B showed a significantly higher incidence of bradycardia (43.3%) compared to group A (20%, $p<0.05$). Group A demonstrated better hemodynamic stability with fewer rescue interventions. Neonatal outcomes were similar in both groups.
Conclusions: A 150 µg bolus of phenylephrine is as effective as 200 µg in preventing hypotension following spinal anesthesia in cesarean delivery, with fewer adverse effects. It is recommended as the preferred dose for prophylaxis.

Keywords: Phenylephrine, Hypotension, Cesarean section, Spinal anesthesia, Bradycardia, Obstetric anesthesia

INTRODUCTION

Spinal anaesthesia is widely regarded as the preferred technique for cesarean delivery due to its rapid onset, reliability, and minimal drug exposure to the fetus. Compared to general anaesthesia, spinal anaesthesia eliminates the risks of airway complications, maternal aspiration, and neonatal respiratory depression, while allowing the mother to remain conscious during childbirth and promoting immediate bonding and breastfeeding initiation.[1] However, a significant limitation of this technique is the high incidence of hypotension, which may lead to adverse maternal and fetal outcomes.[2]

This hypotension results primarily from sympathetic blockade, leading to peripheral vasodilation, decreased venous return, and reduced cardiac output. Furthermore, the gravid uterus compresses the inferior vena cava in the supine position, exacerbating the decrease in preload.[3] In the absence of adequate compensation, these haemodynamic changes can significantly impair uteroplacental perfusion, increasing the risk of fetal hypoxia, acidosis, and low Apgar scores.[4,5]

Over the years, various strategies have been adopted to mitigate spinal-induced hypotension, including intravenous fluid preloading or co-loading, left uterine displacement with wedges, leg wrapping, and pharmacologic intervention using vasopressors. Among these, vasopressor therapy remains the most effective and reliable method.[6,7] Historically, ephedrine was the vasopressor of choice due to its combined alpha- and beta-adrenergic activity. However, its association with fetal acidosis and maternal tachyphylaxis has shifted the preference toward phenylephrine in modern obstetric practice.[8-10]

Phenylephrine acts by inducing arterial and venous vasoconstriction, effectively counteracting the vasodilatory effects of spinal anesthesia. It maintains systolic blood pressure (SBP) and improves venous return without increasing heart rate (HR) or myocardial oxygen consumption. Multiple randomized controlled trials and meta-analyses have demonstrated that phenylephrine provides superior maternal hemodynamic stability, and better neonatal acid-base status, compared to ephedrine.[11]

The use of phenylephrine in obstetric anesthesia has evolved from reactive bolus administration to prophylactic infusions and fixed-dose boluses.[12] However, there remains uncertainty regarding the optimal bolus dose required to effectively prevent hypotension while minimizing side effects such as reflex bradycardia and reduced cardiac output.[13] While higher doses ensure more effective vasoconstriction, they may cause excessive increases in blood pressure and HR reduction through baroreceptor-mediated reflexes.[14,15]

This study was undertaken in this context to compare the efficacy and safety of two prophylactic bolus doses of intravenous phenylephrine-150 µg and 200 µg-administered immediately after spinal anesthesia in parturients undergoing elective cesarean section. The primary aim was to assess the incidence of hypotension, while secondary endpoints included incidence of bradycardia, requirement of rescue vasopressors, and neonatal Apgar scores. By determining the most effective dose with the least adverse effects, this study contributes to optimizing vasopressor use in obstetric anesthetic practice.

METHODS

Study design and setting

This study was designed as a prospective, randomized, double-blind, comparative trial conducted over a period of 18 months at Adichunchanagiri Institute of Medical Sciences, Karnataka, India. Ethical approval was obtained from the institutional ethics committee, and written informed consent was secured from each participant prior to enrolment. The study population consisted of full-term parturients scheduled for elective or emergency cesarean section under spinal anesthesia.

Participants

A total of 60 pregnant women aged between 20 and 35 years, classified as American society of anesthesiologists (ASA) physical status I, were enrolled. All participants were scheduled for cesarean delivery under subarachnoid block. Participants were randomly assigned into two groups of 30 each, using a computer-generated simple randomization technique.

Inclusion criteria

Patients with singleton full-term pregnancy (≥37 weeks gestation), ASA physical status I, age 20-35 years, scheduled for cesarean section under spinal anesthesia were included.

Exclusion criteria

Patients with age <20 or >35 years, height <150 cm or >170 cm; weight >70 kg, pre-existing hypertension (BP>140/90 mmHg), history of preeclampsia/eclampsia, cardiovascular, renal, metabolic, neurological, or psychiatric disorders, thyroid dysfunction, glaucoma, or vascular disease, known hypersensitivity to local anesthetics or phenylephrine, any contraindication to spinal anesthesia, fetal distress or diagnosed fetal anomalies were excluded.

Preoperative assessment

All participants underwent standard preoperative investigations including complete blood count, coagulation profile, renal function tests, viral serology (HIV and HBsAg), urine analysis, random blood glucose, and electrocardiography. A pre-anesthesia evaluation was performed, and patients were counselled about the procedure and potential complications in a language they understood.

Anesthesia protocol

Upon arrival in the operating room, patients were positioned in the left lateral position and preoxygenated with 100% oxygen at 4 l/min via a face mask. Baseline vital parameters-SBP and diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, and peripheral oxygen saturation (SpO_2) were recorded using a multiparameter monitor.

All patients received preload with Ringer's lactate at 10 ml/kg over 15 minutes via an 18G intravenous cannula, and fluid administration continued at 10 ml/min during the procedure.

Spinal anesthesia was administered under strict aseptic precautions using a 25G Quincke spinal needle at the L3-L4 interspace in the lateral decubitus position. A fixed intrathecal dose of 9 mg of 0.5% hyperbaric bupivacaine was administered. Immediately following injection,

patients were repositioned supine with left uterine displacement achieved using a wedge to prevent aortocaval compression.

Study drug administration

Immediately after completion of the spinal injection, patients received the study drug based on the randomization:

Group A (n=30): 150 µg phenylephrine IV bolus.

Group B (n=30): 200 µg phenylephrine IV bolus.

Both phenylephrine doses were diluted in 10 mL of normal saline and administered over 1 minute. The anesthesiologist and the data recorder were blinded to group allocation.

Monitoring and data collection

Hemodynamic parameters (SBP, DBP, MAP, HR, and SpO_2) were recorded at baseline and at 2-minute intervals for the first 20 minutes following subarachnoid block. Sensory level of the spinal block was assessed using pinprick discrimination, targeting a block level of the T5-T6.

Hypotension was defined as SBP falling more than 20% below the baseline value. Bradycardia was defined as HR <60 bpm. Hypotension was treated with additional 50 µg boluses of phenylephrine as needed. Bradycardia episodes were managed with intravenous atropine 0.6 mg.

Nausea and vomiting episodes were noted; if not associated with hypotension, intravenous ondansetron was administered.

After delivery, all patients received 5IU oxytocin as an intravenous bolus. Neonatal status was evaluated using Apgar scores at 1 and 5 minutes.

Outcomes

Primary outcome: Incidence of hypotension within 20 minutes of spinal block.

Secondary outcomes: Incidence of bradycardia, need for rescue vasopressors, Apgar scores at 1 and 5 minutes, and incidence of nausea and vomiting

Sample size

A sample size of thirty participants per group (total n=60) was determined based on previous studies assuming a twenty five-thirty percentages incidence of spinal hypotension, with 80% power and a significance level of five percentages to detect a twenty percentages difference between the groups.

Statistical analysis

Data were analyzed using standard statistical software. Results were expressed as mean±standard deviation for continuous variables and percentages for categorical variables. Intergroup comparisons were made using the unpaired Student's t test for continuous variables and chi-square test for categorical variables. A $p<0.05$ was considered statistically significant; $p<0.01$ highly significant.

RESULTS

Maternal characteristics

Age, weight, and height characteristics of the two groups were comparable. These differences were not statistically significant, as shown in Table 1 below.

Table 1: Maternal characteristics.

Parameters	Group A (Mean±SD)	Group B (Mean±SD)	P value
Age (in years)	24.26±5.1	25.02±4.67	0.41
Weight (in kg)	64.82±4.32	63.6±6.12	0.64
Height (in cm)	153.5±6.02	152.7±4.32	0.78

SBP

Both groups had similar baseline SBP. Group B had significantly higher SBP values from 2 to 6 minutes post-subarachnoid block. Hypotension (>20% drop in SBP) occurred equally in both groups (16.66%).

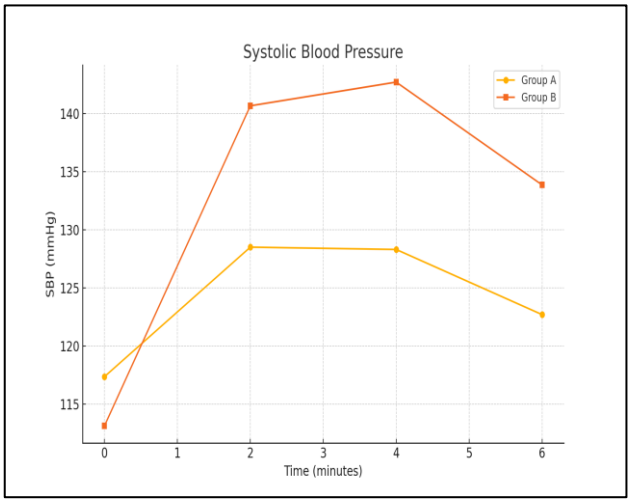

Figure 1: SBP variation over time.

DBP

Group B demonstrated significantly higher diastolic pressures at 2-6 minutes. Baseline DBP was comparable between groups.

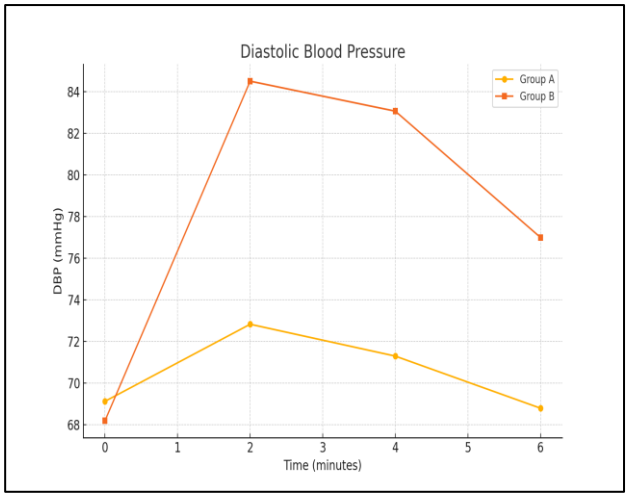

Figure 2: DBP variation over time.

MAP

MAP was higher in group B from 2 to 6 minutes post-drug administration. Baseline MAPs were comparable.

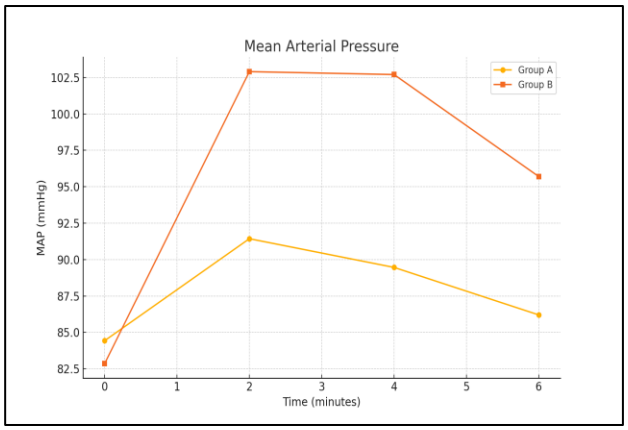

Figure 3: Mean arterial pressure variation over time.

HR

HR was significantly lower in group B at 4 minutes. Other time points were not statistically different.

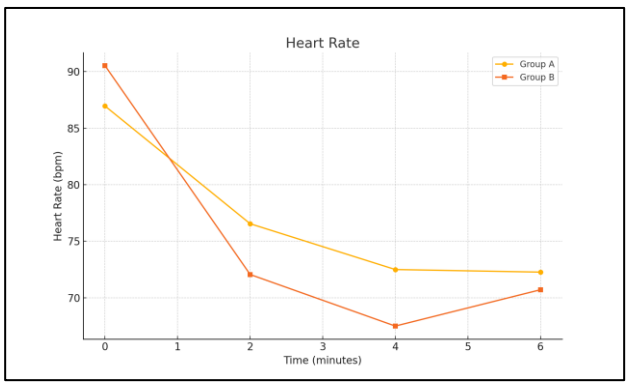

Figure 4: HR variation over time.

Bradycardia

Bradycardia occurred in 20% of group A (6/30) and 43.33% of group B (13/30).

APGAR scores

APGAR scores at 1 and 5 minutes were comparable between groups, as detailed in Table 2 below.

Table 2: APGAR scores.

Time (min)	Group A (Mean±SD)	Group B (Mean±SD)	P value
1	7.53±0.68	7.73±0.63	0.24
5	9.43±0.56	9.4±0.49	0.82

Side effects

No side effects such as nausea or vomiting were reported in either group.

DISCUSSION

Spinal anaesthesia has become the anaesthetic technique of choice for caesarean section due to its rapid onset, dense neural blockade, minimal neonatal drug exposure, and avoidance of airway-related complications inherent to general anaesthesia. This technique permits the mother to remain conscious and participate in the birthing process while providing effective surgical anaesthesia. However, it is not without drawbacks. The most commonly encountered and clinically significant complication of spinal anaesthesia in obstetric patients is maternal hypotension, with an incidence ranging between 75% and 85% in the absence of prophylactic interventions.[6,16]

The hypotension arises due to sympathetic blockade, resulting in vasodilation, decreased systemic vascular resistance, venous pooling, and a reduction in cardiac preload. These haemodynamic changes are further exacerbated by aortocaval compression by gravid uterus in the supine position, contributing to decreased venous return and cardiac output.[17] Clinically, this may manifest as nausea, vomiting, dizziness, loss of consciousness, and in severe cases, cardiovascular collapse. More importantly, significant maternal hypotension may compromise uteroplacental perfusion, resulting in foetal hypoxia, acidosis and low Apgar scores.[4]

Historically, ephedrine was the vasopressor of choice due to its combined alpha and beta agonist activity. It maintains blood pressure primarily by increasing cardiac output via beta-adrenergic stimulation. However, several studies have demonstrated that ephedrine readily crosses the placenta and is associated with a higher incidence of foetal acidosis, attributed to increased foetal metabolic activity and catecholamine surge.[2,8] In contrast, phenylephrine is a selective alpha-1 adrenergic receptor agonist, inducing vasoconstriction without beta-mediated

chronotropic or inotropic effects. It increases systemic vascular resistance and blood pressure without significant changes in HR or cardiac output and is associated with improved neonatal acid-base status.[9,18]

The present study aimed to compare the efficacy and safety of 2 prophylactic bolus doses of phenylephrine (150 mcg and 200 mcg) in preventing hypotension following subarachnoid block in caesarean section. Both doses were found to be equally effective in maintaining SBP, with comparable incidence of hypotension in each group (16.66%). This is consistent with findings by Kee et al who demonstrated that phenylephrine effectively maintains haemodynamic stability when used as a prophylactic bolus or infusion.[11]

However, the 200 mcg dose was associated with significantly higher systolic, diastolic, and mean arterial pressures in the first 6 minutes post-administration, indicating a more potent pressor effect. While this may be desirable in preventing hypotension, it was accompanied by a greater incidence of reflex bradycardia (43.33% in group B vs. 20% in group A). This reflex bradycardia is a known side effect of phenylephrine and results from baroreceptor-mediated vagal stimulation in response to sudden increases in systemic vascular resistance.[19]

Thomas et al and Hall et al similarly reported a higher incidence of bradycardia with phenylephrine, particularly at higher doses.[15,16] Although the bradycardia episodes in our study were transient and easily managed with intravenous atropine, their frequency suggests that lower phenylephrine doses may offer a more favourable safety profile without compromising efficacy. Importantly, bradycardia can reduce cardiac output, which is particularly concerning in context of physiological changes of pregnancy, where stroke volume and HR are both required to maintain adequate uteroplacental perfusion.

No patients in either group experienced nausea or vomiting. This could be attributed to effective maintenance of cardiac preload and blood pressure. Cooper et al postulated that the primary mechanism for nausea during spinal anaesthesia is decreased venous return and vagally mediated reflexes, both of which are mitigated by the vasoconstrictive properties of phenylephrine.[8] This finding was also supported by Saravanan et al who demonstrated a significantly lower incidence of intraoperative nausea in patients managed with phenylephrine.[8]

In terms of neonatal outcomes, APGAR scores at 1 and 5 minutes were comparable in both groups and exceeded the clinically acceptable thresholds. This finding is in accordance with studies by Sharma et al and Moran et al who found that phenylephrine, even in higher doses or infusions, did not negatively affect neonatal well-being.[19,20] Importantly, we did not assess umbilical arterial pH, which would have provided a more objective measure of fetal acid-base status. However, previous literature has demonstrated superior neonatal pH values with phenylephrine when compared to ephedrine.[8,9]

In the context of existing literature, our findings support the notion that phenylephrine is a safe and effective vasopressor for prophylactic use during spinal anaesthesia in caesarean delivery. Studies by Das et al and Mercier et al have shown that phenylephrine, either alone/in combination with ephedrine, offers optimal haemodynamic control.[18,21] Main practical limitation of phenylephrine remains the requirement for dilution and risk of dosing errors.[22]

Limitations

Our study was limited by a relatively small sample size and the lack of umbilical cord blood gas analysis. This was a single-center study and side effects such as shivering were not formally documented.[23] Additionally, inter-individual variations in the timing of baby extraction and positioning may have influenced haemodynamic measurements. Future multicentre trials with larger populations and robust neonatal markers are needed to confirm the optimal dosing strategy.

CONCLUSION

This prospective, randomized study demonstrates that a prophylactic intravenous bolus of 150 µg phenylephrine is as effective as 200 µg in preventing spinal-induced hypotension during caesarean section. Importantly, 150 µg dose was associated with a significantly lower incidence of bradycardia and required fewer rescue interventions, suggesting improved overall hemodynamic stability.

Neonatal outcomes were unaffected by either dose, affirming the safety of both regimens with regard to foetal well-being. However, the side effect profile and need for additional dosing make 150 µg the more favourable option for routine prophylactic use.

In clinical practice, using the lowest effective dose of phenylephrine not only minimizes adverse maternal effects but also simplifies intraoperative management. Future research with larger sample sizes and additional maternal outcome metrics may further validate these findings.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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