Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v6i4.1656
*Biol. Clin. Sci. Res. J., Volume 6(4), **2025**: 1656*
Original Research Article ***NCT06836986***

Comparison Between Efficacy of Norepinephrine and Phenylephrine Boluses for Prevention of Spinal Anesthesia-Induced Hypotension in Obstetrical Patients Undergoing Emergency Cesarean Section

Rabia Kamal*, Muhammad Arsalan Jamil, Shaista Uzair, Syed Farjad Sultan

Department of Anesthesia, Surgical ICU & Pain Management, Dow University of Health Sciences Karachi, Pakistan
**Corresponding author's email address:* rabiakamal.ae@gmail.com

(Received, 4th April 2025, Accepted 28th April 2025, Published 30th April 2025)

Abstract: *Spinal anesthesia-induced hypotension (SAH) is a common complication during emergency cesarean sections, which can negatively affect both maternal and neonatal outcomes. This study aims to compare the efficacy of norepinephrine and phenylephrine boluses in preventing SAH in obstetric patients.* ***Objective:*** *To compare the efficacy of norepinephrine and phenylephrine boluses for preventing spinal anesthesia-induced hypotension (SAH) in obstetric patients undergoing emergency cesarean section.* ***Methods:*** *A double-blind randomized controlled trial was conducted at Dr. Ruth K.M. Pfau Civil Hospital Karachi, Dow University of Health Sciences, from 1st January 2025 to 31st March 2025. A total of 124 obstetric patients undergoing emergency cesarean section under spinal anesthesia were randomly assigned into two groups: norepinephrine (N) and phenylephrine (P). Each group consisted of 62 patients. The primary outcome was the incidence of hypotension following spinal anesthesia, while secondary outcomes included the need for additional vasopressor boluses, maternal and neonatal outcomes, and side effects. Statistical analysis was performed using Chi-square tests, with a p-value <0.05 considered statistically significant.* ***Results:*** *The overall incidence of hypotension was 58 (46.77%). The rate of spinal anesthesia-induced hypotension was significantly higher in the phenylephrine group compared to the norepinephrine group (56.45% vs. 37.1%; p=0.031). The proportion of infants with an Apgar score <7 at one minute was significantly higher in the phenylephrine group than in the norepinephrine group (33.9% vs. 6.5%; p=0.0005).* ***Conclusion:*** *A prophylactic bolus dose of norepinephrine demonstrated superior efficacy compared to phenylephrine for the prevention of spinal anesthesia-induced hypotension in parturients undergoing emergency cesarean section.*

Keywords: Efficacy, Prevention, Spinal anesthesia, Induced hypotension, Emergency cesarean section

[***How to Cite:***Kamal R, Jamil MA, Uzair S, Sultan SF.Comparison between efficacy of norepinephrine and phenylephrine boluses for prevention of spinal anesthesia-induced hypotension in obstetrical patients undergoing emergency cesarean section. *Biol. Clin. Sci. Res. J.*, **2025;** 6(4):31-36.doi: https://doi.org/10.54112/bcsrj.v6i4.1656

Introduction

Spinal anesthesia has become the most common and favoured anesthetic technique for cesarean delivery (1). Obstetric airway management is challenging; thus, spinal anesthesia bypasses airway manipulation in this population. Spinal anesthesia-induced hypotension (SAH) is a common and potentially serious complication encountered in obstetric patients undergoing cesarean section. The incidence of spinal anesthesia-induced hypotension is 56.8% (2). The sympathetic blockade caused by spinal anesthesia leads to vasodilation and reduced venous return, subsequently decreasing cardiac output and systemic vascular resistance. This blood pressure reduction can compromise uteroplacental blood flow, causing adverse feto-maternal outcomes, like nausea, vomiting, fetal acidosis, and in extreme scenarios, intrauterine fetal demise (3).

Various measures are taken to prevent spinal anesthesia-induced hypotension. Preloading with 10- 15ml/kg Crystalloids or co-loading with colloids is a regular practice. Different vasopressors have also been used to overcome vasodilation. The preferred medication for the management of spinal anesthesia-induced hypotension is phenylephrine (4). Phenylephrine is an alpha 1 agonist that overcomes vasodilation secondary to sympatholytic. It maintains preload and improves cardiac output. The worrisome side effect of phenylephrine is reflex bradycardia (5).

Norepinephrine is a relatively new vasopressor that prevents and treats hypotension secondary to neuraxial anesthesia. It is a potent vasopressor having an additional β1 effect. This dual mechanism has the potential to provide more stable hemodynamics compared to phenylephrine, which may reduce the incidence of reflex bradycardia and result in better maternal cardiovascular stability. Recently, it has been safely used for the management of spinal anesthesia-induced hypotension in obstetric (6) and elderly populations. 7Norepinephrine has been used as an infusion and bolus dosage. Most of the studies use infusion pumps (8, 9). Bolus and infusion dosage of norepinephrine have also been safely determined. Different bolus dose allocation studies have been done. In a recent survey, the ED90 values for prophylactic norepinephrine bolus and phenylephrine bolus were found to be 8.0 µg (95% CI 7.1-11.0 µg) & 90.9 µg (95% CI 82.0-123.9 µg), respectively (10, 11).

Neonatal outcomes are also comparable using norepinephrine to manage hypotension, secondary to spinal anesthesia (12, 13). In a recent study, hemodynamic parameters were compared between parturients undergoing elective and emergency c-section, and there was a significant statistical difference in hemodynamics. 14Norepinephrine has been used for the management of spinal anesthesia-induced hypotension in patients undergoing elective cesarean section with promising results (15).

This study aims to determine the effectiveness of prophylactic use of bolus norepinephrine and phenylephrine in patients undergoing emergency caesarian section. The data was lacking in our part of the World, and as we belong to a developing country, bulk use of the drug is cost-effective. Most of the studies have been done in elective cases and using infusion pumps; we studied bolus doses of the drug in patients undergoing emergency cesarean delivery. This trial aims to provide insights into which vasopressor may be optimal for this high-risk patient population by assessing hemodynamic stability, side effects, and maternal and neonatal outcomes.

Methodology

This was a single-centered, prospective randomized controlled trial conducted at Dr Ruth K.M. Pfau Civil Hospital Karachi, Dow University of Health Sciences, from 1st January 2025 to 31st March 2025. The institutional review board approved the study, Dow University of Health Sciences, on 31st December, 2024 (IRB-788/DUHS/Approval/2024/377). This trial was registered at the ClinicalTrials.gov registry, No: NCT06836986.Written informed consent was obtained from all study participants before their inclusion in this trial. A total of 124 pregnant women who were admitted for an emergency cesarean section under spinal anesthesia were enrolled. OpenEpi software was used to calculate sample size, where Alpha=5%, Power of test 1-beta=80, incidence of hypotension is 24% & 6% in norepinephrine and phenylephrine groups, respectively. [16 The] calculated sample size was n=124, and 62 patients were in each group. The inclusion criteria were ASA II & III patients undergoing emergency lower segment cesarean section under spinal anesthesia, age 18-40 years, and gestational age ≥ 32 weeks. All patients with hypertensive disorders of pregnancy having baseline systolic blood pressure ≥160mmHg and diastolic blood pressure ≥99mmHg, baseline Mean arterial pressure <70 mmHg, antepartum hemorrhage/intraoperative blood loss greater than 1000ml, history indicative of cardiovascular or neurological disease, known fetal anomaly, taking serotonin reuptake inhibitor, tricyclic antidepressants,monoamine oxidase inhibitor and maternal situations requiring immediate administration of general anesthesia were excluded. Using a lottery method, participants were randomly assigned to one of the two groups. Group N received norepinephrine boluses, while Group P received phenylephrine boluses. Group N (Norepinephrine Boluses) patients in this group received a prophylactic bolus of norepinephrine 8 µg administered intravenously right after induction of spinal anesthesia. If hypotension persisted, additional boluses of norepinephrine 4 µg were administered at 3-minute intervals until blood pressure was stabilized. Group P (Phenylephrine Boluses) patients in this group received a prophylactic bolus of phenylephrine 100µg intravenously right after induction of spinal anesthesia. If hypotension persisted, additional boluses of phenylephrine 50µg were administered at 3-minute intervals until blood pressure was stabilized.

All patients were monitored with pulse-oximetry and a continuous ECG. Heart rate & blood pressure were monitored continuously via an automated non-invasive blood pressure cuff every 3 minutes during the procedure and for 30 minutes postoperatively. Hypotension was defined as a decrease in systolic blood pressure of>80% from the baseline value. Bradycardia was described as a heart rate <60 beats per minute. The occurrence of bradycardia (heart rate <60 bpm), hypotension, nausea, vomiting, and other adverse events was recorded during the procedure. Neonatal outcomes were assessed using Apgar scores at 1 and 5 minutes post-delivery. Need for rescue boluses, administration of atropine & need for blood transfusion were also recorded**.** After informed consent, patients were included in the study. The obstetrics team had already given aspiration prophylaxis. Co-loading was done with 15ml/kg Inj. Ringer's lactate and hemodynamics were monitored with standard ASA monitoring. At this point, blood pressure and heart rate were labelled as maternal baseline hemodynamic parameters. After aseptic measures, spinal anesthesia was induced in a sitting position by a midline approach. 25 g Quinke's needle was injected at L3-L4 vertebra after subcutaneous infiltration of 2% lignocaine. 0.5% bupivacaine hyperbaric 10-12mg (2-2.2ml) was injected in the subarachnoid space with consideration of the patient's height.The desired sensory block level was T6 to pinprick.Oxygen supplementation with a 5-liter face mask was administered. Prophylactic boluses were given to both groups immediately after spinal anesthesia induction. The immediate hemodynamic parameters after induction were labelled as T0, after every 3 minutes. Maternal mean arterial pressure, systolic blood pressure, diastolic blood pressure, and heart rate were recorded every 3 minutes till delivery of the baby (umbilical cord clamping). The trial was concluded at this point. The data entry & analysis were done through SPSS-23. Kolmogorov-Smirnov test and independent sample t-test were applied between groups. Chi-square or Fisher's exact test was used to compare the proportion difference between groups. P value has remained significant <0.05.

Results

The demographic characteristics, including age, weight, height, and BMI, were comparable in both groups. Additionally, booking status and gravida showed no statistically significant differences between the groups (Table 1, Fig. 1). In groups N & P, the baseline SBPs were127.05±13.08 and 128.26±11.98mmHg, and the baseline Heart rates were 94.81±16.19 and 99±16.13 bpm, respectively. The mean heart rate, systolic blood pressure (BP), diastolic BP, and mean arterial pressure (MAP) were comparable between the groups (Tables 2-4, Figs. 2-3). No significant differences were observed in hemodynamic parameters between the groups, except for diastolic BP, which showed a significant difference at the T6 and T7 time points. This might be becausethe mean duration from induction till delivery of the neonate was 16-18 minutes. Mean arterial pressure was significantly higher in group N vs group P, 86.10±8.86 vs 76.48±11.04 (p value 0.02). Overall incidence of hypotension in this study was 46.77% (58). The rate of spinal anesthesia-induced hypotension was significantly higher in group P as compared to group N [56.45% vs. 37.1%; p=0.031] (Fig. 4). Similarly, the need for rescue bolus was 22.58% in group N and 24.19% in group P, which was not statistically significant between groups (p=0.832).

The rate of bradycardia was not significantly different between the groups (4.84% vs. 6.45%; p=0.999). Similarly, the rate of transfusion showed no statistically significant difference. However, the mean urinary output was significantly higher in Group P compared to Group N (p=0.015). The incidence of an Apgar score <7 at one minute was considerably higher in Group P than in Group N (33.9% vs. 6.5%; p=0.0005). In contrast, the proportion of infants with an Apgar score <7 at five minutes was 1.61% in Group N and 3.23% in Group P, which was not statistically significant (Table 5).

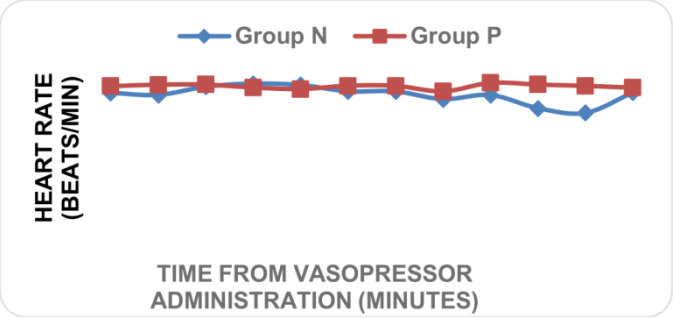

Fig. 1: Trends of heart rate in both groups

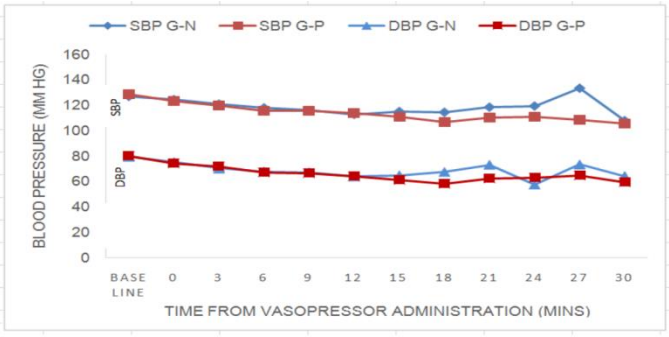

Fig. 2: Trends of blood pressure in both groups

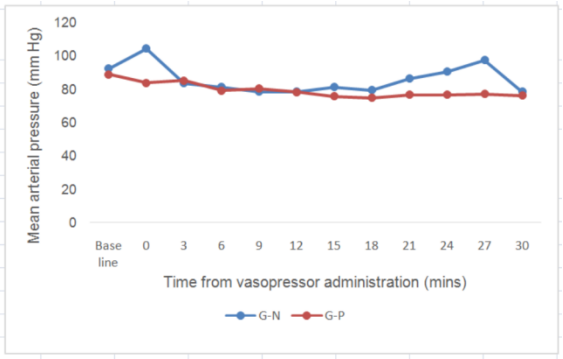

Fig. 3: Trends of mean arterial pressure (MAP)

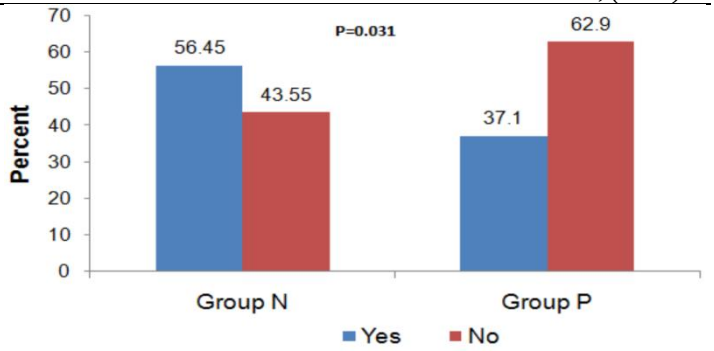

Fig. 4: Comparison of the rate of spinal anesthesia-induced hypotension between groups (n=124).

Table 1: Comparison of demographic characteristics of patients between groups

Variables	Group N (n=62)	Group P (n=62)	P-Value
Age (years)	27.82±5.25	26.85±5.39	0.313
Weight (kg)	65.90±7.75	68.05±8.76	0.151
Height (cm)	155.24±2.74	154.82±1.92	0.326
BMI (kg/m^2)	27.35±3.19	28.40±3.73	0.095
Baseline HB	10.67±1.02	10.86±1.09	0.308
Booking status			
Booked	52 (83.87%)	45 (72.58%)	0.128
Referred	10 (16.13%)	17 (27.42%)	
Gravida			
Primigravida	10 (16.13%)	16 (25.81%)	0.292
Multigravida	47 (75.81%)	39 (62.90%)	
Grand Multigravida	5 (8.06%)	7 (11.29%)	
Twin Pregnancy	7 (11.60%)	10 (16.12%)	0.6135

Table 2: Comparison of mean heart rate between groups over time

Heart Rate [Time (min)]	Group N (n=62)	Group P (n=62)	P-Value
Base line	94.81±16.19	99±16.13	0.15
T0 (induction)	93.4±17.80	99.92±17.60	0.06
T1 (3mins)	98.68±19.47	100.06±20.74	0.70
T2 (6mins)	100.68±19.29	98.11±23.77	0.51
T3 (9mins)	99.71±18.42	97.18±18.86	0.45
T4 (12mins)	95.72±18.74	99.26±20.25	0.35
T5 (15mins)	95.71±17.84	99.24±22.05	0.42
T6 (18mins)	90.71±16.41	95.66±25.08	0.41
T7 (21mins)	93.4±17.62	101.1±18.92	0.28
T8 (24mins)	85.0±6.48	100±16.96	0.12
T9 (27mins)	82.0±2.83	99.17±12.32	0.11
T10 (30mins)	95.0±21.21	98±11.77	0.81

Table 3: Comparison of mean systolic and diastolic blood pressure between groups over time

Time (min)	Diastolic BP			Diastolic BP		
	Group N (n=62)	Group P (n=62)	P value	Group N (n=62)	Group P (n=62)	P value
Base line	127.05±13.08	128.26±11.98	0.592	79.08±10.52	79.95±10.07	0.638
T0 (induction)	124.56±17.43	123.16±15.22	0.634	74.90±13.19	73.82±13.78	0.656
T1 (3mins)	121.03±16.80	119.44±13.91	0.565	69.94±15.30	71.82±15.83	0.501
T2 (6mins)	118.05±20.21	115.44±17.30	0.441	67.55±15.02	66.69±16.06	0.760
T3(9mins)	116.02±15.27	115.41±14.81	0.824	66.89±12.21	66.39±14.93	0.841
T4(12mins)	112.91±13.50	113.74±14.53	0.761	63.61±13.07	64.06±13.37	0.862
T5(15mins)	115.17±10.53	110.88±20.66	0.235	64.55±10.75	60.98±13.76	0.191
T6(18mins)	114.58±15.98	106.84±23.94	0.176	67.17±14.89	58.09±16.66	0.040*
T7(21mins)	118.60±12.11	110.19±13.18	0.099	72.80±8.57	61.95±11.34	0.012*
T8(24mins)	119.50±17.54	110.67±15.96	0.389	57.25±8.36	62.56±11.80	0.701
T9(27mins)	133.50±33.23	108.67±7.45	0.092	73.00±4.24	64.33±14.21	0.448
T10(30mins)	108.00±9.90	105.60±6.11	0.700	64.00±1.41	59.40±9.63	0.553

Table 4: Comparison of mean arterial pressure between groups over time

MAP [Time (min)]	Group N (n=62)	Group P (n=62)	P-Value
Base line	92.48±11.30	88.77±11.06	0.06
T0	104.32±14.25	83.66±13.45	0.16
T1	83.48±14.96	84.95±14.44	0.57
T2	81.26±15.87	79.08±15.20	0.43
T3	78.37±13.64	80.34±12.63	0.40
T4	78.50±12.79	78.15±14.43	0.89
T5	80.98±11.77	75.73±13.29	0.06
T6	79.13±14.66	74.74±11.87	0.22
T7	86.10±8.86	76.48±11.04	0.02*
T8	90.50±6.95	76.67±12.66	0.06
T9	97.50±24.74	77.17±5.15	0.06
T10	78.50±2.12	76.20±4.38	0.53

Table 5: Comparison of secondary outcomes between groups over time

Secondary Outcome	Group N (n=62)	Group P (n=62)	P-Value
Need for rescue boluses	14(22.58%)	15(24.19%)	0.832
Adverse events			
Bradycardia (heart rate <60 bpm)	3(4.84%)	4(6.45%)	0.999
Administration of atropine	3(4.84%)	2(3.23%)	0.999
Need for blood transfusion	1(1.61%)	1(1.61%)	0.999
Others			
Intraoperative Blood Loss	580.65±978.24	613.71±118.79	0.092
Urine output (ml)	107.26±59.26	133.87±60.58	0.015*
Total intravenous fluid administration from preloading till the end of the surgery in liters	1.89±1.33	1.70±0.26	0.260
Duration of surgery (min)	57.77±9.30	55.44±9.97	0.179
Duration from induction to delivery of the baby	16.98±4.79	18.16±6.22	0.240
Neonatal outcomes			
Apgar scores <7 at 1minute	4(6.5%)	21(33.9%)	0.0005
Apgar scores <7 at 5 minutes	1(1.61%)	2(3.23%)	0.999

Discussion

One of the key findings of our study was the reduced incidence of hypotension in the norepinephrine group compared to the phenylephrine group. Another study supported this finding, which showed intermittent norepinephrine bolus maintains greater cardiac output in spinal anesthesia-induced hypotension (17). This finding is consistent with another study that suggests norepinephrine provides more stable hemodynamics, likely due to its dual action as an α- and β-adrenergic agonist. The results align with the survey by Ngan-Kee et al (5).This showed that norepinephrine significantly lowers the incidence of spinal anesthesia-induced hypotension compared to phenylephrine in parturients undergoing cesarean section under spinal anesthesia. 5 In the present study, fewer patients in the norepinephrine group required additional boluses of vasopressors, but this number isn't statistically significant. However, another study has similar findings regarding the requirement of a rescue bolus (18).

This study showed no difference regarding incidence of bradycardia in both groups and finding was supported by other studies where post anesthesia induction heart rate were comparable in both groups(8-16)(19) In contrast, another study showed norepinephrine was superior to phenylephrine for decreased number of incidence of bradycardia (5). Reflex bradycardia is a known side effect of phenylephrine, which increases vascular resistance and triggers a compensatory decrease in heart rate.The difference in our findings might be due to the patient population, as our parturients were in labor, had fluctuations in the heart rate secondary to pain, and were undergoing emergency cesarean section.

In our study, we opted for the most common bolus dosage of the vasopressors for managing spinal anesthesia-induced hypotension. Phenylephrine 100 micrograms is equivalent to norepinephrine 7.6 micrograms. This potency ratio of both drugs was calculated in a graded dose-response study and found to be approximately 1:13 (10). Another study applied the Narayana rule for an up-down sequential allocation method, and the potency ratio of phenylephrine and norepinephrine was found to be 1:11.3, which means 8.8 micrograms of norepinephrine is equipotent with 100 micrograms of phenylephrine (20). Another study was conducted in parturients undergoing emergency cesarean section using similar doses (12). Hence, we opted for this combination of equipotent doses of both drugs.

In our study, group P had significantly higher urine output than group N. Phenylephrine significantly increased urine output without changing creatinine values (21). However, this might not be clinically significant.

In our study, neonatal outcomes were comparable between the two groups concerning Apgar scores at 5 mins, consistent with findings from Zhou et al (22). Both vasopressors were equally safe for the fetus, with no adverse effects on acid-base balance or neonatal vitality.[23] The Apgar scores are significantly better in the norepinephrine group at 1 min. This is supported by a Bayesian network meta-analysis of fetal and maternal outcomes (24). In contrast, recent studies show comparable fetal outcomes in both groups (25, 26). As our study showed better neonatal outcomes in terms of Apgar scores at 1 min, this discrepancy may be because our study included parturients with potential fetal distress. This is a critical consideration, as the safety of the fetus remains a primary concern in obstetric anesthesia, especially when using medications that affect maternal hemodynamics. However, Apgar scores at 1 minute are usually low in parturients undergoing c-section, and they typically

improve at 5 minutes. Low Apgar scores at 5-10 minutes are associated with cerebral palsy (27).

As our study also included pre-eclamptic patients, norepinephrine bolus dosage is equally effective as phenylephrine bolus dosage. Mohta et al (28). Parturients with pre-eclampsia undergoing caesarean delivery, bolus doses of phenylephrine (50μg) and norepinephrine (4μg) used to treat spinal anaesthesia-induced hypotension are equally effective with comparable maternal & neonatal outcomes

Moreover, the total volume of intravenous fluids administered did not differ significantly between the two groups, suggesting that the differences in blood pressure maintenance were due to the vasopressors rather than fluid management. This finding supports the conclusion that norepinephrine's superior efficacy is related to its pharmacodynamic properties rather than any differences in fluid resuscitation. The strength of our study is the bolus use of norepinephrine for the prevention of SAH in the context of emergency cesarean section. The results of this study can be applicable for both the prevention and treatment of spinal anesthesia-induced hypotension. Most previous studies were done in the elective scenario or using infusion pumps. As most operating setups in our part of the World lack infusion pump availability, safe bolus norepinephrine dosage in this population warrants promising neonatal and maternal outcomes.

Conclusion

Strong evidence in favor of norepinephrine boluses for the prevention of spinal anesthesia-induced hypotension in obstetric patients undergoing emergency cesarean section was noted. Norepinephrine appears to offer superior hemodynamic control with better neonatal outcomes, making it a preferable choice over phenylephrine for this patient population.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRB-3788/DUHS/Approval/2024/377).
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

RK (Resident)
Manuscript drafting, Study Design
MAJ (Assistant Professor)
Review of Literature, Data entry, Data analysis, and article drafting
SU (Senior Registrar)
Conception of Study, Development of Research Methodology Design
SFS (Associate Professor)
Review of Literature, Data entry, Data analysis, and article drafting

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

References

Ng KW, Parsons J, Cyna AM, Middleton P. Spinal versus epidural anaesthesia for caesarean section. Vol. 2012, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2004.

2. Chekol WB, Melesse DY, Mersha AT. Incidence and factors associated with hypotension in emergency patients that underwent cesarean section with spinal anaesthesia: Prospective observational study. Int J Surg 2021 Sep 1;35:100378.
3. Xu S, Mao M, Zhang S, Qian R, Shen X, Shen J, et al. A randomized double-masked study comparing prophylactic norepinephrine and ephedrine infusion for preventing maternal spinal hypotension during elective cesarean section under spinal anesthesia: A CONSORT-compliant article. Medicine (United States) 2019;98(51).
4. Nadella H, Islam A, Ina EA, Levin D, Bacoat-Jones T. The management of spinal and epidural anesthesia-related hypotension in the United States during cesarean childbirth. Cureus 2024;16(3).
5. NganKee WD, Lee SWY, Ng FF, Tan PE, Khaw KS. Randomized double-blinded comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anesthesia for cesarean delivery. Anesthesiology 2015;122(4):736-45.
6. Theodoraki K, Hadzilia S, Valsamidis D, Stamatakis E. Prevention of hypotension during elective cesarean section with a fixed-rate norepinephrine infusion versus a fixed-rate phenylephrine infusion: a double-blinded randomized controlled trial. Int J Surg 2020;84(October):41-9.
7. Mostafa M, Hasanin A, Mostafa M, Taha MY, Elsayad M, Haggag FA, et al. Hemodynamic effects of norepinephrine versus phenylephrine infusion for prophylaxis against spinal anesthesia-induced hypotension in the elderly population undergoing hip fracture surgery: a randomized controlled trial. Korean J Anesthesiol 2021;74(4):308-16.
8. Goel K, Luthra N, Goyal N, Grewal A, Taneja A. Comparison of norepinephrine and phenylephrine infusions for maintenance of haemodynamics following subarachnoid block in lower segment cesarean section. Indian J Anaesth 2021;65(8):600–5.
9. Du W, Song Y, Li J, Zhou X, Xu Z, Liu Z. Comparison of prophylactic norepinephrine and phenylephrine infusions during spinal anaesthesia for primary caesarean delivery in twin pregnancies: a randomized double-blinded clinical study. Drug Des Devel Ther 2022; 16(March):789-98.
10. Kee WDN. A random-allocation graded dose-response study of norepinephrine and phenylephrine for treating hypotension during spinal anesthesia for cesarean delivery. Anesthesiology 2017;127(6):934-41.
11. Guo L, Xu X, Qin R, Shi Y, Xue W, He L, et al. Prophylactic norepinephrine and phenylephrine boluses to prevent postspinal anesthesia hypotension during cesarean section: a randomized sequential allocation dose-finding study. Drug Des Devel Ther 2023; 17(May):1547-55.
12. Mohta M, Bambode N, Chilkoti G. Neonatal outcomes following phenylephrine or norepinephrine for treatment of spinal anaesthesia-induced hypotension at emergency caesarean section in. Elsevier, 2021
13. NganKee WD, Lee SWY, Ng FF, Lee A. Norepinephrine or phenylephrine during spinal anaesthesia for caesarean delivery: a randomised double-masked pragmatic non-inferiority study of neonatal outcome. Br J Anaesth 2020;125(4):588-95.
14. Çavuş Z, Vahapoğlu A, Türkmen ÜA, Gencer FK, Yıldız E. Comparing elective and emergency caesarean section by using bioimpedance method. Arch Gynecol Obstet 2024;309(6):2633-41.
15. Pan Z Bin, Sheng ZM, Zhu M, Mei Z, Shen YP, Liu JP, et al. Randomized double-blinded comparison of intermittent boluses of

phenylephrine and norepinephrine for the treatment of postspinal hypotension in patients with severe pre-eclampsia during cesarean section. Drug Des Devel Ther 2024; 18(February):639-50.
16. Chen Z, Zhou J, Wan L, Huang H. Norepinephrine versus phenylephrine infusion for preventing postspinal hypotension during cesarean section for twin pregnancy: a double-blinded randomized controlled clinical trial. BMC Anesthesiol 2022;22(1).
17. Wang X, Mao M, Zhang SS, Wang ZH, Xu SQ, Shen XF. Bolus norepinephrine and phenylephrine for maternal hypotension during elective cesarean section with spinal anesthesia: a randomized, double-blinded study. Chin Med J (Engl) 2020;133(5):509-16.
18. Puthenveettil N, Sivachalam S, Rajan S, Paul J, Kumar L. Comparison of norepinephrine and phenylephrine boluses for the treatment of hypotension during spinal anaesthesia for caesarean section: a randomised controlled trial. Indian J Anaesth 2019;63(12):995–1000.
19. Nguyen TT, Nguyen HC, Nguyen ATH, Doan TH, Ngo QS. Comparison of intermittent boluses of noradrenaline vs. phenylephrine for spinal anesthesia-induced hypotension during cesarean delivery. Anaesthesia Pain Intensive Care 2023;27(5):562–6.
20. Mohta M, Dubey M, Malhotra R, Obstetric ATI Journal of, 2019, undefined. Comparison of the potency of phenylephrine and norepinephrine bolus doses used to treat post-spinal hypotension during elective caesarean section. Elsevier 2021.
21. Ford DJ, Cullis B, Denton M. Dopaminergic and pressor agents in acute renal failure. Therapy in Nephrology and Hypertension: A Companion to Brenner & Rector's The Kidney, Expert Consult - Online and Print. 2008;16;13-34.
22. Zhou Y, Yu Y, Chu M, Zhang Y, Yu X, Chen G. Comparison of metaraminol, phenylephrine, and norepinephrine infusion for prevention of hypotension during combined spinal-epidural anaesthesia for elective caesarean section: a three-arm, randomized, double-masked, non-inferiority trial. Drug Des Devel Ther 2022;16(July 2021):117-27.
23. Liu T, Cheng Z, Zou S, Xu C, Pan S, Zeng H, et al. Effect of weight-adjusted phenylephrine, norepinephrine, and metaraminol for elective cesarean delivery on neonatal acid–base status: a randomized controlled trial. Drug Des Devel Ther. 2022;16(September):3215-23.
24. Singh PM, Singh NP, Reschke M, NganKee WD, Palanisamy A, Monks DT. Vasopressor drugs for the prevention and treatment of hypotension during neuraxial anaesthesia for caesarean delivery: a Bayesian network meta-analysis of fetal and maternal outcomes. Br J Anaesth 2020;124(3):e95–107.
25. Sun L, Tang Y, Guo F, Liu J, Xu L, Zhu G, et al. Norepinephrine or phenylephrine for preventing post-spinal hypotension after caesarean section: a double-blinded, randomized, controlled study of fetal heart rate and cardiac output. J Clin Anesth 2024;1:97.
26. Kang H, Sung TY, Jee YS, Kwon W, Cho SA, Ahn S, et al. A comparison of norepinephrine versus phenylephrine to prevent hypotension after spinal anesthesia for cesarean section: systematic review and meta-analysis. J Personalized Med Multidisciplinary Digital Publishing Institute 2024; 14.
27. Razaz N, Cnattingius S, Persson M, Tedroff K, Lisonkova S, Joseph KS. One-minute and five-minute Apgar scores and child developmental health at 5 years of age: a population-based cohort study in British Columbia, Canada. BMJ Open 2019;9(5).
28. Mohta M, Lakshmi R, Chilkoti GT, Agarwal R, Malhotra RK. A randomised double-masked comparison of phenylephrine and norepinephrine for the management of postspinal hypotension in pre-eclamptic patients undergoing caesarean section. Eur J Anaesthesiol 2021;38(10):1077-84.