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Original article

Comparison of Noradrenaline and Ephedrine for Maintaining Maternal Hemodynamic Stability and Neonatal Outcomes during Spinal Anesthesia for Caesarean Section: A Prospective Comparative Study

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Abstract

Spinal anesthesia-induced hypotension (SAIH) complicates up to 70–80% of caesarean sections performed under spinal block, threatening both maternal organ perfusion and uteroplacental blood flow. Ephedrine has been the traditional first-line vasopressor, but accumulating evidence points to its beta-adrenergic metabolic effects as a source of fetal acidosis. Noradrenaline (norepinephrine), a predominantly alpha (α) adrenergic agent, has emerged as a promising alternative, though data from North African populations remain scarce. Seventy Parturients undergoing elective or urgent caesarean section at Zawia Medical Centre, Libya, were assigned to receive either ephedrine 6 mg IV (Group E, n=35) or noradrenaline 16 µg IV (Group N, n=35) as rescue therapy whenever mean arterial pressure (MAP) fell below 65 mmHg following spinal anesthesia. Hemodynamic parameters were recorded at five-minute intervals for 45 minutes. Primary outcomes were the incidence of hypotension and intraoperative MAP profiles. Secondary outcomes included neonatal Apgar scores at one and five minutes, and maternal side effects (nausea, vomiting, shivering). The two groups were comparable in age, weight, height, and baseline heart rate (all $p>0.05$). Baseline MAP was slightly higher in Group E (93.4 ± 11.3 vs 88.1 ± 8.5 mmHg; $p=0.039$), though this difference did not translate into clinically meaningful differences in intraoperative MAP ($p=0.119$) or hypotension incidence (40.0% vs 33.3%; $p=0.766$). Intraoperative heart rate was significantly higher in Group E (99.4 ± 13.2 vs 92.6 ± 10.9 bpm; $p=0.033$). Neonatal Apgar scores were significantly higher in the noradrenaline group (median 9 vs 8; $p<0.001$). Nausea occurred universally in Group N (100% vs 54.3%; $p<0.001$), while vomiting tended to be more frequent in Group E (40.0% vs 16.7%; $p=0.074$). Noradrenaline and ephedrine produced equivalent maternal hemodynamic profiles during spinal anesthesia for caesarean section. Noradrenaline was associated with better neonatal Apgar scores but a higher rate of maternal nausea. These findings support the use of noradrenaline as a viable first-line vasopressor in obstetric anesthesia in Libya, with attention to antiemetic co-administration.

Keywords. Spinal Anesthesia, Caesarean Section, Noradrenaline, Ephedrine, Maternal.

Introduction

Spinal anesthesia is now the standard approach for caesarean delivery in most tertiary obstetric centers worldwide. It has largely replaced general anesthesia by removing the need for airway instrumentation, cutting the risk of pulmonary aspiration, keeping the mother conscious at birth, and limiting neonatal exposure to pharmacologically active drug levels [1]. The advantages are well established, but the technique has a real hemodynamic downside: sympathetic blockade reduces systemic vascular resistance and impairs venous return, while aortocaval compression from the gravid uterus in the supine position further compromises cardiac preload. Together, these mechanisms produce spinal anesthesia-induced hypotension (SAIH) in 40–80% of Parturients, depending on what prophylactic measures are in place [2]. SAIH creates problems on two fronts simultaneously.

Maternal hypotension of sufficient degree and duration reliably triggers nausea and vomiting during surgery, disrupting operative conditions and diminishing the birth experience [3]. From the fetal side, reduced uteroplacental perfusion pressure reduces oxygen delivery; sustained impairment leads to measurable fetal acidosis: a drop in umbilical artery pH and a rise in lactate even when Apgar scores still look normal [4]. These parallel maternal and neonatal risks have driven intensive research into which vasopressor best manages SAIH in obstetric practice. Ephedrine held the default position for decades. Its combined alpha (α) and beta (β) adrenergic activity was thought to maintain uteroplacental perfusion better than selective alpha agonists, a belief largely extrapolated from sheep data. That reasoning fell apart when randomized clinical evidence showed that ephedrine's beta-adrenergic component crosses the placenta easily, stimulating fetal adrenoceptors, driving fetal glycolysis, and generating lactate and carbon dioxide that push fetal acid-base status toward acidosis even when maternal blood pressure is back on target [5]. Phenylephrine, a selective α_1 agonist without β activity, was shown to protect fetal acid-base status more reliably and has become the first choice agent in well-resourced settings. Its main drawback is that reflex bradycardia with an associated

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fall in cardiac output becomes especially problematic in women who present with tachycardia or intravascular volume deficit [6]. Noradrenaline (norepinephrine) has attracted considerable interest as a mechanistically distinct option.

As an endogenous catecholamine with dominant α_1 adrenergic vasoconstriction and modest β_1 inotropic activity, it restores systemic vascular resistance while partly counteracting the reflex bradycardia and cardiac output depression that pure alpha agonists tend to cause [7]. Placental transfer is limited, which reduces the fetal metabolic load associated with ephedrine. Over the past decade, randomized trials and meta-analyses have shown that noradrenaline produces hemodynamic profiles comparable to phenylephrine and neonatal acid-base outcomes well above those achieved with ephedrine [8,9]. A 2023 dose-response meta-analysis covering ten randomized trials (1,144 Parturients) confirmed a favorable safety profile across the full range of infusion rates tested [10], and a 2024 meta-analysis further established prophylactic noradrenaline infusion as an effective strategy for preventing SAIH during caesarean delivery [11].

Despite all this international evidence, clinical practice in many regions has not kept pace. In North Africa, including Libya, ephedrine remains the most widely used vasopressor, kept in place by local availability, cost pressures, and the absence of regionally generated outcome data. Pharmacological findings from European, East Asian, or North American populations cannot be applied without qualification to settings with different maternal body habitus, baseline cardiovascular physiology, and perioperative infrastructure [12]. This prospective comparative study was conducted at Zawia Medical Centre specifically to address that gap. Noradrenaline and ephedrine were compared as rescue vasopressors in Libyan Parturients undergoing elective or urgent caesarean delivery under spinal anesthesia. The primary outcome was the number of hypotensive episodes, used as a proxy for mean arterial pressure (MAP) stability; MAP was chosen because it integrates systolic and diastolic components and correlates more reliably with organ perfusion than systolic pressure alone [13]. Secondary outcomes included maternal heart rate, intraoperative nausea and vomiting, bradycardia incidence, and neonatal Apgar scores at one and five minutes. The aim is to produce locally grounded, prospective data to guide vasopressor selection in Libyan obstetric anesthesia.

Methods

Study Design and Setting

This was a prospective comparative study conducted at Zawia Medical Centre, Libya, following approval from the institutional ethics committee. The study adhered to the principles of the Declaration of Helsinki. All participants provided written informed consent before enrolment.

Participants

Seventy pregnant women scheduled for either elective or urgent caesarean section under spinal anesthesia were enrolled consecutively between the start of data collection and the completion of the target sample. Inclusion criteria were: age 20–45 years, singleton pregnancy at term, and planned spinal anesthesia. Patients were excluded if they had known hypersensitivity to ephedrine or noradrenaline, pre-existing or pregnancy-induced hypertension (including preeclampsia), or significant cardiovascular, cerebrovascular, or renal co-morbidity.

Group Allocation and Drug Administration

Patients were allocated to receive ephedrine (Group E, n=35) or noradrenaline (Group N, n=35) based on drug availability at the time of surgery, a pragmatic allocation that reflects real-world conditions in the study setting. Group E received 6 mg (2 mL) IV ephedrine as a bolus whenever the MAP fell below 65 mmHg. Group N received 16 µg (1 mL) IV noradrenaline under the same trigger criterion. The dosing regimen was determined by local clinical consensus and is consistent with ranges reported in recent comparative trials.

Anesthetic Procedure

All patients received an intravenous preload of 500 mL of normal saline prior to spinal block. Spinal anesthesia was performed at the L3–L4 intervertebral space using a 27-gauge needle. The intrathecal injectate consisted of 2.2–2.5 mL of 0.5% hyperbaric bupivacaine. Following injection, patients were placed supine with a 30-degree left lateral tilt to minimize aortocaval compression. Supplemental oxygen at 100% was administered via face mask until delivery of the neonate.

Monitoring and Outcome Measurement

Non-invasive MAP, heart rate, and oxygen saturation (SpO_2) were recorded at baseline and at five-minute intervals throughout the procedure until 45 minutes post block. Hypotension was defined as a MAP below 65 mmHg at any recorded time point. Bradycardia (HR <60 bpm) was managed with atropine per standard protocol. Neonatal outcome was assessed using Apgar scores at one and five minutes, assigned by the attending pediatrician who was unaware of the maternal vasopressor allocation. Maternal side effects, such as nausea, vomiting, and shivering, were recorded by the anesthetist.

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Statistical Analysis

Data were analyzed using SPSS Statistics (v26). Normally distributed continuous variables are reported as mean ± standard deviation and compared using independent-samples t-tests. Apgar scores, being ordinal, were compared with the Mann–Whitney U test and reported as median with interquartile range. Categorical variables (incidence of hypotension, complications) were analyzed by chi-square or Fisher's exact test as appropriate. A p-value <0.05 was considered statistically significant. No corrections for multiple comparisons were applied, given the exploratory nature of the study.

Results

Baseline Characteristics

Both groups comprised 30 patients each. They were well matched for age (31.3 ± 5.2 vs 31.9 ± 5.5 years; p=0.312), body weight (80.1 ± 13.6 vs 82.2 ± 11.1 kg; p=0.242), and height (160.6 ± 3.9 vs 160.3 ± 4.3 cm; p=0.672). Baseline heart rate was virtually identical between groups (99.3 ± 16.6 vs 99.7 ± 15.2 bpm; p=0.944). A modest but statistically significant difference in baseline MAP was noted, with Group E starting at a higher value (93.4 ± 11.3 vs 88.1 ± 8.5 mmHg; p=0.039). Full demographic and baseline hemodynamic data are in Table 1.

Table 1. Demographic and baseline hemodynamic characteristics (mean ± SD)

Variable	Group E (Ephedrine) (n= 30)	Group N (Noradrenaline) (n= 30)	p-value
Age (years)	31.3 ± 5.2	31.9 ± 5.5	0.312
Weight (kg)	80.1 ± 13.6	82.2 ± 11.1	0.242
Height (cm)	160.6 ± 3.9	160.3 ± 4.3	0.672
Baseline MAP (mmHg)	93.4 ± 11.3	88.1 ± 8.5	0.039*
Baseline HR (bpm)	99.3 ± 16.6	99.7 ± 15.2	0.944

** p<0.05. MAP = mean arterial pressure; HR = heart rate.*

Hemodynamic Outcomes

The overall incidence of intraoperative hypotension (MAP <65 mmHg at any time point) did not differ significantly between groups: 14 of 30 patients (46.7%) in Group E experienced at least one hypotensive episode, compared with 10 of 30 (33.3%) in Group N (x^2=0.625; p=0.429). Mean intraoperative MAP was similarly comparable (80.2 ± 7.5 vs 77.6 ± 5.2 mmHg; p=0.119), as was the nadir MAP recorded during the procedure (67.6 ± 10.0 vs 67.2 ± 6.0 mmHg; p=0.825). The number of rescue boluses required was not significantly different between groups (2.37 ± 0.89 vs 2.83 ± 1.37; p=0.161). Mean intraoperative heart rate was significantly higher in Group E than in Group N (99.4 ± 13.2 vs 92.6 ± 10.9 bpm; p=0.033), consistent with the chronotropic effect of ephedrine's beta-adrenergic activity. Time-point analysis of MAP showed that the two groups diverged most at baseline and at five minutes post block, reflecting the pre-existing baseline MAP difference, but converged completely from the ten-minute mark onward (all p>0.15; see Table 2 and Table 3).

Table 2. Intraoperative hemodynamic outcomes (mean ± SD)

Outcome	Group E (Ephedrine) (n=30)	Group N (Noradrenaline) (n=30)	p-value
Hypotension incidence	14/30 (46.7%)	10/30 (33.3%)	0.429
Mean intraoperative MAP (mmHg)	80.2 ± 7.5	77.6 ± 5.2	0.119
Nadir MAP (mmHg)	67.6 ± 10.0	67.2 ± 6.0	0.825
Mean intraoperative HR (bpm)	99.4 ± 13.2	92.6 ± 10.9	0.033*
Number of rescue boluses	2.37 ± 0.89	2.83 ± 1.37	0.161

** p<0.05. MAP = mean arterial pressure; HR = heart rate.*

Table 3. Mean arterial pressure (mmHg) at each time point (mean ± SD)

Time Point	Group E (Ephedrine) (n= 30)	Group N (Noradrenaline) (n=30)	p-value
Baseline	93.4 ± 11.3	88.1 ± 8.5	0.039*
5 minutes	89.0 ± 13.1	82.9 ± 8.9	0.038*
10 minutes	76.5 ± 13.5	75.5 ± 10.4	0.751
15 minutes	76.8 ± 12.9	77.6 ± 7.9	0.776
20 minutes	80.1 ± 10.0	76.6 ± 9.7	0.164
25 minutes	77.8 ± 10.6	75.2 ± 7.7	0.279
30 minutes	77.1 ± 9.6	74.3 ± 8.0	0.217
35 minutes	78.8 ± 9.9	77.9 ± 10.1	0.722
40 minutes	80.5 ± 10.0	77.8 ± 8.4	0.251

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45 minutes	85.2 ± 11.2	80.4 ± 8.6	0.067

** p<0.05. Independent-samples t-test at each time point.*

Neonatal Outcomes

Neonatal Apgar scores were significantly higher in Group N. The median one minute Apgar score was 9 (IQR 8–9) in Group N, compared with 8 (IQR 7–8) in Group E (p<0.001). The mean scores were 8.53 ± 0.57 versus 7.87 ± 0.82, respectively (p<0.001). All four neonates with a one-minute Apgar score below 7 were in Group E.

Maternal Side Effects

Maternal nausea was more common in Group N: all 30 patients (100.0%) reported nausea, compared with 16 of 30 patients (53.3%) in Group E (p<0.001). However, progression to frank emesis followed the opposite pattern. Vomiting occurred in 13 of 30 patients in Group E (43.3%) but in only 5 of 30 patients in Group N (16.7%); this difference reached statistical significance (p=0.047). Shivering was infrequent in both groups 2/30 (6.7%) in Group E; 0/30 (0.0%) in Group N; p=0.492). Full neonatal and complication data are presented in Table 4

Table 4. Neonatal outcomes and maternal complications

Outcome	Group E (Ephedrine) (n=30)	Group N (Noradrenaline) (n=30)	p-value
Apgar score (median, IQR)	8.0 (7–8)	9.0 (8–9)	<0.001*
Apgar score (mean ± SD)	7.87 ± 0.82	8.53 ± 0.57	<0.001*
Nausea	16/30 (53.3%)	30/30 (100.0%)	<0.001*
Vomiting	13/30 (43.3%)	5/30 (16.7%)	0.047*
Shivering	2/30 (6.7%)	0/30 (0.0%)	0.492*

** p<0.05. † Fisher's exact test. IQR = interquartile range.*

Discussion

Three main findings came out of this study. First, noradrenaline and ephedrine produced equivalent intraoperative hemodynamic control, with comparable MAP trajectories throughout the perioperative period. Second, noradrenaline was associated with meaningfully better neonatal Apgar scores. Third, the two drugs produced a divergent pattern of gastrointestinal side effects: nausea was universal in the noradrenaline group (100%) but affected just over half of patients in the ephedrine group (53.3%), whereas frank emesis was substantially more common with ephedrine (43.3% versus 16.7%). These results align with the international literature and, to our knowledge, represent the first prospective hemodynamic comparison of these agents in a Libyan obstetric population. The equivalence of MAP profiles between groups fits well with evidence from well-designed randomized trials. Sharkey et al. showed that noradrenaline, titrated against a MAP target using intermittent intravenous boluses, produced hemodynamic stability indistinguishable from phenylephrine in British parturients [14]. Ngan Kee et al. similarly found that noradrenaline infusion maintained MAP at least as effectively as phenylephrine in a double-blinded randomized trial [7]. The pharmacological basis is clear: noradrenaline acts on alpha-1 and, to a lesser extent, beta-1 adrenoceptors, restoring systemic vascular resistance through vasoconstriction while preserving cardiac output through modest inotropy [15]. This corrects MAP without the reflex bradycardia that limits pure alpha agonists like phenylephrine, and without the tachycardia and increased myocardial oxygen demand associated with ephedrine's more pronounced beta-adrenergic activity. [16].

The present data extend this to a rescue-bolus protocol in a resource-limited setting, a practically important point for facilities that cannot reliably run continuous drug infusions. The neonatal outcomes deserve close attention. Apgar scores were significantly higher in the noradrenaline arm (median 9 versus 8 at one minute), and all four neonates with one-minute scores below 7 were in the ephedrine group. The mechanism is well characterized. Ephedrine crosses the placenta more readily than noradrenaline and directly stimulates fetal adrenergic receptors, accelerating glycolysis and oxygen consumption; the resulting lactate production and carbon dioxide accumulation drive fetal pH toward acidosis [5, 17]. Noradrenaline's more selective alpha-adrenergic pharmacology leaves this pathway undisturbed, preserving the fetal metabolic environment, which explains why Apgar scores were better in the noradrenaline group even though MAP nadir values were equivalent between arms. Systematic reviews have consistently documented higher umbilical artery pH with alpha agonists than with ephedrine [18]. The gastrointestinal complication data are striking and deserve careful interpretation. Nausea occurred in every patient in the noradrenaline group (30/30; 100%) but in only 16 of 30 patients in the ephedrine group (53.3%; p<0.001). This is a higher incidence than typically reported in studies comparing noradrenaline with phenylephrine, and it likely reflects the rescue-bolus dosing strategy used here: rapid, intermittent injections of noradrenaline can produce brief, sharp rises in arterial pressure that stimulate baroreceptor-mediated vagal afferents, transiently heightening the emetic threshold without triggering sustained nausea or vomiting [19 The dissociation between nausea incidence and emesis rates supports this interpretation. Despite universal nausea in Group N, only 5 of 30 patients (16.7%) progressed to frank vomiting, far fewer than the 13 of 30 (43.3%) who vomited in Group E (p=0.047).

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Ephedrine's sustained beta-adrenergic stimulation and tachycardia appear to create more prolonged gastric dysmotility, which more readily advances to emesis [20]. Clinically, this means that although noradrenaline produces near universal mild nausea with bolus dosing, it causes significantly less vomiting than ephedrine, an outcome that is arguably more relevant to patient comfort and airway safety during a conscious surgical procedure. Routine antiemetic prophylaxis is advisable regardless of which vasopressor is selected, though the pattern of symptoms differs: noradrenaline patients may benefit from agents that blunt vagal-mediated nausea, while ephedrine patients require more aggressive cover to prevent emesis.

The significantly higher intraoperative heart rate in the ephedrine group (99.4 versus 92.6 bpm; p = 0.033) reflects the direct chronotropic action of this agent—a response that can be distressing for the conscious mother and may complicate interpretation of intraoperative fetal heart rate monitoring in centers using continuous cardiotocography [16]. Noradrenaline, acting through unopposed alpha-adrenergic vasoconstriction, can trigger reflex bradycardia; this occurred more often in the noradrenaline group (14.3% versus 2.9%), though the difference did not reach statistical significance, and all episodes resolved promptly with atropine. This pattern matches observations from Vallejo and colleagues, who found that bolus doses of noradrenaline below 20 µg did not produce clinically significant heart rate changes in obstetric patients [21]. The hemodynamic impact of these brief bradycardic episodes was negligible; none caused circulatory compromise. That said, atropine should always be immediately available when alpha-agonist vasopressors are used, and this trend warrants prospective evaluation in protocols comparing bolus and continuous infusion dosing strategies [22].

Several methodological limitations should be acknowledged. Vasopressor allocation depended on drug availability at the time of surgery rather than formal randomization, which introduces potential allocation bias; while baseline demographic and clinical characteristics were comparable between groups, this source of confounding cannot be ruled out. The modest between-group difference in baseline MAP, negligible in absolute terms, represents a minor systematic imprecision. With 35 participants per arm, the study had sufficient power to detect the hemodynamic differences observed, but it cannot draw definitive conclusions about lower frequency outcomes such as emesis, bradycardia, or serious neonatal adverse events. The most critical limitation is the absence of umbilical cord blood gas analysis, the most sensitive and objective measure of neonatal acid-base status, which was not available at the site during the study period. [5] Apgar scoring, while clinically useful at the bedside, carries well-documented interobserver variability; the score gives no allowance for varying intensities of respiratory support, and assessments performed in retrospect by attending staff are subject to systematic bias [23].

A properly powered, formally randomized trial with umbilical cord blood gas analysis as a co-primary endpoint would provide the objective evidence needed to revise institutional protocols. This limitation aside, the study addresses a real gap. Pharmacological data from European, East Asian, or North American cohorts cannot simply be imported into North African obstetric practice, where maternal body composition, vascular reactivity, and critically, the monitoring infrastructure available during and after spinal anaesthesia differ meaningfully from the conditions under which most landmark trials were conducted [24]. The close alignment between findings from Zawia Medical Centre and comparable studies in Egyptian, Indian, and Chinese centers provides reasonable reassurance that hemodynamic and neonatal responses to these vasopressors are broadly reproducible across genetically and dietarily distinct populations [15, 25, 26]. Noradrenaline achieved hemodynamic equivalence to ephedrine, required a similar number of rescue boluses, and was associated with meaningfully better neonatal Apgar scores. The nausea signal seen with bolus noradrenaline is real but does not translate into a higher rate of vomiting; with routine antiemetic prophylaxis, it should not be a barrier to adoption. A formally randomized, adequately powered trial incorporating umbilical cord blood gas analysis as a co-primary endpoint would consolidate this evidence base and give North African institutions the data they need to update their vasopressor protocols in line with the growing international consensus that noradrenaline should replace ephedrine for SAIH management during obstetric spinal anesthesia.

Conclusion

Noradrenaline and ephedrine provided equivalent maternal hemodynamic protection against spinal anesthesia-induced hypotension during caesarean section at Zawia Medical Centre. The noradrenaline group achieved better neonatal Apgar scores, consistent with the drug's more favorable transplacental metabolic profile. Although nausea was near-universal with bolus noradrenaline dosing, it did not translate into a higher rate of vomiting; ephedrine produced significantly more emesis (43.3% versus 16.7%). These findings support noradrenaline as a clinically acceptable and potentially preferable vasopressor for obstetric spinal anesthesia in Libya, pending confirmation by a properly randomized trial with cord blood gas endpoints.

Conflict of interest. Nil

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