

COMPARISON OF INHALATIONAL INDUCTION USING SEVOFLURANE WITH INTRAVENOUS INDUCTION USING PROPOFOL IN ADULTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING SURGERY IN TERMS OF HEMODYNAMIC STABILITY - A PROSPECTIVE RANDOMIZED, COMPARATIVE STUDY

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Abstract

Background: Anaesthetic induction techniques in patients with coronary artery disease undergoing coronary artery bypass grafting surgery are based on considerations for hemodynamic stability, optimising myocardial oxygen supply demand and minimizing intubation stress response. This study compares the hemodynamic stability of induction between intravenous agent propofol and inhalational agent sevoflurane in patients with coronary artery disease posted for coronary artery bypass grafting surgery (CABG). **Materials and Methods:** This prospective randomized comparative study was conducted at Apollo Hospital, Chennai, from Nov 2017 to Nov 2018. All the patients were informed and consented before entry into the study. All 60 patients in the study were randomized equally in group A sevoflurane and group B propofol. The patient's detailed history, general physical and systemic examination and all necessary investigations were examined thoroughly for anaesthesia. **Result:** The study found no significant difference in age, gender, and BMI between groups, with no significant difference in hypertension, diabetes, or ejection fraction. Propofol had a greater fall in SBP than sevoflurane, with a statistically significant difference at T2 and T3. Propofol had a statistically significant fall in DBP at time points T2 and T3. MAP decreased in both groups, with sevoflurane having statistically more MAP values at T2 and T3. Phenylephrine requirement for hypotension was significantly less in sevoflurane group. Time taken for induction was also shorter in the sevoflurane group than the propofol group. Propofol and sevoflurane induction techniques were satisfactory for 26.7% of patients, but no adverse effects were observed. **Conclusion:** Inhalational induction with sevoflurane is a better alternative for IV induction with propofol due to its quicker and better hemodynamic stability.

INTRODUCTION

General anaesthesia is a drug-induced loss of consciousness during which an individual is not arousable, even by painful stimulation.^[1] Intravenous or inhalational anaesthetic agents are used for inducing general anaesthesia. Induction of anaesthesia in patients with coronary artery disease is a critical part of cardiac anaesthesia practice because the impaired circulatory system in these patients is less tolerant of the haemodynamic disturbances caused by the anaesthetic agents.^[2] Haemodynamic instability and arrhythmias are life-

threatening complications following induction. Anaesthetic induction techniques in patients with coronary artery disease undergoing coronary artery bypass grafting surgery are based on considerations for hemodynamic stability, optimising myocardial oxygen supply-demand and minimizing intubation stress response.^[2-4]

Hence the primary goal of induction in patients with CAD is avoiding hypotension caused by vasodilatation and cardiac depression due to anaesthetic drugs and attenuation of sympathetic responses to noxious stimuli, such as laryngoscopy, intubation to avoid myocardial oxygen supply and

demand mismatch. Intravenous anesthetic agents are used widely for inducing general anaesthesia in patients with coronary artery disease. Propofol and etomidate are considered superior to other intravenous anaesthetic agents in these patients.^[2,4] Etomidate is perceived as one of the hemodynamic stabilities preserving agents during induction of anaesthesia. But it inhibits 11 beta-hydroxylase and causes adrenocortical dysfunction.^[2,5] The advantages of propofol are suppression of airway reflexes, achievement of adequate anaesthesia and lack of lightening of the anaesthetic plane during airway intervention.^[6] However, it has major adverse effects like cardiovascular depression, myoclonus & pain on injection.^[7]

Halothane and sevoflurane are widely used for inhalational induction of general anaesthesia, with sevoflurane being the most suitable agent due to its low blood-gas partition coefficient.^[6] When used in high concentrations for rapid inhalational induction of anaesthesia in adults, it is well tolerated by most cardiac patients.^[8] The benefits of this technique include reduced incidence of hypotension and lower costs compared to some intravenous anaesthetics agents.^[9] Over the last few years, there has been growing interest in using inhalational induction in adults. Studies have shown that inhalational induction with sevoflurane offered a better haemodynamic profile. Hence considered a better alternative to intravenous agents in adults.^[10-13] In cardiac anaesthesia, practising attention towards protecting myocardial function and avoiding myocardial ischaemia is vital. Recent studies prove that volatile anaesthetics exert protection against myocardial ischemia and reperfusion injury in coronary artery disease patients, as they have been shown to cause ischemic preconditioning.^[14,15]

Ischemic preconditioning is the innate ability of the myocardium to protect itself from ischemic events. This protection occurs when the myocardium is exposed to a brief ischemic period before a more extreme ischemic event. Ischemic preconditioning induces a series of molecular pathways that releases adenosine, which induces the mitochondrial KATP channel. Volatile anaesthetics mimic this phase of ischemic preconditioning by inducing mitochondrial KATP channels.^[16] Therefore, volatile induction and maintenance of anaesthesia (VIMA) is gaining popularity versus TIVA.^[17] Hence, the study aims to compare the hemodynamic stability on induction between intravenous agent propofol and inhalational agent sevoflurane in patients with coronary artery disease posted for coronary artery bypass grafting surgery (CABG).

MATERIALS AND METHODS

This prospective randomized comparative study was conducted at the Department of Anaesthesiology Apollo Hospital, Grems Lane, Off Grems Road, Chennai, from Nov 2017 to Nov 2018. After

approval by the ethical committee of Apollo Hospitals, Chennai, all the patients were informed and consented before entry into the study. Patients were admitted for coronary artery bypass grafting after the pre-anaesthetic assessment according to the inclusion and exclusion criteria.

Inclusion Criteria

Age group 30 to 70 years and coronary artery disease with Ejection fraction > 45% posted for CABG were included.

Exclusion Criteria

Allergy to propofol/sevoflurane, ejection fraction <45%, left main coronary artery disease, valvular heart disease, recent myocardial infarctions (<6 weeks), anticipated difficult intubation, emergency CABG, and chronic respiratory diseases were excluded.

Methodology

Preoperative Assessment

All the patients were examined prior to study. Patient's detailed history, general physical and systemic examination and all necessary investigations were examined thoroughly for conduct of anaesthesia. To avoid bias, during the preoperative visit all the patients were educated to perform vital capacity breaths i.e., the patient was asked to first exhale fully and then inhale fully and hold their breath as long as possible.

Informed Consent Form

Those patients who had satisfied the inclusion criteria were explained about the anaesthesia procedure in their vernacular language. A written consent was obtained in each case.

Conduct of Anaesthesia

All preoperative cardiac medications were continued till the morning of the surgery. All the patients received oral diazepam 10 mg on the night before surgery and morphine of 0.2 mg/Kg with promethazine 0.5 mg/kg were injected intramuscularly one hour before anaesthesia induction as per institutional protocol.

After confirming the identity of patient, consent forms and fasting status were checked. Routine preoperative review examination was carried out. As per the computer generated randomization table Group A received sevoflurane and Group B received propofol respectively.

Once the patient was received inside operating room - standard monitoring was applied to all patients: HR, ECG, NIBP and SpO₂. 16 G peripheral venous cannula, 18 G radial artery cannula were placed under local anaesthesia using 2% lignocaine. Normal saline was connected to venous line. BIS monitoring was attached to forehead. All patients received 4microgram/kg fentanyl. All patients were preoxygenated with 100% oxygen for three minutes. Base line parameters SBP, DBP, MAP and HR were measured five minutes after fentanyl administration. Patients were then induced with either Propofol or Sevoflurane.^[4]

- Patients in Group A (sevoflurane) were preoxygenated with 100% oxygen for 3 min

- using an alternative source of oxygen. We used B type cylinder with Bain circuit attached to it.
- During this time the machine circuit was primed with sevoflurane 8% (10,11) with O₂/N₂O 50%:50% at a flow rate of 6 lit/min with the y piece occluded until the inspired limb sevoflurane concentration measured >6% in the gas monitor(39,47).
 - With the primed circuit patient was asked to take vital capacity breaths i.e., the patient was asked to first exhale fully and then inhale fully and hold their breath as long as possible. The time of start of mask placement with sevoflurane 8% was considered as 'starting point of induction'.
 - Loss of consciousness was assessed every 3 to 5 seconds by absence of response to verbal commands and loss of eyelash reflex which was defined as 'induction end point'(21,39) and confirmed with BIS value <60. Time taken for Induction was noted using stop clock.
 - Once the patient was induced, sevoflurane was stepped down and maintained between 1 to 2 MAC titrated to maintain BIS between 40 to 60(21).
 - Patients in Group B (propofol) received Propofol 1% about 1.5mg/kg body weight which was injected manually and slowly over 1 min until loss of consciousness was achieved(10,56).
 - Time of start of injection of propofol was the starting point of induction. Loss of consciousness was assessed every 3 to 5 seconds by absence of response to verbal commands and absence of eyelash reflex which was defined as 'induction end point'(21) and confirmed with BIS value <60. Time taken for Induction was noted using stop clock.
 - Anaesthesia was maintained with 1% Propofol infusion at a rate of 50 to 100mcg/kg/min(56) in a 50ml syringe using infusion pump with N₂O:O₂ at 1:1 ratio. Infusion dose was titrated to maintain BIS between 40 to 60.
 - In both the groups following loss of consciousness, the patients were manually ventilated and a bolus dose of rocuronium a non depolarising muscle relaxant 0.6mg/kg was given in both the groups and patients were ventilated with O₂/N₂O (50%:50%) and then the

- patients were intubated after three minutes with appropriately sized endotracheal tube.
- After intubation-controlled ventilation was established with N₂O:O₂ 50:50 via closed circuit at 10 to 12 breaths/min and a tidal volume of 8 to 10 ml/kg aiming at normocapnia in both the groups.

SBP, DBP, MAP, HR, and SpO₂ were monitored at the following time points: T₀ to T₅. Induction complications like pain on injection, myoclonus, airway irritation, cough, bronchospasm, and laryngospasm were all monitored. Patient satisfaction was assessed with the help of the questionnaire provided in the study proforma. All continuous variables which were normally distributed were represented by mean ± SD. Categorical variables were described by percentage (%). The independent sample 'T' test compared normally distributed continuous variables. A comparison of categorical variables was made by either the Chi-square test or Fisher's exact test. Data entry was done in MS Excel Spread Sheet. Data analysis was carried out by SPSS Version 25.0, and all p-values <0.05 were considered statistically significant.

RESULTS

The study involved 60 patients posted for CABG, 30 in each group. Group A sevoflurane and group B propofol.

In the sevoflurane group, 87% were males, and 13% were female. In the propofol group, 83% were males, and 17% were female patients. There is no statistical significance in age, gender, and BMI between groups.

In the sevoflurane group, 80% of patients were hypertensive, and 67% of the propofol group were hypertensive, and there is no significant difference (p=0.243).

In the sevoflurane group, 63% of patients had diabetes, and 60% of the propofol group had diabetes, and there is no significant difference (p=0.791). There is no significance in ejection fraction between groups.

Table 1: Demographic data of the study

		Sevoflurane	Propofol	P-value
Age		57.03 ± 7.609	56.20 ± 7.444	0.67
BMI		24.39 ± 2.56	23.86 ± 2.73	0.445
Gender	Male	26 (87%)	25 (83%)	0.718
	Female	4 (13%)	5 (17%)	
Hypertension	Present	24 (80%)	20 (67%)	0.243
	Absent	6 (20%)	10 (33%)	
Diabetes mellitus	Present	19 (63%)	18 (60%)	0.791
	Absent	11 (37%)	12 (40%)	
Ejection fraction		53.27 ± 3.22	52.97 ± 2.77	0.700
Number of coronary vessels	2	6 (20%)	4 (13%)	>0.05
	3	24 (80%)	26 (87%)	
Beta-blocker	Taken	24 (80%)	21 (70%)	>0.05
	Not taken	6 (20.0%)	9 (30%)	
ACE inhibitors		23 (77%)	20 (67%)	>0.05

	Not taken	7 (23%)	10 (33%)	
Calcium channel blockers	Taken	23 (77%)	20 (67%)	>0.05
	Not taken	7 (23%)	10 (33%)	

Table 2: Phenylephrine and time took for induction between groups

		Sevoflurane	Propofol	P-value
Phenylephrine	Required	3 (10.0%)	10 (33.3%)	0.028
	Not required	27 (90.0%)	20 (66.7%)	
Time taken for induction (Sec)		47.33 ± 4.56	64.70 ± 9.09	<0.0001

Patients with triple vessel disease in the sevoflurane group were 80% and 87% in the propofol group, and there is no significant difference. 80% of patients took beta blockers in the sevoflurane group and 70% in the propofol group, and there is no significant difference.

77% of patients took ACE inhibitors in the sevoflurane group and 67% in the propofol group, and there is no significant difference. 77% of patients took calcium channel blockers in the sevoflurane group and 67% in the propofol group; there is no significant difference [Table 1].

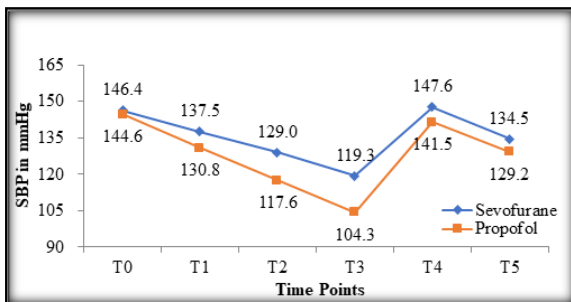


Figure 1: Systolic Blood Pressure (SBP) at different time points between groups

From time point T1, there was a fall in systolic blood pressure in both groups. The fall in SBP was more in the propofol group than the sevoflurane group. Their difference at time points T2 and T3 were statistically significant. At T2 and T3, p-value <0.05, and at time point T4, there was an increase in SBP in both groups [Figure 1].

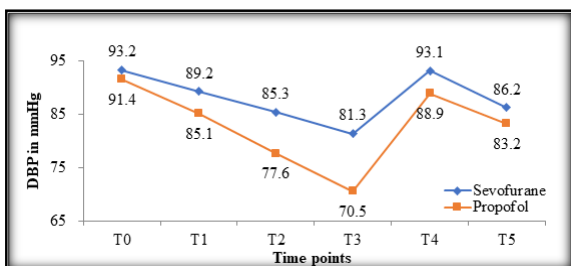


Figure 2: Diastolic Blood Pressure (DBP) at different time points between groups

The fall in DBP was more in the propofol than the sevoflurane group. At time points T2 and T3, there was a statistically significant fall in DBP in the propofol group p-value <0.05. At time point T4 and T5, DBP increased in both groups, but no statistically significant difference was observed between the groups [Figure 2].

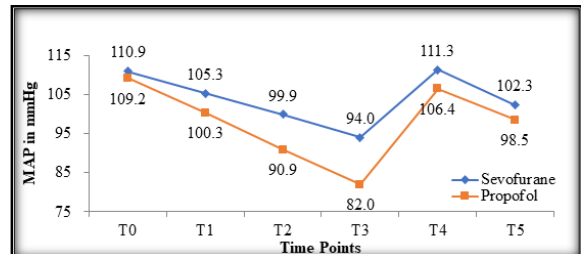


Figure 3: Mean Arterial Pressure (MAP) at different time points between groups

MAP shows a decreasing trend from baseline in both groups. MAP values at T2 and T3 were statistically more in the sevoflurane group than in propofol p value <0.05. At T4, MAP increases in both groups and no statistically significant difference exists between the groups at time points T4 and T5 [Figure 3].

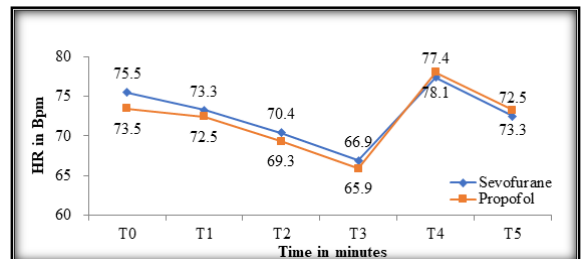


Figure 4: Heart rate at different time points between groups

Heart rate decreased following induction and increased following intubation in both groups. No statistically significant difference exists between the two groups at various time points [Figure 4].

Oxygen saturation and BIS values between the two groups at various intervals show no statistical difference.

Totally 22% of the patients required phenylephrine for hypotension, of which 17% belonged to propofol, and 5% belonged to the sevoflurane group. There is a statistically significant in phenylephrine between groups (p=0.028). Time taken for induction was 47.33 ± 4.6 seconds in the sevoflurane group and 64.7 ± 9.09 seconds in the propofol group, and there is a significant difference (p<0.0001) [Table 2].

All the patients were explained about the technique of induction before the procedure. 26.7% of patients complained of pain during propofol injection, but no one could remember the post-op pain period. Both techniques proved to be satisfactory among the

patients. Our study did not observe other adverse effects like myoclonus with propofol, bronchospasm, laryngospasm, or cough with sevoflurane.

DISCUSSION

During induction of anaesthesia and intubation, hemodynamic changes are very important; especially in patients with CAD. Patients undergoing CABG are more susceptible to hemodynamic lability during induction. Sudden hypotension, arrhythmias and cardio vascular collapse are threatening complications following induction. Also laryngoscopy and endotracheal intubation is a noxious stimulus, which can cause tachycardia, and hypertension which can be deleterious in patients with poor cardiovascular reserve.

These hemodynamic changes may alter the delicate balance between myocardial oxygen demand and supply and consequently precipitate myocardial ischemia in patients with CAD. Hence an induction agent that would cause less incidence of hypotension and also avoiding hypertension and tachycardia post intubation would be preferred in these patients.

Intravenous or inhalational anaesthetics can be used for inducing general anaesthesia. At present intravenous anaesthetic agents are used widely for inducing general anaesthesia in adults. In cardiac anaesthesia propofol and etomidate are commonly used agents.^[4] However propofol has several adverse effects like hypotension, pain on injection, apnoea and rarely neuro-excitatory phenomena like myoclonus.

Over the last few years there is growing interest in using inhalation induction in adults. There have been studies in which inhalation induction with sevoflurane offered a better hemodynamic profile and considered as a better alternative to intravenous agents in adults.^[10-14] In elderly patients sevoflurane induction showed better left ventricular mechanical performance than propofol.^[13] Also sevoflurane induction had caused lesser changes in stroke volume when compared with propofol. Sevoflurane also has properties of myocardial protection through ischemic preconditioning.^[18,19]

Hence in our study we wanted to compare the hemodynamics on induction between sevoflurane and propofol in patients with coronary artery disease who belong to ASA class III. In our study we had included 60 patients as per the inclusion criteria posted for CABG under general anaesthesia requiring endotracheal tube. Among the sixty patients 30 patients received propofol for IV induction and the rest received sevoflurane for inhalational induction.

The pharmacokinetics of propofol may be altered by various factors (gender, weight, pre-existing disease, and concomitant medication like opiates and

benzodiazepines). Concurrent use of fentanyl 4mcg/kg could have influenced hemodynamics, but small doses have shown only minimal cardiovascular changes.^[4] In this study, propofol/sevoflurane were administered five minutes after the patients received fentanyl (4 mcg/kg) and the baseline parameters were taken 5 min after fentanyl administration.

Uzun S et al,^[18] reported that when propofol was injected at a slower rate, the fall in MAP was less, and the amount of drug needed was less. Djaiani G et al,^[10] concluded that the method provided a hemodynamic profile comparable to etomidate and faster induction in patients with coronary artery disease. Vidal M et al,^[8] compared sevoflurane VCRII with tidal volume breathing technique in CABG patients and found that both methods produced the same hemodynamic stability. Lin TC et al. confirmed that VCRII with a high inspiratory concentration of sevoflurane for induction is a safe and practical method. Tidal volume breathing technique or vital capacity induction with a lesser sevoflurane concentration didn't suppress intubation-induced hemodynamic responses.^[19]

Robba C et al,^[11] found that the Propofol group had a significant fall in MAP >20% from the baseline at time point T2 (Sedation steady state) than the 8% sevoflurane group. They concluded that even when injected slowly, propofol induction can cause a significant drop in MAP, and hence it matches our study. Bharti N et al,^[12] found that induction with propofol resulted in a significant decrease in MAP and hypertension following intubation. At the same time, intraoperative haemodynamics were more stable with sevoflurane, which is consistent with the current study's findings. They also observed a decrease in post-induction heart rate in both groups, which matches the results of the present study.

Rawal P et al,^[13] observed that the sevoflurane group had more fall in heart rate than propofol at 1-, 3- and 5-min post-induction ($p < 0.05$). Their study was done on 108 patients, and we might need a larger sample size to observe the difference. In their study, Tan et al,^[20] also found that the heart rate response was the same between sevoflurane and propofol induction, wherein they had performed fiberoptic intubation.

Potocnik et al,^[21] in their study, observed that after induction, the patients anaesthetized with propofol required substantially more ephedrine to maintain the hemodynamic parameters within the normal range. This means that the patients in the propofol group were hemodynamically less stable than those in the sevoflurane group. Thus, sevoflurane proved to be more hemodynamically stable when compared to propofol, as concluded in the studies done by Robba C et al,^[11] and Bharti N et al.^[12]

Lin TC et al,^[19] showed that the speed of induction with sevoflurane was faster with fentanyl pretreatment and was about 48.3 ± 17.9 seconds compared with our study. Prabhat Rawal et al,^[13] showed that 8% sevoflurane induction was faster,

45.31±10.97, compared to propofol, which was 55.91±15.80, and this compares with our study. El-Radaide et al,^[22] also showed that 8% sevoflurane induction was faster than propofol 51.6±4.4 sec vs 59.7±4.9.

Chavan et al,^[23] also observed that propofol, when injected at a rate of 20mg every 5 sec had a faster induction than 8% sevoflurane. The propofol injection rate was faster in both of these studies than ours. No difference in Oxygen saturation was observed between the two groups. None of the patients presented with signs of airway irritation like cough bronchospasm, laryngospasm and myoclonus in our study. Nigro Neto et al, in their case series study on 56 patients undergoing CABG, proved that all the patients accepted sevoflurane induction.^[9] Our study did not observe other adverse effects like myoclonus with propofol, bronchospasm, laryngospasm, or cough with sevoflurane.

Limitations

The sample size of our study was 60, and studies carried out with a larger sample size will yield more reliable results. We didn't include CAD with Left main coronary artery involvement; hence, the results cannot be applied to Left main vessel disease. We didn't have CAD with associated valvular heart disease, and several female patients in our study were less. Ejection fraction less than 45% was excluded from our study; hence, the results cannot be applied to patients with poor Ejection fraction. We could not measure pulmonary artery pressure as the pulmonary artery catheter would be inserted after induction in our institution. Our study couldn't use continuous cardiac output monitoring due to cost constraints.

CONCLUSION

Inhalational induction with sevoflurane thus proved superior to conventional IV induction with propofol, as induction was quicker, with better hemodynamic stability. We hence recommend inhalational induction with sevoflurane as a better alternative modality for IV induction with propofol, as suggested by the study's outcome.

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