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RESEARCH ARTICLE

Comparison of intravenous induction with propofol versus inhalation induction with sevoflurane: A prospective randomized controlled study

Divya John[1], Rachel Cherian Koshy[2], Prathibha V K[3], Gopakumar G[4], Ranju Jayaprakash[5]

[1]Department of Anaesthesiology, Kerala Institute of Medical Sciences, Thiruvananthapuram, Kerala, India, [2]Department of Anaesthesiology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India, [3]Department of Pharmacology, Amala Institute of Medical Sciences, Thrissur, Kerala, India, [4]Department of Anaesthesiology, Azeezia Institute of Medical Sciences, Kollam, Kerala, India, [5]Department of Anaesthesiology, Royal Dental College, Chalissery, Palakkad, Kerala, India

Correspondence to: Gopakumar G, E-mail: drgopakumarg@yahoo.in

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ABSTRACT

Background: Propofol is widely used for the induction of anesthesia. Sevoflurane, a popular inhalational induction agent for pediatric patients, may also be used in adults with needle phobias. **Aims and Objectives:** This study was done to compare the two popular induction agents, namely, propofol and sevoflurane. The speed of achieving the conditions ideal for intubation, in the background of the synergistic action of sevoflurane with vecuronium, the non-depolarizing muscle relaxant was also studied. **Materials and Methods:** In this prospective randomized controlled study, female patients between 20 and 65 years of age belonging to the American Society of Anaesthesiologists Grade I and II who underwent elective surgeries for breast cancer under general anesthesia were allocated randomly into two groups. Group 1 patients received propofol as the induction agent and in Group 2 sevoflurane was used as the induction agent. Induction with vital capacity breath technique using 8% sevoflurane was compared with standard induction with propofol. **Results:** It was found that propofol caused a greater drop in blood pressure (BP), although the time for induction was marginally lower (insignificant) with propofol. Sevoflurane potentiated the effect of vecuronium. One case in the sevoflurane group developed laryngospasm and hence was excluded from the study. Three patients in the propofol group had pain on injection. One patient from each group had abnormal transient groaning sound on induction and two patients from sevoflurane group had coughing on induction. **Conclusion:** Propofol and sevoflurane are equally fast in inducing anesthesia. Sevoflurane potentiates the action of non-depolarizing muscle relaxants when compared to propofol during induction and may be considered as a better option for patients in whom fall in BP is unlikely to be tolerated even for a short period.

KEY WORDS: Sevoflurane; Propofol; Induction

INTRODUCTION

The advances in pharmacology give a wide choice to the anesthesiologists in selecting the mode of induction of anesthesia. Intravenous induction, with the advantages of predictability and non-dependence on patient cooperation, continues to be popular among anesthesiologists. Since ages, inhalational induction was popular in pediatric practice, to ensure that the child does not experience the discomfort of awake intravenous access and halothane became the agent of choice. With the introduction of sevoflurane, anesthesiologists had the option of another nonirritant gas, with an added advantage of rapid onset of action and an equally fast drug elimination and emergence. At present, sevoflurane has a place in adult anesthetic induction as well, especially in those with needle phobias.

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This study compares the two popular induction agents, namely, propofol and sevoflurane. The speed of achieving the conditions ideal for intubation, in the background of the synergistic action of sevoflurane with vecuronium, the non-depolarizing muscle relaxant is also studied.

MATERIALS AND METHODS

This is a prospective randomized controlled study conducted in the Department of Anesthesiology at a tertiary care teaching hospital in South Kerala after getting approval from the Institutional Review Board and clearance from the Hospital Ethics Committee. Population under study included American Society of Anaesthesiologists (ASA) I and II female patients between 20 and 65 years of age who underwent elective surgeries for breast cancer under general anesthesia over a study period of 1 year. Patients with a history of coronary artery disease, cerebrovascular accidents, epilepsy, malignant hyperthermia, ASA III or IV, anticipated difficult airway, allergy to propofol, hepatic disease, renal disease, uncontrolled hypertension, and body mass index >30 kg/m^2 were excluded from the study.

Patients were randomly allocated using the sealed envelope technique into two groups. To get statistically significant results, a sample size of forty was allotted to in each group. Group 1 patients received propofol as the induction agent and in Group 2 sevoflurane was used as the induction agent. Primary data were collected with the help of a pre-structured and pretested proforma by the investigator. Relevant investigations were done for all patients. Cardiology evaluation was done and clearance obtained for all patients treated with anthracycline-based chemotherapeutic agents. Informed consent was obtained from all patients. All patients included in the study were kept fasting for 6 h before surgery and premedicated with oral ranitidine 150 mg at night and oral metoclopramide 10 mg and ranitidine 150 mg 2 h before the surgery.

In the operating room, pre-induction monitors included electrocardiography, non-invasive blood pressure (BP), and pulse oximeter. Baseline recordings of pulse rate, BP, and SpO_2 were noted. Intravenous midazolam 1 mg and intravenous fentanyl 1 microgram/kg were given to all patients 2 min before induction of anesthesia. All patients were pre-oxygenated with 100% oxygen using a Bain's circuit for 3 min and the concerned induction agent was introduced. Loss of verbal contact and loss of eyelash reflex were taken as endpoints of induction. At this point, 50% oxygen in N_2O was given. Once the patient was induced, vecuronium was given at a dose of 0.1 mg/kg intravenously before tracheal intubation. The train of four ratios was monitored using peripheral nerve stimulator and trachea was intubated when train of four ratios reached 0.

In the propofol group, after pre-oxygenation, 2% preservative-free lignocaine 1.5 mg/kg was given intravenously. This was followed by 2 mg/kg of 1% propofol. Once verbal contact and eyelash reflex were lost, 50% oxygen in N_2O was given. In the sevoflurane group, after pre-oxygenation, 2% preservative-free lignocaine 1.5 mg/kg was given intravenously, and sevoflurane 8% was introduced into the circuit, and the patients were asked to take deep breaths. Once verbal contact and eyelash reflex were lost, sevoflurane concentration was reduced to 2% and 50% oxygen in N_2O given. After induction, 0.1 mg/kg vecuronium was given intravenously. If the depth of anesthesia was considered inadequate as indicated by movement, swallowing, tearing, sweating, tachycardia, or mean arterial pressure increases more than 15% of that obtained pre-induction, anesthesia was deepened with the respective induction agent.

Pulse rate, BP, and oxygen saturation were monitored preinduction and every 2 min after the start of induction. The train of four ratios was monitored every 12 s after giving vecuronium. The time intervals recorded included induction time (start of anesthetic until loss of eyelash reflex and verbal response) and time to endotracheal intubation (intravenous vecuronium to train of four ratios zero). Successful induction of anesthesia was defined as the absence of any side effects like pain on injection, coughing, excitement, laryngospasm, excessive secretions, or any other untoward event. Apnea was not considered as a complication in our study.

Hemodynamic instability was defined as a change in BP – systolic, diastolic, or mean ±20% of the baseline value and change in pulse rate ±20% of the baseline value. Rapid infusion of intravenous fluids was the strategy for the management of BP fall. Continued fall in BP, if any, even after intubation was managed with intravenous ephedrine 6 mg boluses in addition to the rapid infusion of intravenous fluids.

The data collected were entered into a master chart. The data were analyzed statistically using SPSS. The hypothesis formulated was tested statistically using statistical tests like Student's t-test in case of quantitative data. To find out the association between variables, the Chi-square test was used.

RESULTS

The sample taken for the study was comparable in terms of age. One patient in the sevoflurane group went out of the study as she developed laryngospasm during induction. Hence, the sample size in the sevoflurane group became 39 for the rest of the study. However, the incident is included in the list of complications. The oxygen saturation monitoring did not show any statistically significant difference between the two groups at any time.

Speed of Induction

The mean induction time in the sevoflurane group was 65.21 s and that in propofol group was 59.42 s. There was no statistically significant difference in the mean induction time between the two groups ($P = 0.212$) [Table 1].

Effect on Muscle Relaxants

The mean time taken for train of four to become zero after giving vecuronium was compared between the sevoflurane group and the propofol group. The time taken by the sevoflurane group was shorter (211.87 s) than that of the propofol group (241.80 s). This variation was statistically significant ($P = 0.003$) [Table 1].

Hemodynamic Stability

Heart rate

At 2 min, 1 patient and at 4 min, 4 patients of 39 in the sevoflurane group showed a pulse rate variation from baseline of more than 20% whereas a similar degree of change was seen in 4 patients at 2 min and 9 patients at 4 min out of 40 in the propofol group. This difference does not reach clinical significance, $P = 0.175$ and 0.142, respectively [Table 2].

BP

At 2 min and 4 min, propofol caused a significantly more BP fall, amounting to hemodynamic instability. At 2 min, 6 of 39 patients in the sevoflurane group showed more than 20% change in systolic BP, whereas 18 patients in the propofol group had a similar change. This systolic BP fluctuation was always a fall from baseline, Chi-square=8.189, $P < 0.01$. At 4 min, a similar change was seen in 29 patients in the sevoflurane group and 39 patients in the propofol group, Chi-square=15.811, $P = 0.000$ [Table 3].

Two patients in the sevoflurane group showed more than 20% change in diastolic BP at 2 min, whereas 23 patients in the propofol group had a similar change. This diastolic BP fluctuation was always a fall from baseline. Statistical

Table 1: Mean induction time and mean time to TOF "0" in sevoflurane and propofol groups (in seconds)

Parameter	Group	Number of patients	Mean	Standard deviation	*t*-value	*P* value
Induction time	Sevoflurane	39	65.21	27.422	1.259	0.212
	Propofol	40	59.42	9.451		
Time to TOF "0"	Sevoflurane	39	211.87	36.393	−3.028	0.003
	Propofol	40	241.80	50.188		

TOF: Train of four

Table 2: Variation in pulse rate at 2 min and 4 min following induction

Group	Variation in pulse rate at 2 min		Chi-square		Variation in pulse rate at 4 min		Chi-square
	Change <20%	Change ≥20%			Change <20%	Change ≥20%	
Sevoflurane (*n*=39)							
Count	38	1	1.842 (*P*=0.175)	Count	35	4	2.153 (*P*=0.142)
Expected count	36.5	2.5		Expected count	32.6	6.4	
Propofol (*n*=40)							
Count	36	4		Count	31	9	
Expected count	37.5	2.5		Expected count	33.4	6.6	

Table 3: Variation in SBP at 2 min and 4 min following induction

Group	Variation in SBP at 2 min		Chi-square		Variation in SBP at 4 min		Chi-square
	Change <20%	Change ≥20%			Change <20%	Change ≥20%	
Sevoflurane (*n*=39)							
Count	33	6	8.189 (***P***<0.01)	Count	15	24	15.811 (***P***=0.000)
Expected count	27.2	11.8		Expected count	7.9	31.1	
Propofol (*n*=40)							
Count	22	18		Count	1	39	
Expected count	27.8	12.2		Expected count	8.1	31.9	

SBP: Systolic blood pressure

analysis showed that propofol caused significantly more diastolic BP fall, amounting to hemodynamic instability, Chi-square=25.039, $P < 0.001$. At 4 min, 35/40 patients in the propofol group showed ≥20% change in diastolic BP compared to 17/39 in the sevoflurane group, Chi-square 16.925, $P = 0.000$ [Table 4].

Regarding mean BP, 2 of 39 patients in the sevoflurane group showed more than 20% change in mean BP at 2 min post-induction, whereas 21 patients in the propofol group had a similar change. Similar to that seen in the case of systolic and diastolic BPs, this was also a fall from baseline and was more in the propofol group, Chi-square=25.039, $P < 0.001$. In the sevoflurane group, 17 of 39 patients showed more than 20% change in mean BP at 4 min post-induction, whereas 34 of 40 patients in the propofol group had a similar change, Chi-square=14.799, $P < 0.000$ [Table 5].

Significantly more number of patients induced with propofol showed a more than 20% fall in BP – systolic (18 vs. 6, $P < 0.01$), diastolic (23 vs. 2, $P < 0.001$), and mean (21 vs. 2, $P < 0.001$) BP when compared to patients induced with sevoflurane at 2 min. At 4 min, the statistical significance of propofol's greater propensity over sevoflurane to cause hemodynamic instability became even more obvious; systolic (39 vs. 24, $P = 0.000$), diastolic (35 vs. 17, $P = 0.000$), and mean (34 vs. 17, $P = 0.000$) BP.

Complications During Induction

Complications during induction were studied in the two groups and did not reach any statistically significant level in any particular group. $P = 0.499$ [Figure 1]. In the propofol group, complications noted include pain on injection (3) and abnormal sound (1). In the sevoflurane group, movement (2), abnormal sound (1), laryngospasm (1), cough (2) (Abnormal sound refers to a transient groaning sound emitted by the patient). There was no incidence of an unexpected delay in intubation in the entire study group.

DISCUSSION

In our study, we found that patients in the propofol group reached induction criteria 5.79 s earlier (59.42 vs. 65.21) than those in the sevoflurane group. This difference is small and did not reach statistical significance ($P = 0.212$). In our study, 2 mg/kg bolus of propofol was used in the propofol group and in the sevoflurane group, patients encouraged to breathe deeply into a circuit filled with oxygen into which 8% sevoflurane was introduced. The difference in induction time was small and not significant enough to give an advantage to any agent. In our observations more than 20% change in baseline pulse rate was observed in 4 (of 40) patients in the propofol group (10%) and 1 (of 39) patient in the sevoflurane group at 2 min and 9 (of 40) patients in propofol group (22.5 %) and 4 (of 39) in sevoflurane group (10.25%) at 4 min. These values

Table 4: Variation in DBP at 2 min and 4 min following induction

Group	Variation in DBP at 2 min		Chi-square		Variation in DBP at 4 min		Chi-square
	Change <20%	Change ≥20%			Change <20%	Change ≥20%	
Sevoflurane (*n*=39)							
Count	37	2	25.039 (*P*<0.001)	Count	22	17	16.925 (*P*=0.000)
Expected count	26.7	12.3		Expected count	13.3	25.7	
Propofol (*n*=40)							
Count	17	23		Count	5	35	
Expected count	27.3	12.7		Expected count	13.7	26.3	

DBP: Diastolic blood pressure

Table 5: Variation in MBP at 2 min and 4 min following induction

Group	Variation in MBP at 2 min		Chi-square		Variation in MBP at 4 min		Chi-square
	Change <20%	Change ≥20%			Change <20%	Change ≥20%	
Sevoflurane (*n*=39)							
Count	37	2	21.472 (*P*<0.001)	Count	22	17	14.799 (*P*=0.000)
Expected count	27.6	11.4		Expected count	13.8	25.2	
Propofol (*n*=40)							
Count	19	21		Count	6	34	
Expected count	28.4	11.6		Expected count	14.2	25.8	

MBP: Mean blood pressure

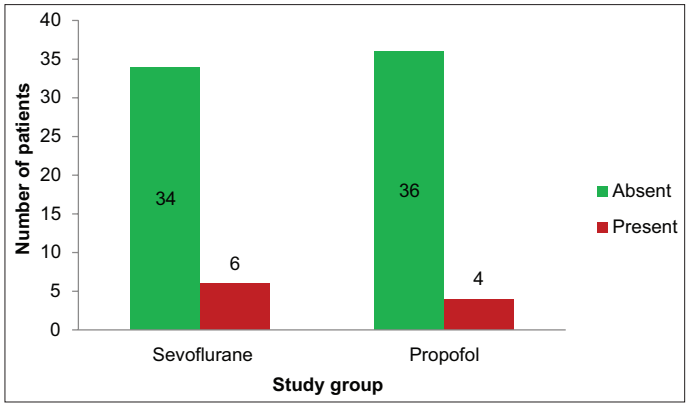

Figure 1: Distribution of patients in groups based on incidence of complications. *Chi – square = 0.457; *P* = 0.499

did not reach statistical significance (*P* = 0.175 and 0.142 at 2 and 4 min respectively). There was a significantly greater burden of hemodynamic instability – systolic, diastolic, and mean BP for propofol over sevoflurane at 2 min. This became even more evident at 4 min, even though the rapid infusion of fluids was always given. The time taken for the train of four to become zero was shorter for the sevoflurane group (211.87 s) when compared to the propofol group (241.80 s). This difference reached statistical significance (*P* = 0.003).

In literature, several studies have shown significantly faster induction with intravenous propofol as against sevoflurane inhalation.[1-8] One study, however, showed faster induction time with vital capacity breath technique using 8% sevoflurane.[9] Yet another study showed no significant difference in induction time with propofol or sevoflurane.[10] These differences appear to be due to differences in technique such as a higher concentration of sevoflurane, and larger inhalational volumes when vital capacity induction is used. The speed of the injection of propofol is also a factor to be considered. Both inhalational volume and speed of injection can have a subjective element depending on the cooperation and vital capacity of the patient and the size and flow rate of the venous line used. The variations in heart rate in our study correspond with the observations in literature.[11] The observations in our study with respect to variation in BP are consistent with literature, with most studies unequivocally demonstrating this potential risk with propofol induction over sevoflurane.[12] However, the impact of this parametric observation on the overall clinical picture of the patient was benign in our study group with no attributable complication. It is well documented in the literature that sevoflurane potentiates the neuromuscular-blocking effect of non-depolarizing muscle relaxants.[13-16] Propofol, in most studies, does not have this effect.[17] Our observations correspond with the classic teaching in literature.

It is reported that post-operative nausea and vomiting are less with propofol than with sevoflurane.[18] However, we did not study this aspect in the present study.

CONCLUSION

Propofol and sevoflurane are equally fast in inducing anesthesia in controlled circumstances in adult patients. Heart rate remains reasonably stable during induction for both agents. Propofol causes greater BP fall than sevoflurane. Sevoflurane potentiates the action of non-depolarizing muscle relaxants when compared to propofol during induction. Complications attributable to either of the agents are infrequent and can be detected early with alert monitoring and managed with routine interventions. Sevoflurane may be considered as a better option than propofol as an induction agent for patients in whom fall in BP is unlikely to be tolerated even for a short period.

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