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Original article

Effect of Different Vasopressors for the Management of Spinal Anesthesia-Induced Hypotension during Cesarean Section and Postnatal Chart in Tripoli, Libya

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Abstract
Spinal-induced hypotension (SIH) remains a prevalent and clinically consequential complication of neuraxial anaesthesia for cesarean delivery. Its pathophysiological sequelae include maternal symptomatology (nausea, vomiting, dizziness) and impaired uterine-placental perfusion, predisposing to fetal acidosis and diminished fetal Apgar scores. Judicious selection of a vasopressor agent is therefore paramount. This study sought to compare the efficacy of ephedrine, norepinephrine, and a combined regimen in the management of SIH during cesarean section, with respect to maternal hemodynamic stability, neonatal outcomes, and adverse event profiles. This study was a prospective cross-sectional clinical analysis conducted at Al-Hadba Al-Khadra General Hospital in Tripoli, Libya. A total of 170 parturients were enrolled and divided into four groups: ephedrine (n = 60), norepinephrine (n = 60), combined (n = 20), and a control group (n = 30). Hemodynamic parameters were recorded at eleven perioperative time points. Apgar scores were assessed at both one and five minutes after delivery, and maternal adverse effects were documented. Statistical analysis was carried out using SPSS version 25, applying one-way ANOVA, the Kruskal-Wallis test, repeated-measures ANOVA, Pearson correlation, and chi-square tests. A p-value of less than 0.05 was considered statistically significant. Baseline demographic and clinical characteristics were comparable across all groups. All vasopressor regimens successfully restored blood pressure within 30–45 minutes. The combined group exhibited the most pronounced early reduction in systolic and mean arterial pressures at the five-minute interval, whereas norepinephrine demonstrated the most stable hemodynamic profile with minimal fluctuation relative to ephedrine. Apgar scores did not differ significantly among groups. Nausea and vomiting were reported across all cohorts; tachycardia was predominantly observed in the ephedrine group, while sporadic bradycardia occurred in those receiving norepinephrine. All vasopressor agents effectively controlled SIH without compromising neonatal outcomes. Norepinephrine may be the preferred agent owing to its superior hemodynamic stability and reduced propensity for tachyarrhythmia. Larger-scale, multi-centre investigations are warranted to corroborate these findings.
Keywords. Vasopressors, Spinal Anaesthesia, Anaesthesia, Hypotension, Cesarean Section, Apgar Score.

Introduction

Vasopressors such as ephedrine, phenylephrine, and norepinephrine are routinely employed to prevent maternal hypotension by counteracting sympathetic blockade, stabilising cardiovascular function, and reducing maternal and neonatal complications [1]. Ephedrine, a mixed α- and β-adrenergic agonist, has historically been favoured due to its relative preservation of utero-placental blood flow compared with pure α-adrenergic agents. However, its use may increase systemic vascular resistance (SVR) and compromise placental perfusion, raising concerns about fetal outcomes. In contrast, α-adrenergic agonists like phenylephrine and norepinephrine, while effective in maintaining blood pressure, can induce uterine vasoconstriction and contribute to fetal acidosis [2,3]. Despite these pharmacological distinctions, the Libyan healthcare system lacks standardised protocols, leaving vasopressor selection largely dependent on drug availability. Cesarean section (CS), defined as delivery of the fetus via laparotomy and hysterotomy [4], is the most frequently performed major surgical procedure worldwide [5]. It may be elective or emergent, with rising utilisation across both developed and developing regions [6].

Spinal anaesthesia, first introduced by August Bier in 1898, remains the predominant anaesthetic technique for CS, owing to its efficacy in surgeries below the umbilical level [7,8]. Despite its widespread use, neuraxial anaesthesia carries contraindications, notably maternal hypotension [9]. Spinal anaesthesia–induced hypotension lacks a standardised definition, with criteria varying across studies. Commonly applied thresholds include an absolute systolic blood pressure of 80–100 mmHg, a relative decline of up to 30% from baseline, or a combination of both parameters [10]. During labour, vasopressors such as phenylephrine and ephedrine are administered to restore maternal blood pressure and maintain placental perfusion [11]. Their effects on neonatal outcomes, particularly Apgar scores, remain inconclusive. The Apgar score, endorsed by the American College of Obstetricians and Gynaecologists and the American Academy of Pediatrics, provides a rapid, standardised assessment of neonatal status immediately after birth and following resuscitation [12]. Spinal anaesthesia-induced maternal hypotension during cesarean section represents a frequent clinical challenge, occurring in up to 75% to 90% of obstetric patients due to preganglionic sympatholysis and aortocaval compression. This hemodynamic instability compromises uteroplacental perfusion, increasing the risk of fetal hypoxia, acidosis, and subsequent adverse neurodevelopmental sequelae.

To mitigate these complications, evidence-based obstetric protocols advocate for the targeted administration of vasopressors, such as phenylephrine and norepinephrine, to stabilise maternal blood pressure and safeguard neonatal

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outcomes [13]. Accordingly, this clinical study is designed to evaluate and compare the efficacy of diverse vasopressor management strategies on spinal-induced hypotension and postnatal indices during cesarean sections conducted over nine months at Al-Hadba Al-Khadra General Hospital in Tripoli.

Methods

Study Subjects

This study was designed as a cross-sectional clinical analysis and was conducted at Al-Hadba Al-Khadra General Hospital in Tripoli over a period of nine months. The methodology outlines the ethical approval from the hospital (24/249), subject selection criteria, anaesthesia techniques, administration of vasopressors, and monitoring procedures. It also explains the data collection methods, neonatal evaluations, and statistical analysis employed to ensure the reliability and validity of the findings.

Patient Groups

The study involved women with full-term pregnancies (gestational age between 37 and 40 weeks) who were scheduled for elective cesarean sections under spinal anaesthesia. Participants were classified according to the American Society of Anesthesiologists (ASA) physical status classification as I or II and were aged between 19 and 45 years. Exclusion Criteria: Women were excluded from the study if they refused participation, had maternal comorbidities, fetal abnormalities, or contraindications to spinal anaesthesia. Additional exclusions included gestational diabetes, preeclampsia, placenta previa, systemic hypertension, or any other chronic medical conditions.

Patient Preparation and Preoperative Evaluation

Patients arrived at the gynaecology department of Al-Hadba Al-Khadra General Hospital in the morning after an overnight fast. Preparation included the insertion of two green intravenous cannulas, administration of prophylactic antacids, and a 500 mL crystalloid preload (normal saline or Ringer's lactate). Standard assessments were conducted collaboratively by the gynaecology and anesthesiology teams, which included measuring baseline hemodynamic parameters such as heart rate, oxygen saturation, electrocardiogram, and blood pressure.

Anaesthesia Technique

After completing the baseline assessments, the surgical site was disinfected and infiltrated with a 1% lidocaine hydrochloride injection (10 mg/mL; sourced from the Republic of Korea). Spinal anaesthesia was then administered intrathecally while the patient was in a sitting position, using a 25-, 26-, or 27-gauge spinal needle. This involved delivering 10–12 mg of hyperbaric bupivacaine without fentanyl (5 mg/mL).

Vasopressor Preparation and Administration

Vasopressors were prepared preoperatively by the attending anaesthesia team as follows. Norepinephrine tartrate (2 mg/mL; Laboratorio Farmacologico at Bergamo, Italy) and ephedrine hydrochloride (25 mg/mL; same manufacturer) were employed.

Apgar Score Assessment (Neonatal Evaluation)

Neonatal evaluation was performed by an assistant paediatrician, with Apgar scores assigned at 1 and 5 minutes following delivery. The assessors were blinded to maternal vasopressor exposure to minimise bias. Birth weight and sex were systematically recorded in the medical records. An Apgar score <7 at either time point was defined as neonatal distress.

Statistical Analysis

All analyses were conducted using SPSS software, version 25.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were applied to summarise the data: continuous variables were expressed as mean ± standard deviation (SD) or as median with range, whereas categorical variables were presented as frequencies and percentages. Comparisons of variables were performed using paired t-tests and one-way ANOVA for continuous variables, and chi-square for categorical variables. A p-value <0.05 was considered statistically significant.

Results

Study Population and Baseline Characteristics

A total of 170 pregnant women undergoing cesarean section were enrolled and allocated to one of four groups: ephedrine, norepinephrine, combined treatment, and control. Baseline demographic and clinical characteristics of the study population are presented in Table 1. No statistically significant differences in maternal age were observed across the treatment groups. The mean ages of the ephedrine and norepinephrine groups were comparable (31.92 ± 5.51 and 31.73 ± 5.42 years, respectively), whereas the control and combined-treatment groups exhibited marginally higher mean ages of 33.93 and 33.70 years, respectively. Body mass index (BMI) values were similarly distributed among all groups, ranging from 32.54 to 32.92 kg/m^2, indicating the absence of clinically meaningful intergroup differences in obesity status. Although modest variations in body weight and height were noted across groups, the combined-treatment group

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demonstrated the highest mean body weight at 87.65 kg. Moreover, clinical assessment revealed greater estimated intraoperative blood loss within this group. This finding likely reflects a greater degree of underlying hemodynamic instability necessitating dual vasopressor support, underscoring the importance of accounting for baseline clinical severity when interpreting intergroup differences.

Table 1 summarises the baseline data, providing a solid framework for investigating the study's objectives, specifically the comparative effectiveness of vasopressors and their associated maternal-neonatal outcomes. Both ephedrine and norepinephrine were similarly effective in correcting hypotension; however, norepinephrine produced a hemodynamic response that more closely resembled the spontaneous recovery pattern observed in the control group. In contrast, the combination therapy group exhibited increased hemodynamic variability and a higher incidence of side effects, while the control subjects maintained physiological stability.

Table 1. Demographic and clinical continuous variables by group

Variables	Ephedrine (n=60)	Norepinephrine (n=60)	Combined (n=20)	Controls (n=30)
Age (yrs)	31.92 ± 5.51 (21–43)	31.73 ± 5.42 (20–42)	33.70 ± 6.12 (22–45)	33.93 ± 5.87 (23–46)
Weight (kg)	86.12 ± 12.34 (60–115)	85.45 ± 11.98 (62–112)	87.65 ± 13.45 (65–120)	84.23 ± 10.67 (63–108)
Height (cm)	162.45 ± 5.67 (150–175)	161.89 ± 5.23 (149–174)	160.23 ± 6.12 (148–172)	162.12 ± 5.34 (150–173)
BMI (kg/m^2)	32.67 ± 4.23 (25–42)	32.54 ± 4.12 (24–41)	32.92 ± 4.56 (26–43)	32.78 ± 4.01 (25–40)
Fasting Time (hr)	8.45 ± 2.34 (4–12)	8.67 ± 2.12 (5–13)	8.23 ± 2.45 (4–12)	8.56 ± 2.23 (5–12)
Blood Loss (ml)	771.67 ± 245.12 (400–1200)	664.17 ± 198.45 (350–1000)	860.00 ± 270.62 (500–1400)	602.33 ± 167.89 (300–900)

Neonatal Outcomes

The APGAR scores are generally healthy, with values above 7; however, there is a slight dip observed in the combined group. Clinically, we noted that the higher blood loss in both groups may indicate greater hemodynamic instability, which necessitated the use of dual vasopressors. While the combined group's APGAR scores show a slight decline, the control group, which did not require vasopressor use, exhibited the lowest blood loss. This difference might be attributed to less severe hypotension or varying surgical factors. Additionally, the combined group's blood loss displayed higher variability, with a standard deviation (SD) of 270.62.

Table 2. Neonatal APGAR scores in each group, and the results are expressed as mean ± SD

Groups	APGAR 1st min	APGAR 5th min
Ephedrine	8.32 ± 0.87 (6–9)	9.25 ± 0.45 (8–10)
Norepinephrine	8.12 ± 0.92 (6–9)	9.18 ± 0.50 (8–10)
Combined	7.65 ± 1.12 (5–9)	8.80 ± 0.67 (7–10)
Controls	8.03 ± 0.95 (6–9)	9.13 ± 0.52 (8–10)

Maternal Hemodynamic Parameters Across Time Points

Vital signs were analysed at all predefined time points to assess hemodynamic changes, with complete data presented in Tables 3 and 4.

Pre-Induction

One-way ANOVA revealed significant between-group differences in systolic blood pressure (SBP; $F = 3.12$, $p = 0.028$) and mean blood pressure (MBP; $F = 2.78$, $p = 0.042$). Post-hoc analysis using Tukey's Honestly Significant Difference (Tukey's HSD) test demonstrated that the ephedrine group exhibited significantly higher SBP and MBP compared with the norepinephrine group ($p < 0.05$). No significant differences were observed in heart rate (HR; $F = 2.45$, $p = 0.065$), diastolic blood pressure (DBP; $F = 1.89$, $p = 0.132$), or oxygen saturation (SpO2; $F = 0.87$, $p = 0.458$).

Three Minutes Post-Induction

Significant intergroup differences were observed for HR ($F = 4.56$, $p = 0.004$), SBP ($F = 6.78$, $p < 0.001$), DBP ($F = 5.23$, $p = 0.002$), and MBP ($F = 7.12$, $p < 0.001$). Tukey's HSD revealed that the ephedrine, norepinephrine, and combined vasopressor groups had significantly lower SBP, DBP, and MBP than the control group ($p < 0.05$). Notably, the combined vasopressor group demonstrated higher HR than both the ephedrine and norepinephrine groups ($p < 0.05$). No significant differences in SpO2 were detected ($F = 1.34$, $p = 0.263$).

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Five Minutes Post-Induction

Significant differences were identified in HR (F = 3.89, p = 0.010), SBP (F = 8.45, p < 0.001), DBP (F = 6.67, p < 0.001), MBP (F = 9.12, p < 0.001), and SpO2 (F = 3.45, p = 0.018). The combined vasopressor group recorded the lowest SBP (91.85 ± 25.66 mmHg) and MBP (65.32 ± 16.45 mmHg), both significantly lower than the control group (p < 0.05). Additionally, SpO2 in the combined vasopressor group was significantly lower than in both the ephedrine and control groups (p < 0.05).

Ten to Twenty-Five Minutes Post-Induction

Significant differences persisted in SBP, DBP, and MBP (p < 0.05), with vasopressor-treated groups maintaining lower values than controls; however, these differences diminished progressively over time. No significant differences in HR or SpO2 were observed (p > 0.05).

Thirty to Forty-Five Minutes Post-Induction

No significant intergroup differences were observed across any parameter (p > 0.05), indicating hemodynamic stabilisation by this time point.

Table 3. Maternal systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) Across Time Points; all results are expressed as (Mean ± SD)

Time Point	PARAMETERS	EPHEDRINE (N=60)	NOREPINEPHRINE (N=60)	COMBINED (N=20)	CONTROLS (N=30)
Pre_induction	SBP (mmHg)	129.3 ± 15.2	131.8 ± 14.9	124.0 ± 16.3	129.5 ± 13.5
	DBP (mmHg)	78.1 ± 10.2	77.9 ± 9.9	79.8 ± 11.5	79.2 ± 9.3
	MBP (mmHg)	95.2 ± 11.6	96.9 ± 11.0	94.5 ± 12.3	96.3 ± 10.2
3 min Post_induction	SBP (mmHg)	108.5 ± 19.9	109.1 ± 18.6	93.5 ± 24.8	112.3 ± 14.9
	DBP (mmHg)	56.8 ± 11.9	62.3 ± 11.0	53.1 ± 13.5	62.5 ± 9.9
	MBP (mmHg)	74.3 ± 13.6	78.1 ± 12.8	66.9 ± 15.7	79.1 ± 10.3
5 min Post_induction	SBP (mmHg)	106.8 ± 20.3	108.2 ± 19.6	91.9 ± 25.7	111.7 ± 15.8
	DBP (mmHg)	55.6 ± 12.6	62.0 ± 12.0	52.1 ± 14.2	62.0 ± 10.1
	MBP (mmHg)	72.7 ± 14.2	77.4 ± 13.9	65.3 ± 16.5	78.6 ± 11.5
10 min Post_induction	SBP (mmHg)	113.5 ± 18.2	114.8 ± 17.5	112.3 ± 20.1	115.9 ± 14.6
	DBP (mmHg)	64.1 ± 11.3	65.3 ± 10.7	62.5 ± 12.3	66.8 ± 9.5
	MBP (mmHg)	80.6 ± 12.9	81.9 ± 12.1	79.1 ± 13.7	83.1 ± 10.8
15 min Post_induction	SBP (mmHg)	113.8 ± 17.9	114.1 ± 17.1	113.5 ± 19.3	116.1 ± 13.9
	DBP (mmHg)	64.5 ± 10.9	65.8 ± 10.3	63.8 ± 11.9	67.1 ± 9.1
	MBP (mmHg)	80.9 ± 12.5	81.6 ± 11.9	80.3 ± 13.1	83.5 ± 10.3
20 min Post_induction	SBP (mmHg)	114.1 ± 17.6	114.5 ± 16.9	113.8 ± 18.9	116.5 ± 13.5
	DBP (mmHg)	65.8 ± 10.7	66.1 ± 10.1	64.5 ± 11.6	67.5 ± 8.9
	MBP (mmHg)	81.9 ± 12.1	82.3 ± 11.6	81.12 ± 12.89	83.8 ± 10.1
25 min Post_induction	SBP (mmHg)	114.3 ± 17.3	114.8 ± 16.7	113.9 ± 18.6	116.8 ± 13.1
	DBP (mmHg)	66.1 ± 10.5	66.5 ± 9.9	65.1 ± 11.3	67.8 ± 8.7
	MBP (mmHg)	82.3 ± 11.9	82.8 ± 11.3	81.5 ± 12.7	84.1 ± 9.9
30 min Post_induction	SBP (mmHg)	114.5 ± 18.1	115.2 ± 17.9	114.0 ± 19.5	116.1 ± 14.2
	DBP (mmHg)	68.9 ± 11.3	70.1 ± 10.9	67.9 ± 12.6	71.5 ± 9.9
	MBP (mmHg)	84.1 ± 13.5	85.5 ± 13.0	83.3 ± 14.2	86.3 ± 11.2
35 min Post_induction	SBP (mmHg)	114.8 ± 17.9	115.5 ± 17.6	114.3 ± 19.1	116.3 ± 13.9
	DBP (mmHg)	69.1 ± 11.1	70.3 ± 10.7	68.1 ± 12.3	71.7 ± 9.7
	MBP (mmHg)	84.3 ± 13.1	85.8 ± 12.8	83.6 ± 13.9	86.6 ± 11.1
40 min Post_induction	SBP (mmHg)	115.1 ± 17.6	115.8 ± 17.3	114.7 ± 18.9	116.7 ± 13.7
	DBP (mmHg)	69.3 ± 10.9	70.7 ± 10.5	68.5 ± 12.1	71.9 ± 9.5
	MBP (mmHg)	84.8 ± 12.9	86.1 ± 12.6	83.9 ± 13.7	86.9 ± 10.9
45 min Post_induction	SBP (mmHg)	115.5 ± 17.3	116.1 ± 17.1	115.1 ± 18.7	117.1 ± 13.5
	DBP (mmHg)	69.7 ± 10.7	71.1 ± 10.2	68.78 ± 11.9	72.1 ± 9.2
	MBP (mmHg)	85.1 ± 12.7	86.5 ± 12.3	84.3 ± 13.5	87.3 ± 10.7

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Table 4. Maternal heart rate (beats per minute) and SpO_2 (%) across Time Points before and during anaesthesia; all results are expressed as (Mean ± SD)

Time Point	Parameters	Ephedrine (N=60)	Norepinephrine (N=60)	Combined (N=20)	Controls (N=30)
Pre-Induction	HR (bpm)	97.9 ± 12.5	101.9 ± 13.1	102.4 ± 14.2	94.6 ± 11.9
	SpO_2 (%)	99.2 ± 1.7	98.9 ± 1.2	99.1 ± 1.5	99.2 ± 0.7
3 min Post-induction	HR (bpm)	92.3 ± 13.1	94.6 ± 12.5	94.3 ± 14.9	96.8 ± 11.5
	SpO_2 (%)	99.1 ± 1.5	98.8 ± 1.3	98.3 ± 2. 6	99.2 ± 0.9
5 min Post-induction	HR (bpm)	90.8 ± 13.6	92.77 ± 12.9	90.45 ± 15.34	98.8 ± 12.3
	SpO_2 (%)	99.2 ± 1.7	98.83 ± 1.5	97.60 ± 4.32	99.2 ± 1.0
10 min Post-induction	HR (bpm)	91.7 ± 12.8	91.42 ± 11.9	90.60 ± 14.23	92.9 ± 11.1
	SpO_2 (%)	99.0 ± 1.6	98.83 ± 1.2	98.70 ± 1.89	99.0 ± 0.8
15 min Post-induction	HR (bpm)	92.5 ± 12.3	91.89 ± 11.6	91.45 ± 13.78	92.7 ± 10.9
	SpO_2 (%)	99.0 ± 1.5	98.83 ± 1.1	98.80 ± 1.67	99.0 ± 0.9
20 min Post-induction	HR (bpm)	93.1 ± 12.1	92.34 ± 11.3	92.45 ± 13.45	93.5 ± 10.7
	SpO_2 (%)	99.0 ± 1.3	98.83 ± 1.1	98.80 ± 1.56	99.0 ± 0.8
25 min Post-induction	HR (bpm)	93.5 ± 11.9	92.67 ± 11.1	92.78 ± 13.12	93.8 ± 10.5
	SpO_2 (%)	99.0 ± 1.2	98.83 ± 1.1	98.80 ± 1.5	99.0 ± 0.8
30 min Post-induction	HR (bpm)	95.3 ± 12.3	94.32 ± 11.9	95.25 ± 13.5	94.7 ± 11.2
	SpO_2 (%)	99.0 ± 1.5	98.83 ± 1.2	98.80 ± 1.7	99.0 ± 0.9
35 min Post-induction	HR (bpm)	95.5 ± 12.1	94.45 ± 11.7	95.45 ± 13.34	94.9 ± 11.1
	SpO_2 (%)	99.0 ± 1.3	98.83 ± 1.1	98.80 ± 1.56	99.0 ± 0.8
40 min Post-induction	HR (bpm)	95.7 ± 11.9	94.67 ± 11.5	95.67 ± 13.12	95.1 ± 10.9
	SpO_2 (%)	99.0 ± 1.2	98.83 ± 1.1	98.80 ± 1.45	99.0 ± 0.8
45 min Post-induction	HR (bpm)	95.9 ± 11.7	94.89 ± 11.2	95.89 ± 12.89	95.3 ± 10.7
	SpO_2 (%)	99.0 ± 1.1	98.83 ± 1.1	98.8 ± 1.3	99.0 ± 0.8

Post-Hoc Analysis

At 5 min post-induction, Ephedrine (p=0.038) and combined (p=0.025) had significantly lower HR than control; Norepinephrine approached significance (p=0.069). No differences at other time points (p>0.05), as illustrated in (Figure 1).

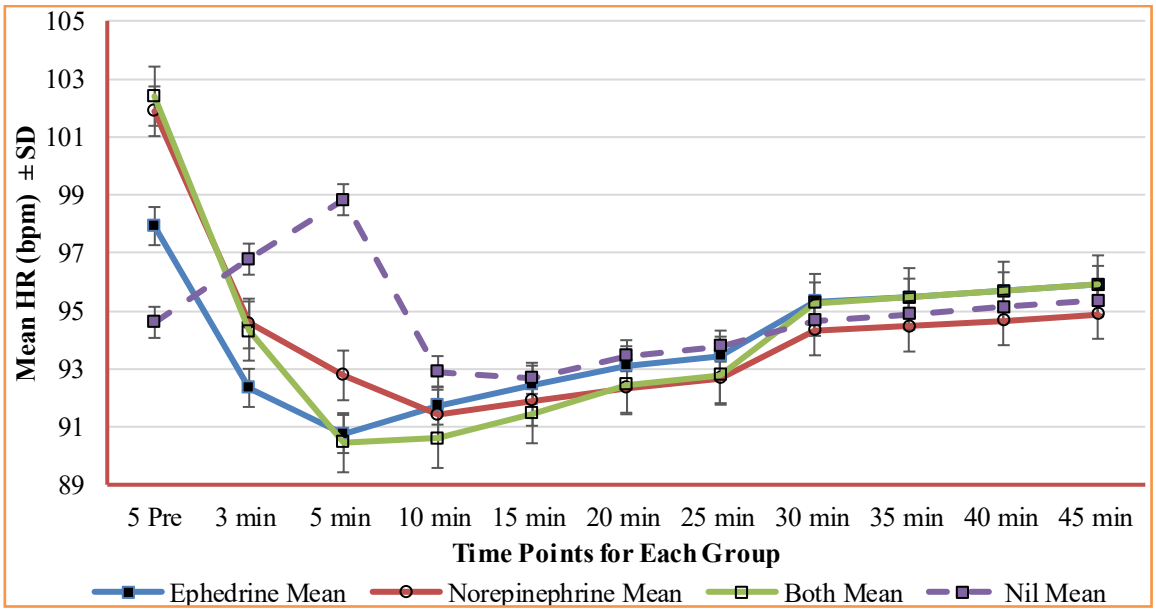

Figure 1. Mean HR (bpm) Across Time Points in all the groups that participated in this study

Discussion

Optimising vasopressor administration is a critical imperative in obstetric spinal anaesthesia, where maternal haemodynamic stability directly shapes both maternal well-being and neonatal outcomes. Uncontrolled hypotension can precipitate serious maternal complications, ranging from nausea, vomiting, and dizziness to, in severe cases, cerebral hypoperfusion and cardiac arrest. In the neonate, prolonged or profound maternal hypotension compromises uterine-placental perfusion, potentially resulting in fetal distress, acidosis, and diminished Apgar scores [14]. Baseline demographic and clinical characteristics, including age, weight, height, body mass index (BMI), and fasting time, demonstrated no statistically significant differences among the ephedrine, norepinephrine, combined, and control groups

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(F = 1.89, p = 0.132 for age; p > 0.05 for all other variables) [15]. This baseline homogeneity reflects successful randomisation and constitutes a cornerstone of internal validity, substantially mitigating the risk of confounding and enhancing the reliability of subsequent comparisons [16].

Observed differences in haemodynamic stability, maternal outcomes, or neonatal well-being can therefore be attributed more confidently to the vasopressor interventions themselves rather than to pre-existing patient characteristics. For example, comparable age distributions across groups reduce the likelihood that age-related differences in drug metabolism or cardiovascular responsiveness confound the results; similarly, concordant BMI and weight profiles minimise the influence of variations in drug distribution volume or dose requirements on the primary outcomes [17]. Although the control group exhibited a slightly higher mean age (33.93 ± 5.87 years) and the combined group a marginally higher mean weight (87.65 ± 13.45 kg), the absence of statistical significance reinforces overall baseline comparability. It lends further support to the validity of the inter-group comparisons that follow.

Neonatal assessment, based on Apgar scores recorded at the 1st and 5th minutes after delivery (Table 2), revealed no statistically significant intergroup differences across the four study arrays (ephedrine, norepinephrine, combined, and control) [18,19]. This finding indicates that, within the present study, the choice of vasopressor strategy did not exert an apparent effect on immediate perinatal adaptation as reflected by this composite measure. Nevertheless, the combined regimen (ephedrine plus norepinephrine) consistently showed marginally lower mean Apgar scores at both the 1st minute (7.65 ± 1.12) and the 5th minute (8.80 ± 0.67) than the other groups. These differences, although consistently directionally unfavourable, did not attain statistical significance (1st min: F = 2.34, p = 0.087; 5th min: F = 2.12, p = 0.112). While this trend falls short of statistical strength, it merits interpretive caution. The observed pattern may be attributable to the relatively small sample size, which limits statistical power to detect modest effect sizes or may reflect a true, albeit subtle, pharmacological interaction. The direction of this trend aligns with, and lends preliminary support to, the existing evidence implicating cumulative sympathomimetic exposure in the modulation of fetal acid–base homeostasis. Ephedrine, a mixed α- and β-adrenergic agonist, has historically been favoured in obstetric anaesthesia owing to its perceived minimal influence on uterine-placental blood flow. Its principal mechanism of action is indirect, operating through the displacement of endogenous norepinephrine from presynaptic stores, which produces concurrent α_1-mediated vasoconstriction and β_1-mediated augmentation of cardiac output. However, ephedrine undergoes transplacental transfer more readily than do pure α-agonists such as phenylephrine, and its administration has been associated with a higher incidence of fetal metabolic acidosis, particularly at elevated doses or with protracted maternal hypotension [20].

The principal pathophysiological model attributes this metabolic acidosis to β-adrenergic-mediated stimulation of fetal metabolic rate and oxygen consumption, which predisposes to lactic acid accumulation and a consequent reduction in fetal pH [21]. These pharmacokinetic and pharmacodynamic considerations, taken together with the trend observed in the present combined group, underscore the need for cautious dose selection and ongoing vigilance with respect to fetal acid–base status when combining sympathomimetic agents. Norepinephrine, predominantly an α_1-adrenergic agonist with modest β_1-agonist activity, has emerged as a viable alternative to both ephedrine and phenylephrine in obstetric anaesthesia. Converging evidence indicates that norepinephrine maintains maternal blood pressure effectively while preserving uterine-placental perfusion and fetal acid–base equilibrium. This favourable profile is attributed to its direct vasoconstrictive action, which achieves hemodynamic stabilisation without the pronounced β_2-adrenergic effects characteristic of ephedrine—thereby minimising potentially adverse metabolic stimulation of the fetus (22). The absence of a statistically significant difference in neonatal outcomes between the norepinephrine and ephedrine groups in the present study is consistent with a growing body of recent literature supporting comparable neonatal safety profiles for these two vasopressors when administered within careful dose ranges [23,24]. This concordance lends external validity to our findings and suggests that, at clinically effective doses, both agents may be considered acceptable first-line options with respect to short-term neonatal wellbeing. The marginally lower, although statistically non-significant, Apgar scores observed in the combined group should be interpreted with caution.

One possible explanation is a pharmacodynamic interaction between the two agents. The additive or potentially synergistic effects of ephedrine and norepinephrine, which both stimulate the sympathetic nervous system, could increase fetal metabolic demand and/or affect placental perfusion. Even small changes in these factors might lead to a slight, clinically insignificant decrease in neonatal scores. However, this hypothesis is still speculative, and the observed trend could also be due to chance or residual confounding rather than a true effect of the drugs. Future investigations employing larger, adequately powered cohorts and more granular measures of neonatal wellbeing, particularly umbilical cord blood gas analysis and continuous fetal monitoring, are warranted to definitively characterise the dose-response relationships and combined effects of vasopressor regimens on neonatal outcomes. Moreover, exploration of genomic variability in adrenergic receptor signalling may offer insight into individual predisposition to adverse fetal responses, thereby advancing toward a more personalised approach to intraoperative hemodynamic management in the obstetric population. This section examines the efficacy of the vasopressor strategies through One-Way ANOVA of hemodynamic parameters across designated time points (Tables 1, 3, 4), enabling direct intergroup comparisons and informing which regimen confers superior hemodynamic stability.

In Pre-Induction: Consistent with the descriptive analysis, significant intergroup differences in SBP and MBP were observed pre-induction, with the ephedrine group demonstrating higher values than the norepinephrine group ($p < 0.05$) [25]. Moreover, 3–5 Minutes Post-Induction (Critical Phase): This interval represents the most dynamic and clinically

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significant period in managing spinal-induced hypotension. ANOVA robustly confirmed that all vasopressor groups (ephedrine, norepinephrine, combined) maintained significantly lower SBP, DBP, and MBP than the control group ($p < 0.05$). This finding reinforces the clinical imperative of vasopressor intervention to counteract the profound hypotensive effect of spinal anaesthesia [26]. Notably, the persistence of lower blood pressure in actively treated groups relative to the non-hypotensive control underscores the hemodynamic severity of spinal anaesthesia, indicating that while vasopressors effectively attenuate the magnitude of hypotension, they may not entirely avert transient episodes, thereby emphasising the need for rapid, precise dosing [27]. However, 10–25 Minutes Post-Induction (Recovery Phase): Significant differences in SBP, DBP, and MBP between vasopressor and control groups persisted throughout this extended period, although the intergroup gap progressively narrowed over time, indicating gradual hemodynamic normalisation. This indicates that while vasopressors effectively mitigated the severity of hypotension, they did not consistently restore blood pressure to pre-induction levels, particularly relative to the control group, which may have experienced less profound initial drops or faster spontaneous recovery in some individuals [28]. The absence of significant differences in heart rate or oxygen saturation during this period suggests that the transient effects on these parameters had resolved, leaving blood pressure maintenance as the principal remaining challenge. Finally, by 30–45 minutes post-induction, all hemodynamic parameters had stabilised, with no significant intergroup differences observed. This indicates that the acute effects of spinal anaesthesia and vasopressor administration had largely subsided, and patients had achieved a stable hemodynamic state irrespective of the initial vasopressor regimen, a critical prerequisite for maternal safety throughout the remainder of the cesarean section and into the postpartum period [22].

Conclusion

This study provides a detailed comparative analysis of ephedrine, norepinephrine, and their combination in managing spinal-induced hypotension during cesarean section, yielding critical insights into their differential effects on maternal hemodynamics, neonatal outcomes, and adverse events. Our findings underscore both the immediate and significant hypotensive impact of spinal anaesthesia and the indispensable role of vasopressors in attenuating this effect. Although all tested vasopressor strategies ultimately achieved hemodynamic stability, the early post-induction phase posed distinct challenges, and most notably for the combination group, which exhibited unexpected transient hemodynamic instability and lower oxygen saturation.

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Conflicts of Interest

The authors declare no conflicts of interest.

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