Section: Anaesthesiology

Original Research Article

EFFECT OF VARYING TIME INTERVALS BETWEEN FENTANYL AND PROPOFOL ADMINISTRATION ON PROPOFOL REQUIREMENT FOR INDUCTION OF ANAESTHESIA: RANDOMISED CONTROLLED TRIAL

A. Muthusamy[1], J. Sasikala[2], T. Rajesh Khanna[3], I. Samson Ebenezer[4]

[1]Assistant Professor, Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tamilnadu, India.
[2]Assistant Professor, Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tamilnadu, India.
[3]Assistant Professor, Department of Anaesthesiology, Government Ariyalur Medical College Hospital, Tamilnadu, India.
[4]Postgraduate, Department of Anaesthesiology, Thanjavur Medical College, Tamilnadu, India.

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Corresponding Author:
Dr. I.Samson Ebenezer,
Email: samsonebenezar@gmail.com.

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Abstract

Background: Fentanyl administration before propofol induction of anaesthesia should enable a smooth induction and reduce the induction dose of propofol and its side effects. This study investigated the impact of different times between the injection of fentanyl and propofol on the propofol needed to induce anaesthesia. **Materials and Methods:** This randomised control trial was conducted at the Department of Anaesthesiology, Thanjavur Medical College and Hospital between January 2020 and May 2021. One hundred twenty cases were randomly allocated to one of the three groups (40 in each). Group 1- Propofol administration immediately after fentanyl administration. Group 2- Propofol administration 3 minutes after fentanyl administration. Group 3- Propofol administration 5 minutes after fentanyl administration. **Results:** There was no significant difference between the gender, age, and weight of the three groups. The mean systolic, diastolic blood pressures, and mean arterial pressures were statistically significant between the groups. The mean propofol dose for the three groups was 143.39±19.48, 121.4±15.65 and 110.04±17.15 mg, with a statistically significant ($p<0.001$). The mean dose per weight for the three groups were 2.23±0.14, 1.89±0.08 and 1.69±0.09 mg/kg, with a statistically significant ($p<0.001$). The mean movement % and incidence of vocalisation % were statistically significant ($p<0.001$). The mean incidence of hypotension, which required fluid bolus and vasopressors among the three groups, was 34.3±7.12, 18.4±5.69, and 13.7±4.87 %, with a statistically significant ($p<0.001$). **Conclusion:** Fentanyl is given 5 minutes before propofol, which considerably reduces the latter's dose required and the likelihood of hypotension during induction.

INTRODUCTION

Propofol is the most frequently utilised intravenous induction agent nowadays.[1,2] The common use of propofol is that it possesses many properties of the elusive ideal anaesthetic agent, such as a quick onset of hypnosis and an equally quick waking with little excitation. However, some characteristics make this drug less ideal for utilisation as a single induction agent, like the considerable reduction in cardiac output and systemic vascular resistance with a concurrent drop in systemic blood pressure. Hypotension is a common side effect of rapid propofol infusion. Negative effects include myocardial injury, stroke, acute renal injury, and mortality can result from intraoperative hypotension.[1-3]

The idea of balanced anaesthesia has been developed to include giving an opioid before giving propofol, which significantly lowers the latter dose and enhances haemodynamic stability. The most often utilised intravenous opioid for intraoperative analgesia worldwide is fentanyl, a strong synthetic mu-receptor agonist. Fentanyl and propofol work together synergistically when given before intravenous induction, and they also lessen the haemodynamic response to laryngoscopy and endotracheal intubation.[2,4-6]

The time relationship of administration of both of these drugs has not received enough attention;

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however, the dose-effect relationships of propofol and fentanyl have both been documented.[1] We anticipate that injecting propofol after fentanyl reaches its full impact will significantly reduce the amount of propofol needed and the adverse effects that come with it. Therefore, this study was undertaken to examine the effect of varying intervals between fentanyl and propofol administration on the propofol dose required for anaesthesia induction.

MATERIALS AND METHODS

This randomised control trial was conducted at the Department of Anaesthesiology, Thanjavur Medical College and Hospital, for one and a half years (between January 2020 and May 2021) on 120 patients posted for elective surgery.

Inclusion Criteria

Patients scheduled for elective surgery with an anticipated duration of more than 1 hr under general anaesthesia, American Society of Anesthesiologists (ASA) physical status I, II patients, and ages 18-65 years were included.

Exclusion Criteria

Patients who declined participation, had allergies to propofol or fentanyl, exhibited obesity (with a body mass index exceeding 30 kg/m2), anticipated difficult airway cases, patients with respiratory, cerebrovascular, renal, and cardiovascular conditions, including hypertension, individuals receiving medications that might influence propofol requirements, patients with unstable hemodynamic parameters, those experiencing dehydration, or were scheduled for emergency surgery were excluded from the study.

A total of 120 cases were randomly assigned to one of three groups, with 40 patients in each. Group 1 received propofol immediately after fentanyl administration, Group 2 received propofol 3 minutes after fentanyl administration, and Group 3 received propofol 5 minutes after fentanyl administration.

In preparation for surgery, patients underwent an 8-hour fasting period and received intravenous premedication with metoclopramide and IV ranitidine, with an 18-gauge cannula securely in place. Standard pre-induction monitoring, encompassing electrocardiography, pulse oximetry, and blood pressure assessments, was conducted. Intravenous infusion of Ringer's lactate, administered at a rate of 10 ml/kg/hour, was initiated, and oxygen was administered via facemask. The first anesthesiologist in the operating room administered fentanyl and recorded the injection time. A second anesthesiologist, unaware of the fentanyl injection time, administered propofol per group randomization, employing a slow injection rate of 1 ml over 3 seconds while verbally communicating with the patient. Induction of anesthesia was considered complete upon the loss of verbal contact, and the required propofol dose for induction was documented. After confirming mask ventilation, atracurium (0.5 mg/kg iv) facilitated tracheal intubation. Additional propofol doses in 20 mg aliquots were given for any observed movement, vocalization, or bucking during mask ventilation initiation. The total dose, including the induction dose and additional boluses, was recorded. Heart rate, non-invasive systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were monitored every minute, from fentanyl administration to the completion of anesthesia induction. Hypotension, defined as a 20-30% decrease in blood pressure from baseline, received an intravenous bolus of 300 ml of Ringer's lactate. Hypotension unresponsive to fluid bolus received a 6 mg bolus of intravenous ephedrine. Incidences of hypotension, bradycardia, and the need for fluid boluses and vasopressors were documented. Demographic parameters, including age, sex, weight, and ASA physical status, were recorded. Primary outcome measures included the total propofol dose and propofol requirement per kg of body weight for anesthesia induction. Secondary outcome measures encompassed heart rate, SBP, DBP, MAP immediately following fentanyl injection and induction, and the incidence of movement, bucking, and vocalization.

Statistical Analysis

All the data were entered into MS Excel, and IBM SPSS version 22 was used for statistical analysis. ANOVA with post hoc tests for quantitative variables, Chi-square test for categorical variables. A p-value of < 0.05 was taken to be statistically significant for all parametric and categorical data.

RESULTS

Sex distribution was comparable between the study groups. Mean ages of groups I, II and III were 38.58 ± 11.79, 39.33 ± 10.35 and 39.83 ± 11.30. The participants' mean weights in the three groups were 64.2±7.48, 63.5±7.88 and 64.7±8.43, respectively. There was no significant difference between the gender, age, and weight of the three groups (Table 1). Mean systolic blood pressures of Group 1, 2 and 3 after 5 minutes and 7.5 minutes were 80.47±4.98, 124.70±3.52, 124.20±3.03 and 100.1±6.98, 124.45±4.54, 124.45±2.58 mmHg respectively, with a statistically significant ($p<0.001$) (Figure 1).

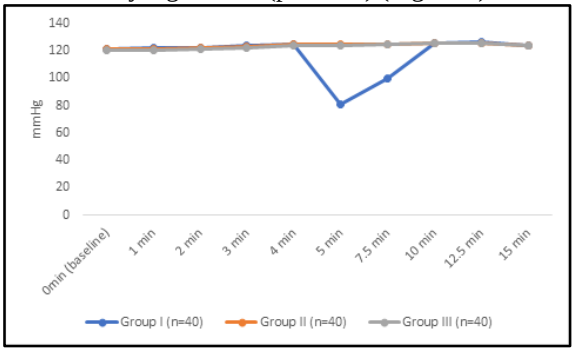

Figure 1: Systolic blood pressure between the three groups

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Mean diastolic blood pressures of Group 1, 2 and 3 after 5 minutes and 7.5 minutes were 56.50±7.93, 80.65±5.46, 80.70±6.08 and 61.25±7.75, 77.17±5.53, 77.08±5.57 mmHg respectively, with a statistically significant (p<0.001) (Figure 2).

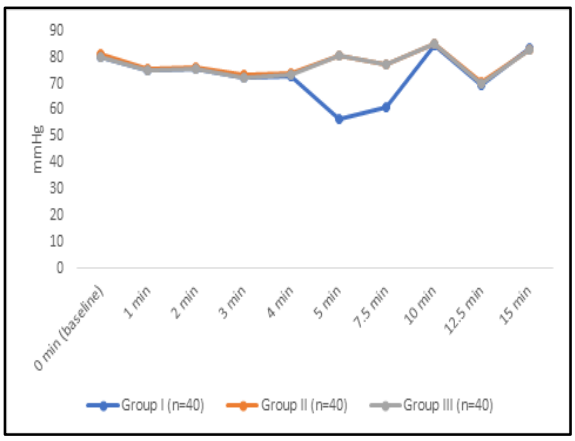

Figure 2: Diastolic blood pressure between the three groups

Mean arterial pressures of Group 1, 2, and 3 after 5 minutes were 64.49±5.76, 95.33±3.76, 95.20±4.23 and 74.20±5.77, 92.93±4.21, 92.88±3.79 mmHg respectively, with a statistically significant (p<0.001) (Figure 3).

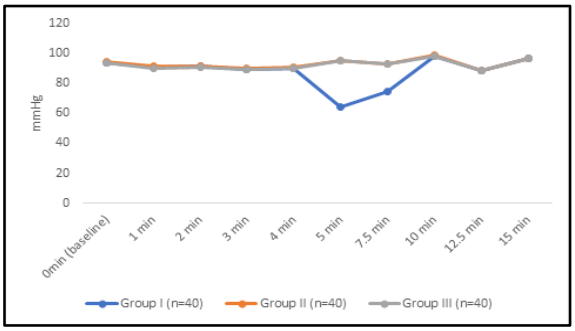

Figure 3: Mean arterial pressure between the three groups

The mean propofol dose for the three groups was 143.39±19.48, 121.4±15.65 and 110.04±17.15 mg, with a statistically significant (p<0.001). The mean dose per weight for the three groups were 2.23±0.14, 1.89±0.08 and 1.69±0.09 mg/kg, respectively, with a statistically significant (p<0.001).

The mean movement % in the three groups were 25.20±4.62, 28.60±5.57 and 11.50±3.78 %, with a statistically significant (p<0.01). The mean incidence of vocalisation % in the three groups was 19.5±6.24, 9.7±4.53, and 3.6±3.28 %, with a statistically significant (p<0.001). The mean incidence of hypotension, which required fluid bolus and vasopressors among the three groups, was 34.3±7.12, 18.4±5.69, and 13.7±4.87 %, with a statistically significant (p<0.001) (Table 3).

Table 1: Demographic data between the groups

		Group I (n=40)	Group II (n=40)	Group III (n=40)	P value
Sex	Male	28	30	29	0.882
	Female	12	10	11	
Age	< 30	11	8	10	0.881
	31 – 40	11	14	12	
	41 – 50	9	10	9	
	> 50	9	8	9	
	Mean ± SD	38.58 ± 11.79	39.33 ± 10.35	39.83 ± 11.3	
Weight	< 60	15	17	14	0.802
	61 – 70	16	15	15	
	> 70	9	8	11	
	Total	40	40	40	
	Mean ± SD	64.2 ± 7.481	63.525 ± 7.884	64.7 ± 8.434	

Table 2: Propofol dose, DPW, movement, vocalisation, hypotension, and fluid bolus among the three groups

		Group I	Group II	Group III	P value
Inj. Propofol dose [TD (mg)]	Mean ± SD	143.39 ± 19.48	121.38 ± 15.65	110.04 ± 17.15	<0.001
DPW (mg/kg)	1.6 - 1.8	0	0	40	<0.001
	1.9 - 2.0	0	40	0	
	2.1 - 2.5	40	0	0	
	Mean ± SD	2.233 ± 0.138	1.895 ± 0.0815	1.697 ± 0.092	
Movement %	Mean ± SD	25.2 ± 4.62	28.6 ± 5.57	11.5 ± 3.78	<0.01
Vocalisation %	Mean ± SD	19.5 ± 6.24	9.7 ± 4.53	3.6 ± 3.28	<0.001
Hypotension and fluid bolus	Mean ± SD	34.3 ± 7.12	18.4 ± 5.69	13.7 ± 4.87	<0.001

DISCUSSION

Induction of anaesthesia is the most significant and striking period of general anaesthesia. Propofol is the recommended intravenous anaesthetic because of its quick onset, offset, and inhibition of airway reflexes. However, hemodynamic instability and pain during injection are the anaesthesiologists' top concerns when using propofol. The cardiovascular system has a biphasic response to propofol induction. Numerous research examining propofol co-induction techniques with fentanyl were conducted to evaluate ways to avoid these negative effects.[1-5]

Propofol inductions are known to cause hypotension.[1,2] A decreased systemic vascular

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resistance and a lowering of myocardial contractility have been identified as the causes of this hypotension. Fentanyl was employed for the adjuvant induction of anaesthesia with propofol. Small dosages of fentanyl have negligible effects on the heart. However, it may intensify propofol's bradycardia and hypotensive effects when used with it to induce anaesthesia.[6-9]

In our study, patients who received fentanyl as premedication 5 minutes before induction required a significantly lower mean dose of propofol than those who received fentanyl at 1-minute and 3-minute intervals before induction. This suggests that a 5-minute premedication interval with fentanyl may be more effective in reducing the propofol dose for anaesthesia induction. A higher incidence of hypotension was observed in patients who received a higher induction dose of propofol. This finding emphasises the importance of carefully monitoring blood pressure during anaesthesia induction, especially when higher propofol doses are administered.

Administering fentanyl 5 minutes before propofol induction resulted in a marked reduction in unwanted movements, vocalisation, and bucking during the induction process. This indicates that the 5-minute premedication interval with fentanyl may contribute to smoother and more comfortable anaesthesia inductions by minimising patient discomfort and movement. The study suggests that optimising the timing of fentanyl administration, specifically with a 5-minute premedication interval, can favour propofol dose requirements, reduce the risk of hypotension, and improve patient comfort during anaesthesia induction. The ideal fentanyl dosage to lessen systemic haemodynamic fluctuations during the induction was investigated by Yukari et al. To reduce the changes in vital signs and cardiac output brought on by tracheal intubation, the researchers found that fentanyl 2 mcg/kg in individuals without hypertension and 4 mcg/kg in those with hypertension was preferable.[10]

Fentanyl's peak plasma concentration and onset time depend on the dosage and method of administration, respectively. Fentanyl may begin to relieve pain as fast as one minute after intravenous injection.[11,12] With only two time points to compare, it may be difficult to accurately understand the haemodynamic fluctuation pattern, particularly the interval between the drop before intubation and the rise following intubation. The haemodynamic variations may be harmful to patients.[11-13]

CONCLUSION

Fentanyl was given 5 minutes before propofol, considerably reducing the latter's dose requirement and the likelihood of hypotension, undesired movements, vocalisation, and bucking during induction.

Limitations

Due to logistical limitations, we were unable to measure plasma concentrations of fentanyl and propofol, which could have provided additional insights into the results. The assessment of anesthesia induction endpoints relied solely on clinical evaluation, and electroencephalography-based monitors were not incorporated. The study excluded hemodynamically unstable patients, for whom the findings might be particularly relevant, and did not explore varying fentanyl dosages.

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