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Haemodynamic Response to Induction and Intubation Using Propofol with Etomidate and Propofol with Phenylephrine – A Prospective Observational Study

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ABSTRACT

Background: Endotracheal intubation can cause significant hemodynamic fluctuations, necessitating the use of appropriate induction agents to ensure stability. Propofol is commonly used but may cause hypotension, while Etomidate offers better cardiovascular stability. Phenylephrine, a vasopressor, can counteract Propofol-induced hypotension. This study compares the hemodynamic effects of Propofol with Etomidate versus Propofol with Phenylephrine during induction and intubation.the objective of the study is to compare hemodynamic changes during induction and intubation using a combination of Propofol with Etomidate and Propofol with Phenylephrine by assessing blood pressure and heart rate variations.

Methods: A prospective, randomized study was conducted on 50 patients undergoing elective surgery under general anesthesia with endotracheal intubation. Patients were randomly assigned to two groups: Group P received Propofol (2.5 mg/kg) with Phenylephrine (100 mcg), while Group E received Propofol (1.25 mg/kg) with Etomidate (0.15 mg/kg). Hemodynamic parameters, including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR), were recorded at baseline, immediately after induction, and at 1, 2, 3, and 5 minutes post-intubation. Additionally, postoperative adverse events such as nausea, vomiting, arrhythmias, and thrombophlebitis were monitored for 6 hours following surgery.

Results: A statistically significant variation in SBP, DBP, and MAP was observed immediately after induction, with Group P demonstrating better hemodynamic stability and minimal blood pressure decline. No significant differences in HR were noted at any time point. Additionally, no statistically significant variations were observed between the two groups in hemodynamic parameters at 1, 2, 3, and 5 minutes post-intubation.

Conclusion: The combination of Propofol with Phenylephrine resulted in better hemodynamic stability than Propofol with Etomidate, particularly in maintaining blood pressure post-induction. However, both regimens were comparable in terms of heart rate stability and postoperative complications.

Keywords: *Propofol, Etomidate, Phenylephrine, Hemodynamic Stability, Endotracheal Intubation, Blood Pressure, Heart Rate*

1. INTRODUCTION

Induction of general anaesthesia is a critical phase in surgical procedures, requiring careful selection of agents to ensure haemodynamic stability. Propofol, a widely used induction agent, is favored for its rapid onset, short half-life, and smooth recovery profile. However, it is associated with significant hypotension due to myocardial depression, impaired baroreflex mechanisms, and systemic vasodilation (1-3). To mitigate these haemodynamic effects, adjuncts such as Etomidate and Phenylephrine are often employed.

Etomidate is a short-acting hypnotic agent known for its cardiovascular stability, making it a preferred choice in patients at risk of haemodynamic instability (4). It provides stable conditions for laryngoscopy and intubation but is associated with transient adrenal suppression and postoperative nausea and vomiting (5,6). On the other hand, Phenylephrine, an alpha-1 adrenergic agonist, is commonly used to counteract Propofol-induced hypotension by increasing systemic vascular resistance and maintaining blood pressure during anaesthetic induction (7,8).

Several studies have investigated the efficacy of combining Propofol with either Etomidate or Phenylephrine to reduce haemodynamic fluctuations during induction (9,10). However, there remains a lack of direct comparison between these two approaches to determine the optimal strategy for maintaining haemodynamic stability.

This prospective observational study aims to compare the haemodynamic response to induction and intubation using Propofol with Etomidate versus Propofol with Phenylephrine. The study will evaluate changes in blood pressure, heart rate, and overall stability during anaesthetic induction to determine which combination provides superior haemodynamic control.

2. MATERIAL AND METHODS

Study Design and Population: This was a prospective observational comparative study consisting of 50 cases, with 25 cases in each group. After obtaining approval from the ethical committee and informed consent from patients who fulfilled the inclusion criteria, the study was conducted in the Department of Anaesthesiology, Baby Memorial Hospital, Kozhikode, Kerala. Adult patients of the American Society of Anesthesiologists (ASA) physical status 1 and 2 who were posted for elective surgeries under general anaesthesia with endotracheal intubation at Baby Memorial Hospital, Kozhikode, were included in the study.

Sample Size:

The sample size was calculated using the formula:

$$n = \frac{Z^2(1-\alpha/2)\,[P1(1-P1)\ +\ P2}{d^2}$$

Where:

P1: Proportion in the first group

P2: Proportion in the second group

d^2: Population risk difference

1-α: Desired confidence level

From similar past studies, P1 = 17, P2 = 11, $d^2 = 0.2$, and by keeping the desired confidence level at 95%, the minimum sample size required in each group was 23. A total of 25 patients were included in each group.

Duration of Study: The study was conducted from December 2020 to July 2021.

Selection Criteria:

Patients aged 25–50 years, classified as ASA I or II, undergoing elective surgery under general anesthesia were included in the study. Eligible participants had a body weight between 50 and 80 kg. Exclusion criteria included refusal to participate, known allergy to the study drugs, history of alcohol or drug abuse, difficult airway, or pre-existing hypertension with blood pressure exceeding 140/90 mmHg. Additionally, patients requiring more than one attempt at laryngoscopy, those with intubation lasting longer than 30 seconds, or those needing additional doses for induction were excluded from the study.

Methodology: The combinations of Inj. Propofol with Inj. Etomidate and Inj. Propofol with Inj. Phenylephrine were routinely used in the hospital for better haemodynamic control during induction. A prospective observational study was conducted to compare the efficacy of these two combinations in terms of haemodynamic stability during induction and intubation.

Elective surgical patients who met the inclusion criteria and consented to participate were selected the day before surgery after obtaining informed consent and explaining the study details. A thorough pre-anaesthetic evaluation, including routine laboratory investigations such as complete haemogram, blood sugar, blood urea, serum creatinine, and electrocardiography (ECG), was carried out in all patients.

On the day of surgery, after ensuring an adequate NPO period of at least 8 hours, the patients were pre-medicated with Inj. Midazolam 1 mg and Inj. Ondansetron 4 mg intravenously in the preoperative room after securing an IV cannula in the non-dominant hand. A volume of 5 ml/kg of Ringer's Lactate was administered over 30 minutes before induction.

Patients were divided into two groups of 25 each by convenient sampling. Patients in Group E received a combination of Inj. Propofol 1.25 mg/kg body weight with Inj. Etomidate 0.15 mg/kg body weight, while patients in Group P received a combination of Inj. Propofol 2.5 mg/kg body weight with Inj. Phenylephrine 100 mcg as the induction agent. One ml of Inj. Lignocaine was added to both combinations to reduce pain during drug administration. The principal investigator observed the procedure and had no role in assigning cases to different modalities of induction.

After shifting the patient to the operating room, all standard monitors were attached, including electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse oximeter, and baseline readings were noted. General anaesthesia was administered after pre-oxygenation with 100% oxygen for 3 minutes. The patients were given Inj. Fentanyl 2 mcg/kg five minutes before induction. The patients were then induced with one of the aforementioned combinations over 30 seconds by the consultant in charge of the particular case. Loss of consciousness was confirmed by the absence of the eyelash reflex. After confirming bag and mask ventilation, Inj. Succinylcholine 1.5 mg/kg was administered intravenously as the muscle relaxant. Bag and mask ventilation was continued for one minute with 100% oxygen to maintain an SpO2 of > 95%.

Laryngoscopy was performed with a Macintosh laryngoscope, and the airway was secured with an appropriate endotracheal tube within 30 seconds. Correct placement of the endotracheal tube was confirmed with capnography and auscultation of both lungs for air entry. The endotracheal tube was then connected to the anaesthesia machine with a closed circuit. Anaesthesia was maintained with 40% O2, nitrous oxide, and sevoflurane, while Inj. Atracurium 0.5 mg/kg was administered intravenously for muscle relaxation.

Hypotension was defined as a decrease in SBP < 20% from baseline, hypertension as SBP > 20%, bradycardia as HR < 60/min, and tachycardia as HR > 20% of baseline heart rate. Patients with oxygen saturation < 90% were considered desaturating.

At the end of surgery, residual neuromuscular blockade was antagonised with Inj. Neostigmine 0.05 mg/kg IV and Inj. Glycopyrrolate 0.01 mg/kg. Extubation was performed when respiration became adequate and patients began to obey verbal commands.

Parameters Recorded:Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were continuously monitored and recorded before induction (Baseline), immediately after induction, and at 1, 2, 3, and 5 minutes after intubation. The incidence of postoperative nausea and vomiting (PONV), arrhythmias, superficial thrombophlebitis, or any other significant events during the first 6 hours of the postoperative period was noted and recorded.

Plan for Statistical Analysis:Continuous data with normal distribution was measured as mean ± standard deviation, while skewed data was represented as median. Testing for the significance of mean for independent continuous scale variables was done using an independent t-test, whereas for non-normal distribution data, the Mann-Whitney test was used. The test of association for proportions was done using the Chi-square test. The data was expressed using appropriate charts and bar diagrams.

A p-value < 0.05 was considered statistically significant. IBM SPSS Version 22 was used for statistical analysis.

Ethical Clearance:Ethical clearance for the study was obtained from the Institutional Ethical Committee of Baby Memorial Hospital, Calicut.

Informed Consent:Patients fulfilling the selection criteria were briefed about the nature of the study during pre-anaesthetic evaluation, and written informed consent was obtained from selected patients.

3. RESULT

In this prospective observational study comparing the hemodynamic response to induction and intubation, 50 patients were enrolled and equally divided into two groups using convenience sampling:

- Group P: Received Propofol 2.5 mg/kg + Phenylephrine 100 mcg
- Group E: Received Propofol 1.25 mg/kg + Etomidate 0.15 mg/kg

Both groups had comparable baseline characteristics in terms of gender distribution (P = 0.612), age (P = 0.524), and weight (P = 0.773), ensuring a homogeneous population for analysis. (Table 1)

Table 1: Comparison of Basic Demographics Between Study Groups (n=50)

Parameter		Group P (n=25)	Group E (n=25)	P-Value
Gender	**Male**	11(44%)	11(44%)	
	Female	14(56%)	14(56%)	
Age Group in years	**24-30**	8 (32%)	5 (20%)	0.52
	30-35	2 (8%)	7 (28%)	
	35-40	3 (12%)	2 (8%)	
	40-45	4 (16%)	5 (20%)	
	45-50	6 (24%)	4 (16%)	
	50-55	2 (8%)	2 (8%)	
Total		25(100%)	25 (100%)	
Weight (kg) mean± SD		63.40 ± 7.87	62.76 ± 7.15	0.773

Hemodynamic Parameters Between Study Groups (n=50)

Heart Rate (HR) Comparison

The mean heart rate (HR) at baseline was slightly higher in Group E (73.28 ± 4.56 bpm) compared to Group P (70.40 ± 8.05 bpm), though this difference was not statistically significant (p = 0.126). Following induction and intubation, HR increased in both groups, with a peak at 5 minutes post-intubation (84.60 ± 9.88 bpm in Group P vs. 88.84 ± 9.965 bpm in Group E). However, none of the time points showed a statistically significant difference between the two groups, indicating similar hemodynamic responses in terms of HR. (Table 2, Fig1)

Table 2: Comparison of Mean Heart Rate Between Study Groups

Variable	Time Point	Group P (Mean ± SD)	Group E (Mean ± SD)	P-value
Heart Rate	Baseline	70.40 ± 8.05	73.28 ± 4.56	0.126
	After Induction	68.24 ± 9.71	69.36 ± 4.18	0.599
	After Intubation 1 Min	80.96 ± 7.13	79.12 ± 3.60	0.255
	After Intubation 2 Min	80.64 ± 9.21	79.32 ± 7.47	0.581
	After Intubation 3 Min	82.08 ± 8.58	85.92 ± 13.87	0.245
	After Intubation 5 Min	84.60 ± 9.88	88.84 ± 9.965	0.138

Systolic Blood Pressure (SBP) Comparison

At baseline, SBP was comparable between the groups (121.68 ± 10.43 mmHg in Group P vs. 118.36 ± 10.84 mmHg in Group E, p = 0.276). A significant drop in SBP was observed after induction in Group E (106.32 ± 10.31 mmHg) compared to Group P (116.12 ± 13.10 mmHg), with a statistically significant difference (p = 0.005). Although SBP increased following intubation in both groups, the differences at later time points were not significant, suggesting transient intraoperative hemodynamic fluctuations rather than sustained effects. (Table 3, Fig.2)

Table 3: Comparison of Mean Systolic Blood Pressure (SBP) Between Study Groups

Variable	Time Point	Group P (Mean ± SD)	Group E (Mean ± SD)	P-value
Blood Pressure (SBP)	Baseline	121.68 ± 10.43	118.36 ± 10.84	0.276
	After Induction	116.12 ± 13.10	106.32 ± 10.31	0.005*
	After Intubation 1 Min	131.64 ± 11.88	125.56 ± 16.16	0.136
	After Intubation 2 Min	119.08 ± 15.41	123.36 ± 7.20	0.214
	After Intubation 3 Min	114.76 ± 11.56	115.80 ± 13.30	0.769
	After Intubation 5 Min	113.60 ± 11.67	109.24 ± 14.77	0.253

Significant at P < 0.05

Diastolic Blood Pressure (DBP) Comparison

Baseline DBP values did not show a significant difference between the groups (p = 0.308). However, after induction, DBP decreased more in Group E (64.56 ± 11.54 mmHg) than in Group P (71.84 ± 10.19 mmHg), reaching statistical significance (p = 0.022). While DBP values fluctuated post-intubation, no significant differences were observed at subsequent time points, implying that the initial drop was likely due to the anesthetic agents used during induction. (Table 4, Fig.3)

Table 4: Comparison of Mean Diastolic Blood Pressure (DBP) Between Study Groups

Variable	Time Point	Group P (Mean ± SD)	Group E (Mean ± SD)	P-value
Diastolic Blood Pressure (DBP)	Baseline	96.88 ± 8.96	71.32 ± 7.75	0.308
	After Induction	71.84 ± 10.19	64.56 ± 11.54	0.022*
	After Intubation 1 Min	81.20 ± 11.21	77.72 ± 13.70	0.331
	After Intubation 2 Min	77.80 ± 10.19	82.04 ± 9.28	0.130
	After Intubation 3 Min	70.36 ± 11.43	69.69 ± 10.17	0.897
	After Intubation 5 Min	69.52 ± 12.86	71.88 ± 12.86	0.485

Significant at P < 0.05

Mean Arterial Pressure (MAP) Comparison

MAP values at baseline were nearly identical between the groups (p = 0.833). Following induction, a significant reduction in MAP was observed in Group E (78.48 ± 8.77 mmHg) compared to Group P (86.60 ± 8.56 mmHg), with a p-value of 0.002. This difference was no longer statistically significant after intubation, as both groups demonstrated a recovery in MAP. This suggests that the transient drop in MAP was more pronounced in Group E but did not persist post-intubation. (Table 5, Fig.4)

Table 5: Comparison of Mean Arterial Blood Pressure (MAP) Between Study Groups

Variable	Time Point	Group P (Mean ± SD)	Group E (Mean ± SD)	P-value
Mean Arterial Blood Pressure (MAP)	Baseline	86.48 ± 9.03	87.00 ± 8.30	0.833
	After Induction	86.60 ± 8.56	78.48 ± 8.77	0.002*
	After Intubation 1 Min	98.01 ± 9.44	93.67 ± 11.18	0.144
	After Intubation 2 Min	91.56 ± 9.22	95.61 ± 6.77	0.069
	After Intubation 3 Min	85.16 ± 8.90	85.24 ± 11.07	0.978
	After Intubation 5 Min	84.21 ± 8.64	84.33 ± 12.27	0.968

Significant at P < 0.05

Fig 1: Comparative Analysis of Hemodynamic Parameters Between Study Groups Over Time

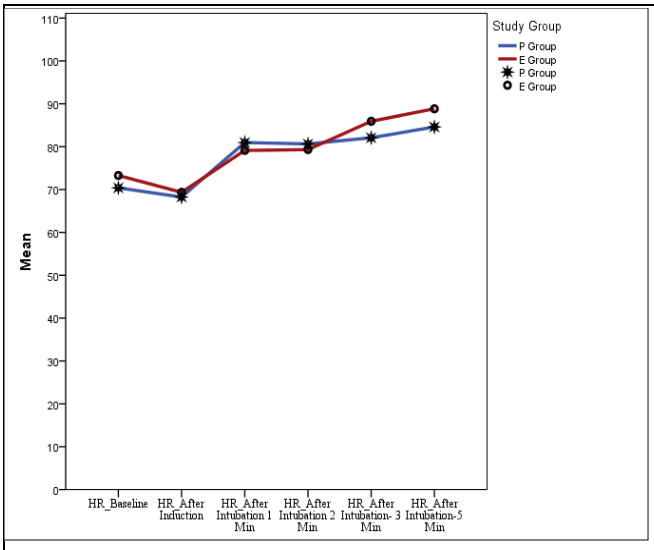

Fig:1

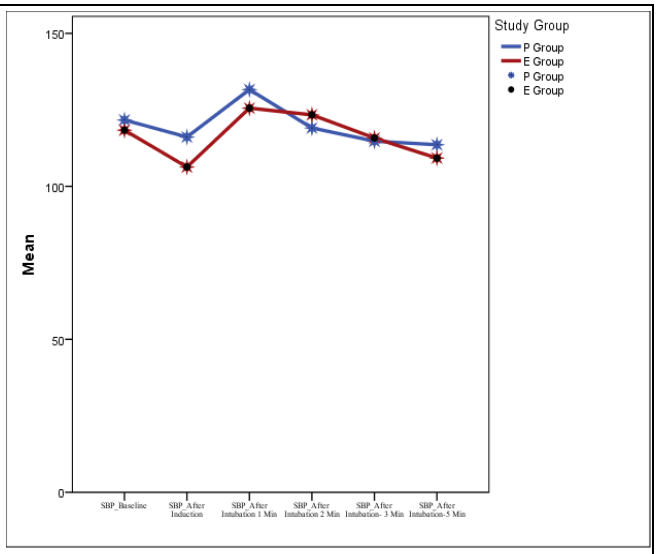

Fig:2

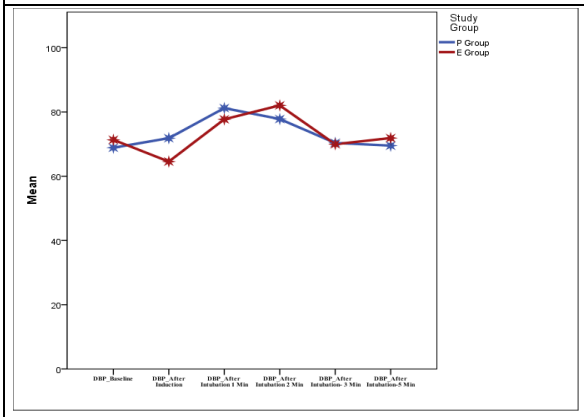

Fig:3

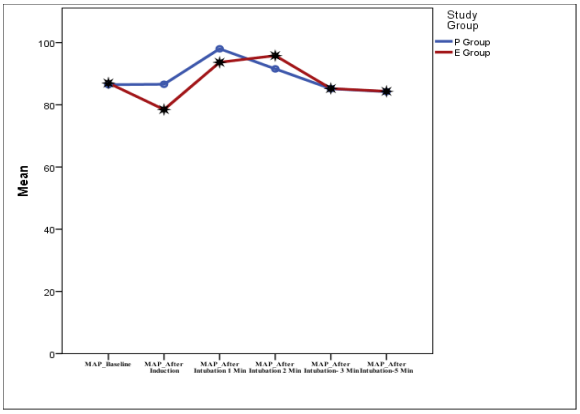

Fig:4

While both groups exhibited similar hemodynamic trends, significant differences were observed in SBP, DBP, and MAP after induction, with Group E experiencing a more pronounced decrease. However, these differences were transient, and no significant variations were seen in HR or postoperative complications. These findings suggest that while both anesthetic approaches maintain hemodynamic stability, Group E may require closer monitoring immediately after induction to manage transient hypotension.

4. POSTOPERATIVE COMPLICATIONS

No postoperative complications, including postoperative nausea and vomiting (PONV), arrhythmias, or superficial thrombophlebitis, were observed in either group within the first 6 hours after anesthesia induction. This indicates that both anesthetic techniques were well tolerated and did not lead to immediate postoperative hemodynamic instability or adverse effects.

5. DISCUSSION

The present study compared the haemodynamic response to induction and intubation using a combination of Propofol with Etomidate (Group E) and Propofol with Phenylephrine (Group P) in patients undergoing elective surgeries under general anaesthesia. The primary outcome measures included changes in HR, SBP, DBP, and MAP at baseline, immediately after induction, and at 1, 2, 3, and 5 minutes post-intubation. Secondary outcomes included the incidence of postoperative nausea and vomiting (PONV), arrhythmias, and other complications.

Our findings suggest that while both combinations effectively attenuate Propofol-induced hypotension, Group P (Propofol + Phenylephrine) demonstrated better haemodynamic stability in terms of SBP, DBP, and MAP immediately after induction. However, no significant difference in haemodynamic parameters was observed between the two groups at 1, 2, 3, and 5 minutes post-intubation.

These findings are in line with previous studies. Mahesh V et al.[11] And Meena K et al.[12] Reported that the combination of Propofol and Etomidate maintained heart rate within 20% of baseline values throughout induction and intubation. This is consistent with our study, where no significant heart rate variation was noted between Group P and Group E at any recorded time points. Similarly, Hussein M et al. Found that the use of Phenylephrine minimized fluctuations in haemodynamic parameters during induction, further supporting our observations.

However, Imran M et al. Observed a transient decrease in heart rate when Phenylephrine was combined with Propofol, a finding that contrasts with our results. This discrepancy may be due to differences in injection rate. In our study, the combination was administered over 30 seconds, whereas in Imran M et al.'s [13] study, it was given over 20 seconds, potentially leading to a more pronounced initial bradycardic response.

With regard to SBP, DBP, and MAP, a statistically significant difference was noted between Group P and Group E immediately after induction, with Group P exhibiting higher values. This suggests that Phenylephrine effectively counteracted Propofol-induced hypotension. However, at subsequent time points (1, 2, 3, and 5 minutes post-intubation), no significant intergroup differences were found, indicating that both combinations ultimately stabilized haemodynamics after the initial response to induction. Similar findings were reported in the study by Imran M et al., where Phenylephrine preserved blood pressure levels immediately after induction but showed comparable effects to Etomidate at later stages.

Clinical Implications:

The choice of induction agents in anaesthesia should be tailored to the patient's haemodynamic profile. While Etomidate offers a cardio-stable alternative to Propofol, the addition of Phenylephrine to Propofol appears to be an effective strategy to mitigate its hypotensive effects. Our findings suggest that Phenylephrine is beneficial in maintaining haemodynamic stability, particularly in the immediate post-induction phase. However, Etomidate remains a viable alternative, especially in patients with compromised cardiovascular function.

Limitations and Future Directions:

Our study was limited by its relatively small sample size (50 patients). Larger, multi-center trials with a more diverse patient population (including ASA III and IV patients) would provide stronger evidence regarding the optimal strategy for induction in high-risk surgical patients. Additionally, future studies should explore the long-term effects of these induction strategies on postoperative recovery and complications.

6. CONCLUSION

We conclude that the combination of Inj. Propofol with Inj. Phenylephrine showed better haemodynamic stability compared to Inj. Propofol with Inj. Etomidate soon after induction in terms of SBP, DBP and MAP, while both the combinations were of comparable efficacy in maintaining the haemodynamic stability after endotracheal intubation.

Conflict of interest: Nil

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