Comparison of Mephentermine, Ephedrine and Phenylephrine for Treating Hypotension after Spinal Anesthesia in Caesarean Section

Shakya S[1], Shakya A[2], Nepal A[1], Khatik C[1]

ABSTRACT

Introduction: Hypotension is a common complication during spinal anesthesia in the caesarean section, often requiring vasopressors for correction. This study compares the effects of Mephentermine, Ephedrine, and Phenylephrine in maintaining arterial pressure. **Aims:** To evaluate the onset time and efficacy of three vasopressors in reversing hypotension, comparing heart rate responses (bradycardia or tachycardia) and assessing side effects such as nausea, vomiting or shivering. Additionally, neonatal outcomes are assessed using Apgar scores at 1 and 5 minutes to evaluate the impact of each vasopressor. **Methods:** A prospective, randomized interventional study was conducted among 105 parturients undergoing elective or emergency caesarean section under spinal aesthesia at Nepalgunj Medical College Teaching Hospital. Participants were randomly divided into three equal groups (n=35) to receive intravenous boluses of either Mephentermine 6 mg, Ephedrine 6 mg, or Phenylephrine 80 µg when hypotension occurred. Hemodynamic parameters (Systolic blood pressure, diastolic blood pressure and heart rate), neonatal outcomes and complications were recorded. **Results:** The Phenylephrine group demonstrated a significantly greater and quicker rise in systolic blood pressure during the first six minutes post-administration ($p<0.05$). However, Bradycardia was more frequent in this group. Ephedrine and Mephentermine maintained heart rate more effectively with fewer bolus doses. Neonatal APGAR scores at 1 and 5 minutes were comparable among all three groups. **Conclusion:** All three vasopressors effectively correct spinal anesthesia-induced hypotension. Phenylephrine results in higher blood pressure and reduces heart rate, offering an advantage when tachycardia is undesirable. None show significant adverse maternal or neonatal effects.

Keywords: Apgar score, Caesarean section, Hypotension, Spinal anesthesia, Vasopressors

Authors:

1. Dr. Shailendra Shakya
2. Dr. Anuka Shakya
3. Dr. Ashmita Nepal
4. Dr. Chandra Khatik

[1]Department of Anaesthesiology, Nepalgunj medical College and Teaching Hospital, Kohalpur, Banke

[2]Department of Community Medicine, Kathmandu Medical College and Teaching Hospital, Kathmandu

Address for Correspondence:

Dr. Shailendra Shakya
Assistant Professor
Dept of Anesthesiology and Critical Care
Nepalgunj Medical College Teaching Hospital
Kohalpur, Banke, Nepal
Email: drshailenshakya@gmail.com

INTRODUCTION

Spinal anesthesia is the most commonly used regional anesthetic techniques for caesarean sections due to its rapid onset, profound sensory blockade and minimal fetal drug exposure. However, spinal anesthesia often causes maternal hypotension through sympathetic blockade, potentially compromising both maternal and fetal health. During caesarean delivery, this hypotension can lead to maternal nausea, dizziness, and reduced cardiac output, as well as fetal complications including transient hypoxia and acidosis.[1] Effective management of hypotension is therefore crucial for achieving optimal maternal and fetal outcomes. Several vasopressors are used to counteract spinal-induced hypotension, each with different mechanisms and safety profiles. Mephentermine, an indirectly acting sympathomimetic stimulates both alpha- and beta-adrenergic receptors, thereby increasing cardiac output and vascular tone. Ephedrine, a mixed-acting sympathomimetic with alpha- and beta-agonist properties, causes vasoconstriction while also increasing heart rate and cardiac contractility. Phenylephrine, a direct alpha-1 agonist, causes rapid vasoconstriction and is increasingly preferred because it effectively restores blood pressure with minimal effects on fetal acid–base status.[2] The rationale for comparing these vasopressors in treating hypotension after spinal anesthesia is to identify the most effective and safest vasopressor for improving maternal blood pressure and fetal outcomes. This study aims to evaluate the onset time and efficacy of three vasopressors in reversing hypotension, comparing heart rate responses (bradycardia or tachycardia) and assessing side effects such as nausea, vomiting or shivering. Additionally,

neonatal outcomes are assessed using Apgar scores at 1 and 5 minutes to evaluate the impact of each vasopressor.

METHODS

This prospective, comparative clinical study was conducted in the Department of Anaesthesia at Nepalgunj Medical College Teaching Hospital, Kohalpur from November 2024 to April 2025. Ethical approval was obtained from the Institutional Review Committee of Nepalgunj Medical College, and written informed consent was secured from all participants.

The sample size was calculated with an α error of 5% and β error of 20%[4] resulting in 105 patients. Patients (N = 105) who developed hypotension after spinal anesthesia were randomly assigned to one of three groups (n = 35 per group) using a sealed opaque envelope method.

Group A: Mephentermine 6 mg in 1 ml as intravenous (IV) bolus,

Group B: Ephedrine 6 mg in 1 ml as IV bolus, and

Group C: Phenylephrine 80 mcg in 1 ml as IV bolus was used as indicated.

Inclusion Criteria:

• Pregnant women aged 18-40 years undergoing elective caesarean section under spinal anesthesia.

• ASA Physical Status I or II (patients who are healthy or have mild systemic disease).

Exclusion Criteria:

• Patients' refusal for consent, fetal distress and contraindications to spinal anesthesia.

• Patients with known allergies to Mephentermine, Ephedrine, or Phenylephrine.

• Patients with comorbidities such as preeclampsia, eclampsia, pregnancy-induced hypertension (PIH), and heart disease.

On arrival of the patients in operation theater, IV line was initiated with 18-G cannula; all patients were given 20 ml/kg of Ringer's lactate solution intravascular loading before spinal anesthesia. All patients were given premedication consisting of 50 mg of intravenous ranitidine and 10 mg of metoclopramide before surgery, according to institutional protocol, to prevent the risk of regurgitation and aspiration. Under aseptic precautions, spinal anaesthesia was administered in the sitting position using a 25-gauge Quincke needle at the L3-L4 level. A total dose of 2.2 mL of heavy Bupivacaine was given for spinal anaesthesia. The level of sensory blockade was targeted to T4-T6 dermatomes. Sensory block was assessed using the pinprick method, and motor block was evaluated with the Bromage scale to ensure adequate anaesthesia for lower segment cesarean section.The wedge was placed under right buttock for left uterine displacement in all patients. Additionally, all patients were kept in oxygen at 5L/min through facemask and intravenous oxytocin 5U were given after the delivery of baby.

Hypotension is defined as a decrease in systolic blood pressure of ≥20% from the baseline value or an absolute value of <100 mmHg, whichever will be higher.[5] Hemodynamic parameters (SBP, DBP, HR) of patient were recorded at baseline, immediately after the intervention, and at 2, 4, 6, 8, 10, 15 and 20 minutes post-intervention and every 10 minutes until the end of surgery. Intraoperatively, hypotension was recorded and managed with intravenous study drugs to restore blood pressure.

The incidence of adverse effects like nausea, vomiting, shivering and bradycardia were noted and managed according to the institution protocol. Nausea and vomiting was treated with 4mg of intravenous odansetron. The bradycardia i.e. a pulse rate of 60/min or less was treated with atropine 0.6mg intravenous while shivering was managed with pethidine 25 mg IV slowly. Paediatrician blinded to the study drugs assessed Apgar score of every neonate at 1 and 5 minutes after delivery and recorded.

Statistical analysis

Data were collected and recorded as per proforma. Statistical analysis was done by SPSS version 20. Data were presented in tables and figures as appropriate and comparability of groups were analyzed with Analysis of variance (ANOVA) test and Chi-square test. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic and Baseline Parameters: There were no statistically significant differences between the three groups in terms of age, weight, physical status and duration of surgery.

Variables	Group A	Group B	Group C	p-value
Age(yrs)	26.54± 4.84	27.11 ± 5.58	25.31 ± 3.91	0.28
Weight(Kg)	77.89 ± 7.5	77.37 ±7. 9	77.51 ±7. 8	0.96
Physical Status				
ASA I	28(80)	25(71.4)	24(68.6)	0.5
ASA II	7(20)	10(28.6)	11(31.4)	
Duration of Surgery(min)	66.86 ±8.67	64.00±8.81	62.57±7.41	0.09

Table I: Study population demographic data

Hemodynamic Response:

Intervals	Systolic Blood Pressure			Value		Inter Group Comparison		
	Group A	Group B	Group C	F	p	A-B	A-C	B-C
Baseline	128.03± 9.46	127.40± 10.68	129.34± 9.7	0.346	0.71	-	-	-
B1T0	95.63± 4.4	96.77± 4.83	95.31± 4.4	0.995	0.373	-	-	-
B1T2	113.57± 9.78	117.34± 11.93	127.03± 11.01	14.086	0.001	-	++	++
B1T4	119.86± 13.48	117.11± 13.17	127.66± 10.49	6.76	0.002	-	-	++
B1T6	126.71± 11.78	127.06± 11.81	119.06± 11.92	5.11	0.008	-	-	+
B1T8	128.31± 9.48	129.51± 7.01	128.00± 11.05	0.257	0.77	-	-	-
B1T10	123.57± 14.71	119.63± 16.31	122.06± 15.33	0.579	0.56	-	-	-
B1T15	127.77± 11.61	129.06± 9.32	126.97± 11.43	0.330	0.72	-	-	-
B1T20	127.94± 10.17	126.43± 14.85	126.66± 15.41	0.125	0.88	-	-	-
B1T30	119.23± 13.83	124.03± 13.57	122.24± 12.98	1.134	0.326	-	-	-
B1T40	121.49± 12.85	126.54± 11.89	126.06± 11.02	1.911	0.15	-	-	-
B1T50	127.77± 11.61	129.06± 9.32	126.11± 12.99	0.585	0.56	-	-	-
B1T60	121.64± 16.56	118.27± 16.55	118.45± 16.05	0.429	0.65	-	-	-
B1T70	127.88± 11.57	125.13± 12.21	126.09± 15.93	0.241	0.79	-	-	-
B1T80	125.40± 11.33	134.00± 4.32	135.00± 7.07	1.415	0.298	-	-	-

Table II: Comparison of the Systolic BP among three groups

B1T0: At the time of hypotension B1T2: 2 minutes after study drugs

(Within 2 groups: ++: p value <0.0001 +:p value<0.05 -: p value>0.05)

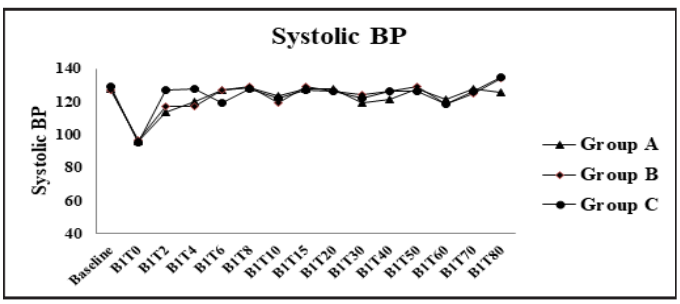

Figure 1: Comparison of the Systolic BP among three groups

The baseline systolic blood pressure among all three groups was statistically similar. Both systolic and diastolic pressures decreased similarly at the onset of hypotension and increased following the bolus dose in all groups. A significant rise in systolic and diastolic blood pressure was observed in the Phenylephrine group compared to the other two groups at 2 and 4 minutes post-intervention (p = 0.001 and 0.002, respectively). On intergroup comparison, the increase in diastolic pressure at 2 and 4 minutes was less pronounced in the Ephedrine and Mephentermine groups than in the Phenylephrine group (p < 0.001). No significant difference was noted between the Ephedrine and Mephentermine groups (p > 0.05).

Intervals	Diastolic Blood Pressure			Value		Inter Group Comparison		
	Group A	Group B	Group C	F	p	A-B	A-C	B-C
Baseline	82.83± 9.46	81.86± 10.91	83.26± 10.19	0.173	0.84	-	-	-
B1T0	57.89± 4.39	56.63± 4.13	55.17± 4.54	3.39	0.052	-	+	-
B1T2	65.00± 3.89	70.91± 10.18	78.09± 10.47	19.75	0.001	-	++	+
B1T4	75.09± 11.22	72.57± 11.05	79.80± 9.93	4.08	0.02	-	-	+
B1T6	80.43± 5.12	81.26± 3.63	81.29± 2.69	0.534	0.59	-	-	-
B1T8	81.66± 10.83	83.37± 6.23	80.74± 10.37	0.708	0.50	-	-	-
B1T10	80.00± 11.46	78.60± 11.47	80.20± 11.67	0.200	0.82	-	-	-
B1T15	81.69± 11.02	80.74± 9.75	82.00± 8.70	0.154	0.86	-	-	-
B1T20	82.29± 3.82	76.83± 11.61	80.40± 11.26	2.92	0.06	-	-	-
B1T30	74.77± 11.38	79.17± 10.72	76.50± 11.42	1.377	0.26	-	-	-
B1T40	82.17± 7.97	83.00± 5.68	82.29± 7.01	0.146	0.86	-	-	-
B1T50	82.66± 4.84	82.63± 4.79	81.37± 5.26	0.764	0.47	-	-	-
B1T60	77.48± 11.53	76.80± 11.83	74.87± 12.38	0.409	0.67	-	-	-
B1T70	81.24± 9.55	82.63± 6.39	78.45± 11.06	0.698	0.50	-	-	-
B1T80	74.00± 8.94	80.00± 8.20	85.00± 7.07	1.359	0.31	-	-	-

Table III: Comparison of the Diastolic BP among three groups

B1T0: At the time of hypotension B1T2: 2 minutes after study drugs

(Within 2 groups: ++: p value <0.0001 +:p value<0.05 -: p value>0.05)

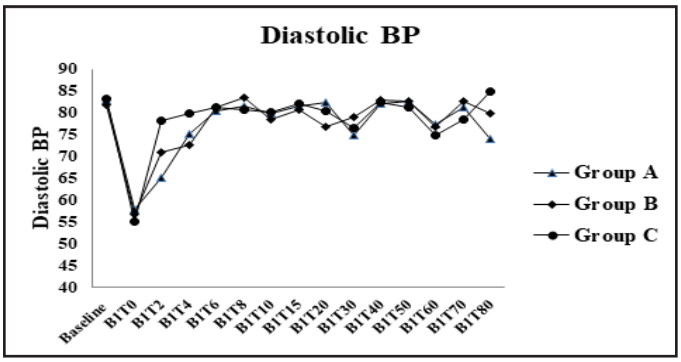

Figure 2: Comparison of the Diastolic BP among three groups

The baseline heart rate among all three groups was statistically similar. A clinically significant rise in heart rate was observed in all groups during hypotension, though this was not statistically significant. However, a significant decrease in heart rate was noted in the Phenylephrine group compared to the Ephedrine and Mephentermine groups at 4, 6, and 8 minutes after administration of the study drug. No significant difference in heart rate changes was observed between the Ephedrine and Mephentermine groups.

Intervals	Heart Rate			Value		Inter Group Comparison		
	Group A	Group B	Group C	F	p	A-B	A-C	B-C
Baseline	83± 11.14	85.03± 12.7	86.20± 11.65	0.654	0.52	-	-	-
B1T0	103.14± 7.69	104.00± 8.22	104.63± 8.01	0.306	0.74	-	-	-
B1T2	78.97± 12.54	80.60± 12.28	83.77± 9.57	1.57	0.2	-	-	-
B1T4	84.00± 13.22	81.26± 14.97	72.34± 8.77	8.2	0.0001	-	++	+
B1T6	81.63± 13.85	87.20± 14.10	65.86± 9.50	28.76	0.0001	-	++	++
B1T8	81.63± 13.86	90.11± 13.68	68.11± 10.66	26.24	0.0001	-	++	++
B1T10	84.20± 12.95	86.26± 14.07	82.51± 13.17	0.68	0.51	-	-	-
B1T15	85.80± 13.49	83.54± 11.06	83.80± 12.79	0.34	0.71	-	-	-
B1T20	85.09± 13.78	81.86± 14.50	85.43± 13.48	0.70	0.50	-	-	-
B1T30	85.34± 13.38	80.20± 11.74	83.77± 14.08	1.42	0.25	-	-	-
B1T40	84.26± 14.12	81.89± 13.42	85.26± 13.44	0.56	0.57	-	-	-
B1T50	84.11± 12.94	81.49± 13.41	85.03± 13.85	0.66	0.52	-	-	-
B1T60	80.00± 10.37	85.03± 13.97	80.65±1 2.77	1.49	0.23	-	-	-
B1T70	80.38± 10.41	87.33± 13.99	84.27± 12.84	1.45	0.25	-	-	-
B1T80	82.67± 15.16	92.50± 9.85	75± 7.07	1.34	0.32	-	-	-

Table IV : Comparison of the Heart Rate among three groups

B1T0: At the time of hypotension B1T2: 2 minutes after study drugs

(Within 2 groups: ++: p value <0.0001 +:p value<0.05 -: p value>0.05)

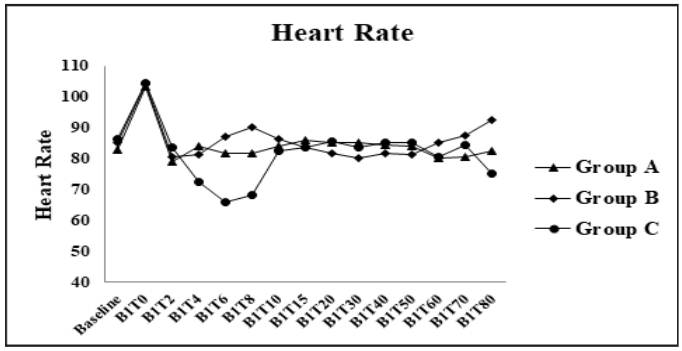

Figure 3: Comparison of the Heart Rate among three groups

Nausea was observed in 5.7% of patients in both the mephentermine and phenylephrine groups, and 2.9% in the ephedrine group. Shivering occurred in 11.4%, 8.6%, and 14.3% of patients in the mephentermine, phenylephrine, and ephedrine groups, respectively. Bradycardia was reported in 2.9%, 5.7%, and 8.6% of patients across the groups.(Figure 4) None of these differences were statistically significant (nausea p = 0.81; shivering p = 0.75; bradycardia p = 0.59).

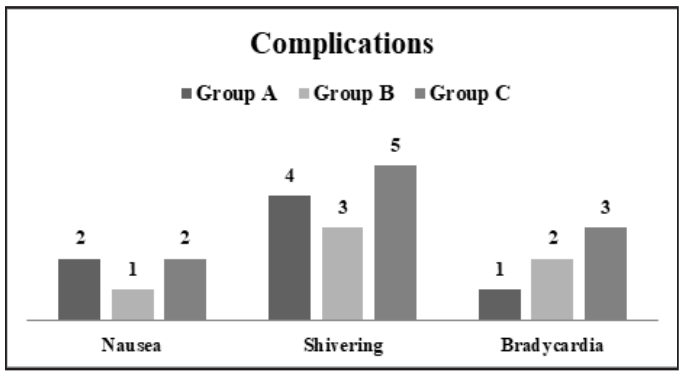

Figure 4: Comparison of the adverse effects among three groups

There was no statistical significant difference among three groups in context of total number of bolus of study drugs (p=0.74). Apgar scores at 1 and 5 minutes were ≥7 in all neonates among the three groups. No significant differences in neonatal outcomes were observed (p<0.05).

	Group A	Group B	Group C	p-value
Number of Bolus	1.26±0.51	1.26±0.50	1.34±0.60	0.74
Apgar Score@				
1min	7.54±0.51	7.57±0.50	7.6±0.55	0.9
5min	9.09±0.51	9.06±0.48	9.11±0.47	0.89

Table V: Comparison of the mean Number of Bolus and Apgar score of Neonates among three groups

DISCUSSION

Hypotension is one of the serious complications seen during caesarean section performed under subarachnoid block. This can be minimized with intravenous fluid, avoidance of aortocaval compression and judicious use of vasopressor agent. Careful positioning and volume preloading with intravenous crystalloid and colloid solution have been standard practice for prevention of hypotension but these are not complete measures. Primary cause of arterial pressure reduction is vasodilation. So, it is better to use vasopressor to correct hypotension.[3]

Our study included a total of 35 patients in each group receiving Mephentermine, Ephedrine and Phenylephrine. Percentage decrease in placental perfusion is related to percentage reduction in maternal arterial pressure and not to absolute reduction in pressure. In this study, Hypotension is defined as a decrease in mean arterial pressure below 20% of baseline or systolic blood pressure of < 100 mm of Hg.[5,6]

Among the vasopressors used Ephedrine have got a mixed action directly as well as indirectly on alpha and beta receptors whereas Mephentermine is an indirectly acting sympathomimetic amine and phenylephrine has pure alpha receptor activity.[2]

Ganeshanavar et al[6] stated that rise of systolic and diastolic blood pressure at 2, 4 and 6 minutes were significantly less in ephedrine and mephentermine group as compared to phenylephrine group. No significant difference (p>0.05) were observed between changes in systolic and diastolic pressure of ephedrine and mephentermine group which shows similar result as our group. In our study arterial blood pressure was maintained within 20% baseline limit by all three vasopressors though phenylephrine maintained better in first 6 minute of bolus dose (p<0.05) as compared to ephedrine and mephentermine. This may be due to the reason that phenylephrine has peak effect within one minute whereas ephedrine has 2-5 minutes and mephentermine has 5 minutes.[3]

Simin et al[7] and Nazir et al[8] concluded ephedrine and phenylephrine are effective vasopressors for treatment of hypotension associated to spinal shock during caesarean section without adverse effect on neonates.

Bhardwaj et al[9] compared phenylephrine, ephedrine and mephentermine and found all these vasopressors were equally effective in maintaining maternal blood pressure as well as umbilical pH without any detrimental effect on foetal and maternal outcome which shows similar result as our study.

According to study done by Sahu D et al[3] cardiovascular stability was better with phenylephrine as it caused significant reduction in heart rate after the bolus dose. In case of ephedrine and mephentermine group heart rate is increased compared to preoperative value which showed similar result as our study.

In this study, the mean number of bolus doses required to maintain systolic blood pressure within 20% of baseline was similar among the three groups indicating no statistically significant difference (p>0.05). This suggests that all study drugs were equally effective in stabilizing intraoperative hemodynamics. These findings align with previous literature. Ngan Kee et al[5] observed comparable rescue bolus requirements between phenylephrine and ephedrine in caesarean sections under spinal anesthesia, with no significant difference in total doses administered. There were no appreciable differences (p>0.05) in the incidences of nausea and shivering between any of the three groups which is in accordance with studies by Singh PM et al[10] and Tiwari JP et al.[11]

Our study showed the APGAR Scores at 1 and 5 minutes after delivery of baby were >7 among all the three study groups (p >0.05). Our findings were similar to the study conducted by Sahu D. et al[3], Thomas D.G. et al[12], Gunda C.P. et al[13] and Kee WD. et al[14] who gave IV boluses of these vasopressors and observed that APGAR scores at 1 and 5 minutes were >7 for all the neonates among the groups. Overall, mephentermine, phenylephrine, and ephedrine appear to have similar safety profiles, supporting their use as effective and well-tolerated vasopressors for intraoperative hemodynamic management.

LIMITATIONS

This study was limited by its single-centre design and short follow-up period restricted to intraoperative and immediate neonatal outcomes. Arterial blood gas analysis was not performed, limiting precise evaluation of fetal acid–base status.

CONCLUSION

In conclusion, we found that all three vasopressors mephentermine ephedrine and phenylephrine are effective as IV boluses form in maintaining maternal arterial pressure within 20% of baseline values. Among them, phenylephrine resulted in higher BP and reduction in heart rate, which may be advantageous when tachycardia is undesirable. All the three vasopressors had no significant adverse effects on maternal and neonatal outcome.

REFERENCES

1. Fakherpour A, Ghaem H, Fattahi Z, Zaree S. Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: a multinomial logistic regression. Indian J Anaesth. 2018;62(1):36–46.

2. Chandak AV, Bhuyan D, Singam AP, Patil B. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. Res J Pharm Technol. 2021;14(3):1349–52.

3. Sahu D, Kothari D, Mehrotra A. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section–a clinical study. Indian J Anaesth. 2003;47(2):125–8.

4. Sharma H, Senger VS, Gajbhiye S. A comparative study of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. Eur J Mol Clin Med. 2021;8(4):1744–53.

5. Kee WD, Khaw KS, Lee BB, Lau TK, Gin T. A randomized double-blinded comparison of phenylephrine and ephedrine for the maintenance of arterial pressure during spinal anesthesia for cesarean section. Anesthesiology. 2001;95(2):307–13.

6. Ganeshanavar A, Ambi US, Shettar AE, Koppal R, Ravi R. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anesthesia in caesarean section. J Clin Diagn Res. 2011;5(5):948–52.

7. Simin A, Zahra F, Pouya H, Reza T. Comparison of effect of ephedrine and phenylephrine in treatment of hypotension after spinal anesthesia during cesarean section. Open J Obstet Gynecol. 2012;2(3):192–6.

8. Nazir I, Bhat MA, Qazi S, Buchh VN, Gurcoo SA. Comparison between phenylephrine and ephedrine in preventing hypotension in spinal anesthesia for cesarean section. J Obstet Anesth Crit Care. 2012;2(2):92–7.

9. Bhardwaj N, Jain K, Arora S, Bharati N. A comparison of three vasopressors for tight control of maternal blood pressure during cesarean section under spinal anesthesia: effect on maternal and fetal outcome. J Anaesthesiol Clin Pharmacol. 2013;29(1):26–31.

10. Singh PM, Singh NP, Reschke M, Ngan Kee 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–e107. doi:10.1016/j.bja.2019.09.045

11. Tiwari JP, Verma SJ, Singh AK. A prospective randomized study comparing the bolus doses of norepinephrine and phenylephrine for the treatment of spinal-induced hypotension in cesarean section. Cureus. 2022;14(7):e27166. doi:10.7759/cureus.27166

12. Thomas DG, Robson SC, Redfern N, Hughes D, Boys RJ. Randomized trial of bolus phenylephrine or ephedrine for maintenance of arterial pressure during spinal anaesthesia for caesarean section. Br J Anaesth. 1996;76:61–5.

13. Gunda CP, Malinowski J, Tegginmath A, Suryanarayana VG, Chandra SBC. Vasopressor choice for hypotension in elective caesarean section: ephedrine or phenylephrine? Arch Med Sci. 2010;6:257–63.

14. Kee WD, Khaw WD, Lau KS, Ng TK, Chui FF, et al. Randomised double-blinded comparison of phenylephrine vs ephedrine for maintaining blood pressure during spinal anaesthesia for non-elective caesarean section. Anaesth. 2008;63:1319–26.