A comparative study of intraoperative analgesic consumption and recovery profile between sevoflurane- and propofol-based general anesthesia in adults

Abanish Ray¹, Debojyoti Das², Sweta Shaw³, Soma Chakraborty⁴, Arpita Laha⁵, Mohanchandra Mandal⁶

Background: Many researches were performed in the past to compare propofol and

sevoflurane as sole anesthetics. While some studies have reported the advantages of

propofol regarding better recovery profile and post-operative analgesic sparing effect, the

contrast reporting does exist. Hence, there is a further need of research to explore recovery

characteristics. Whether either of these two as sole anesthetics can yield any benefit regarding

intraoperative analgesics consumption has not been evaluated. Aims and Objectives: The

study primarily aimed at determining total analgesic consumption in the intraoperative period (primary outcome), between those receiving either sevoflurane or propofol for induction as well as maintenance of anesthesia. In addition, intraoperative hemodynamics (heart rate and

mean arterial pressure) and recovery profile were compared. Materials and Methods: Total

of 168 patients, aged 18-60 years, the American Society of Anesthesiologists' physical status I/II, undergoing elective and emergency surgeries under general anesthesia for 2-3 h

finally recruited. Patients were randomly allocated to receive either sevoflurane (group S, n = 84) or propofol (group P, n = 84) for both induction and maintenance. Anesthetics were titrated to achieve bispectral index (BIS) value of 60. For both the groups, additional fentanyl

was considered aliguots of 25 mcg whenever the hemodynamics changes occurred despite

maintaining BIS value in the above-mentioned range. Results: The total intraoperative

analgesic consumption was found comparable in both groups of patients. Induction time (38 vs. 59 s) and emergence time (8 vs. 10 s, P < 0.001) were found shorter in the propofol group than in sevoflurane. Aldrete score >9 was achieved earlier with propofol compared with sevoflurane (8.5 vs. 12 min). Conclusion: Propofol-based shows no advantage over sevoflurane in view of intraoperative consumption of analgesics and intraoperative hemodynamic stability. However, the use of propofol was associated with faster induction

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ABSTRACT

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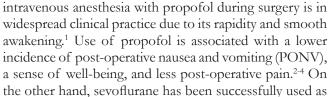
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INTRODUCTION

Nowadays, propofol and sevoflurane are being used widely among the commonly used intravenous and inhalational anesthetics owing to their safe and satisfactory recovery profile. They have their merit and demerit. The use of

Key words: Aldrete score; Anesthesia; Propofol; Recovery; Sevoflurane

as well as quicker emergence from anesthesia.



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an alternative to propofol for various daycare procedures as induction agent.⁵ Sevoflurane maintains a good hemodynamic stability and has a cardioprotective effect at the cost of a high incidence of PONV.⁶

When compared the effects of propofol anesthesia with sevoflurane anesthesia on post-operative pain after radical gastrectomy, it was found that there was better analgesic outcome for the propofol group, especially in the early post-operative period.⁷ In a study, comparing "single-agent" anesthesia using either sevoflurane or propofol, the recovery profile (emergence time, post-operative nausea, vomiting, and pain) was found to be unaffected by the anesthetic technique.8 In that study, both techniques maintained comparable cardiovascular stability, and the majority of patients found either technique acceptable.8 In another study, sevoflurane showed an advantage over propofol in respect of intraoperative cardiovascular stability without increasing recovery time.⁹ In a recent study, propofol was found to be advantageous in having considerably shorter time to emergency from anesthesia over sevoflurane whereas the latter was found to blunt the hemodynamics better.¹⁰ There are further contrasting reports regarding the advantages of propofol. While some studies^{4,11-13} have reported a considerable reduction in post-operative pain others^{3,14} have observed a non-significant effect.

In the recent past, Peng et al.,¹⁵ observed in a metaanalysis that a high level of heterogeneity exist among the reported studies performed in a wide range of surgeries, and concluded that none of the post-operative pain outcomes was considerably changed using propofol instead of sevoflurane for maintenance of anesthesia. Hence, there is further scope of evaluating these two drugs as sole anesthetic agents. Till the time of designing the study, no research has been carried out regarding intraoperative analgesia consumption. Consequently, the present study was designed to compare intraoperative analgesic requirements and post-operative recovery profile between those receiving either sevoflurane or propofol for induction as well as maintenance of anesthesia.

Aims and objectives

The study aimed at determining total analgesic consumption in the intraoperative period (primary outcome) between those receiving either sevoflurane or propofol for induction as well as maintenance of anesthesia. In addition, the recovery characteristics in terms of extubation time, time to reach Aldrete score >9, and the incidence of PONV were compared. Furthermore, the changes in hemodynamics (heart rate and mean arterial pressure [MAP]) in the intraoperative period were compared.

MATERIALS AND METHODS

This parallel group, single-blinded, and randomized controlled study was conducted in the general surgery operating room under the Department of Anesthesiology, IPGME&R and SSKM Hospital after obtaining the approval from Institute's Ethics Committee (IEC/2022/092). A total of 168 patients, aged 18–60 years, conforming to the American Society of Anesthesiologists' physical status I/II, admitted undergoing elective and emergency surgeries under general anesthesia for 2–3 h were finally recruited (Figure 1) for this study. The study was registered with the Clinical Trial Registry of India in a prospective manner with trial number CTRI/2022/08/044983.

Exclusion criteria

The following exclusion criteria were considered:

- Patient's refusal to give consent
- Patient having sensory or motor deficit
- Patient on medications such as hypnotics, narcotics analgesics, or sedatives
- History of seizure disorders
- Anticipated difficult airway.

Sample size

The sample size was calculated using nMaster version 2.0 (Department of Biostatistics, Christian Medical College, Vellore, 2011) software. The sample size calculation is based on the total analgesic (fentanyl) requirement as the primary outcome measure. On calculation, total of 84 individuals per group was the requirement in order to detect a difference of 20 mcg in this parameter with 90% power and 5% probability of type I error. This calculation assumed the standard deviation of fentanyl requirement to be 40 mcg and two-sided testing.

Patients remained fasted for 6 h before surgery and received premedication with alprazolam 0.25 mg and ranitidine 150 mg tablets orally at night before surgery. The purpose and protocol of the study were explained to all patients and an informed and written consent was taken.

In the operating room, standard monitors such as electrocardiogram, non-invasive blood pressure, peripheral arterial oxygen saturation (SpO_2) , and bispectral index (BIS) were used. Intravenous fluids were administered at 2 mL/kg before start of induction.

Patients were randomly allocated to receive either sevoflurane (group S, n=84) or propofol (group P, n=84) using computer-generated random numbers. The allocated patients of any group received either sevoflurane or propofol alone as assigned for both induction and

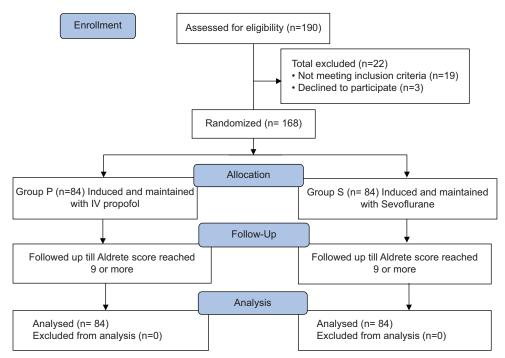


Figure 1: Consort flow diagram

maintenance. All patients received fentanyl 2 μ g/kg 3 min before induction.

In group P, anesthetic induction was carried out with propofol in 20 mg increments every 5 s till the BIS value reached 60 and maintained with propofol infusion started at the rate of 150 μ g/kg/min adjusted gradually by 25 μ g/kg/min to maintain the BIS value between 40 and 60 and then the time for induction was noted down.

In group S, anesthesia was induced with sevoflurane with 60% nitrous oxide in oxygen, with a total gas flow of 6 L/min. Sevoflurane was started at 5% then increased gradually up to 8% till BIS reached to 60, and then the time for induction was noted down. For maintenance of anesthesia, 2% sevoflurane was given with 60% N_2O in oxygen and adjusted in the steps of 0.4% to maintain BIS value of 40–60.

For both the groups, additional fentanyl was considered aliquots of 25 mcg whenever the hemodynamics changes occurred despite maintaining BIS value in the abovementioned range. Muscle relaxation was achieved with atracurium 0.5 mg/kg and after intubation with proper size endotracheal tube additional boluses (0.1 mg/kg) were given if required. The total amount of muscle relaxants required was recorded. Fluids were replaced accordingly and fentanyl was repeated as required. The total dose of fentanyl was recorded. Intermittent positive pressure ventilation was used to maintain $E_{\rm T}CO_2$ within 35–40 mmHg. Patient's heart rate and MAP were observed at pre-induction, after

induction, after intubation, after insertion of ET Tube, and then in the intraoperative period till extubation. Adverse events such as cough, laryngeal spasm, and bradycardia, if any, were recorded during induction. Hypertension and hypotension were determined by a change in MAP >20% of the pre-induction value. The administration of sevoflurane and propofol was discontinued at the end of the surgery. Reversal of neuromuscular blockade was obtained by injection of neostigmine (0.05 mg/kg) and injection of glycopyrrolate (10 μ g/kg). The endotracheal tube was removed when patients regain consciousness and breathing adequately. The time to extubation (from cessation of anesthetics to extubation of trachea) was noted. The total dose of analgesics in the intraoperative period was calculated. Patients were shifted to the postanesthesia recovery area and the time to reach a modified Aldrete score of >9 was noted down (Table 1) in the case of every patient.¹⁶ The incidence of PONV was recorded.

This was a single-blinded study. The resident who recorded intraoperative data from the monitor remained blind as he was kept unaware of the propofol infusion and sevoflurane vaporizer used under curtain. The resident in the recovery room who observed post-operative vitals and modified Aldrete's scores was blind about the anesthesia procedure.

Statistical analysis plan

Data were summarized by routine descriptive statistics, namely mean and standard deviation for numerical variables that are normally distributed, median and interquartile range for skewed numerical variables, and counts and percentages for categorical variables. Numerical variables were compared between groups by student's independent sample t-test, if normally distributed, or by Mann–Whitney U test, if otherwise. Fisher's exact test or Pearson's Chi-square test was employed for intergroup comparison of categorical variables Changes over time in numerical variables were assessed for statistical significance by repeated measures analysis of variables (ANOVA) or Friedman's ANOVA, as appropriate. Analyses were two-tailed and the statistical significance level was set at P=<0.05 for all comparisons.

RESULTS

The study spanned over 18 months (from March 2021 to August 2022). Data from all 168 participants were available for analysis (Figure 1).

Demographic data and duration of anesthesia were comparable between the two groups (Table 2).

Induction time was considerably shorter in patients receiving propofol compared with sevoflurane. The total intraoperative analgesic consumption was found comparable in both groups of patients (Table 3).

The total consumption of analgesic (fentanyl) in the intraoperative (left side graph) and post-operative period (right side graph) is presented as a raincloud plot (Figure 2).

The plot shows combined depiction of data distribution (the 'cloud'), with jittered raw data (the 'rain'). It also contains boxplots and measures of central tendency. It provides a visual impact about how the data is distributed, its bimodal nature and other crucial aspects.

Although heart rates at pre-induction and recovery were found to be considerably less in those receiving sevoflurane,

Table 1: I	Nodified aldrete scoring	
Activity	Moves all four limbs voluntarily/on	2
	command	
	Moves two limbs	1
	No movements	0
Respiration	Breaths deeply and coughs freely	2
	Dyspneic, shallow or limited breathing	1
	Apneic	0
Circulation	BP±20 mmHg of preanesthetic level	2
	BP±20–50 mmHg of preanesthetic level	1
	BP±50 mmHg of preanesthetic level	0
Awareness	Fully awake	2
	Arousable on calling	1
	Not responding	0
Oxygen	$SpO_2 > 92\%$ on room air	2
saturation	Supplemental O2 required to maintain	1
	SpO ₂ >92%	
	$SpO_2 < 92\%$ with O_2 supplementation	0

the values are in the physiological range. Hence, it was not of any clinical significance (Table 4). It can be commented that both propofol and sevoflurane maintained heart rate well within comfortable range at different time points of perioperative period. In other words, although at certain time points the difference of heart rates was statistically significant, it has no clinical importance.

On analysis, there was a considerable difference of MAP between the two groups at different time points except at recovery (Table 5). However, the values are within physiological range. Hence, it can be commented that both propofol and sevoflurane maintained MAP within the clinically acceptable range at different time points of perioperative period.

Emergence time after propofol-based anesthesia was found to be considerably shorter than sevoflurane. The time to

Table 2: Demographic parameters and durationof anaesthesia				
Parameters	Propofol (n=84)	Sevoflurane (n=84)	P-value	
Age (years)	39.33±8.52	34.87±7.97	0.791	
Gender (Male/	51/33	53/31	0.750	
Female)*				
Weight (Kg)	64.81±3.12	63.44±3.52	0.249	
BMI (kg/m ²)	25.88±2.11	24.24±1.78	0.172	
ASA-PS (I/II)	55/29	43/41	0.603	
Duration of	2.84±0.17	2.9±0.14	0.06	
anesthesia (hours)				

ASA-PS: American Society of Anesthesiologists' Physical Status

Table 3:	Intrao	perative	paramet	ters
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Parameters	Group P (n=84)	Group S (n=84)	P-value
Induction time in seconds	38.3±3.2	59.7±7.1	<0.001
Muscle Relaxant required	79.4±6.49	66.8±5.79	<0.001
Intraoperative analgesics consumed	315.5±17.76	312.3±19.58	0.271
Post-operative analgesics consumed	366.9±77.06	557.7±61.69	<0.001

Atracurium was used as muscle relaxant and data presented as mg; Fentanyl was used as intraoperative and postoperative analgesic, data is presented as microgram

Table 4: Perioperative heart rate at various timepoints

Data of heart rate is expressed as beats per minute				
Parameters (heart rate)	Group P (n=84)	Group S (n=84)	P-value	
Preinduction	85.1±8.733	75.9±8.773	<0.001*	
Just after intubation	89.3±8.816	87.6±6.384	0.206	
Intraoperative	83.2±7.466	83.8±7.889	0.6	
Just after recovery	80.3±8.498	77.6±9.578	0.024*	

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reach Aldrete score >9 was found considerably lower after propofol-based anesthesia compared with sevoflurane. The incidence of PONV was significantly higher with sevoflurane compared to propofol (Table 6).

DISCUSSION

The present study observes comparable consumption of analgesics in the intraoperative period in propofolbased and sevoflurane-based anesthesia (315 vs. 312 mcg, respectively). This is in contrast with the observation of Saad et al.,¹⁷ who found higher fentanyl consumption in the propofol group compared with the sevoflurane group (mean 223 vs. 158 mcg, approximated). Inhalational anesthetics at a minimum alveolar concentration of 0.1 can produce hyperalgesic effects which may increase pain perception.¹⁸ Further investigation is required to determine the effect of propofol and sevoflurane before drawing any consolidated inference.

Table 5: Perioperative mean arterial pressure atvarious time points				
Parameters (MAP)	Group P (n=84)	Group S (n=84)	P-value	
Pre-induction Immediately after intubation	79.6±7.173 70.8±7.222	81.6±5.801 76.3±5.713	0.042 <0.001	
Average intraoperative Just after recovery	68.3±7.469 78.3±7.585	78.0±5.392 79.6±5.385	<0.001 0.211	
Mean arterial pressure (in mm Hg)				

iviean arter	iai pressure	e (in mm Hg)

Table 6: Recovery characteristics				
Parameters	Group P (n=84)	Group S (n=84)	P-value	
Time to emergence (in minutes)	8.11±0.45	10.31±0.61	0.045	
Time to reach aldrete score >9 (min) PONV	8.54±0.54	12.03±0.95	<0.0001	
Yes (%) No (%)	28 (33.3) 56 (66.7)	10 (11.9) 74 (88.1)	0.0009	

The present study finds a shorter induction time (mean 38 vs. 59 s) during the use of propofol compared with sevoflurane. However, the requirement of muscle relaxant was more during the use of propofol. Chung and Dhanrajani¹⁰ found both propofol target-controlled infusion and sevoflurane to be comparable regarding induction and maintenance of anesthesia for short day-case surgery.

In the present study, no clinically significant difference was observed regarding intraoperative heart rate during propofol and sevoflurane anesthesia. In a study, Orhon et al.¹⁹ found that intraoperative hemodynamic parameters were comparable between propofol-based and sevofluranebased anesthesia where both sevoflurane concentration and propofol infusion rate were adjusted according to BIS values. Bindra et al.²⁰ also found that hemodynamic parameters such as heart rate and MAP were comparable in both sevoflurane and propofol-based anesthesia throughout surgery with lower readings at some time points in the propofol group without any statistically significant difference. Overall, sevoflurane provided better stability compared to propofol.

In the study of Chung and Dhanrajani¹⁰ propofol was found to be inferior in blunting the hemodynamic response to sudden, severe stimuli compared with sevoflurane. Chung and Dhanrajani¹⁰ opined that it may be considered a concern in patients with cardiac comorbidities. Bharti et al.⁹ found that the changes in heart rate were comparable between propofol-based and sevofluranebased anesthesia. However, the MAP was found to be considerably lower after induction and higher during laryngoscopy in the propofol group as compared to the sevoflurane group. Overall, in their study, sevoflurane was found to be advantageous over propofol in respect of intraoperative cardiovascular stability without increasing recovery time9 In a study, Chaudhary et al.21 found lower heart rate but higher MAP in the intraoperative period during use of propofol compared with sevoflurane.

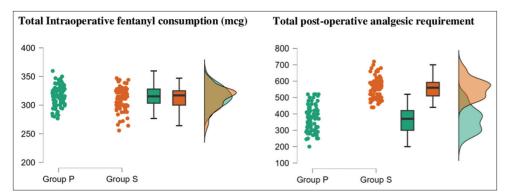


Figure 2: Raincloud plots showing total consumption of intraoperative and post-operative analgesia

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In the present study, emergence time was found to be considerably shorter with the use of sevoflurane compared with propofol (mean 8.11 vs. 10.31 min, respectively). The finding of the present study is in line with the study of Orhon et al.,¹⁹ who found that maintenance of anesthesia using sevoflurane was associated with faster recovery than propofol-based anesthesia. A similar observation was also reported by Chaudhary et al.,²¹ who found emergence time, extubation time, and recovery time to be considerably shorter with the use of sevoflurane. In contrast, Bharti et al.⁹ found comparable emergence time between propofol and sevoflurane (mean 7.8 vs. 8.2 min, respectively).

In the present study, considerable longer time was needed to reach Aldrete score >9 after propofol-based anesthesia compared with sevoflurane-based anesthesia (12 vs. 8.5 min, respectively). Contrast reporting does exist in this regard, where Bharti et al.,⁹ observed that considerably shorter time was needed to reach Aldrete score 9 using propofol compared with sevoflurane (mean 9.4 vs. 11.2 min, respectively).

Propofol was found to be comparable with sevoflurane for maintenance of anesthesia in surgeries such as open cholecystectomy with an additional benefit of lower incidence of PONV owing to its intrinsic antiemetic properties.²² Orhon et al.¹⁹ also found that the use of propofol resulted in a considerably lower incidence of PONV. Amiri et al.23 observed that the incidence of PONV and the requirement of antiemetic rescue drug and the severity of nausea were found to be considerably lower in patients receiving total intravenous anesthesia (propofol) compared with inhalational (isoflurane) anesthetics (3.8% vs. 11.3%, respectively). Maintenance of anesthesia using propofol was found to be associated with a decreased incidence of early PONV compared with sevoflurane or desflurane in patients undergoing ambulatory surgery.² Bindra et al.²⁰ opined that sevoflurane can be considered a useful alternative to propofol in providing anesthesia, especially in such situations where rapid emergence and recovery of cognitive function are mostly desired.

The present study finds that post-operative analgesic consumption was lower in patients receiving propofolbased anesthesia compared with sevoflurane-based anesthesia (approximated mean 367 mcg vs. 558 mcg, respectively). The findings of the present study are in contrast with Pokkinen et al.,¹⁴ who compared sevoflurane with propofol for maintenance of general anesthesia and found that the choice of anesthetic had no effect on the requirement of analgesic or intensity of pain in the post-operative period. Moreover, a recent study²⁴ evaluated propofol-remifentanil and sevoflurane-remifentanil anesthesia for shoulder arthroscopic surgery and found comparable post-operative analgesia. In a systematic review and meta-analysis on the impact of propofol on post-operative pain outcome. Wong et al.²⁵ have reported that the use of propofol-based anesthesia can reduce postoperative pain scores and reduce opioid consumption after surgery. In another meta-analysis Peng et al.,¹⁵ concluded in a contrast way that none of the post-operative pain outcomes was significantly changed or improved using propofol instead of sevoflurane for maintenance of anesthesia. They opined that this might be attributed to substantially high level of heterogeneity of the reported studies and the small number of studies included in the metaanalysis.¹⁵

Limitations of the study

In the present study, the propofol or sevoflurane was titrated to maintain the level of anesthesia to a close range of BIS value. However, the level of intraoperative analgesia could not be titrated in an objective manner. This remained a major limitation. Further study is warranted in future using sophisticated monitors capable of indicating level of hypnosis and analgesia in a measurable way.

CONCLUSION

There is no discernible difference in the intraoperative consumption of analgesic between propofol-based and sevoflurane-based anesthesia. Both techniques have achieved intraoperative hemodynamic stability. The use of propofol showed faster induction as well as quicker emergence from anesthesia in the present study.

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