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Original Research Article

COMPARATIVE EVALUATION OF INTRAVENOUS PHENYLEPHRINE AND EPHEDRINE FOR THE MANAGEMENT OF HYPOTENSION FOLLOWING SPINAL ANAESTHESIA IN ELECTIVE CAESAREAN SECTION

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ABSTRACT

Background: Hypotension is the commonest haemodynamic disturbance during spinal anaesthesia for caesarean delivery and, if uncorrected, can compromise uteroplacental perfusion and neonatal well-being. Phenylephrine and ephedrine remain the vasopressors most widely used in obstetric anaesthesia, yet debate continues over which offers the better balance of maternal control and fetal safety. The objective is to compare the haemodynamic effects, vasopressor requirement, and adverse-event profile of intravenous phenylephrine versus ephedrine for managing hypotension after spinal anaesthesia for caesarean section.

Materials and Methods: Fifty American Society of Anesthesiologists class I–II parturients scheduled for elective caesarean section were enrolled in this prospective, randomised, double-blind, parallel-group study and allocated equally to receive intravenous ephedrine (10 mg bolus) or phenylephrine (100 µg bolus) after spinal anaesthesia. Systolic blood pressure, heart rate, incidence of hypotension, bradycardia, hypertension, nausea, vomiting, and patient satisfaction were recorded and compared using the chi-square test, Student t-test, and Mann–Whitney U test, with $p<0.05$ considered significant.

Results: The two groups were demographically comparable at baseline. Phenylephrine produced significantly better post-intervention systolic blood pressure control and shorter hypotensive episodes but was associated with a lower post-intervention heart rate than ephedrine. The phenylephrine group required fewer additional vasopressor doses and reported higher satisfaction during haemodynamically unstable episodes, while overall rates of hypotension, bradycardia, nausea, and vomiting were similar between groups.

Conclusion: Intravenous phenylephrine offers more stable and efficient control of post-spinal hypotension than ephedrine, with a comparable safety profile, supporting its preferential use during elective caesarean delivery under spinal anaesthesia.

Keywords: Spinal anaesthesia; Caesarean section; Hypotension; Phenylephrine; Ephedrine; Vasopressors.

INTRODUCTION

Spinal anaesthesia is the technique of choice for caesarean delivery because of its rapid onset, technical simplicity, and reliable sensory and motor block, but the sympathetic blockade it produces frequently causes a sharp fall in systemic vascular resistance and venous return, leading to maternal hypotension.[1] The supine position adopted during surgery further aggravates this fall in blood pressure through aortocaval compression, a phenomenon described decades ago and still central to the pathophysiology of spinal-induced hypotension in pregnancy.[2] Left uncorrected, hypotension exposes

the mother to nausea, vomiting, and light-headedness, and exposes the fetus to reduced placental perfusion, acidosis, and, in severe or prolonged cases, hypoxic injury.[3] Because of these risks, prompt and effective correction of blood pressure is considered an essential part of safe obstetric anaesthesia practice.[4]

Vasopressor therapy, together with fluid co-loading, forms the mainstay of management, and ephedrine and phenylephrine remain the two agents most widely used for this purpose.[5] Ephedrine, a mixed alpha- and beta-adrenergic agonist, raises blood pressure largely by increasing heart rate and cardiac output, and for many years was regarded as the safer choice in pregnancy because of concerns that pure alpha-agonists might reduce uterine blood flow.[3] This concern has been substantially revised over the past two decades: several trials and reviews have shown that phenylephrine, a selective alpha-1 agonist, restores maternal blood pressure rapidly and predictably, and is associated with less fetal acidosis than ephedrine, largely because the reflex bradycardia it produces is not accompanied by the metabolic stimulation seen with ephedrine.[6] As a result, current obstetric anaesthesia practice now generally favours phenylephrine as the first-line agent for prophylaxis and treatment of spinal-induced hypotension, although ephedrine continues to have a role, particularly when bradycardia limits the use of a pure alpha-agonist.[7]

Despite this shift in practice, the two drugs continue to be used somewhat interchangeably in many resource-limited settings, and direct comparative data generated from such settings remain relatively limited.[8] Differences in dosing protocol, patient population, and outcome definitions across published trials make it difficult to generalise findings to every clinical context, and much of the existing evidence originates from high-income centres with different baseline obstetric risk profiles. There is, therefore, a continuing need for prospective comparative data generated in routine clinical settings to guide vasopressor selection at the bedside, particularly using simple bolus-dosing protocols that are practical in busy obstetric units rather than the infusion pumps and closed-loop systems used in many published trials.

Both phenylephrine and ephedrine act swiftly once injected, but the speed and predictability with which they restore blood pressure, the degree to which they alter maternal heart rate, and the number of repeat doses needed to maintain stability are not interchangeable, and small differences in these parameters can meaningfully affect maternal comfort and the smooth conduct of surgery. A clearer, locally generated comparison of the two drugs along these practical dimensions, rather than relying solely on findings from other healthcare settings, was therefore felt to be of direct value to anaesthetic practice in this institution.

MATERIALS AND METHODS

This prospective, randomised, double-blind, parallel-group observational study was conducted in the Department of Anaesthesiology at Sarojini Naidu Medical College, Agra, a 750-bed tertiary care teaching hospital, over a period of 18 months, including six months allotted to data analysis and thesis preparation. All women scheduled for elective caesarean section under spinal anaesthesia during the study period and meeting the eligibility criteria were considered for enrolment. Patients were included if they belonged to American Society of Anesthesiologists (ASA) physical status class I or II, were aged between 18 and 60 years, had given written informed consent, had a Glasgow Coma Scale score of 15, and were undergoing surgery expected to last less than two hours. Women with ASA class III or IV status, haemodynamic instability, a Glasgow Coma Scale score below 13, anticipated surgical duration beyond two hours, known allergy to opioids or local anaesthetics, a history of substance dependence, coagulopathy or antiplatelet therapy, inability to communicate or comprehend the visual analogue scale, anticipated need for postoperative ventilatory support, or pre-eclampsia, eclampsia, or pregnancy-induced hypertension were excluded. Fifty eligible patients were randomly allocated in a 1:1 ratio, using a computer-generated randomisation sequence, to receive either ephedrine (Group A, n=25) or phenylephrine (Group B, n=25).

After preoperative assessment on the day prior to surgery, all patients fasted for at least eight hours and received no premedication. In the operating room, an 18-gauge intravenous cannula was secured and baseline blood pressure and heart rate were recorded as the mean of three readings taken one minute apart, with continuous non-invasive monitoring of blood pressure, heart rate, and oxygen saturation thereafter. With the patient in the sitting position, spinal anaesthesia was administered at the L2–L3 or L3–L4 interspace using a Quincke or Whitacre needle, and 2.0 ml of hyperbaric bupivacaine was injected intrathecally once free flow of cerebrospinal fluid was confirmed; co-loading with 10 ml/kg of Ringer's lactate was begun at the time of injection. Patients were then placed supine with a standard left lateral tilt and observed for development of a bilateral sensory block to the T4 dermatome within ten minutes; failure to achieve this level led to exclusion from the final analysis. Immediately after confirmation of an adequate block, Group A received an intravenous bolus of 10 mg ephedrine and Group B received an intravenous bolus of 100 µg phenylephrine, both diluted in normal saline.

Blood pressure and heart rate were recorded at two-minute intervals from the time of the spinal block until delivery, and at five-minute intervals thereafter. Hypotension was defined as a fall in systolic blood pressure of 20% or more from baseline, or an absolute value below 100 mmHg; hypertension as a rise of

20% or more above baseline; and bradycardia as a heart rate below 60 beats per minute. Episodes of hypotension were treated with a repeat bolus of the same study drug; if two consecutive doses failed to restore blood pressure, vasopressin was used as rescue therapy. Bradycardia accompanied by a heart rate below 55 beats per minute was treated with intravenous atropine 0.5 mg. Nausea and vomiting were recorded as patient-reported events. Time points corresponding to induction of spinal anaesthesia, skin incision, delivery, and any intraoperative complication were logged for each patient, and maternal satisfaction with anaesthetic care was assessed using a 0–10 visual analogue scale (VAS).

Data were entered in Microsoft Excel and analysed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Between-group comparisons of continuous variables were performed using the Student t-test or Mann–Whitney U test as appropriate, while categorical variables were compared using the chi-square test or Fisher's exact test. A two-tailed p-value of less than 0.05 was considered statistically significant throughout.

RESULTS

A total of 50 patients completed the study, 25 in each group, with no patient excluded for failed block or protocol deviation.

Table 1: Baseline demographic, clinical, and comorbidity profile (N=50)

Characteristic	Group A – Ephedrine (n=25)	Group B – Phenylephrine (n=25)	p-value
Age, years (mean ± SD)	31.5 ± 5.2	30.8 ± 4.9	0.62
BMI, kg/m² (mean ± SD)	24.3 ± 3.1	25.1 ± 3.4	0.48
ASA class I, n (%)	20 (80%)	19 (76%)	0.74
ASA class II, n (%)	5 (20%)	6 (24%)	–
Occupation – Homemaker, n (%)	15 (60%)	16 (64%)	0.78
Occupation – Professional, n (%)	7 (28%)	6 (24%)	–
Occupation – Labourer, n (%)	3 (12%)	3 (12%)	–
No comorbidity, n (%)	20 (80%)	19 (76%)	0.74
Hypertension, n (%)	3 (12%)	4 (16%)	–
Diabetes mellitus, n (%)	2 (8%)	2 (8%)	–
Surgery <60 min, n (%)	10 (40%)	8 (32%)	0.64
Surgery 60–120 min, n (%)	15 (60%)	17 (68%)	–

The two groups were closely matched at baseline. Mean age (31.5 ± 5.2 vs 30.8 ± 4.9 years, p=0.62) and body mass index (24.3 ± 3.1 vs 25.1 ± 3.4 kg/m², p=0.48) did not differ significantly, nor did ASA grade distribution, occupation, comorbidity burden, or duration of surgery (all p>0.05). This balance indicates that any differences detected in subsequent outcomes are unlikely to be explained by baseline confounding [Table 1].

Table 2: Comparison of haemodynamic parameters between groups (N=50)

Parameter	Group A – Ephedrine	Group B – Phenylephrine	p-value
Baseline SBP, mmHg	120 ± 10	118 ± 12	0.42
Post-intervention SBP, mmHg	112 ± 8	115 ± 9	0.04
Baseline heart rate, beats/min	75 ± 8	76 ± 7	0.67
Post-intervention heart rate, beats/min	80 ± 7	75 ± 8	<0.001

Baseline systolic blood pressure and heart rate were comparable between groups. After the study drug was administered, Group B (phenylephrine) maintained a significantly higher systolic blood pressure than Group A (115 ± 9 vs 112 ± 8 mmHg, p=0.04), while Group A (ephedrine) showed a significantly higher post-intervention heart rate (80 ± 7 vs 75 ± 8 beats/min, p<0.001), consistent with the relative beta-adrenergic activity of ephedrine and the reflex bradycardic tendency of phenylephrine [Table 2].

Table 3: Onset and duration of hypotensive episodes (N=50)

Time interval	Group A – Ephedrine (n=25)	Group B – Phenylephrine (n=25)	p-value
Onset of hypotension <5 min	6 (24%)	4 (16%)	0.03
Onset of hypotension 5–10 min	10 (40%)	12 (48%)	–
Onset of hypotension >10 min	9 (36%)	9 (36%)	–
Episode duration <2 min	8 (32%)	15 (60%)	0.03
Episode duration 2–5 min	10 (40%)	6 (24%)	–
Episode duration >5 min	7 (28%)	4 (16%)	–

Hypotension developed within the first five minutes more often in Group A than in Group B (24% vs 16%, p=0.03), although the overall distribution of onset times beyond five minutes was similar. Once hypotension occurred, episodes resolved within two minutes in 60% of Group B patients compared with only 32% of Group A patients (p=0.03), and prolonged episodes lasting more than five minutes were correspondingly less frequent with phenylephrine, suggesting faster correction of blood pressure with this agent [Table 3].

Table 4: Vasopressor requirement and incidence of hypotension, bradycardia, and hypertension (N=50)

Variable	Group A – Ephedrine (n=25)	Group B – Phenylephrine (n=25)	p-value
No additional dose required	8 (32%)	15 (60%)	0.02
1–2 additional doses	12 (48%)	7 (28%)	–
>2 additional doses	5 (20%)	3 (12%)	–
Hypotension, n (%)	8 (32%)	6 (24%)	0.53
Bradycardia, n (%)	12 (48%)	10 (40%)	0.15
Hypertension, n (%)	2 (8%)	3 (12%)	0.64

Significantly more patients in Group B required no additional vasopressor dose beyond the initial bolus (60% vs 32%, p=0.02), and fewer needed repeated dosing. The overall incidence of hypotension, bradycardia, and hypertension across the full study period was statistically similar between the two drugs, indicating that the dose-sparing advantage of phenylephrine was not accompanied by a corresponding rise in haemodynamic side effects [Table 4].

Table 5: Maternal adverse events (N=50)

Adverse event	Group A – Ephedrine (n=25)	Group B – Phenylephrine (n=25)	p-value
Nausea, n (%)	5 (20%)	4 (16%)	0.72
Vomiting, n (%)	2 (8%)	1 (4%)	0.55
Need for rescue vasopressor, n (%)	6 (24%)	4 (16%)	0.47

Nausea, vomiting, and the need for rescue vasopressor therapy occurred at low and statistically comparable rates in both groups, supporting an equivalent overall maternal safety profile for the two drugs at the doses used in this study [Table 5].

Table 6: Maternal satisfaction (VAS 0–10) overall and by haemodynamic stability (N=50)

Satisfaction category	Group A – Ephedrine (n=25)	Group B – Phenylephrine (n=25)	p-value
VAS 0–4 (low)	2 (8%)	1 (4%)	0.18
VAS 5–7 (moderate)	18 (72%)	20 (80%)	–
VAS 8–10 (high)	5 (20%)	4 (16%)	–
Satisfied when haemodynamically stable, n (%)	18 (72%)	22 (88%)	0.12
Satisfied when haemodynamically unstable, n (%)	7 (28%)	3 (12%)	0.03

Overall VAS satisfaction scores did not differ significantly between groups. However, when analysed by haemodynamic stability, the picture reversed direction in the two subgroups: among patients with a stable course, satisfaction tended to favour Group B (88% vs 72%, p=0.12), whereas among patients with an unstable course, satisfaction was significantly lower in Group B than in Group A (12% vs 28%, p=0.03) [Table 6].

DISCUSSION

The present study found that intravenous phenylephrine produced more stable post-intervention systolic blood pressure control and shorter hypotensive episodes than ephedrine, while ephedrine maintained a relatively higher post-intervention heart rate. The phenylephrine group also required fewer additional vasopressor boluses, although the overall incidence of hypotension, bradycardia, hypertension, nausea, and vomiting did not differ significantly between the two drugs. These findings are broadly consistent with the pattern reported across several decades of comparative obstetric anaesthesia literature.

One of the earliest comparative trials, by Hall and colleagues, found that higher-dose ephedrine infusion controlled blood pressure more effectively than phenylephrine, with phenylephrine associated with a longer duration of hypotension,[9] a pattern that contrasts with the shorter hypotensive episodes seen with phenylephrine in the present cohort and likely reflects differences in dosing regimen (bolus versus infusion) and in the definition of hypotension used between the two studies. In contrast, Simin et al. and Moslemi et al. both reported essentially equivalent efficacy between ephedrine and phenylephrine when matched for clinical effect, with neither drug showing a clear advantage in maternal blood pressure control or neonatal outcome,[10,11] a finding that aligns with the comparable overall incidence of hypotension observed in our patients.

The reduced need for repeat vasopressor dosing with phenylephrine in our study mirrors the dose-sparing effect described with weight-adjusted phenylephrine infusion regimens,[12] and is consistent with the relative potency advantage of pure alpha-agonists reported in graded dose-response work comparing phenylephrine with other vasopressors, where considerably smaller incremental doses were needed to achieve an equivalent pressor effect.[14] The lower post-intervention heart rate seen with phenylephrine in our cohort is consistent with the reflex bradycardia repeatedly described with pure alpha-1 agonists, an effect that has prompted some authors to favour agents with combined alpha- and beta-adrenergic activity, such as norepinephrine, in selected populations.[13,15]

With respect to comparative safety, several of the larger trials and the multicentre work by McDonnell

et al. have generally found phenylephrine to produce outcomes at least as favourable as alternative vasopressors with respect to maternal haemodynamics, even though both phenylephrine and ephedrine remain considered acceptable choices in routine obstetric practice.[13,16,17] Although the present study was not designed to capture neonatal acid–base parameters, the absence of any excess in maternal nausea or vomiting with phenylephrine is in keeping with these reports and supports its continued use as a first-line agent in this setting.

The improved maternal satisfaction observed in the phenylephrine group during episodes of haemodynamic instability is a clinically relevant finding that has received comparatively less attention in the literature, although a similar trend toward greater haemodynamic predictability with phenylephrine, and with related alpha-agonist strategies, has been noted in other randomised comparisons.[18,19] Taken together with more recent fetal monitoring data reported by Sun et al., which found no clinically meaningful difference between phenylephrine and norepinephrine on fetal cardiac output,[20] our results support the view that the choice between ephedrine and phenylephrine can reasonably be individualised to maternal heart rate and haemodynamic trend rather than dictated by a single uniform protocol.

Several limitations should be acknowledged. The sample size of 50 patients, while adequate to detect the differences reported, limits the power of the study to detect rarer adverse events or subtle differences in neonatal outcome, which was not directly assessed. The single-centre design and fixed bolus-dosing protocol may not be generalisable to infusion-based regimens used elsewhere, restricting direct comparison with several of the larger trials discussed above. Future multicentre work incorporating fetal acid–base measures and weight-adjusted dosing strategies would help to clarify the optimal vasopressor strategy for this patient population.

CONCLUSION

In this comparative study of fifty women undergoing elective caesarean section under spinal anaesthesia, intravenous phenylephrine provided more effective control of post-spinal hypotension than ephedrine, reflected in better post-intervention systolic blood pressure, shorter hypotensive episodes, and a reduced requirement for additional vasopressor doses. Ephedrine, in turn, was associated with a higher post-intervention heart rate, an effect that may be advantageous in patients prone to bradycardia. Both drugs demonstrated a comparable and acceptable safety profile, with no significant difference in the overall incidence of hypotension, bradycardia, hypertension, nausea, or vomiting. These findings support the use of phenylephrine as a reliable first-line vasopressor for the prevention and treatment of spinal-induced hypotension during caesarean delivery, while reserving ephedrine for situations in which heart-rate preservation is a specific clinical priority.

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