Khalij Libya Journal of Dental and Medical Research. 2025;9(2):312-317
https://doi.org/10.47705/kjdmr.259226
eISSN:2708-888X

Original article

Impact of Intravenous Bolus Norepinephrine *versus* Ephedrine on Post-Spinal Hypotension during Cesarean Section in Libyan Patients

Fathi Abulifa[1,2]*, Ibrahim Garta[1,2], Elsonosi Elferjani[1,2], Abdalrahman Elzufri[1,2], Omar Danfour[1,2], Ahmed Aniba[2], Omar Alhaddad[3]

[1]*Anesthesia and Intensive Care Department, Misrata Medical Center, Misurata, Libya*
[2]*Department of Surgery, Faculty of Medicine, Misurata University, Libya*
[3]*Department of Family and Community Medicine, Faculty of Medicine, Misurata University, Libya.*
Corresponding email. *f.abulifa@med.misuratau.edu.ly*

Abstract
Spinal anaesthesia-induced hypotension (SAIH) is a frequent and significant complication during Cesarean section (CS) performed under neuraxial blockade, with the potential to cause adverse maternal and neonatal outcomes. The main management involves administration of vasopressors such as Ephedrine (EP) and phenylephrine. Recently, Norepinephrine (NE) has gained considerable attention as a viable alternative due to its favorable hemodynamic profile. This study was conducted to compare the efficacy and safety of NE versus Ephedrine for the treatment of established SAIH in a specific cohort of Libyan patients undergoing CS. This retrospective comparative study included 120 female patients undergoing elective CS under spinal anesthesia, randomized into two groups (n=60 each): the Norepinephrine (NE) group received 8 µg bolus of NE, and the ephedrine (EP) group received 10 mg bolus of Ephedrine (EP) for treating hypotension (Systolic Blood Pressure (SBP) < 90 mmHg or a 20% decrease from baseline). Hemodynamic parameters (SBP, Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), and Heart Rate (HR)) were recorded every 5 minutes from baseline (0 min) up to 60 minutes. Maternal side effects (nausea/vomiting, bradycardia) and neonatal Apgar scores at 1 and 5 minutes were also recorded. Baseline characteristics were comparable between the two groups. The Norepinephrine (NE) group showed significantly higher MAP and SBP values during the initial 20 minutes post-spinal block compared to the Ephedrine (EP) group (e.g., MAP at 5 min: NE 85.27 ± 15.63 mmHg vs. EP 74.82 ± 12.47 mmHg, P < 0.001). The EP group exhibited a significantly higher HR throughout the 60-minute monitoring period (e.g., HR at 10 min: NE 83.35 ± 18.19 bpm vs. EP 107.15 ± 14.88 bpm, P < 0.001). The incidence of maternal bradycardia was significantly higher in the NE group (25.0%) compared to the EP group (1.7%, P < 0.001). The incidence of nausea and vomiting was similar (NE 53.3% vs. EP 58.3%, P = 0.713). Neonatal Apgar scores at 1 and 5 minutes were comparable between the two groups (P > 0.05). Intravenous bolus norepinephrine was more effective than ephedrine in maintaining maternal blood pressure (MAP and SBP) during the critical period following spinal anesthesia for Cesarean section. However, Norepinephrine was associated with a higher incidence of maternal bradycardia. Both vasopressors demonstrated comparable neonatal outcomes.
Keywords. *Norepinephrine, Ephedrine, Spinal Anesthesia, Hypotension.*

Received*:09/10/25*
Accepted*: 08/12/25*
Published*: 13/12/25*

Introduction

Spinal anesthesia (SA) remains the gold standard for elective Cesarean section (CS) due to its superior safety profile compared to general anesthesia [1]. However, the resultant sympathetic blockade leads to a high incidence of maternal hypotension, often exceeding 60% [2]. This reduction in systemic vascular resistance can critically impair uteroplacental perfusion, leading to fetal distress, and is a major cause of maternal discomfort, including nausea and vomiting [4]. The timely administration of a vasopressor is essential for treating SA-induced hypotension. Ephedrine (EP), a mixed α and β agonist, was historically favored, but its use is limited by its propensity to cause maternal tachycardia and its potential to cross the placenta, which may lead to fetal acidosis [5]. Consequently, Phenylephrine (PE), a pure α_1-agonist, has become the preferred agent in many international guidelines due to its rapid onset and minimal effect on fetal acid-base status [2].
Recently, Norepinephrine (NE), a potent α_1-agonist with minor β_1 activity, has emerged as a promising alternative. Norepinephrine is thought to provide effective vasoconstriction while maintaining cardiac output better than Phenylephrine and causing less tachycardia than Ephedrine [3]. Several recent studies have compared norepinephrine to phenylephrine, but direct comparisons between norepinephrine and ephedrine, particularly using bolus doses for treatment rather than prophylaxis, remain relevant, especially in settings where ephedrine is still commonly used [6].

Khalij Libya Journal of Dental and Medical Research. 2025;9(2):312-317
https://doi.org/10.47705/kjdmr.259226
eISSN:2708-888X

Given the need for robust, contemporary data to guide clinical practice, especially in specific regional populations, this study aimed to compare the efficacy and safety of intravenous bolus norepinephrine (8 µg) versus Ephedrine (10 mg) for the treatment of SAIH in Libyan patients undergoing elective CS. The primary outcome was the comparison of maternal hemodynamic stability, and secondary outcomes included the incidence of maternal side effects and neonatal Apgar scores.

Methods

Study Design and Participants

This was a retrospective, comparative study conducted at the Misrata Medical Center, Misrata, Libya, and Alsalam International Hospital, Misrata, Libya. Data were collected from April 2024 to April 2025. The study included 120 Libyan female patients classified according to ASA (American Society of Anesthesia) as physical status II, aged 18–45 years, who underwent elective CS under spinal anesthesia. Ethical approval was obtained from the Institutional Review Board (IRB) of the Misrata Medical Center. Patients with pre-eclampsia, placenta previa, known cardiac disease, or contraindications to spinal anesthesia were excluded.

Anaesthesia and Intervention

All patients received a standardized pre-load of crystalloid solution. Spinal anaesthesia was performed using a pencil-point spinal needle at the L3-L4 or L4-L5 interspace. The anesthetic mixture consisted of Heavy-Bupivacaine 2-2.5 ml (10mg to 12.5mg). Patients were divided into two groups (n=60 each). The Norepinephrine (NE) Group received an intravenous bolus of 8 µg NE for the treatment of hypotension. The Ephedrine (EP) Group received an intravenous bolus of 10 mg EP for the treatment of hypotension.
Hypotension was defined as a Systolic Blood Pressure (SBP) less than 90 mmHg or a decrease of more than 20% from the baseline SBP. The vasopressor bolus was repeated if hypotension persisted after 1 minute.

Data Collection and Outcome Measures

Maternal hemodynamic parameters—including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR)—were systematically recorded at baseline (0 minutes) and at 5-minute intervals for a total of 60 minutes.
The primary outcome of the study was the comparison of maternal hemodynamic stability, assessed through the mean values of SBP, DBP, and MAP across the observation period. The secondary outcomes included the incidence of maternal side effects, specifically nausea, vomiting, and bradycardia, with bradycardia defined as a heart rate of fewer than 60 beats per minute. In addition, neonatal outcomes were evaluated using Apgar scores at both one minute and five minutes following delivery.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables were presented as Mean ± Standard Deviation (SD) and compared using the independent samples t-test. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test or Fisher's exact test, as appropriate. A P-value of less than 0.05 was considered statistically significant.

Results

Baseline Characteristics

The baseline demographic and clinical characteristics of the patients are presented in (Table 1). There were no statistically significant differences between the Norepinephrine (NE) and Ephedrine (EP) groups regarding age, height, or weight (P > 0.05 for all). This confirms the homogeneity of the two study groups.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Groups.

Characteristic	Norepinephrine Group (NE) (n=60)	Ephedrine Group (EP) (n=60)	P-value
Age (years), Mean ± SD	29.30 ± 6.14	29.93 ± 5.75	0.561
Height (cm), Mean ± SD	162.73 ± 3.10	163.15 ± 5.21	0.595
Weight (kg), Mean ± SD	81.73 ± 8.19	80.75 ± 10.65	0.572

Maternal Hemodynamic Parameters

The time course of maternal SBP, DBP, MAP, and HR is illustrated in (Figures 1-4) and summarized in (Table 2).

Mean Arterial Pressure (MAP)

Khalij Libya Journal of Dental and Medical Research. 2025;9(2):312-317
https://doi.org/10.47705/kjdmr.259226
eISSN:2708-888X

The Mean arterial pressure (MAP) was significantly higher in the Norepinephrine (NE) group compared to the Ephedrine (EP) group during the initial 25 minutes following spinal anesthesia (P < 0.05). The most pronounced difference was observed at 5 minutes (NE 85.27 ± 15.63 mmHg vs. EP 74.82 ± 12.47 mmHg, P < 0.001) and 10 minutes (NE 82.45 ± 15.73 mmHg vs. EP 72.00 ±11.15 mmHg, P < 0.001). After 30 minutes, the MAP values were comparable between the two groups (P > 0.05).

Systolic Blood Pressure (SBP)

Similar to MAP, SBP was significantly higher in the Norepinephrine (NE) group at 10 minutes (NE 114.33 ± 19.69 mmHg vs. EP 107.53 ± 13.78 mmHg, P = 0.030) and 20 minutes (NE 120.10 ± 16.24 mmHg vs. EP 113.87 ± 14.29 mmHg, P = 0.027). Conversely, the EP group showed a significantly higher SBP at 30 minutes (NE 113.75 ± 13.10 mmHg vs. EP 120.40 ± 12.11 mmHg, P = 0.005).

Diastolic Blood Pressure (DBP)

DBP was significantly higher in the Ephedrine (EP) group at 30 minutes (NE 63.57 ± 11.50 mmHg vs. EP 68.35 ± 11.44 mmHg, P = 0.024) and 45 minutes (NE 69.22 ± 8.72 mmHg vs. EP 73.02 ± 8.18 mmHg, P = 0.015).

Heart Rate (HR)

The HR was significantly lower in the Norepinephrine (NE) group compared to the Ephedrine (EP) group throughout the entire monitoring period from 5 minutes to 60 minutes (P < 0.001 for most time points). For instance, at 10 minutes, the mean HR was 83.35 ± 18.19 bpm in the NE group versus 107.15 ± 14.88 bpm in the EP group (P < 0.001).

Table 2. Comparison of Maternal Hemodynamic Parameters (Mean ± SD) at Different Time Points. (Bold P-values indicate statistical significance, P < 0.05)

Tim (min)	SBP (mmHg)		DBP (mmHg)		MAP (mmHg)		HR (bpm)	
	NE (Mean ± SD)	P-value	NE (Mean ± SD)	P-value	NE (Mean ± SD)	P-value	NE (Mean ± SD)	P-value
0	118.93 ± 9.92	0.260	72.37 ± 7.90	0.333	87.90 ± 9.36	0.055	89.20 ± 13.76	0.437
5	115.57 ± 18.37	0.210	67.82 ± 13.33	0.247	85.27 ± 15.63	<0.001	83.93 ± 15.78	<0.001
10	114.33 ± 19.69	0.030	63.67 ± 13.22	0.170	82.45 ± 15.73	<0.001	83.35 ± 18.19	<0.001
15	116.30 ± 16.00	0.063	67.03 ± 12.54	0.130	86.70 ± 12.24	<0.001	80.43 ± 15.53	<0.001
20	120.10 ± 16.24	0.027	67.67 ± 13.15	0.887	86.30 ± 13.62	0.001	83.10 ± 14.62	<0.001
25	117.62 ± 14.99	0.627	63.68 ± 11.73	0.188	83.57 ± 11.16	0.013	87.70 ± 15.81	<0.001
30	113.75 ± 13.10	0.005	63.57 ± 11.50	0.024	81.57 ± 11.71	1.000	84.27 ± 11.75	<0.001
35	115.12 ± 12.56	0.202	64.70 ± 11.17	0.057	82.78 ± 10.82	0.905	85.53 ± 11.39	<0.001
40	117.12 ± 10.06	0.199	67.88 ± 11.28	0.185	84.75 ± 9.35	0.355	83.97 ± 10.24	0.001
45	119.10 ± 9.31	0.348	69.22 ± 8.72	0.015	84.90 ± 7.47	0.248	79.37 ± 10.02	0.003
50	118.48 ± 7.17	0.884	70.50 ± 8.55	0.260	84.97 ± 7.14	0.408	77.67 ± 10.21	0.004
55	119.83 ± 6.23	0.254	73.08 ± 6.30	0.759	86.57 ± 5.50	0.731	75.63 ± 7.90	<0.001
60	121.00 ± 4.65	0.342	75.02 ± 4.93	0.072	88.78 ± 4.13	0.515	75.68 ± 7.34	<0.001

Maternal Side Effects

The incidence of nausea and vomiting was high in both groups, with no statistically significant difference (Norepinephrine (NE) 53.3% vs. Ephedrine (EP) 58.3%, P = 0.713). The incidence of bradycardia (HR < 60

Khalij Libya Journal of Dental and Medical Research. 2025;9(2):312-317
https://doi.org/10.47705/kjdmr.259226
eISSN:2708-888X

bpm) was significantly higher in the Norepinephrine (NE) group (25.0%) compared to the Ephedrine (EP) group (1.7%, P < 0.001).

Table 3. Comparison of Maternal Side Effects

Side Effect	Norepinephrine Group (NE) (n=60)	Ephedrine Group (EP) (n=60)	P-value
Nausea and Vomiting, n (%)	32 (53.3%)	35 (58.3%)	0.713
Bradycardia, n (%)	15 (25.0%)	1 (1.7%)	<0.001

Neonatal Outcome

Neonatal Apgar scores at 1 minute and 5 minutes were excellent and comparable between the two groups (Table 4).

Table 4. Comparison of Neonatal Apgar Scores.

Outcome	Norepinephrine Group (NE) (n=60)	Ephedrine Group (EP) (n=60)	P-value
Apgar Score at 1 min, Mean ± SD	9.38 ± 0.52	9.35 ± 0.55	0.734
Apgar Score at 5 min, Mean ± SD	9.93 ± 0.25	9.93 ± 0.25	1.000

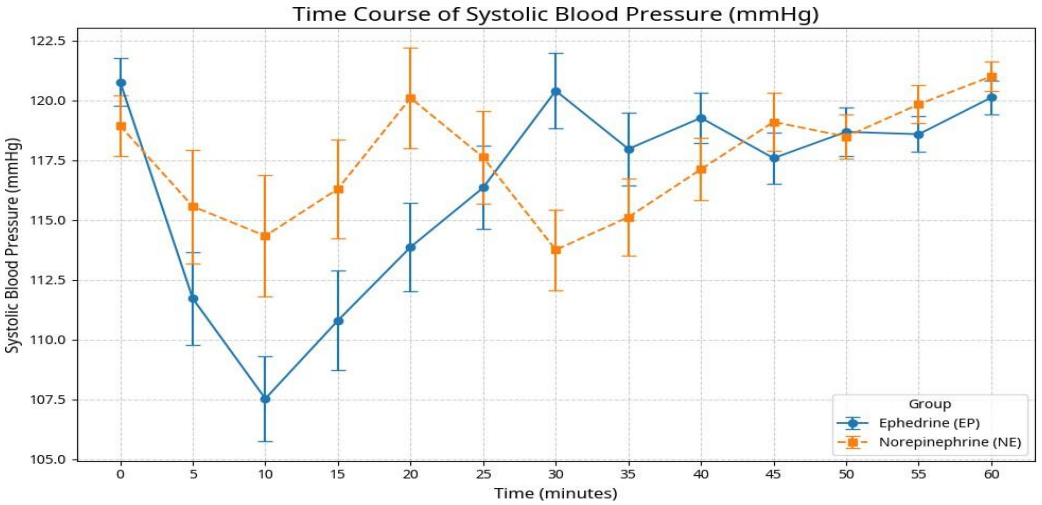

Figure 1. Time Course of Systolic Blood Pressure (SBP)

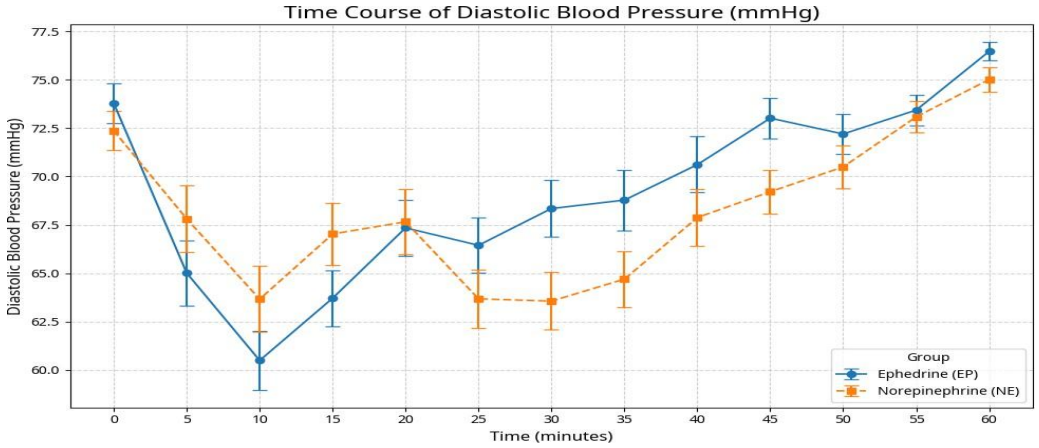

Figure 2. Time Course of Diastolic Blood Pressure (DBP)

Khalij Libya Journal of Dental and Medical Research. 2025;9(2):312-317
https://doi.org/10.47705/kjdmr.259226
eISSN:*2708-888X*

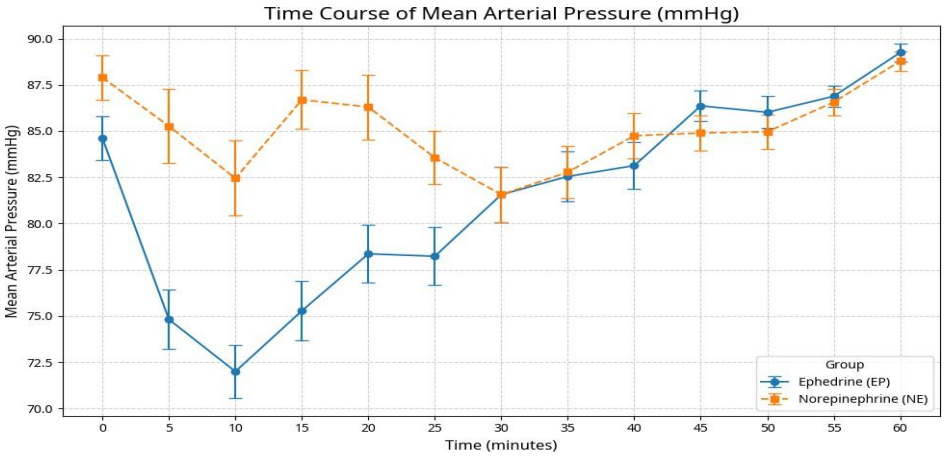

Figure 3: Time Course of Mean Arterial Pressure (MAP)

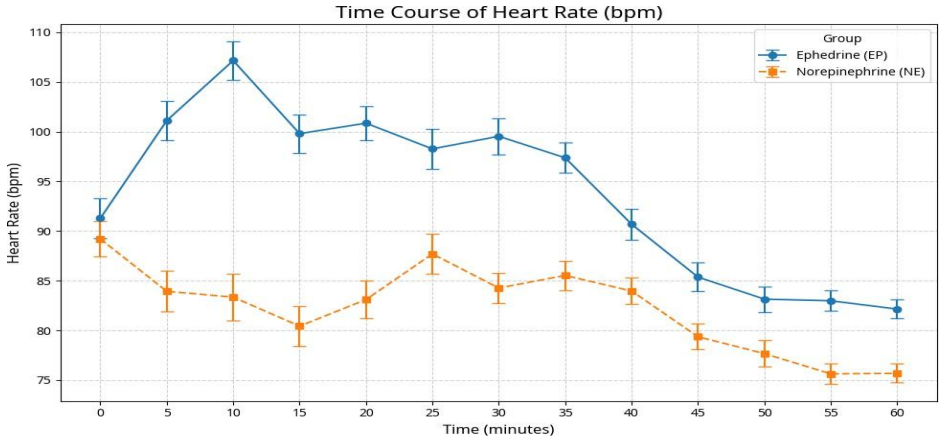

Figure 4: Time Course of Heart Rate (HR)

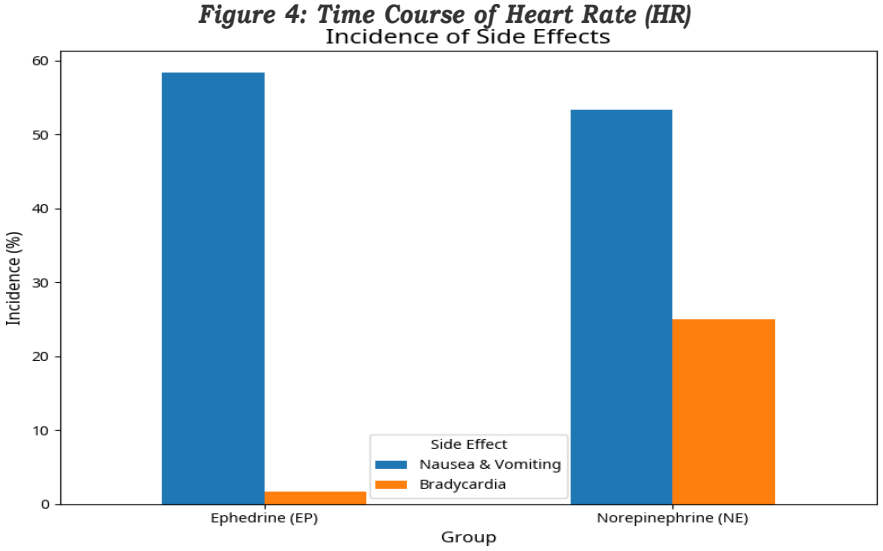

Figure 5: Incidence of Maternal Side Effects

Discussion

The key finding of this comparative study is the superior efficacy of intravenous bolus norepinephrine (NE) (8 µg) over ephedrine (10 mg) in maintaining maternal blood pressure stability, specifically Mean Arterial Pressure (MAP) and Systolic Blood Pressure (SBP), during the initial 25 minutes following spinal anesthesia for Cesarean section. This is demonstrated by the significantly higher MAP and SBP values in the norepinephrine (NE) group during this critical period (Table 2, Figures 1 and 3). This result is consistent with the pharmacological profile of norepinephrine (NE) as a potent a_1-adrenergic agonist, which provides rapid and effective peripheral vasoconstriction [6]. In contrast, the indirect and mixed action of Ephedrine may account for the less robust blood pressure support observed in the Ephedrine group during the immediate post-block phase [10].

Khalij Libya Journal of Dental and Medical Research. 2025;9(2):312-317
https://doi.org/10.47705/kjdmr.259226
eISSN:*2708-888X*

A significant difference was observed in maternal heart rate (HR). The Ephedrine group consistently exhibited a significantly higher HR throughout the entire 60-minute monitoring period compared to the Norepinephrine group (Table 2, Figure 4). This is a predictable consequence of Ephedrine's substantial β-adrenergic activity, which induces tachycardia [5]. The Norepinephrine group, with its predominantly α-agonist action, maintained a more stable and lower HR, which is generally preferred in obstetric anesthesia. However, the Norepinephrine group showed a significantly higher incidence of maternal bradycardia (25.0%) compared to the Ephedrine group (1.7%) (Table 3). This finding is a common trade-off with potent α-agonists like Norepinephrine, where intense vasoconstriction can trigger a baroreceptor-mediated reflex bradycardia [7]. Clinicians must be prepared to manage this side effect, typically with atropine or a reduction in the vasopressor dose [9]. The low incidence of bradycardia in the Ephedrine group is expected due to its inherent chronotropic effect [8].
The incidence of nausea and vomiting was comparable and high in both groups (NE 53.3% vs. EP 58.3%), suggesting that the choice of vasopressor did not significantly influence this common complication, which is often linked to the degree of hypotension or the use of intrathecal adjuncts [4]. Importantly, the neonatal outcomes, as reflected by the 1-minute and 5-minute Apgar scores, were excellent and statistically comparable between the two groups (Table 4). This reinforces the safety of both agents in terms of immediate neonatal well-being when used to treat hypotension. This finding is particularly relevant for Ephedrine, addressing historical concerns about its potential to cause fetal acidosis due to placental transfer [5]. The strengths of this study include its comparative design and the detailed, time-course analysis of hemodynamic parameters, which clearly delineate the temporal effects of the two vasopressors. The inclusion of a specific regional cohort (Libyan patients) also adds valuable data to the global literature. On the other hand, the study was limited to ASA II patients undergoing elective CS. Further studies are required to study the higher-risk group or emergency obstetrics cases.

Conclusion

Intravenous bolus Norepinephrine is superior to ephedrine in maintaining maternal blood pressure stability during the critical initial phase following spinal anesthesia for Cesarean section, while simultaneously maintaining a significantly lower maternal heart rate. The primary drawback of Norepinephrine was a higher incidence of maternal bradycardia. Both vasopressors demonstrated comparable, favorable neonatal outcomes. Based on these results, Norepinephrine is the preferred vasopressor for the treatment of post-spinal hypotension. Future research should focus on optimizing Norepinephrine bolus and infusion strategies to mitigate bradycardia while ensuring optimal hemodynamic support.

Conflict of interest. Nil

References

1. Mathew M, Manah YM, Ahuja P, Shetty AR. Managing spinal anesthesia-induced hypotension in cesarean section: emerging techniques and evidence-based strategies – a narrative review. Ann Med Surg. 2025;110:.
2. Kang H, Kim YH, Kim HS, Kim JH. A comparison of norepinephrine versus phenylephrine to prevent hypotension during spinal anesthesia for cesarean section: a systematic review and meta-analysis. Medicina. 2024;60(8):803.
3. Zhang C, et al. Prophylactic norepinephrine infusion to treat hypotension after spinal anaesthesia in caesarean delivery patients. J Matern Fetal Neonatal Med. 2024;37(1):2393379.
4. Sonsale AR, et al. Comparison of phenylephrine versus ephedrine in managing maternal hypotension during cesarean section under spinal anesthesia. Healthc Bull. 2025;4(1):4188.
5. Phogat A, et al. Comparison of norepinephrine with ephedrine boluses for treatment of hypotension in patients undergoing cesarean section under spinal anesthesia. J Obstet Anesth Crit Care. 2023;13(2):.
6. Elagamy AE, et al. Norepinephrine versus ephedrine for hypotension prophylaxis during spinal anesthesia for cesarean delivery: a randomized controlled trial. Ain-Shams J Anesthesiol. 2021;14(1):1-.
7. Hassabelnaby YS, et al. Comparison of two norepinephrine rescue bolus doses for management of hypotension during cesarean section under spinal anesthesia. Ain Shams J Anesthesiol. 2020;12(1):1–7.
8. George RB, et al. A comparative study of bolus norepinephrine, phenylephrine, and ephedrine in parturient women with preeclampsia who had hypotension during cesarean delivery with spinal anesthesia. Biomed Res Int. 2019.
9. Norepinephrine vs phenylephrine infusions for maintaining blood pressure during spinal anesthesia for cesarean section. Int J Obstet Anesth. 19(4):387–392.
10. Ngan Kee WD, Khaw KS, Lau TK, Ng FF, Chui K, Ng KL. Randomised double-blinded comparison of phenylephrine vs ephedrine for maintaining blood pressure during spinal anaesthesia for non-elective caesarean section. Anaesthesia. 2008;63(12):1319–26.