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Original Research Article

A COMPARATIVE STUDY OF EPHEDRINE AND PHENYLEPHRINE TO COUNTERACT PROPOFOL INDUCED HYPOTENSION

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Abstract

Background: Propofol is a potent and widely accepted anaesthetic, used for inducing and sustaining general anaesthesia via intravenous administration. Despite its extensive use in the field of medicine, propofol is known to cause significant hypotension during induction of anaesthesia which can lead to detrimental outcomes. Preventive interventions using prophylactic drugs such as is crucial to alleviate propofol-induced hypotension during general anaesthesia. Thus, this study aims to assess the efficacy of ephedrine and phenylephrine as prophylactic drugs, compare their effects in counteracting hypotension during general anaesthesia and evaluate their safety as well as associated side-effects. **Materials and Methods:** The current prospective study cohort includes 225 patients who were further divided into three groups of 75 individuals each. Group A, B and C received a mixture of 2mg/kg of 1% propofol with saline, ephedrine (6mg/ml) and phenylephrine (50mcg/ml) respectively. All patients were pre-medicated with oral midazolam 7.5 mg, 1 hour before the operation. In the operating room, after securing intravenous access, intravenous glycopyrrolate (4mcg/kg) was given right before induction. Standard monitoring (pulse oximetry, non-invasive blood pressure, and electrocardiogram) was instituted and the baseline systolic BP, diastolic BP, MAP and heart rate that were noted from an average of two readings taken 5 min apart. All patients were pre-oxygenated with 100% oxygen for 3 min. **Result:** Phenylephrine and ephedrine led to significant increase in the systolic BP, diastolic BP and MAP as compared to the control group where, ephedrine group exhibited tachycardia and phenylephrine group exhibited bradycardia. When compared amongst phenylephrine and ephedrine, by the end of 5 minutes, phenylephrine was more effective in counteracting the significant hypotension occurring because of induction dose of propofol. **Conclusion:** Phenylephrine was able to confer superior effects in alleviating significant hypotension and related symptoms caused by propofol-induced general anaesthesia as compared to ephedrine.

INTRODUCTION

Propofol is a potent and widely accepted anaesthetic, used for inducing and sustaining general anaesthesia via intravenous administration. It is a hypnotic drug with a short half-life that leads to a rapid and smoothly induced anaesthesia and sedation.[1] Though it does not exhibit analgesic effects, it can be used to sedate adults who require mechanical ventilation in intensive care units.[2] Moreover, because of a quick recovery time and minimal incidences of nausea and vomiting, propofol has a multitude of medical applications. [3,4]

Despite its extensive use, there have been reports indicating the adverse effects of propofol induction which include apnea, myoclonus, and thrombophlebitis. Direct myocardial depression and a reduction in systemic vascular resistance have been suggested to be contributing factors in causing drug-induced cardiovascular depression in a dose-dependent manner. Moreover, propofol causes venodilation in addition to arterial vasodilation, which contributes to its hypotensive impact.[5]
Clinically, hypotension becomes significant with a reduction in the end-organ blood flow. The degree of hypotension necessary to lower end-organ blood flow

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is determined by the patient's health and the ability of individual organ vascular beds to autoregulate blood flow. During deliberate hypotensive anaesthesia, the mean arterial blood pressure of a young, fit individual falls as low as 50-65 mm Hg and it still tolerable but at this blood pressure renal blood flow is significantly reduced. Renal blood flow is compromised when the mean arterial blood pressure falls below 80 mm Hg. Thus, an elderly, pregnant, or medically compromised patient will not endure hypotension to the same degree as a young, healthy patient and it is difficult to determine the level at which end-organ blood flow is reduced. Considering these parameters, a decline in arterial blood pressure of greater than 20% below baseline denotes a clinically significant drop in arterial blood pressure, but is unlikely to cause end-organ hypoperfusion, especially in a healthy patient.[4]

Various methods have been tested to counter the hypotensive effects caused by the induction dose of propofol, for instance, pre-loading with crystalloid fluids.[4,6] slow drug administration, (7) and co-administration with ephedrine.[6,8] phenylephrine,[5] ketamine etc.

Phenylephrine is a synthetic non-catecholamine alpha-1 adrenergic agonist. It has minimal effect on beta-adrenergic receptors. Numerous studies have demonstrated the effectiveness of phenylephrine as a vasopressor to maintain arterial blood pressure.

Similarly, ephedrine is an alpha and beta-adrenergic agonist that functions as a vasopressor and sympathomimetic. It has been used safely and successfully for both the prevention and treatment of anesthesia-induced hypotension. Furthermore, it can decrease the hemodynamic responses caused by the administration of bolus propofol.[8,9] Ephedrine has previously been administered as a single bolus, continuous infusion or intramuscular injection.[10,11] When used in high doses, it can effectively treat propofol-induced hypotension but may cause marked tachycardia.[2] Prophylactic use of ephedrine has been also associated with hypertension in some clinical situations.[10] However, several investigations concluded that smaller doses of ephedrine prevented propofol-induced hypotension without significant increases in HR or dysrhythmias.[12] The justification for using a drug as a preventative measure to avoid hypotension and bradycardia stems from the adverse effects of these side-effects, which are frequently overlooked since clinicians are unable to continually monitor hemodynamic variables in certain clinical scenarios.

Due to the extensive utilization of propofol in general anaesthesia, the present investigation was conducted to evaluate the efficacy of phenylephrine and ephedrine with normal saline for the prevention of propofol-induced hypotension.

The primary objective of this study was to assess the effectiveness of ephedrine as well as phenylephrine and comparing the efficacy of both the drugs in counteracting Propofol-induced hypotension in induction of general anaesthesia. Furthermore, the secondary objective was to assess the safety of these drugs and observe the side-effects associated with them.

MATERIALS AND METHODS

Study Design

This single center, prospective, randomized controlled, double-blind study was conducted at the Department of Anesthesia, DY Patil Hospital and Research Centre, Navi Mumbai, from January 2020 to September 2021. The present study was duly approved by Institutional Ethics Committee of D. Y. Patil Deemed to be University (DYP/IECBH/2020/31). Each participant provided a valid informed written and signed consent before being included in the research.

Study Population

225 cases (randomly divided in three groups of 75 cases, each) undergoing elective surgery requiring general anesthesia, during the study period and meeting the inclusion and exclusion criteria.

Eligibility Criteria

The study population comprised patients aged 18-60yrs undergoing elective surgery with general anesthesia, including ASA I and II patients of any gender who provided consent. Patients were excluded from the research if they had emergency surgery, ischemic heart disease, systemic comorbidities (e.g., diabetes, hypertension, thyroid disorder), peripheral vascular disease, allergy to study drugs, or refused to give consent.

Study Protocol

The drugs were prepared by drawing 2mg/kg of 1% propofol in a syringe. The study drugs were added to propofol containing syringe according to the study groups as follows:

- Group A: Saline group: 2 ml of 0.9% sodium chloride as placebo control (n=75)
- Group B: Phenylephrine group: 2ml (50mcg/ml) of Phenylephrine (n=75)
- Group C: Ephedrine group: 2ml (6mg/ml) of Ephedrine (n=75)

All patients were pre-medicated with oral midazolam 7.5 mg, 1 hour before the operation. In the operating room intravenous Glycopyrrolate (4mcg/kg) was given right before induction.

Various parameters such as pulse, blood pressure, electrocardiogram was monitored. Baseline measurements of systolic BP, diastolic BP, MAP, and heart rate were recorded from two readings taken 5 minutes apart. Pre-oxygenation with 100% oxygen was administered for 3 minutes.[13]

Statistical Analysis

Data analysis utilized IBM SPSS software. Descriptive statistics included Mean ± SD for numerical data and percentages for categorical data. Analytical tests included 'Paired t test', 'Unpaired t test', 'One way ANOVA' for numerical data. Significance was denoted by a p value < 0.05 (* in Tables).

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RESULTS

[Tables 1-4] represent demographic data of individuals aged 18 to 65 included in the study. Mean ages in Group A, Group B, and Group C were 34.15 ± 11.29, 36.57 ± 11.14, and 38.55 ± 12.46 years, respectively [Table 1]. No significant age or gender differences were found between the groups (p=0.07 and p=0.160, respectively) [Table 2]. Most cases (87.55%) belonged to orthopedics, surgery, gynecology, and ENT specialties [Table 3]. ASA grades did not significantly differ among the three groups (p=0.641) [Table 4].

[Table 5] displays the baseline and 5-minute systolic blood pressure (BP) in Groups A, B, and C. All groups showed a consistent and significant decrease in BP from 1 to 5 minutes compared to baseline (p<0.001). No significant differences were found in systolic BP among the three groups (p=0.793). Group A had the lowest BP at 5 minutes, followed by Group C, and Group B had the highest BP (p<0.05).

[Table 6] presents baseline and 5-minute BP in Groups A, B, and C. All groups showed a consistent and significant decline in diastolic BP from 1 to 5 minutes compared to baseline (p<0.001). Baseline diastolic BP was similar in all three groups (p=0.997). Group A had the lowest diastolic BP at 5 minutes, followed by Group B, and Group C had the highest (p<0.05). These findings are consistent with Farhan M. et al., who also reported similar baseline diastolic BP values among groups and observed increased diastolic BP from 1 to 5 minutes in the Phenylephrine (PP) and Ephedrine (PE) groups compared to the control Saline (PS) group.

[Table 7] displays baseline and 5-minute Mean Arterial Pressure (MAP) in Groups A, B, and C. All groups showed a consistent and significant decline in MAP from 1 to 5 minutes compared to baseline (p<0.001). Baseline MAP was similar in all three groups (p=0.972). Group A had the lowest MAP at 5 minutes, followed by Group C, and Group B had the highest (p<0.05).

Table 8 presents baseline and 5-minute heart rates in Groups A, B, and C. In Group A, heart rate increased from 79.61 ± 11.43 to 81.69 ± 15.40 beats/minute. In Group B, heart rate initially decreased significantly (67.85 ± 11.64 beats/minute) and then increased significantly (71.99 ± 12.73 beats/minute) compared to baseline (p<0.001). In Group C, heart rate initially increased significantly (83.05 ± 12.39 beats/minute) and then decreased significantly (82.77 ± 11.48 beats/minute) compared to baseline (p<0.05). Baseline heart rates were similar in all groups (p=0.526). The general trend for heart rate from 1 to 5 minutes was lowest in Group B, followed by Group A, and highest in Group C (p<0.05).

The study observed a consistent increase in significant hypotension prevalence in all groups from 1 to 5 minutes [Table 9]. Control Group A had the highest prevalence, followed by Group B and Group C (p<0.001). At 4 and 5 minutes, the control group had the highest prevalence, followed by ephedrine and phenylephrine groups (p<0.05). The proportion of patients requiring treatment increased from 1 to 5 minutes [Table 10]. Significant differences were found at 2 and 5 minutes (p<0.05). Group A had the highest proportion at 2 minutes, followed by Group B, and Group C. At 5 minutes, Group C had a higher proportion than Group B.

Table 1: Age (in years) distribution of the study population in the three groups

Age Group	Group A		Group B		Group C	
	N	%	N	%	N	%
18 to 25	21	28	17	22.67	12	16
26 to 33	21	28	14	18.67	15	20
34 to 41	12	16	14	18.67	18	24
42 to 49	11	14.67	17	22.67	11	14.67
50 to 57	8	10.67	12	16	13	17.33
58 to 65	2	2.66	1	1.32	6	8
Total	75	100	75	100	75	100
Mean ± sd	34.15 ± 11.29		36.57 ± 11.14		38.55 ± 12.46	
Range	18 to 64 years					
P-value	0.070					
Statistical significance	Not significant					

Data is represented as mean+S.D or absolute numbers. P-value <0.05 is statistically significant. The three groups were similar in age distribution; P-value: 0.070.

Table 2: Gender-wise distribution of the study population in the three groups

Gender	Group A		Group B		Group C	
	N	%	N	%	N	%
Females	35	46.67	46	61.33	37	49.33
Males	40	53.33	29	38.67	38	50.67
Total	75	100	75	100	75	100
P-value	0.160					
Statistical significance	Not significant					

Data is represented as mean+S.D or absolute numbers. P-value <0.05 is statistically significant. The three groups were similar in terms of gender distribution; P-value: 0.160.

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Table 3: Distribution of the surgical specialty in the study population

Speciality	N	%
Orthopedics	55	24.44
Surgery	55	24.44
Gynecology	44	19.56
Ent	43	19.11
Oromaxillofacial	11	4.89
Urosurgery	7	3.11
Oncosurgery	5	2.22
Ophthalmology	3	1.34
Plastic surgery	2	0.89
Total	225	100

Orthopedics was the most common specialty while plastic surgery was the least common specialty.

Table 4: Distribution of the study population in the three groups according to the ASA grade

ASA Grade	Group A		Group B		Group C	
	N	%	N	%	N	%
ASA I	36	48	41	54.67	36	48
ASA II	39	52	34	45.33	39	52
TOTAL	75	100	75	100	75	100
P value	0.641					
Statistical Significance	Not significant					

Data is represented as mean+S.D or absolute numbers. P value <0.05 is statistically significant. The three groups were similar in terms of ASA grade; P value: 0.641.

Table 5: Intra-group and inter-group comparison of Systolic BP of Groups A, B and C

	Intra-Group			Inter-Group
	Group A	Group B	Group C	P-value
Baseline	120.28 + 8.05	119.39+ 10.07	120.37+11.03	0.793
1	107.48 + 11.30 a***	113.55+ 12.57 a**	113.81+ 11.39a***	0.001*
2	100.41 + 10.41 a***	109.72+ 12.19 a***	106.76 + 11.14a***	<0.001*
3	95.07+ 9.46 a***	105.83+ 12.17a***	100.27 + 10.67a***	<0.001*
4	90.91+ 8.80 a***	101.97+ 12.44a***	93.91+ 10.06a***	<0.001*
5	87.2 + 8.42 a***	99.16+ 13.45 a***	88.31+ 9.81 a***	<0.001*

Data is represented as mean+S.D or absolute numbers. The symbol "a" used in the table represents statistical significance where each timepoint is compared to the baseline (intragroup), *p<0.05, **p<0.01, ***p<0.001, NS-Not significant.

Table 6: Intra-group and inter-group comparison of Diastolic BP of Groups A, B and C

		Intra-Group		Inter-Group
	A	B	C	P-value
Baseline	76.79 + 10.91	76.91+ 9.59	76.77+11.81	0.997
1	66.17+ 13.06 a***	71.01+ 12.03 a***	73.48+ 11.23 a***	0.001*
2	61.40 + 12.69 a***	66.65+ 11.90 a***	69.08+ 11.14 a***	<0.001*
3	57.25+ 12.37 a***	62.45+ 11.76 a***	65.08+ 11.50 a***	<0.001*
4	52.89+ 11.65 a***	57.85+ 11.47 a***	60.85+ 11.15a***	<0.001*
5	48.79+ 11.07 a***	53.13+ 10.96 a***	56.65+ 10.98 a***	<0.001*

Data is represented as mean+S.D or absolute numbers. The symbol "a" used in the table represents statistical significance where each timepoint is compared to the baseline (intragroup), *p<0.05, **p<0.01, ***p<0.001, NS-Not significant.

Table 7: Intra-group and inter-group comparison of MAP of Groups A, B and C

		Intra-Group		Inter-Group
	A	B	C	P-value
Baseline	91.23+ 8.11	91.05 + 8.79	90.87 + 10.70	0.972
1	79.88 + 10.68 a***	84.88 + 11.60 a***	86.69 + 10.48 a***	0.001*
2	74.43 + 10.17 a***	80.6 + 11.13 a***	81.35 + 10.14 a***	<0.001*
3	69.92 + 9.72 a***	76.85 + 10.95 a***	76.59 + 10.29 a***	<0.001*
4	65.61 + 9.16 a***	72.59 + 10.80 a***	71.57 + 9.82 a***	<0.001*
5	61.59 + 8.66 a***	68.49 + 10.63 a***	66.91 + 9.72 a***	<0.001*

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Data is represented as mean+S.D or absolute numbers. The symbol “a” used in the table represents statistical significance where each timepoint is compared to the baseline (intragroup), *p<0.05, **p<0.01, ***p<0.001, NS-Not significant.

Table 8: Intra-group and inter-group comparison of Heart Rate of Groups A, B and C

	Intra-Group			Inter-Group
	A	B	C	P-value
Baseline	79.61 + 11.43	79.21 + 11.76	81.28 + 12.29	0.526
1	80.37+ 11.46 a^{NS}	73.47 + 11.96 a***	82.96 + 12.23 a***	<0.001*
2	79.91+ 11.59 a^{NS}	67.85 + 11.64 a***	83.05 + 12.39 a**	<0.001*
3	80.73+ 12.73 a^{NS}	68.87 + 11.64 a***	82.77 + 11.21 a**	<0.001*
4	82.03+ 14.00 a^{NS}	70.01 + 12.10 a***	82.13 + 11.48 a^{NS}	<0.001*
5	81.69+ 15.40 a^{NS}	71.99 + 12.73 a***	81.91 + 11.28 a^{NS}	<0.001*

Data is represented as mean+S.D or absolute numbers. The symbol “a” used in the table represents statistical significance where each timepoint is compared to the baseline (intragroup), *p<0.05, **p<0.01, ***p<0.001, NS-Not significant.

Table 9: Distribution of study population according to the presence of significant hypotension (N=225)

Duration	Group A		Group B		Group C		P value
	No	Yes	No	Yes	No	Yes	
1	62 (82.67%)	13 (17.33%)	72 (96%)	3 (4%)	75 (100%)	0 (0%)	<0.001*
2	49 (965.33%)	26 (34.67%)	67 (89.33%)	8 (10.67%)	73 (97.33%)	2 (2.67%)	<0.001*
3	27 (36%)	48 (64%)	62 (82.67%)	13 (17.33%)	64 (85.33%)	11 (14.67%)	<0.001*
4	8 (10.67%)	67 (89.33%)	39 (52%)	36 (48%)	32 (42.67%)	43 (57.33%)	<0.001*
5	2 (2.67%)	73 (97.33%)	12 (16%)	63 (84%)	8 (10.67%)	67 (89.33%)	0.022*

Data is represented as mean+S.D or absolute numbers. P value <0.05 is statistically significant.
There was a consistent increase in the prevalence of significant hypotension in all the groups, from 1 to 5 minutes. At the end of 5 minutes, prevalence was more in Group A>Group C>Group B.

Table 10: Distribution of requirement of treatment according to MAP in the study population (N=225)

Duration	Group A		Group B		Group C		P value
	Treat	No treat	Treat	No treat	Treat	No treat	
1	3 (4%)	72 (96%)	0 (0%)	75 (100%)	1 (1.33%)	74 (98.67%)	0.168
2	11 (14.67%)	64 (85.33%)	4 (5.33%)	71 (94.67%)	1 (1.33%)	74 (98.67%)	0.005*
3	13 (17.33%)	62 (82.67%)	7 (9.33%)	68 (90.67%)	7 (9.33%)	68 (90.67%)	0.220
4	21 (28%)	54 (72%)	11 (14.67%)	64 (85.33%)	11 (14.67%)	64 (85.33%)	0.056
5	30 (40%)	45 (60%)	15 (20%)	60 (80%)	18 (24%)	57 (76%)	0.016*

Data is represented as mean+S.D or absolute numbers. P value <0.05 is statistically significant.
There was a consistent increase in the prevalence of patients requiring treatment according to the MAP in all the groups, from 1 to 5 minutes. At the end of 5 minutes, prevalence was more in Group A>Group C>Group B.

DISCUSSION

Propofol is a short-acting intravenous hypnotic used for anaesthesia, sedation, and ICU patient sedation. It lacks analgesic effects and is commonly used in medical procedures and mechanical ventilation.[2] Propofol is commonly used in clinics for its recovery benefits but can cause significant drops in blood BP and HR. [14,15] Propofol lacks neuromuscular blocking properties and may require an additional muscle relaxant for tracheal intubation. It can cause pain on injection, myoclonus, apnoea, and rarely thrombophlebitis. However, the most critical side-effect is the decrease in systemic blood pressure due to direct myocardial depression and decreased vascular resistance, as propofol causes arterial and venous dilation. [16] The slight increase in heart rate caused by propofol may result in a more significant reduction in arterial pressure compared to an equipotent dose of thiopental. [17] This cardio-depressant effect is more pronounced with age, necessitating dosage adjustments in administration. Although controlled hypotensive techniques in certain elective cases utilize propofol's hypotensive effect, this approach may not be suitable for sick and older patients.

Prophylactic drug use to prevent hypotension and bradycardia is crucial in anaesthesia practice. In certain clinical conditions, constant hemodynamic monitoring is not feasible, making preventive measures essential. Anaesthetic induction agents often lead to rapid blood pressure decline, underscoring the importance of managing hemodynamic stability proactively.[18] To counteract propofol's hypotensive effects, techniques like slow administration, preloading, and vasoactive drug use are investigated.

Phenylephrine is a synthetic non-catecholamine that primarily acts through direct modulation of alpha-1 adrenergic receptors. Its impact on beta-adrenergic receptors is minimal. Intravenous administration of phenylephrine at doses ranging from 50 to 200 mg is commonly utilized to counteract the decrease in blood pressure associated with sympathetic nervous system blockade during regional anaesthesia and the peripheral vasodilation resulting from the administration of injected or inhaled anaesthetics. [19]

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Ephedrine, an indirect sympathomimetic drug, exerts its efficacy by stimulating the adrenergic receptor system, leading to increased noradrenaline activity at postsynaptic α and β receptors. As a prophylactic agent, ephedrine successfully mitigates propofol-induced hypotension during general anaesthesia. It can be administered through intravenous bolus, intramuscular injection, or continuous infusion routes.[8] However, it causes marked tachycardia when used in large dosages to manage propofol-induced hypotension.[19] This study aimed to assess and compare the effects of intravenous phenylephrine, ephedrine, and normal saline in preventing hypotension during propofol-induced anaesthesia, which has not been extensively investigated despite being a common occurrence.

In this double-blinded study, 225 patients undergoing major surgery were selected, with demographics similar to previous studies by Farhan et al in terms of age and gender distribution. [20] The present study's demographic variables are also aligned with results from Gamlin F. et al and El-Tahan M. et al, indicating similarity among all the groups. [21,22] The ASA grades of patients in the three groups were similar (p value=0.641), consistent with Farhan M. et al findings (p value=0.73). The study included major surgery cases from various specialties, with Orthopaedics, Surgery, and Gynaecology having the highest number of patients. Other specialties constituted less than 5% of the cases each.

In this study, all three groups showed a consistent and significant decline in systolic blood pressure from 1 to 5 minutes compared to baseline (p value<0.05). Baseline systolic BP was similar among the groups. The general trend for systolic BP was lowest in Group A, followed by Group C, and highest in Group B (p value<0.05). These results aligned with Farhan M. et al findings, where the groups showed similar baseline systolic BP, and systolic BP was lowest in the saline group, followed by ephedrine and phenylephrine groups, remaining significant from 1 to 5 minutes, similar to our study.[20] Gamlin F. et al compared ephedrine, colloid (Haemaccel), and control groups, finding similar baseline systolic BP (p = 0.138). Our study showed significantly higher systolic BP in the ephedrine group compared to the control group (p value<0.05). Similar results were reported by Kwok F. and Venugobal S. et al studying the effects of prophylactic phenylephrine during propofol induction.[23] They observed that there was significant increase in systolic BP in the phenylephrine group as compared to the saline group. Thus, it can be effectively concluded that both phenylephrine and ephedrine significantly increased systolic BP compared to the control group (normal saline), with phenylephrine leading to a greater increase than ephedrine.

Additionally, all three groups exhibited a consistent and significant decrease in diastolic blood pressure from 1 to 5 minutes compared to baseline (p <0.05). The trend for diastolic BP was lowest in Group A, followed by Group B, and highest in Group C (p <0.05). Farhan M. et al results also showed similar baseline diastolic BP among the three groups. They observed an increase in diastolic BP from 1 to 5 minutes in the Phenylephrine and Ephedrine groups compared to the control group. Our results were similar to Kwok F. and Venugobal S. et al's study, reporting a higher increase in diastolic BP in the Ephedrine group compared to the Saline group. Therefore, both Phenylephrine and Ephedrine significantly increased diastolic BP compared to the control group, with a higher increase observed with Ephedrine than with Phenylephrine. Additionally, diastolic BP decreased over time. [23] Thus, it can be effectively concluded that both Phenylephrine and Ephedrine led to significant increase in diastolic BP as compared to the control group with normal saline, though the increase is more with ephedrine than with phenylephrine. There is also decrease in diastolic BP through time.

In this study, MAP values declined significantly from 1 to 5-minute intervals (p<0.05). The trend for MAP was lowest in Group A, followed by Group C, and highest in Group B (p<0.05). Similar results were reported by Farhan M. et al, where the MAP remained significant across the 1 to 5-minute intervals in the saline, ephedrine, and phenylephrine groups. El-Tahan M. et al also observed a significant increase in MAP in the ephedrine group compared to the placebo group during cardiac surgery. Kwok F. and Venugobal S. et al concluded that there was a significant increase in MAP in the Phenylephrine group compared to the Saline group, similar to our study. Therefore, both phenylephrine and ephedrine significantly increased MAP compared to the control group (normal saline). MAP also decreased over time. [20-23]

The baseline heart rate was similar in all three groups. Group B (phenylephrine) showed a consistent decline in heart rate until the 2-minute interval, followed by an elevated heart rate (p<0.001). Group C (ephedrine) exhibited a consistent increase in heart rate until the 2-minute interval (p<0.05), followed by a decrease at the 3-minute interval. The general trend for heart rate was lowest in Group B, followed by Group A, and highest in Group C from 1 to 5 minutes (P value<0.05). Our results aligned with Farhan M. et al's study, showing significant heart rate differences between phenylephrine and ephedrine groups. Gamlin F. et al and El-Tahan M. et al reported tachycardia in the ephedrine group and phenylephrine group, respectively, which differed from our study where phenylephrine led to relative bradycardia.[21] Gopalakrishna M. et al and El-Beheiry et al reported tachycardia with ephedrine. [24,25] Kwok F. and Venugobal S. et al observed significant heart rate decreases with phenylephrine, matching our results.[23] Thus, phenylephrine decreased heart rate while ephedrine increased it compared to the control group with normal saline.

In this study, there was a steady increase in the prevalence of severe hypotension in all groups. The prevalence of hypotension was highest in the control

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Group A, followed by Group B and Group C (p value<0.001). At 4 and 5-minute intervals, the prevalence of significant hypotension was highest in the control group, followed by the ephedrine and phenylephrine administered groups (p value<0.05). Similar results were reported by Farhan M. et al, showing higher prevalence of hypotension in the saline group compared to ephedrine and phenylephrine groups. [20] Gamlin F. et al and El-Tahan M. et al also observed a lower prevalence of hypotension in the ephedrine group compared to the control group, supporting our findings. [21] Thus, phenylephrine was more effective in counteracting significant hypotension caused by the induction dose of propofol by the end of 5 minutes.

In this study, the proportion of patients requiring treatment for hypotension increased from 1 to 5 minutes. Significant differences in treatment requirements were observed at 2 and 5 minutes (p value<0.05). Previous reports also suggest that ephedrine was more effective initially (up to 2 minutes), while phenylephrine became more effective afterward. [20][23]

CONCLUSION

Thus, in this study, it can be effectively concluded that both phenylephrine and ephedrine led to significant increase in the systolic BP, diastolic BP and MAP as compared to the control group with normal saline. Furthermore, there is tachycardia in the ephedrine group and bradycardia in the phenylephrine group. When compared amongst phenylephrine and ephedrine, by the end of 5 minutes, phenylephrine was more effective in counteracting the significant hypotension occurring because of induction dose of propofol.

REFERENCES

1. Sahinovic MM, Struys MMRF, Absalom AR. Clinical Pharmacokinetics and Pharmacodynamics of Propofol. Clin Pharmacokinet. 2018;57(12):1539.
2. Smith I, White PF, Nathanson M, Gouldson R. Propofol: an update on its clinical use. Anesth Prog. 1995;2(42):63.
3. Claeys M, Gepts E, Camu F. Haemodynamic changes during anaesthesia induced and maintained with propofol. BJA Br J Anaesth. 1988;60(1):3–9.
4. Turner RJ, Gatt SP, Kam PC, Ramzan I, Daley M. Administration of a crystalloid fluid preload does not prevent the decrease in arterial blood pressure after induction of anaesthesia with propofol and fentanyl. Br J Anaesth. 1998;80(6):737–41.
5. Kassam SI, Lu C, Buckley N, Lee RM. The mechanisms of propofol-induced vascular relaxation and modulation by perivascular adipose tissue and endothelium. Anesth Analg. 2011;112(6):1339–45.
6. Dhungana Y, Bhattarai BK, Bhadani UK, Biswas BK, Tripathi M. Prevention of hypotension during propofol induction: a comparison of preloading with 3.5% polymers of degraded gelatin (Haemaccel) and intravenous ephedrine. Nepal Med Coll J. 2008;10(1):16–9.
7. Aitkenhead AR, Smith G, Rowbotham DJ. Textbook of anaesthesia. Elsevier Health Sciences; 2007.
8. Michelsen I, Helbo-Hansen HS, Kohler F, Lorenzen AG, Rydlund E, Bentzon MW. Prophylactic ephedrine attenuates the hemodynamic response to propofol in elderly female patients. Anesth Analg. 1998;86(3):477–81.
9. Billard V, Moulla F, Bourgain JL, Megnigbeto A, Stanski DR. Hemodynamic response to induction and intubation: propofol/fentanyl interaction. J Am Soc Anesthesiol. 1994;81(6):1384–93.
10. Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev. 2006;(4).
11. Ranjbar MS, Sheybani S, Jahanbin F. Prophylactic effects of ephedrine, ondansetron and ringer on hemodynamic changes during cesarean section under spinal anesthesia—a randomized clinical trial. Ginekol Pol. 2018;89(8):454–9.
12. Özkoçak I, Altunkaya H, Özer Y, Ayoğlu H, Demırel CB, Çıçek E. Comparison of ephedrine and ketamine in prevention of injection pain and hypotension due to propofol induction. Eur J Anaesthesiol. 2005;22(1):44–8.
13. Saravanan S, Kocarev M, Wilson RC, Watkins E, Columb MO, Lyons G. Equivalent dose of ephedrine and phenylephrine in the prevention of post-spinal hypotension in Caesarean section. Br J Anaesth. 2006;96(1):95–9.
14. Hug Jr CC, McLeskey CH, Nahrwold ML, Roizen MF, Stanley TH, Thisted RA, et al. Hemodynamic effects of propofol: data from over 25,000 patients. Anesth Analg. 1993;77(4 Suppl):S21-9.
15. Monk CR, Coates DP, Prys-Roberts C, Turtle MJ, Spelina K. Haemodynamic effects of a prolonged infusion of propofol as a supplement to nitrous oxide anaesthesia: studies in association with peripheral arterial surgery. BJA Br J Anaesth. 1987;59(8):954–60.
16. Muzi M, Berens RA, Kampine JP, Ebert TJ. Venodilation contributes to propofol-mediated hypotension in humans. Anesth Analg. 1992;74(6):877–83.
17. Gauss A, Heinrich H, Wilder-Smith OHG. Echocardiographic assessment of the haemodynamic effects of propofol: a comparison with etomidate and thiopentone. Anaesthesia. 1991;46(2):99–105.
18. Masjedi M, Zand F, Kazemi AP, Hoseinipour A. Prophylactic effect of ephedrine to reduce hemodynamic changes associated with anesthesia induction with propofol and remifentanil. J Anaesthesiol Clin Pharmacol. 2014;30(2):217–21.
19. 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(1):61–5.
20. Farhan M, Hoda MQ, Ullah H. Prevention of hypotension associated with the induction dose of propofol: a randomized controlled trial comparing equipotent doses of phenylephrine and ephedrine. J Anaesthesiol Clin Pharmacol. 2015;31(4):526.
21. El-Tahan MR. Preoperative ephedrine counters hypotension with propofol anesthesia during valve surgery: a dose dependent study. Ann Card Anaesth. 2011;14(1):30.
22. Gamlin F, Freeman J, Winslow L, Berridge J, Vucevic M. The haemodynamic effects of propofol in combination with ephedrine in elderly patients (ASA groups 3 and 4). Anaesth Intensive Care. 1999;27(5):477–80.
23. Kwok FY, Venugobal S. The effect of prophylactic phenylephrine on systemic hypotension during induction of anaesthesia with propofol in patients over 55 years old. Med J Malaysia. 2016;71(4):166–70.
24. El-Beheiry H, Kim J, Milne B, Seegobin R. Prophylaxis against the systemic hypotension induced by propofol during rapid-sequence intubation. Can J Anaesth. 1995;42(10):875–8.
25. Gopalakrishna MD, Krishna HM, Shenoy UK. The effect of ephedrine on intubating conditions and haemodynamics during rapid tracheal intubation using propofol and rocuronium. Br J Anaesth. 2007;99(2):191–4.

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