RESEARCH
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MATERNAL HEMODYNAMICS AND FETAL pH AFTER ADMINISTRATION PHENYLEPHRINE AND EPHEDRINE FOR C-SECTION

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Abstract

Background: Hypotension, a significant complication of spinal anesthesia, can disrupt uteroplacental blood flow and impact fetal well-being if severe and prolonged. Phenylephrine and ephedrine are preferred vasopressors used to prevent and treat hypotension after spinal anesthesia. This study aims to determine effects of phenylephrine and ephedrine on maternal hemodynamics and fetal pH in patients undergoing C-Section with spinal anesthesia. **Methods**: This research adopts a randomized controlled trial (RCT) design. The sample comprises 40 parturients undergoing cesarean section who met the inclusion criteria and consented to follow the research protocol at Wahidin Sudirohusodo General Hospital. The sample was divided into two groups: the Phenylephrine Group (PG) received 100 mcg IV phenylephrine, while the Ephedrine Group (EG) received 10 mg IV ephedrine immediately after spinal anesthesia. Parameters including blood pressure, heart rate, rescue vasopressor use, fetal pH, and Apgar scores were assessed and analyzed. **Results**: Administering phenylephrine at 100 mcg is demonstrated to be more stable than ephedrine at 10 mg for both prophylaxis and therapy of hypotension following spinal anesthesia during C-section. It reduces the need for vasopressor rescue and leads to better fetal pH compared to ephedrine administration. **Conclusions**: Administering phenylephrine (100 mcg) reduces the requirement for rescue vasopressors and improves fetal pH compared to ephedrine (10 mg) in preventing and treating hypotension after spinal anesthesia during cesarean section.

Keywords: Blood Pressure, C-Section, Ephedrine, Fetal pH, Hypotension, Phenylephrine, Spinal Anesthesia.

INTRODUCTION

Around 15-30% of births annually in developing countries, including Indonesia, are delivered via C-section with spinal anesthesia. Hypotension is a common complication of spinal anesthesia during C-section procedures, with an incidence of up to 80%. This hypotension is typically characterized by a decrease in systemic vascular resistance rather than a decrease in cardiac output, which usually increases. Severe hypotension can disrupt uteroplacental perfusion, leading to fetal hypoxia, acidosis, and neonatal depression. In mothers, hypotension can result in nausea, vomiting, decreased consciousness, aspiration, apnea, and cardiac arrest.[1]

Several methods have been explored to prevent hypotension during neuraxial anesthesia, including crystalloid or colloid loading and the administration of vasopressor drugs like ephedrine or phenylephrine. Although ephedrine is frequently utilized, phenylephrine has demonstrated equal or greater effectiveness in preventing

hypotension and is less likely to affect umbilical artery blood pH and base excess. Furthermore, phenylephrine crosses the placenta less frequently than ephedrine, potentially decreasing fetal metabolic stimulation and the risk of associated acidosis.[2]

Based on the opinion from previous studies on the use of phenylephrine or ephedrine for preventing fetal hypotension and acidosis after spinal anesthesia, we aim to investigate the effects of phenylephrine compared to ephedrine for this purpose during C-Section. This interest is further fueled by the absence of research on phenylephrine in C-Section in Indonesia.

RESEARCH METHOD

Patient Population

This research involved mothers delivering via C-Section with spinal anesthesia at Wahidin Sudirohusodo Hospital, Makassar, Indonesia, during December 2024. The sample comprised 40 delivering mothers who met the inclusion criteria and agreed to follow the research protocol.

Inclusion and exclusion criteria

The inclusion criteria were as follows: elective C- Section cases without any comorbid disease and agree to join the study by signing a consent form. The exclusion criteria included contraindications to the research materials, a history of comorbid disease, twin pregnancies, and fetal distress or intrauterine fetal death.

Clinical Data and Sample Collection

Clinical and demographic data were obtained from medical history, physical examinations, and medical records. Subsequently, hemodynamic parameters were recorded during the surgical procedure. Fetal pH was assessed using ABG I-Stat.

Statistical Analysis

A statistical analysis using SPSS version 26. Blood pressure, heart rate, rescue vasopressor, fetal ph, and apgar scores were assessed which were then analyzed using the mann-whitney test, friedman test, wilcoxon signed ranks test.

RESULTS AND DISCUSSIONS

Research Result

The characteristics of the study sample in both groups can be seen in Table 1. The study found both groups had similar age ranges and BMI ranges with no statistically significant variances (p>0.05), indicating data homogeneity.

Table 1:Sample Characteristics

Variabel	Group	n	Min	Maks	Mean	SD
Age	PG	20	18	37	27,6	0,818
	EG	20	20	35	27,8	
BMI	PG	20	25	29	26,5	0,357
	EG	20	22	29	26,9	
ASA PS	PG	20	2	2	2	0,000
	EG	20	2	2	2	
Mann-Whitney test						

Systolic Blood Pressure Comparison

Comparing systolic blood pressure (SBP) between the phenylephrine (PG) and ephedrine (EG) groups during C-section surgery revealed significant differences at 4, 6, and 8 minutes post-spinal anesthesia ($p < 0.05$). SBP was notably higher in PG. Both groups showed significant variations in SBP changes across all time measurements ($p < 0.05$). The Friedman test indicated more stable SBP changes in PG (27.8) compared to EG (36.0). See Table 2 and Figure 1.

Diastolic Blood Pressure Comparison

Comparing diastolic blood pressure (DBP) between the phenylephrine group (PG) and the ephedrine group (EG) during C-section surgery revealed significant differences at 4 and 6 minutes post-spinal anesthesia ($p < 0.05$). DBP was notably higher in PG at these time points. Both groups exhibited significant variations in DBP changes from baseline to end measurements ($p < 0.05$). The Friedman test indicated more stable DBP changes in PG (40.8) compared to EG (44.6). Refer to Table 2 and Figure 1 for details.

Comparison of Mean Arterial Pressure

Table 2 and Figure 1 show significant differences in MAP measurements at 4, 6, and 8 minutes post-spinal anesthesia. Mean MAP was significantly higher in the Phenylephrine group (PG) compared to the Ephedrine group (EG) at these time points (all $p < 0.05$). Both groups also exhibited significant variations in MAP changes from baseline to the end of surgery (all $p < 0.05$). The Friedman test indicated smaller variation in MAP changes in PG (45.4) compared to EG (48.5), suggesting greater stability in PG.

Heart Rate Comparison

Table 2: Blood pressure and heart rate comparison

Time	Group	n	Systolic Blood Pressure			Diastolic Blood Pressure			Mean Arterial Pressure			Heart Rate		
			Mean	SD	p	Mean	SD	p	Mean	SD	p	Mean	SD	p
Basal	PG	20	118,9	6,8	0,481	72,8	5,7	0,222	87,0	6,2	0,456	81,4	9,9	0,303
	EG	20	117,9	8,1		76,0	8,9		88,2	8,6		84,6	7,8	
2 min	PG	20	119,4	10,3	0,222	68,7	8,3	0,645	85,5	8,5	0,616	75,3	11,4	0,001
	EG	20	115,4	10,0		69,6	9,5		82,3	10,2		89,9	12,9	
4 min	PG	20	115,9	12,9	0,002	68,2	9,8	0,021	81,5	10,0	0,003	70,8	11,2	0,000
	EG	20	102,4	12,8		58,9	12,2		70,6	10,3		94,3	16,5	
6 min	PG	20	114,3	10,8	0,006	70,0	10,5	0,010	82,5	9,0	0,007	72,5	11,6	0,000
	EG	20	102,5	14,9		60,4	11,0		72,5	11,7		93,9	19,1	
8 min	PG	20	114,3	8,7	0,048	67,2	8,0	0,090	81,0	6,8	0,008	71,6	10,4	0,007
	EG	20	108,1	13,1		62,8	8,8		74,3	8,0		86,2	17,1	
10 min	PG	20	112,7	8,5	0,473	64,7	10,0	0,705	78,9	8,0	0,787	68,7	11,1	0,002
	EG	20	110,5	13,1		65,6	11,8		78,5	12,4		86,2	17,4	
12 min	PG	20	114,4	10,1	0,645	63,4	11,2	0,490	78,4	12,6	0,533	71,2	11,4	0,001
	EG	20	113,5	10,6		65,0	8,8		78,4	8,1		86,6	14,2	
14 min	PG	20	109,7	9,9	0,695	62,3	10,8	0,655	75,0	10,8	0,695	75,3	8,5	0,012
	EG	20	112,0	10,8		63,1	7,5		75,7	7,6		86,9	14,8	
16 min	PG	20	112,7	8,0	0,935	64,2	9,6	0,935	77,4	7,7	0,464	72,9	17,6	0,002
	EG	20	112,2	10,2		62,9	8,0		75,4	9,0		84,7	10,2	
26 min	PG	20	114,0	7,7	0,551	63,0	9,4	0,828	76,9	8,6	0,745	75,9	9,5	0,025
	EG	20	112,2	8,1		63,8	9,5		76,3	7,9		84,1	9,1	
End Of Surgery	PG	20	114,9	5,6	0,664	61,6	9,5	0,179	75,6	8,3	0,350	78,1	9,1	0,076
	EG	20	115,3	7,1		65,3	9,2		78,2	7,7		84,2	10,0	

Table 2 shows significant differences in heart rate (HR) measurements from baseline until the end of surgery. Mean HR was notably lower in the Phenylephrine group (PG) compared to the Ephedrine group (EG) from 2 minutes until 26 minutes (all with $p < 0.05$). Significant variation in mean HR change from baseline to T10 measurements

was observed in the PG group ($p < 0.05$), while no significant variation was found in the EG group ($p > 0.05$). Friedman test results indicated greater variation in HR changes in the PG group (37.5) compared to the EG group (16.6), indicating less stability in the PG group.

Rescue Comparison

In Table 3, rescues were significantly lower in the Phenylephrine group (PG) with a mean of 0.3 compared to the Ephedrine group (EG) with a mean of 1.4 ($p < 0.05$), indicating the superiority of phenylephrine in preventing hypotension during spinal anesthesia. Notably, 50% of the EG group (10 out of 20) required rescue, with 20% needing more than one dose. In contrast, only 25% of the PG group (5 out of 20) needed rescue, with none requiring more than one dose.

Table 3: Rescue comparison

Group	n	Mean	SD	p
PG	20	0,3	0,6	0,000
EG	20	1,4	0,8	
Mann Whitney Test				

Fetal pH and APGAR Score Comparison

The summary of analysis results in Table 4 reveals a significantly higher mean fetal pH in the Phenylephrine group (PG) at 7.308 compared to the Ephedrine group (EG) at 7.234 ($p < 0.05$). However, there were no significant differences in the mean APGAR scores between the two groups at both 1 minute and 5 minutes after birth (all with $p > 0.05$).

Table 4: Fetal pH and APGAR Score Comparison

Group	n	Fetal pH			APGAR Score 1 min			APGAR Score 5 min		
		Mean	SD	p	Mean	SD	p	Mean	SD	p
PG	20	7,308	0,040	0,000	7,9	0,4	1,000*	9,9	0,4	1,000*
EG	20	7,234	0,044		7,9	0,4		9,9	0,4	
Mann Whitney Test, * wilcoxon signed ranks test										

DISCUSSION

Maternal Hemodynamic

Spinal anesthesia possesses hemodynamic risks due to sympathetic nervous system block. Several techniques have been used to prevent complications of spinal anesthesia, including the use of ephedrine, phenylephrine, and other drugs combined with fluid therapy.[8]

The study found significant differences in blood pressure between the phenylephrine and ephedrine groups, with higher averages in the phenylephrine group. Hypotension incidence was lower in the phenylephrine group (25%) compared to the ephedrine group (50%), with fewer rescue doses needed (5 vs. 14 doses). Heart rates were significantly lower in the phenylephrine group, tachycardia was more common in the ephedrine group (50%).

This study's results align with Patel et al.'s research on 80 pregnant women, concluding that prophylactic phenylephrine was more effective than ephedrine in preventing hypotension during C-Section. They found fewer rescue doses needed and

no postoperative complications with phenylephrine and tachycardia was notably higher in the ephedrine group (47%) compared to none in the phenylephrine group.[3]

Sheleg et al. conducted a study on 60 pregnant women undergoing elective C-Section. They found that a bolus of 100 mcg phenylephrine and 12 mg ephedrine immediately after spinal anesthesia equally prevented maternal hypotension without significant cardiovascular or respiratory effects. The higher dose of ephedrine used in their study might explain the variance in results.[4]

An explanation of the mechanism of action of phenylephrine and ephedrine helps understand the findings of this study. Phenylephrine, as a pure α1 adrenergic receptor agonist, acts by contracting vascular smooth muscle and increasing blood pressure. On the other hand, ephedrine, as a mixed α and β adrenergic receptor agonist, works by activating β adrenergic receptors. Thus, ephedrine increase blood pressure primarily by increasing heart rate, myocardial contractility, and cardiac output. Therefore, the finding that the incidence of bradycardia was higher in the phenylephrine group may be explained by the reflex effect of decreasing heart rate after administration of phenylephrine. In contrast, the higher incidence of tachycardia in the ephedrine group could be attributed to the activation of β-adrenergic receptors by ephedrine, which stimulates an increase in heart rate.[5]

The results of the meta-analysis conducted by Lin and colleagues provide significant insight regarding the use of phenylephrine and ephedrine in the context of C-Section surgery under spinal anesthesia. The main conclusion of this study is that overall, phenylephrine is superior to ephedrine in producing higher cord blood pH values when used to treat maternal hypotension. The importance of cord blood pH as an indicator of newborn health suggests that the choice of vasopressor agent can have a direct impact on this parameter. However, this study also shows that both ephedrine and phenylephrine prophylaxis are equally effective in preventing maternal hypotension when administered either intravenously or intramuscularly. This illustrates that both can be relied upon as prophylactic treatment options, providing flexibility in the choice of route of administration according to clinical needs and patient preferences.[6,7]

Fetal pH and APGAR Score

In this study, from table 4, the average fetal pH was higher in the phenylephrine group compared to the ephedrine group. However, neither group showed fetal acidosis. Meanwhile, there was no significant difference in APGAR scores between the phenylephrine and ephedrine groups ($p > 0.05$). These findings align with research conducted by Asokan et al. on 100 pregnant women, where they found that the average neonatal umbilical cord pH was 7.2 ± 0.06 in the ephedrine group and 7.37 ± 0.04 in the phenylephrine group, with a statistically significant p-value of 0.002. However, there was no difference in the incidence of fetal acidosis between the two groups..[8]

Kumari, et al stated that the use of phenylephrine was associated with better fetal acid-base status compared to the use of ephedrine, but there was no difference in the Apgar score, provided consistency with the findings carried out in this study. Also supported by data from previous research by Nazir et al, and Cooper et al. Where they found that the average fetal pH in the group treated with phenylephrine had higher fetal pH compared to ephedrine.[9,10,11]

An RCT conducted by Ngan E maregd that ephedrine has greater liposolubility compared to phenylephrine and crosses the placenta more easily, causing increased oxygen consumption and increased glucose and lactic acid concentrations. Therefore, fetal metabolism is also stimulated by the activation of β adrenergic receptors due to the administration of ephedrine, causing a more acidic status in the fetus.[12]

CONCLUSIONS

This study shows that blood pressure including systolic and diastolic and mean arterial pressure more stable by administration phenylephrine 100 mcg than ephedrine 10 mg as prophylaxis and therapy for hypotension after spinal anesthesia during C-Section. Additionally, compared to ephedrine, the administration of phenylephrine reduces the need for rescue vasopressors and the fetal pH is found to be higher with administration of phenylephrine 100 mcg compared with ephedrine 10 mg.

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Ethıcs Committee Approval

This research was approved by the Ethics Committee of Biomedical Research on Humans at the Faculty of Medicine, Hasanuddin University, Makassar, Indonesia, based on recommendation letter Number: 871/UN4.6.4.5.31/PP36/2023 with protocol number: UH23100766

Author's Contribution

The principal investigators of this study are Fadil Ahmad Halomoan Siregar, Muhammad Ramli Ahmad, and Muhammad Rum. Furthermore, Hisbullah, Nur Surya Wirawan, and Ari Santri Palinrungi were involved in shaping the research concept and design. Arifin Seweng played a significant role in conceptualizing the research, designing the study, and conducting statistical analysis on the data. All authors participated in drafting, revising, and evaluating the manuscript content. They have read and agreed to the manuscript's content and confirm the accuracy and integrity of every detail of this research.

Conflict Of Interest

There are no conflict of interest for any of the researchers.

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