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Bolus Norepinephrine Versus Phenylephrine for the Management of Maternal Hypotension During Caesarean Delivery Under Spinal Anaesthesia -A Double Blind Randomized Controlled Trial

(Norepinephrine vs phenylephrine in spinal hypotension)

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KEYWORDS:

Caesarean delivery, spinal anaesthesia, hypotension, norepinephrine, phenylephrine, bradycardia

ABSTRACT:

Background: Spinal anaesthesia-induced hypotension is a frequent challenge during caesarean delivery and may compromise maternal comfort and uteroplacental perfusion. Phenylephrine is the standard vasopressor(1), while norepinephrine has emerged as a potential alternative because it may preserve heart rate better(2,3).

Methods: This prospective double-blind randomized study included 128 ASA II parturients undergoing elective caesarean delivery under spinal anaesthesia. Patients received intravenous norepinephrine 5 mcg or phenylephrine 50 mcg boluses when systolic blood pressure fell below 80% of baseline. Hemodynamic variables were recorded every minute until delivery. Neonatal APGAR scores and umbilical cord blood gas values were assessed(4).

Results: Both vasopressors effectively treated hypotension. Heart rate was lower in the norepinephrine group at selected time points ($p<0.05$), but clinically significant bradycardia was uncommon (3.13% vs 0%). Neonatal APGAR scores and cord blood gas values were comparable between groups(4).

Conclusion: Intermittent bolus norepinephrine and phenylephrine were both effective and safe for treatment of post-spinal hypotension during caesarean delivery. Norepinephrine showed a favorable hemodynamic profile with acceptable neonatal outcomes(2,5).

Introduction

Spinal anaesthesia is the preferred technique for most elective caesarean deliveries because it provides rapid onset, reliable anaesthesia, and allows the mother to remain awake during birth while avoiding airway manipulation risks associated with general anaesthesia(1,6). However, maternal hypotension occurs frequently due to sympathetic blockade and aortocaval compression by the gravid uterus, with incidence rates up to 71%(4,7).

Untreated hypotension may cause maternal nausea, vomiting, dizziness, and reduced uteroplacental perfusion leading to fetal acidosis(8). Since uteroplacental blood flow correlates directly with maternal perfusion pressure, prompt correction is essential(9). Standard preventive measures include left uterine displacement, crystalloid co-loading, and vasopressor administration(10).

Phenylephrine has been the vasopressor of choice for two decades because it reliably restores blood pressure and maintains favorable fetal acid-base status compared to ephedrine(1,11). Its major limitation is reflex bradycardia due to pure alpha-1 adrenergic activity, which may reduce cardiac output(12). Norepinephrine, with combined alpha and mild beta-1 activity, may

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better preserve maternal heart rate while maintaining vasoconstriction(2,3,13).

This study compared intermittent bolus norepinephrine (5 mcg) versus phenylephrine (50 mcg) for treatment of spinal anaesthesia-induced hypotension during elective caesarean delivery, focusing on maternal bradycardia incidence, hemodynamic stability, and neonatal outcomes(4).

Materials and Methods

Thisprospective double-blind randomized controlled study wasconducted on patients undergoing elective caesarean sections fulfilling inclusion criteria atShri Dharmasthala Manjunatheshwara College of medical science and hospital, Dharwad,during the period of December 2019 to May 2021.Institutional ethics committee approval and informed consent were obtained . One hundred twenty-eight ASA II parturients aged 18-40 years scheduled for elective caesarean delivery under spinal anaesthesia were included. Exclusion criteria comprised refusal, ASA III-IV status, placenta previa/accreta, eclampsia, fetal distress, or extreme body weight(4).

Patients were randomized using sealed opaque envelopes into two groups: norepinephrine (NE, n=64) receiving 5 mcg IV boluses, or phenylephrine (PE, n=64) receiving 50 mcg IV boluses. Study drugs were prepared by an anaesthesiologist not involved in patient care.

After standard monitoring (ECG, NIBP, SpO2), patients received 10 ml/kg Ringer lactate co-loading. Spinal anaesthesia was performed in left lateral position at L3-L4 interspace using 25G Quincke needle with 2.5 ml hyperbaric bupivacaine 0.5% plus 0.2 mg morphine. Patients were positioned supine with left uterine displacement(4,10).

Hypotension was defined as systolic blood pressure <80% of baseline. Bradycardia was defined as heart rate <60 bpm. Rescue boluses were administered for hypotension, with repeats every minute for up to three doses if required. Atropine 0.6 mg IV was available for bradycardia. Heart rate and blood pressure were recorded every minute from intrathecal injection until delivery. APGAR scores (1 and 5 minutes) and umbilical cord arterial blood gas analysis were documented(4).

STASTICAL ANALYSIS Data was analysed using R software version 4.1.1 and Excel. Categorical variables are presented in the form of a frequency table. Continuous variables are presented as Mean ± SD/ Median (Min, Max) form. A Chi-square test was applied to find the association of APGAR score with group. Two sample t-test/Mann Whitney U test was used to compare mean/distributions of parameters over group. P-value ≤0.05 was considered statistically significantData were analyzed using SPSS 22.0. Continuous variables were compared using independent t-test or Mann-Whitney U test. Categorical variables used chi-square test. P<0.05 was significant.

Results

CONSORT DIAGRAM

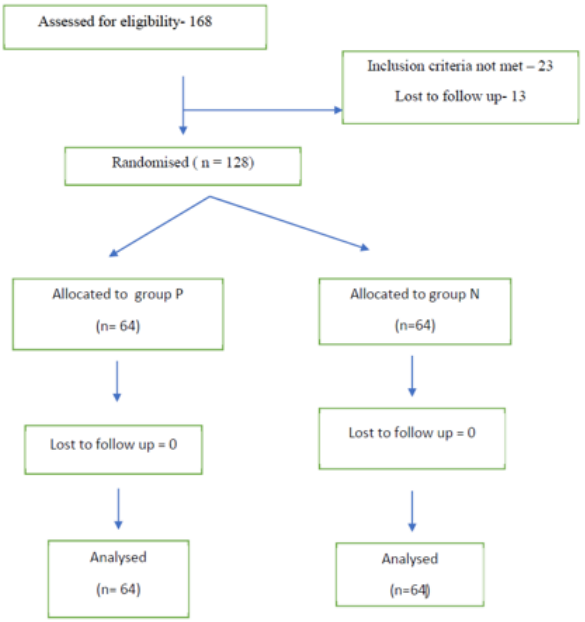

Table 1: Comparison of different demographic variables with groups.

Variables	Sub Category	Group NE (n=64)	Group PE (n=64)	Total	p-value
Age (years)	Mean ± SD	26.83 ± 4.22	26.47 ± 4.53	26.66 ± 4.35	0.6624[T]
	Median (Min, Max)	26 (19, 39)	25 (19, 38)	26 (19, 39)	
Weight (Kg)	Mean ± SD	65.23 ± 9.2	65.95 ± 9.37	65.59 ± 9.26	0.6623[T]
	Median (Min, Max)	64 (46, 88)	66 (40, 84)	66 (40, 88)	

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Demographic characteristics were comparable between groups. Mean age was 26.66±4.35 years and mean weight was 65.59±9.26 kg. Baseline heart rate (86.4±8.2 vs 87.1±7.9 bpm) and systolic blood pressure (118.3±9.4 vs 117.8±10.1 mmHg) were similar(4).

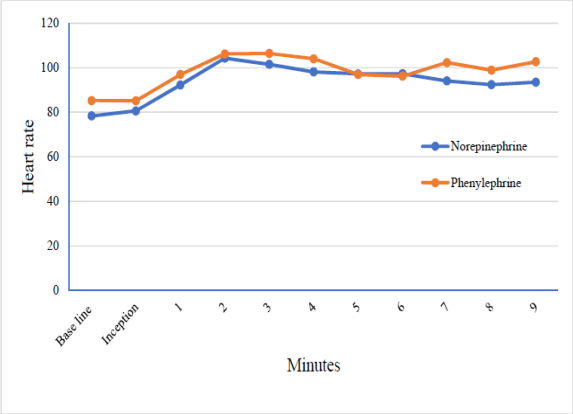

Fig 1. Heart rate at different time points in groups

Heart rate: NE group showed significantly lower heart rates at 4th (p=0.032), 7th (p=0.021), and 8th (p=0.018) minutes compared to PE group. Clinically significant bradycardia occurred in 2/64 (3.13%) NE patients versus 0/64 PE patients (p=0.497). No atropine was required(4).

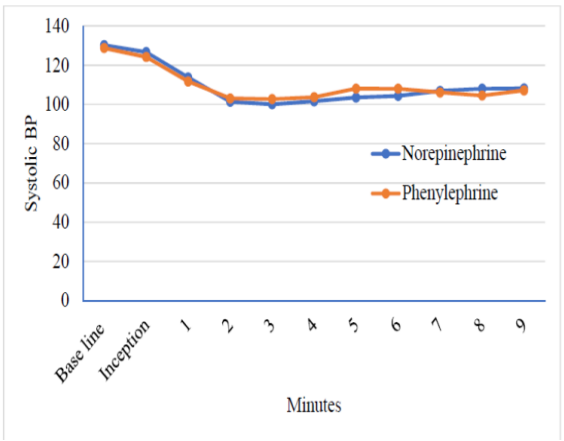

Fig. 2 . Systolic blood pressure at different time points with groups

Blood pressure: Systolic BP differed significantly at 5th (p=0.0259) and 8th (p=0.0293) minutes but remained clinically acceptable in both groups. Diastolic BP showed differences at 3rd (p=0.043) and 5th (p=0.037) minutes. Mean arterial pressure was comparable except at 2nd minute(4).

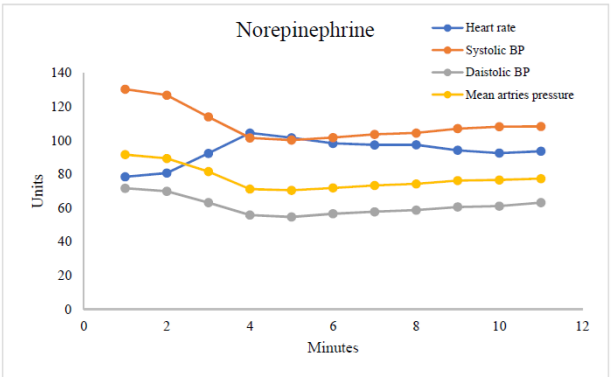

Fig 3 . Impact of norepinephrine

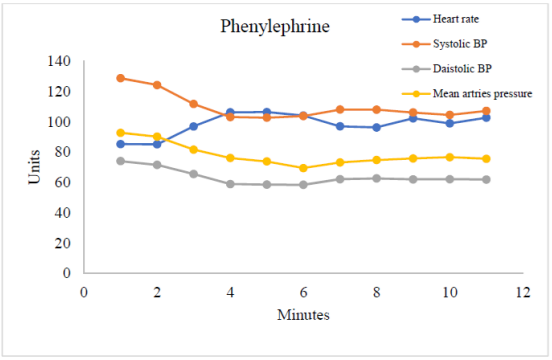

Fig 4 . Impact of phenylephrine

Vasopressor usage: Most boluses were required within first 5 minutes post-spinal injection, consistent with sympathectomy onset. Total boluses per patient were similar between groups(4).

Variables	APGAR score	Group NE (n=64)	Group PE (n=64)	Total	p-value
APGAR 1min	7	1 (1.56%)	12 (19.67%)	13 (10.4%)	**<0.001^{C}***
	8	63 (98.44%)	49 (80.33%)	112 (89.6%)	
APGAR 5min	7	1 (1.56%)	(0%)	1 (0.8%)	**0.036^{MC}***
	8	4 (6.25%)	12 (19.67%)	16 (12.8%)	
	9	59 (92.19%)	49 (80.33%)	108 (86.4%)	

*Abbreviations- C – Chi square test, MC – Chi square test with Monte Carlo simulation, * indicates statistical significance*

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Table 2 . Neonatal outcome of APGAR Score

Neonatal outcomes: Cord blood pH (7.28±0.06 vs 7.29±0.05), PCO2 (48.2±6.1 vs 47.8±5.9 mmHg), and base excess (-2.1±1.2 vs -1.9±1.1 mEq/L) were comparable. APGAR scores ≥8 at 1 and 5 minutes were achieved by all neonates(4).

Discussion

This study demonstrates that both norepinephrine and phenylephrine boluses effectively treat spinal anaesthesia-induced hypotension during elective caesarean delivery. Norepinephrine showed modestly lower heart rates at selected time points but minimal clinically significant bradycardia(4).

Phenylephrine's pure alpha-1 agonism reliably increases systemic vascular resistance but frequently causes reflex bradycardia(1,11). Norepinephrine's mild beta-1 activity appears to attenuate this effect while maintaining vasoconstriction, consistent with recent trials(2,5,13). The 3.13% bradycardia incidence in NE group versus 0% in PE group was not statistically significant and required no intervention.

Blood pressure control was clinically adequate with both agents despite transient statistical differences. This aligns with meta-analyses showing comparable efficacy between vasopressors when titrated appropriately(14). Early bolus requirement reflects predictable sympathectomy timing post-spinal injection(7).

Neonatal outcomes constitute the most important safety endpoint. Both APGAR scoring and cord blood gas analysis showed excellent fetal condition, supporting either vasopressor's safety profile(4). This corroborates systematic reviews finding no fetal outcome differences between norepinephrine and phenylephrine(12,14,15).

Study strengths include double-blinding, adequate sample size for primary outcome, and comprehensive neonatal assessment. Limitations comprise elective-only population, excluding emergency cases or comorbidities where vasopressor response may differ. Total vasopressor dose analysis and cardiac output measurement were not performed(4).

Clinical Implications

Both vasopressors are suitable for bolus rescue therapy during elective caesarean delivery. Norepinephrine offers theoretical hemodynamic advantages and practical simplicity as a dilute solution. Phenylephrine remains the established standard with extensive familiarity.

Institutional protocols should incorporate prompt titration alongside uterine displacement and fluid co-loading(10,16).

Conclusion

Bolus norepinephrine 5 mcg and phenylephrine 50 mcg were equally effective for managing spinal hypotension during elective caesarean delivery. Norepinephrine demonstrated acceptable heart rate preservation with excellent neonatal outcomes, supporting its role as a phenylephrine alternative(4,5).

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