



Original Research Article

Comparison of the effects of propofol and sevoflurane on postoperative cognitive functions and memory in patients undergoing general anaesthesia

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ABSTRACT

This study finds out the effect of propofol and sevoflurane on cognitive function and memory and also compares the effect on postoperative recovery profile in patients undergoing general anaesthesia. Aim of the study is to compare the effects of propofol and sevoflurane on cognitive and memory function in terms of psychometric test pre and post general anaesthesia. 60 patients of age group 18–60 years and ASA grade I, II, III scheduled for general anaesthesia were included in this study. Patients were divided into two groups in maintenance: group P: Inj. propofol infusion and group S: sevoflurane. Assessment of cognitive function and memory of patients in both groups was done preoperatively by following

Materials and Methods: MMSE score, CVLT, DST, RBMT and Recalling the names of surgeon and anaesthetist. After extubation, Patients were observed for recovery by alderate recovery score up to 1 hour and assessed for pain by visual analogue scale up to 4 hours postoperatively. Cognitive function and memory up to 4 hours was assessed postoperatively. The recovery characteristics were better with sevoflurane than propofol up to 10 mins. Sevoflurane had less impact on cognitive function as compared to propofol up to 30 mins postoperative. Effect on verbal and numerical memory was less with sevoflurane as compared to propofol up to 30 mins. Effect on semantic memory was less with sevoflurane as compared to propofol up to 5 mins except recall memory. We concluded from above study that when rapid recovery of cognitive function and memory are desired, sevoflurane is more favourable than propofol for a faster recovery and emergence from anaesthesia.

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1. Introduction

Cognition is defined as ‘the mental processes of perception, memory and information processing which allows the individual to acquire knowledge, solve problems and plan for the future’. It includes the mental processes required for day to day living and not to be confused with intelligence. Cognitive dysfunction is impairment of all these processes.¹ There are two type of memory:[1] explicit memory [2] implicit memory. Explicit memory is conscious recollection of previous experiences. Implicit memory is changes in performances and behavior produced by previous experiences.²

In 1955, Bedford was first described that ‘some of the elderly patients who were subjected to operations under general anaesthesia “were never the same” post operatively’. This change is termed post-operative cognitive dysfunction (POCD), which is a recognized clinical phenomenon after anaesthesia and surgery.³

Sevoflurane was synthesized in the 1970. Sevoflurane is relatively insoluble in blood and has a low blood–gas partition coefficient (0.65) and slightly more soluble than nitrous oxide and desflurane. Induction and recovery from anaesthesia are extremely rapid, and the level of anaesthesia is easily controlled as its tissue–blood partition coefficients are also low.⁴ Sevoflurane exposure can lead to neurodegeneration with aggregation of β -amyloid protein levels, changes in exploratory and anxiety like behavior in these subjects and activation of specific kinases that lead to

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phosphorylation of tau and spatial memory deficits.³

Since the introduction of propofol in the late 1980s, intravenous anaesthesia is also now commonly used.⁵ Propofol is short acting intravenous anesthetic drug used as an induction agent, sedation and also for maintenance of anaesthesia. In propofol hypnotic activity is mostly mediated through enhancing γ -aminobutyric acid (GABA) induced chloride current through its binding to the β -subunit of GABA receptor. Propofol is rapidly metabolized mostly in the liver and its metabolites are considered inactive. Half-life of propofol after initial dose is 2 to 8 minutes, and even after prolonged infusions, propofol provides rapid recovery.⁶

So this study was undertaken to find out the effect of propofol and sevoflurane on cognitive function and memory and also compare the effect on postoperative recovery profile in patients undergoing general anaesthesia.

2. Materials and Methods

This observational study was conducted from December 2016 to June 2017, after approval from institutional ethical committee, written informed consent from patients was taken. 60 patients of age group 18-60 years and ASA grade I, II, III scheduled for general anaesthesia were included in this study. Patients receiving anti-anxiety drugs, history of allergy to drugs, pregnant and lactating mother, patients education below 10th std. and preoperative MMSE score <23, patients with history of alcohol and drug abuse, patients with psychiatric illness were excluded from the study. Patients were divided into two groups by anesthesia maintenance: group P: Inj. propofol infusion and group S: sevoflurane. Each group had 30 patients in each.

Thorough pre-anaesthetic evaluation was carried out. Patient was kept nil by mouth minimum for 6hrs. Tab. Alprazolam 0.25mg HS was given day before surgery and Tab. Ranitidine 150 mg HS was given day before surgery and 1 hour before on the day of surgery. Assessment of cognitive function and memory was done preoperatively by following method: MMSE Score, CVLT, DST, RBMT, Recall names of surgeon and a naesthetist. CVLT (California Verbal Learning Test): It is a measure of episodic verbal learning and memory. Patient were asked the names of any 5 fruits preoperatively and asked to remember same names of 5 fruits postoperatively. (Mango, Apple, Grapes, Pineapple, Orange). DST (Digit Span Test): It measures numerical memory. Patients were asked their vehicle no (4 digit number) and mobile no (6 digit number) preoperatively and asked same questions postoperatively. RBMT (Rivermed behavioral memory test): It assesses semantic memory. Patient were shown picture of animal, to identify that animal and its location and their own birth date preoperatively. Patients were asked again to identify this animal and its location and their own birth date postoperatively. Recall names of surgeons and anaesthetist:

Patient were informed about the name of surgeon and anaesthetist preoperatively and told to remember it and ask for the same postoperatively. MMSE Score : It is 30 point questionnaire. It is used to estimate the severity of progression of cognitive impairment (24-30: no cognitive impairment, 18-23: mild cognitive impairment 0-17: severe cognitive impairment).

Pre-operatively pulse rate, blood pressure, ECG, SPO₂ and BIS were noted in the operation room before giving the study drug and considered as baseline. Premedication was given Inj. Glycopyrrolate 10 μ g/kg IV, Inj. Ondansetron 4 mg IV and Inj. Fentanyl 2 μ g/kg IV, just before induction in patients of both groups. Pre oxygenation was done with 100% Oxygen for 3 min. In the both the groups general anaesthesia was administered with Inj. Propofol 2 mg/kg IV to produce loss of eyelash reflex followed by Inj. Succinylcholine 2 mg/kg IV. All patients were ventilated with 100% O₂ and on achieving complete relaxation intubation was done with appropriate sized cuff portex endotracheal tube. Maintenance of anaesthesia in group P via Inj Propofol infusion 100-300 μ g/kg/min and in group S via Sevoflurane (1.2%-1.5%) along with O₂ (50%), N₂O (50%), Inj. Vecuronium 0.1 mg/kg as bolus dose and 0.01 mg/kg as maintenance with IPPV. Inj. Paracetamol 15 mg/kg was given IV. intraoperatively in patients in whom analgesia is inadequate [BP > 20% from baseline, pulse rate >20% from baseline]. Intraoperatively pulse, blood pressure SPO₂ BIS value and ETCO₂ were recorded 15 minutes and 30 minutes after induction, and then every 30 minutes till extubation. At the end of surgery when the last suture was inserted, N₂O and anaesthetic agents were stopped and O₂ was administered at flow rate of 6 L/min. Reversal was done by using Inj. Glycopyrrolate 0.01mg/kg IV + Inj. Neostigmine 0.05 mg/kg IV at the end of the surgery. Duration of surgery was recorded. After extubation, Patients were observed for recovery by alderate recovery score at 0 min, 5 min, 10 min, 15 min, 30 min and 60 min. Assessment of cognitive function and memory of patients in both groups was done by same method: MMSE Score, CVLT, DST, RBMT, and recall names surgeons and anaesthetist at 5 minutes, 30 minutes and then every hourly up to 4 hours postoperatively. Pain was assessed by visual analogue scale (0-10) at 30 minutes and then every hourly up to 4 hours postoperatively.

2.1. Statistical Analysis

Data was analyzed using SPSS version 22. Tests performed were descriptive, Unpaired T- test with Levene's test of equal variances for intergroup comparison.

3. Result and discussion

The term cognition comes from the Latin verb *congnoſco* (con 'with' + *gnōscō* 'know').⁷ Post operative's cognitive

dysfunction is characterized by impairment of memory working memory, long-term memory, information processing, attention or cognitive flexibility.⁸ Despite technological development in field of surgery and anesthesiology during the last decades, postoperative cognitive dysfunction is still relatively frequent complication in surgical patients.⁶

In present study baseline mean pulse rate, systolic blood pressure, diastolic blood pressure, SPO₂ ETCO₂ and BIS value were comparable in both the groups. So, the difference was statistically not significant in both the groups ($p > 0.05$).

Intraoperatively BIS value was maintained between 40–60 with propofol infusion and sevoflurane in group P and group S respectively. Hence difference between the groups were not significant at different time interval ($p > 0.05$).

Mean alderate recovery score was 8.93 ± 0.25 , 9.79 ± 0.41 and 10 ± 0 in groups and 8.13 ± 0.7 , 8.63 ± 0.67 and 9.7 ± 0.53 in group p at 0 min, 5 min and 10 min interval after extubation respectively. Thus this difference was highly significant ($p < 0.001$). So early recovery was observed with sevoflurane as compared to propofol at 30 min, 60 min after extubating aldrate recovery score were comparable in both the groups ($p > 0.01$) (Figure 1). In 2000, V.A.Peduto, D.Mezzeti et al.⁴ and in 2015, Upasana Goswami, Savita Babbar, Saurabh Tiwari et al.,⁷ observed that Sevoflurane has low blood gas partition coefficient 0.65 which means that anaesthetic concentration in alveoli is attained rapidly and elimination is also quicker. So, there was early recovery seen in sevoflurane due to discontinuation of sevoflurane leads to rapid fall in alveolar concentration due to low blood gas solubility.

Preoperatively baseline mean MMSE score was comparable in both the Groups. Postoperatively at 5 min after extubation, mean MMSE score was 26.75 ± 1.37 in group S and 24.13 ± 1.59 in group P, at 30 min interval 27.65 ± 1 in group S and 25.83 ± 1.82 in group P respectively. Though value of MMSE score was ranging between 23-30. There was less cognitive impairment observed in group S as compared to group P. So this difference was statistically highly significant ($p < 0.001$) but after 30 minutes, there was no cognitive impairment seen with sevoflurane and propofol (Figure 2). In contrast to present study in 2015, Yong Qiao, Hao Feng, et al., suggested that sevoflurane increases the risk of POCD in elderly patients undergoing major surgery because sevoflurane increased the plasma concentration of IL6 and TNF- α throughout the first postoperative week. So there was reduction in MMSE and MoCA scores in first postoperative period in those exposed to sevoflurane rather than propofol.⁸ Also Jeong-yeon hongjong in oh and Soomie kim (2002) et al., observed that there were no significant differences between the sevoflurane nitrous oxide and target controlled propofol with fentanyl for MMSE score at all time intervals. They found that recovery of cognitive function (ability to perform mini mental state test) were

similar between two groups. The discrepancy between results, on recovery of cognitive functions may be due to variation in protocol and different surgical time.⁹

Preoperatively baseline mean no of names of fruits (CVLT test) asked by patients was comparable in both the Groups. At 5 minutes interval after extubation, mean no of names of fruits remembered by patients was 4.62 ± 0.73 in group S and 1.6 ± 0.62 in group P, at 30 minutes interval 4.89 ± 0.31 in group S and 3.87 ± 0.81 in group P respectively. Thus there were more numbers of fruits remembered by patients in group S as compared to group P. Thus this difference was statistically highly significant ($p < 0.001$). So effect of sevoflurane on verbal memory was less affected than propofol up to 30 minutes. After 30 minutes, there was no effect on verbal memory both with sevoflurane and propofol (Table 1). Preoperatively all patients remembered their own mobile no and vehicle no (DST test). Thus there was no statistically significant difference in both the groups ($p > 0.05$). At 5 minutes interval and at 30 minutes interval after extubation, 30 (100%) number of patients in group P and 9 (30 %) number of patients in group S and 15 (50 %) number of patients in group P and 0 number of patients of group S respectively were not able to remember their own mobile number and vehicle number which was asked preoperatively. Thus there were more number of patients remembered their own mobile number and vehicle number in group S as compared to group P. Thus this difference was statistically highly significant ($p < 0.001$). So effect of sevoflurane on numerical memory was less affected than propofol up to 30 minutes. After 30 minutes, there was no effect on numerical memory both with sevoflurane and propofol (Table 2). There were more no of patients had identified animal and its location and recalled their birthdate (RBMT test) in group S as compared to group P ($p < 0.001$) postoperatively. So effect of sevoflurane on semantic memory was less affected than propofol up to 5 minutes. There was no effect on semantic memory both with sevoflurane and propofol after 5 minutes (Table 3). Postoperatively, all patients remembered names of surgeon and anaesthetist in both the groups. So there was no effect on recall memory both with sevoflurane and propofol (Table 4). Upasana Goswami, Savita Babbar, Saurabh Tiwari et al., (2015) observed that sevoflurane had blood gas partition coefficient 0.65 leads to low solubility in blood and tissue causes rapid induction and recovery has been found to have less effect on memory than propofol. Therefore it is better drug for preservation of short term memory.⁷ VAS score was comparable in both the groups at different time interval in postoperative period. Thus this difference was statistically insignificant in both the groups ($p > 0.05$) (Figure 3).

There are many differences in literature suggest choice of test batteries (either very easy or very difficult), the time of post-operative assessment, interval between multiple

Table 1: California verbal learning test

Duration	Group P		Group S		p value
	Mean	SD	Mean	SD	
Preoperative	5	0	5	0	-
5 min after extubation	1.6	0.62	4.62	0.73	<0.001**
30 min after extubation	3.87	0.81	4.89	0.31	0.001**
60 min after extubation	5	0	5	0	-
120 min after extubation	5	0	5	0	-
180 min after extubation	5	0	5	0	-
240 min after extubation	5	0	5	0	-

** - Statistically highly significant ($p < 0.01$)

Table 2: Digit span test

Duration	Group P		Group S		Chi sq	p value
	N=30	%	N=30	%		
Preoperative	0	0	0	0	-	-
5 min after extubation	30	100	9	30	39.227	<0.001**
30 min after extubation	15	50	0	0	16.23	<0.001**
60 min after extubation	0	0	0	0	-	-
120 min after extubation	0	0	0	0	-	-
180 min after extubation	0	0	0	0	-	-
240 min after extubation	0	0	0	0	-	-

** - Statistically highly significant ($p < 0.01$)

Table 3: Rivermad behavioral memory test

Duration	Group P		Group S		Chi sq	p value
	N=30	%	N=30	%		
Preoperative	0	0	0	0	-	-
5 min after extubation	23	76.67	1	3.33	29.371	<0.001**
30 min after extubation	1	3.33	0	0	2.172	0.671**
60 min after extubation	0	0	0	0	-	-
120 min after extubation	0	0	0	0	-	-
180 min after extubation	0	0	0	0	-	-
240 min after extubation	0	0	0	0	-	-

** - Statistically highly significant ($p < 0.01$), NS – Not significant ($p > 0.05$)

Table 4: Recall Names (surgeon and anaesthetist)

Duration	Group P		Group S		chi sq	p value
	N=30	%	N=30	%		
Preoperative	0	0	0	0	-	-
5 min after extubation	1	3.33	0	0	2.127	0.671**
30 min after extubation	0	0	0	0	-	-
60 min after extubation	0	0	0	0	-	-
120 min after extubation	0	0	0	0	-	-
180 min after extubation	0	0	0	0	-	-
240 min after extubation	0	0	0	0	-	-

** - NS - Not significant ($p > 0.05$)

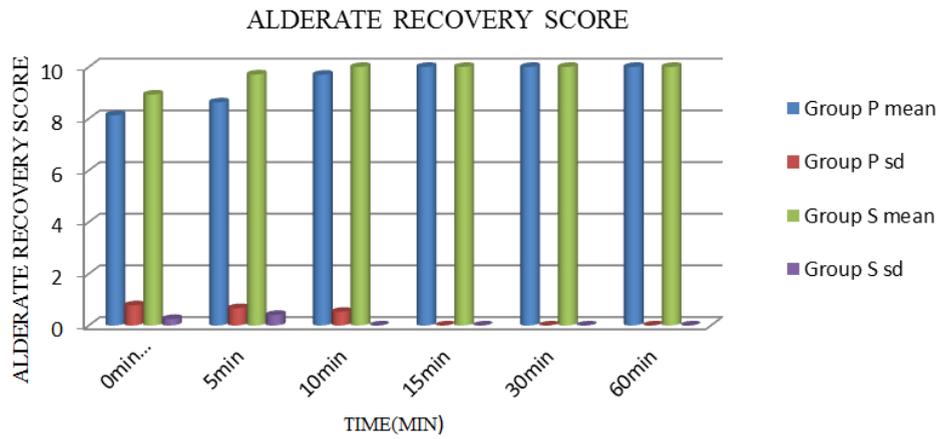


Fig. 1: Alderate recovery score

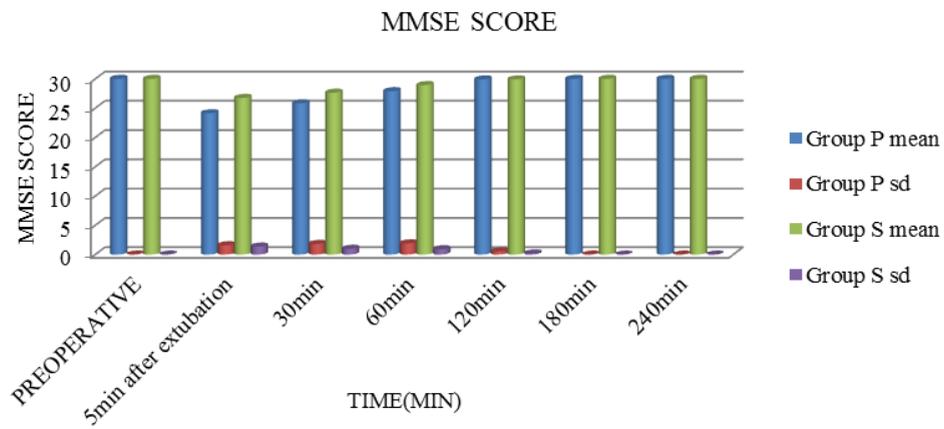


Fig. 2: Mini mental status examination score

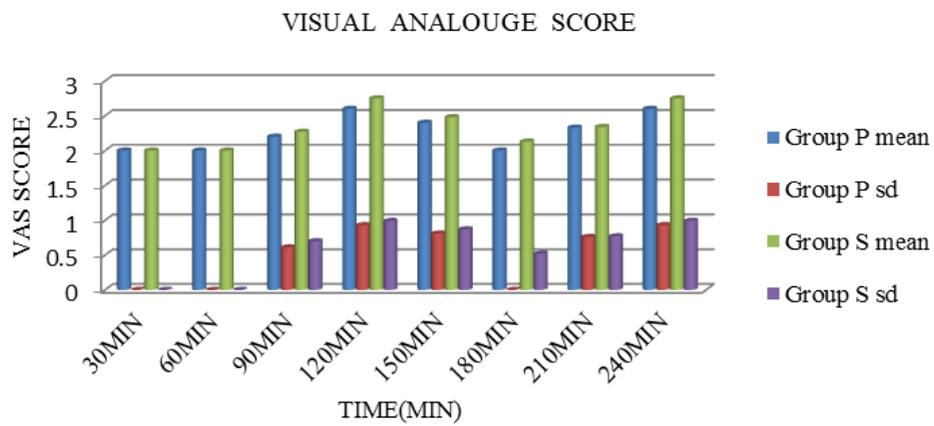


Fig. 3: Visual analogue score

observation for a shorter period and longer duration, the number of parameters were included for evaluation and also on the type of population and sample size. There is variability in evaluation of the test such as time of day when the test was performed, distraction in examining room, the place of examination, therefore on the contrary it has been suggested that a test batteries (multiple cognitive test) rather than one single test may be more appropriate.^{4,10,11} Limitation of present study was that- it was performed for a shorter period (4 hours postoperatively) and there are many variations and different results in using different test, hence further more studies are recommended.

4. Conclusion

From our study, we concluded that titration of anaesthetics to BIS value at 40-60 did not necessarily curb cognitive function and memory under anesthesia. The recovery characteristics were better with sevoflurane than propofol up to 10 minutes. Sevoflurane had less impact on cognitive function as compared to propofol up to 30 minutes postoperative. Effect on verbal and numerical memory was less with sevoflurane as compared to propofol up to 30 minutes. Effect on semantic memory was less with sevoflurane as compared to propofol up to 5 minutes except recall memory. Therefore sevoflurane is more favorable than propofol for a faster recovery and emergence from anesthesia, where rapid recovery of cognitive function and memory are desired.

5. Source of Funding

None.

6. Conflict of Interest

None.

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