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ORIGINAL ARTICLE

Hemodynamic Effects of Phenylephrine 100 µg versus Ephedrine 5 mg During Propofol-Induced General Anesthesia: A Randomized Study

Nicholas Hamonangan Sibarani,[1] Andriamuri Primaputra Lubis,[1] Chrismas Gideon Bangun,[1] Yuki Yunanda[2]

[1]Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Sumatera Utara, Adam Malik General Hospital, Medan, Indonesia

[2]Department of Community Medicine, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

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Corresponding Author:
Andriamuri Primaputra Lubis
Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Universitas Sumatera Utara/Adam Malik General Hospital, Medan, Indonesia
E-mail:
andriamuri@usu.ac.id

Abstract

Background: Propofol is widely used for induction of general anesthesia; however, it frequently associated hypotension due to vasodilation and myocardial depression. Vasopressors such as phenylephrine and ephedrine are commonly administered to counteract this effect, but evidence comparing their hemodynamic efficacy during induction remains limited.

Methods: This randomized double-blind clinical trial included 80 patients undergoing elective surgery under general anesthesia. Patients were randomly allocated into two groups to receive either phenylephrine 100 µg or ephedrine 5 mg at the time of propofol induction. Demographic characteristics (sex, age, body mass index, and ASA physical status) were recorded. Hemodynamic parameters, including systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate, were measured after premedication and 30 seconds following propofol administration.

Results: Baseline characteristics were comparable between the two groups. At 30 seconds after induction, there were no statistically significant differences in systolic blood pressure, diastolic blood pressure, mean arterial pressure, or heart rate between the phenylephrine and ephedrine groups. Both vasopressors effectively maintained hemodynamic stability during propofol induction.

Discussion: The findings suggest that phenylephrine and ephedrine have similar hemodynamic profiles when administered during propofol induction. Despite their differing pharmacological mechanisms, both agents were equally effective in preventing early hypotension without significant differences in heart rate or blood pressure responses.

Conclusion: Phenylephrine 100 µg and ephedrine 5 mg demonstrated comparable efficacy in maintaining hemodynamic stability during propofol-induced general anesthesia, with no significant difference in their ability to prevent hypotension.

Keywords: APGAR score; caesarean section; early ambulation; enhanced recovery after surgery

Introduction

Propofol is one of the most commonly used intravenous agents for the induction of general anesthesia because of its rapid onset and favorable recovery profile.[1–3] However, propofol is frequently associated with hypotension during induction.[4,5] Propofol-induced hypotension is clinically significant,

as it may impair tissue perfusion and has been associated with adverse intraoperative and postoperative outcomes, particularly in patients with limited cardiovascular reserve.[1,6]

Several strategies have been proposed to prevent or attenuate hypotension during propofol induction, including fluid loading, slow induction agent administration, and the use of vasoactive drugs.[2,3] Among these strategies, vasopressors are widely used due to their rapid onset and predictable hemodynamic effects. Phenylephrine is a selective α1-adrenergic agonist that increases systemic vascular resistance with minimal direct effect on heart rate. In contrast, ephedrine is a mixed α- and β-adrenergic agonist that increases blood pressure by enhancing endogenous catecholamine release, thereby maintaining heart rate and cardiac output.[7] Previous studies have shown that both phenylephrine and ephedrine are effective in counteracting hypotension associated with propofol induction; however, the comparative hemodynamic effects of these agents remain inconsistent across studies.[7,8]

Despite the widespread use of phenylephrine and ephedrine in clinical practice, direct comparisons using standardized dosing during propofol-induced general anesthesia are still limited, and there is no clear consensus regarding the superiority of one agent over the oth-er.[7,8] Therefore, this study aimed to compare the hemodynamic effects of phenylephrine 100 µg and ephedrine 5 mg during the induction of general anesthesia with propofol, focusing on changes in systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate.

Subjects and Methods

This study was a randomized, double-blind clinical trial conducted in the operating rooms of Haji Adam Malik General Hospital and Universitas Sumatera Utara Hospital, Medan, Indonesia, in February 2024. Ethical approval was obtained from the Health Research Ethics Committee of Universitas Sumatera Utara (No. 03/KEPK/USU/2024), Haji Adam Malik General Hospital (No. DP.04.03/D. XXVIII/1937/2024), and Universitas Sumatera Utara Hospital (No. 179/UN5.4.1.1.3/ KPM/2024). Written informed consent was obtained from all participants.

The study population consisted of adult patients scheduled for elective surgery under general anesthesia at Haji Adam Malik General Hospital and Universitas Sumatera Utara Hospital. Subjects were recruited using a consecutive sampling technique, whereby all eligible patients meeting the inclusion criteria during the study period were invited to participate until the required sample size was achieved. Inclusion criteria were patients aged 18–40 years, ASA physical status I–II, body mass index (BMI) between 18 and 30 kg/m^2, and planned induction of general anesthesia with propofol. Exclusion criteria included pregnancy, history of hypertension or ischemic heart disease, baseline hypotension before induction, and sinus tachycardia on pre-induction electrocardiography.

Dropout criteria included the occurrence of intraoperative shock or intraoperative death. The sample size was calculated using a formula for comparison of two independent means. Based on differences in diastolic blood pressure reported in previous studies, a minimum of 40 subjects per group was required. Therefore, 80 patients were included. Subjects were randomly allocated into two groups using computer-generated simple randomization. Group allocation was concealed using sealed opaque envelopes. This study employed a double-masked design, in which both the anesthesiologist performing hemodynamic measurements and the patients were blinded to group assignment. Study drugs were prepared and administered by an independent anesthesiologist not involved in data collection.

All patients followed standard preoperative fasting guidelines, including fasting from solid food for at least 6 hours and allowance of clear fluids up to 2 hours before anesthesia induction. No sedative premedication was administered. Lidocaine and other vasoactive agents were not given prior to induction.

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Baseline blood pressure and heart rate were recorded before induction. General anesthesia was induced with intravenous propofol at a dose of 2 mg/kg, administered manually at a standardized injection rate over approximately 30 seconds in all patients. No target-controlled infusion (TCI) system was used. Immediately after propofol administration, patients received either phenylephrine 100 µg or ephedrine 5 mg as a bolus intravenously, according to group allocation.

Non-invasive blood pressure, heart rate, and oxygen saturation were continuously monitored. Hemodynamic measurements were recorded at baseline (before induction) and at 30 seconds after propofol administration. To ensure the accuracy of the 30-second measurement, the non-invasive blood pressure cuff was activated immediately after induction, ensuring the measurement cycle was completed at the designated time point. Hypotension was defined as a decrease in mean arterial pressure (MAP) of ≥20% from baseline or a MAP <65 mmHg. Descriptive statistics were used to summarize subject characteristics. Numerical data were presented as mean ± standard deviation or median, while categorical data were presented as frequencies and percentages. Data normality was assessed using the Shapiro–Wilk test. Normally distributed variables were compared using the unpaired t-test, whereas non-normally distributed variables were analyzed using the Mann– Whitney U test. Statistical analysis was performed using SPSS software, and a p-value < 0.05 was considered statistically significant.

Result

A total of 80 subjects who met the inclusion and exclusion criteria were included in the analysis, with 40 subjects in the phenylephrine group and 40 subjects in the ephedrine group. Baseline characteristics of the study subjects, including sex, age, body mass index (BMI), and ASA physical status, are presented in Table 1. There were no statistically significant differences between the two groups in any baseline characteristic ($p > 0.05$), indicating that the groups were comparable before intervention.

Changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and mean arterial pressure (MAP) before induction (T0) and 30 seconds after induction (T1) are summarized in Tables 2–5.

Both groups experienced a decrease in SBP and DBP following propofol induction. However, comparison between the phenylephrine and ephedrine groups showed no statistically significant differences in SBP or DBP at either time point ($p>0.05$). Similarly,

Table 1 Characteristics of Research Subjects

Variable	Groups		p-value
	Phenylephrine	Ephedrine	
Gender			
Male	10 (25%)	12 (30%)	0.617*
Female	30 (75%)	28 (70%)	
Age (years)	34 (18–40)	33 (14–49)	0.566
BMI (kg/m^2)	24.25 (20.7–29.1)	23.55 (19.9–28.1)	0.205
PS-ASA			
1	18 (45%)	15 (37.5%)	0.496
2	22 (55%)	25 (62.5%)	

Note:*Data are presented as median (minimum–maximum) or number (percentage). Mann–Whitney U test and Chi-square test were used as appropriate

Table 2 Comparison of Systolic Blood Pressure (SBP) in Phenylephrine 100 mcg and Ephedrine 5 mg Groups

SBP	Groups		p-value
	Phenylephrine	Ephedrine	
T0	135 (110–180)	130 (100–180)	0.229*
T1	100 (85–160)	100 (80–135)	0.718*

Note: *Data are presented as median (minimum–maximum); Wilcoxon test

Table 3 Comparison of Diastolic Blood Pressure (DBP) in Phenylephrine 100 mcg and Ephedrine 5 mg Groups

DBP	Groups		p-value
	Phenylephrine	Ephedrine	
T0	79 (60–95)	75 (60–95)	0.767*
T1	65 (50–82)	65 (45–85)	0.65*

Note: *Data are presented as median (minimum–maximum); Wilcoxon test

heart rate decreased after induction in both groups, with no significant difference between groups.

After the administration of phenylephrine and ephedrine, most subjects maintained a mean arterial pressure (MAP) ≥65 mmHg. However, there was no significant difference between the two drugs in preventing hypotension (p>0.05). The detailed comparison of MAP values between the groups is presented in Table 5.

Most subjects in both groups maintained a MAP ≥65 mmHg after induction. There was no statistically significant difference between the phenylephrine and ephedrine groups in the incidence of hypotension as defined by MAP <65 mmHg (p>0.05).

Discussion

Hypotension remains a common complication during general anesthesia, particularly following induction with propofol. The reported incidence varies widely, ranging

Table 4 Comparison of Heart Rate Between the 100 µg Phenylephrine Group and the 5 mg Ephedrine Group

Heart Rate	Groups		p-value
	Phenylephrine	Ephedrine	
T0	81 (70–98)	88 (69–98)	0.796*
T1	75 (53–100)	76 (60–115)	0.552*

Note: *Data are presented as median (minimum–maximum);Wilcoxon test

Table 5 Comparison of MAP in Phenylephrine 100 mcg and Ephedrine 5 mg groups

Variable	Groups		p-value
	Phenylephrine	Ephedrine	
<65	3 (7.5%)	4 (10%)	0.692
>65	37 (92.5%)	36 (90%)	

Note: * Hypotension was defined as mean arterial pressure <65 mmHg. Chi-square test.

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from 5% to nearly 100%, depending on patient characteristics, anesthetic technique, and the definition used, and often requires pharmacological intervention in a significant proportion of cases.[1,6] Propofol is widely used for its rapid onset and favorable recovery profile; however, it is well known to cause dose-dependent hypotension through a combination of direct myocardial depression, reduced systemic vascular resistance, and impaired baroreflex responses.[1–5]

The present study demonstrated that prophylactic administration of either phenylephrine 100 μg or ephedrine 5 mg was effective in maintaining hemodynamic stability during the propofol-induced general anesthesia. There were no statistically significant differences between the two groups in systolic blood pressure, diastolic blood pressure, heart rate, or mean arterial pressure at baseline or 30 seconds after induction. These findings suggest that both agents provide comparable protection against early induction-related hypotension in this clinical setting.

Regarding heart rate, the median values after induction were nearly identical between the phenylephrine and ephedrine groups. Therefore, it cannot be concluded that ephedrine increased heart rate in this study. Although ephedrine has β_1- adrenergic activity that may increase heart rate, this effect was not reflected in the median heart rate values observed in our results. This highlights the importance of interpreting central tendency measures appropriately, particularly when non-parametric statistical tests are used.[8]

In this study, hypotension was assessed 30 seconds after induction, reflecting the early hemodynamic effects of propofol administration. While post-induction hypotension is commonly defined as hypotension occurring within the first 20 minutes after induction, the present study focused specifically on the immediate phase, during which the most abrupt decreases in blood pressure are frequently observed. This limited observation window should be considered when comparing the present findings with studies that evaluated more extended post-induction periods.[6]

Previous studies have shown mixed results regarding the relative efficacy of phenylephrine and ephedrine, particularly in the context of spinal anesthesia. Several investigations in obstetric spinal anesthesia have reported that phenylephrine is associated with better blood pressure control but a higher incidence of bradycardia, whereas ephedrine tends to preserve heart rate.[9,10,13–15] However, these findings may not be directly applicable to general anesthesia, as the mechanisms of hypotension differ between spinal anesthesia and propofol-induced vasodilation. Studies conducted during general anesthesia induction have generally demonstrated comparable effectiveness of phenylephrine and ephedrine, consistent with the results of the present study.[7,8]

Several potential confounding factors should be considered when interpreting these results. Individual variations in intravascular volume status, vascular tone, and autonomic responsiveness may influence hemodynamic responses to both propofol and vasopressors. Additionally, differences in drug dosage, timing of administration, and anesthetic technique across studies may contribute to inconsistent findings in the literature. A key limitation of this study is the short observation period, limited to the early induction phase, which may not capture delayed hypotensive events. Furthermore, the single-center design A relatively small sample size may limit the generalizability of the results. Future studies with longer monitoring periods and larger populations are needed to examine further examine the comparative effects of these agents during general anesthesia induction

Conclusion

In this randomized, double-masked clinical trial, there was no statistically significant difference between phenylephrine 100 μg and ephedrine 5 mg in maintaining systolic, diastolic, heart rate, and mean arterial pressure

at 30 seconds after induction of general anesthesia with propofol. These findings indicate that both vasopressors provide comparable hemodynamic effects during the early phase of propofol-induced anesthesia.

However, because this study did not include a placebo or control group, the effectiveness of each drug in preventing hypotension cannot be independently determined. Further studies with more extended observation periods and appropriate control groups are required to evaluate the actual efficacy of vasopressors in preventing post-induction hypotension.

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