Section: Anaesthesiology

Original Research Article

A COMPARATIVE STUDY TO EVALUATE THE EFFECTIVENESS OF PROPHYLACTIC PHENYLEPHRINE VERSUS NOREPINEPHRINE INFUSION FOR THE PREVENTION OF POST-SPINAL HYPOTENSION IN CAESAREAN DELIVERY

R. Priyanga[1], Hassaan Muhammed[2], Aswin Mohanram[3], Karthick S[4], Alekya Sai Guntupalli[5]

[1]Post Graduate III, Department of Anaesthesiology, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India.
[2]Assistant Professor Department of Anaesthesia, King Faisal University, Hofuf 36362, KSA.
[3]Assistant Professor, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India
[4]Senior Resident, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India
[5]Senior Resident, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India

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Corresponding Author:
Dr. R. Priyanga,
Email: priyangaprithumbbs678@gmail.com

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ABSTRACT

Background: Spinal anaesthesia is the preferred technique for caesarean delivery but is frequently complicated by maternal hypotension. Phenylephrine is the established first-line vasopressor, while norepinephrine, with mixed α1- and modest β1-adrenergic activity, has emerged as a promising alternative that may preserve heart rate and cardiac output better than phenylephrine. The objective is to compare the effectiveness of prophylactic phenylephrine versus norepinephrine infusion in preventing post-spinal hypotension in parturients undergoing caesarean delivery. **Materials and Methods:** Prospective randomised comparative trial of 120 ASA II parturients aged 18–40 years undergoing elective/emergency caesarean section under spinal anaesthesia at PESIMSR, randomised to Group P (phenylephrine infusion 25 mcg/min, n=60) or Group N (norepinephrine infusion 3 mcg/min, n=60), both commenced immediately after spinal block. Heart rate, blood pressure, and SpO_2 were recorded at 1, 3, and 5 minutes, at delivery, and at intervals thereafter; incidence of hypotension, bradycardia, rescue vasopressor requirement, physician intervention, reactive hypertension, nausea/vomiting, and neonatal outcomes were compared using the independent t-test and chi-square test. **Results:** Baseline demographic, obstetric, and haemodynamic parameters were comparable between groups (all $p>0.05$). Post-spinal hypotension occurred in 33.3% of Group P versus 28.3% of Group N ($p=0.68$), and severe hypotension in 3.3% versus 1.6% ($p=0.55$); rescue vasopressor requirement was similar ($p=0.66$). Bradycardia (HR ≤50 bpm) was significantly more frequent in Group P (8.3% vs 5.0%; $p=0.046$), and physician intervention was required more often in Group P (41.6% vs 28.3%; $p=0.04$). Reactive hypertension and nausea/vomiting were comparable between groups ($p=0.34$ and $p=0.73$). APGAR scores and umbilical arterial/venous pH did not differ significantly between groups. **Conclusion:** Norepinephrine infusion is non-inferior to phenylephrine in preventing post-spinal hypotension during caesarean delivery, with the added advantages of better heart rate preservation, fewer episodes of bradycardia, and reduced need for physician intervention, without compromising maternal or neonatal safety.

INTRODUCTION

Spinal anaesthesia is the technique of choice for elective and emergency caesarean delivery owing to its rapid onset, dense block, and minimal fetal drug transfer, but it is frequently complicated by maternal hypotension, reported in 60–80% of cases, which can cause maternal symptoms and reduced uteroplacental perfusion.[1]

Hypotension after spinal anaesthesia results mainly from sympathetic blockade causing decreased systemic vascular resistance and venous return, compounded by aortocaval compression and increased vascular capacitance of pregnancy; if

untreated, it can lead to fetal acidosis and poor neonatal outcomes, making prophylactic haemodynamic strategies essential.[2]

Phenylephrine, a pure α1-agonist, is the current first-line vasopressor owing to its predictable onset and favourable neonatal outcomes, though it may cause reflex bradycardia and reduced cardiac output at higher prophylactic doses.[3,4] Norepinephrine, with both α1-mediated vasoconstriction and modest β1-cardiac stimulation, may better preserve cardiac output and heart rate, prompting growing interest in its use as a prophylactic alternative to phenylephrine.[5,6]

Prophylactic vasopressor infusions provide more stable maternal haemodynamics than bolus regimens, but the optimal choice between phenylephrine and norepinephrine remains under investigation.[7] This study was therefore undertaken to compare the effectiveness of prophylactic phenylephrine versus norepinephrine infusion in preventing post-spinal hypotension during caesarean delivery.

Aims and Objectives

To compare the effectiveness of prophylactic phenylephrine and norepinephrine infusion in preventing post-spinal hypotension during caesarean delivery, assessed by blood pressure, heart rate, and SpO_2 at 1, 3, and 5 minutes after injection, until delivery, and every 10 minutes thereafter.

MATERIALS AND METHODS

Study design and setting: Prospective, randomised, comparative clinical trial conducted in the Department of Anaesthesiology, PES Institute of Medical Sciences and Research (PESIMSR), Kuppam, after Institutional Human Ethics Committee approval.

Study population and sampling: Parturients aged 18–40 years, ASA physical status II, with singleton term pregnancy (≥37 weeks) scheduled for caesarean section under spinal anaesthesia were enrolled after written informed consent. Patients with premature rupture of membranes, pregnancy-induced hypertension, antepartum haemorrhage, significant medical comorbidities, severe pre-eclampsia/eclampsia, or caesarean delivery under general anaesthesia were excluded. Participants were randomised using computer-generated codes in sealed, sequentially numbered opaque envelopes to Group P (phenylephrine, n=60) or Group N (norepinephrine, n=60).

Intervention: After standard monitoring and spinal anaesthesia (25-gauge Quincke needle, L3–L4, 2 mL 0.5% hyperbaric bupivacaine) with left uterine displacement and co-loading with Ringer Lactate 20 mL/kg, Group P received phenylephrine infusion at 25 mcg/min and Group N received norepinephrine infusion at 3 mcg/min, both commenced immediately after the block via syringe pump and continued until delivery. Hypotension (≥20% fall from baseline systolic blood pressure) was treated with rescue boluses (25 mcg phenylephrine or 3 mcg norepinephrine as per group), and bradycardia (HR ≤50 bpm with hypotension) with IV atropine 0.6 mg.

Outcome measures: The primary outcome was effectiveness in maintaining maternal blood pressure after spinal anaesthesia. Secondary outcomes were incidence of hypotension, heart rate variations and atropine requirement, total rescue boluses, physician intervention, reactive hypertension, nausea/vomiting, and neonatal outcomes (APGAR scores, umbilical arterial/venous pH).

Statistical analysis

Data were analysed using SPSS version 23. Continuous variables were expressed as mean ± standard deviation and compared using the independent t-test; categorical variables were expressed as frequencies/percentages and compared using the chi-square test. $p<0.05$ was considered statistically significant.

RESULTS

One hundred and twenty parturients (60 per group) were studied. Age, height, weight, BMI, gravida status, type of caesarean section, and baseline heart rate, blood pressure, and SpO_2 were comparable between Group P and Group N (all $p>0.05$), confirming adequate randomisation. [Table 1]

Table 1: Baseline demographic, obstetric, and haemodynamic characteristics

Parameter	Group P (n=60)	Group N (n=60)	p value
Age 23–30 years, n (%)	43 (71.6%)	44 (73.3%)	0.97
BMI ≥25 (overweight/obese), n (%)	49 (81.6%)	46 (76.6%)	0.604
Primigravida, n (%)	42 (70.0%)	40 (66.6%)	0.603
Elective caesarean section, n (%)	41 (68.3%)	39 (65.0%)	0.68
Baseline heart rate 80–89 bpm, n (%)	25 (41.6%)	26 (43.3%)	0.90
Baseline SBP 110–119 mmHg, n (%)	30 (50.0%)	29 (48.3%)	0.98
Baseline MAP 80–89 mmHg, n (%)	30 (50.0%)	29 (48.3%)	0.99

The overall incidence of post-spinal hypotension, severe hypotension, and rescue vasopressor bolus requirement did not differ significantly between groups, though bradycardia and physician intervention were significantly more frequent in Group P. [Table 2]

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Table 2: Maternal haemodynamic outcomes and adverse events

Outcome	Group P (n=60)	Group N (n=60)	p value
Post-spinal hypotension, n (%)	20 (33.3%)	17 (28.3%)	0.68
Severe post-spinal hypotension, n (%)	2 (3.3%)	1 (1.6%)	0.55
No rescue bolus required, n (%)	43 (71.6%)	46 (76.6%)	0.66
Bradycardia (HR ≤50 bpm), n (%)	5 (8.3%)	3 (5.0%)	0.046*
Physician intervention required, n (%)	25 (41.6%)	17 (28.3%)	0.04*
Reactive hypertension, n (%)	7 (11.6%)	4 (6.6%)	0.34
Nausea/vomiting, n (%)	4 (6.6%)	5 (8.3%)	0.73

Neonatal outcomes, surgical timing, and level of sensory block achieved were comparable between the two groups. [Table 3]

Table 3: Neonatal outcomes and surgical/block characteristics

Parameter	Group P (n=60)	Group N (n=60)	p value
APGAR ≤7 at 1 min, n (%)	4 (6.6%)	3 (5.0%)	0.69
APGAR >7 at 5 min, n (%)	60 (100%)	60 (100%)	1.00
Umbilical arterial pH <7.20, n (%)	1 (1.6%)	0 (0.0%)	0.66
Sensory block level T5, n (%)	30 (50.0%)	28 (46.6%)	0.83
Duration of surgery 31–45 min, n (%)	32 (53.3%)	30 (50.0%)	0.64
Time SAB to delivery ≤8 min, n (%)	28 (46.6%)	30 (50.0%)	0.94

DISCUSSION

In this study of 120 parturients, baseline age, anthropometric, obstetric, and haemodynamic parameters were comparable between groups, consistent with NganKee et al,[8] Goel et al,[9] and the systematic review by Liu et al,[10] all of whom reported similar baseline equivalence between phenylephrine and norepinephrine groups, supporting attribution of subsequent differences to the study drugs.

Post-spinal hypotension occurred in 33.3% of Group P and 28.3% of Group N, with no significant intergroup difference (p=0.68), indicating non-inferior efficacy of norepinephrine, consistent with Goel et al,[9] Ali and Bajaj,[11] and Saharia et al,[12] who similarly reported comparable hypotension rates between the two vasopressors despite differing absolute incidences attributable to variation in infusion protocols and monitoring frequency.

Bradycardia was significantly more frequent with phenylephrine (8.3% vs 5.0%; p=0.046), in keeping with its pure α1-agonism and lack of chronotropic activity, and consistent with Goel et al,[9] who reported higher atropine use with phenylephrine, and with Vallejo et al,[13] who observed fewer heart-rate-related corrective interventions with norepinephrine. This heart-rate-preserving effect likely also explains the significantly lower requirement for physician intervention in Group N (28.3% vs 41.6%; p=0.04), a pattern indirectly supported by the pooled reduction in bradycardia and reactive hypertension with norepinephrine reported by Liu et al.[10]

Reactive hypertension and nausea/vomiting did not differ significantly between groups, consistent with Liu et al,[10] and Chen et al,[14] who reported low and comparable incidences of these adverse effects with both vasopressors. Neonatal outcomes, including APGAR scores and umbilical arterial/venous pH, were similar between groups, in agreement with the non-inferiority findings of NganKee et al.8 and Pauline et al,[15] confirming that norepinephrine does not compromise fetal wellbeing relative to phenylephrine.

Limitations

This was a single-centre study with a sample size not powered to detect differences in rare outcomes such as severe hypotension or neonatal acid–base disturbance. Haemodynamic monitoring was non-invasive, with heart rate used as a surrogate for cardiac output rather than direct measurement.

CONCLUSION

Norepinephrine infusion is non-inferior to phenylephrine in preventing post-spinal hypotension during caesarean delivery, with comparable incidences of hypotension, severe hypotension, rescue vasopressor requirement, reactive hypertension, and nausea/vomiting. Norepinephrine offered a significant advantage in preserving maternal heart rate, with fewer episodes of bradycardia and a correspondingly reduced need for physician intervention, while neonatal outcomes remained equivalent between groups. These findings support norepinephrine as a safe and effective alternative to phenylephrine for prophylactic management of spinal anaesthesia-induced hypotension in caesarean section.

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