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RESEARCH ARTICLE

Propofol-Based Anaesthesia in Association with Lower Incidence of Postoperative Cognitive Dysfunction in Older Adults Compared to Sevoflurane

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Abstract: Postoperative cognitive dysfunction (POCD), commonly under-recognized complication following surgery, particularly in elderly patients, characterized by impairments in memory, attention, and executive function that can negatively impact recovery and quality of life. Anaesthetic technique is a potentially modifiable factor influencing the development of POCD. This prospective, randomized controlled trial conducted in the Department of Anaesthesiology at a tertiary care teaching hospital over a six-month period, involving 100 patients aged 65 years and above undergoing elective non-cardiac, non-neurosurgical procedures under GA. Participants randomly assigned to two groups: Group P received propofol-based total intravenous anaesthesia (TIVA),Group S received sevoflurane-based inhalational anaesthesia. Cognitive assessments performed using Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Digit Span, and Trail Making Tests A/B (TMT-A/B) preoperatively and postoperative days 1 and 7. POCD, defined as a decline of ≥1 standard deviation in two or more cognitive tests on day 7. Baseline characteristics were similar between the groups. On postoperative day 7, POCD occurred in 12% of the propofol group and 34% of the sevoflurane group ($p = 0.01$). Patients in the propofol group had significantly better cognitive test scores and exhibited faster recovery in terms of orientation, ambulation, and hospital discharge. Multivariate analysis identified the use of sevoflurane and lower educational level as independent predictors of POCD. In conclusion, propofol-based anaesthesia was associated with a lower incidence of POCD in elderly, suggesting potential neuroprotective effects and supporting its use in this population.

Keywords: Propofol, Sevoflurane, POCD, Elderly, General Anaesthesia, Neurocognitive Outcomes, TIVA

INTRODUCTION

Postoperative cognitive dysfunction (POCD) is a common yet often underdiagnosed complication following surgery, especially in older adults. It encompasses a spectrum of neurocognitive impairments—ranging from subtle memory deficits and reduced attention to executive dysfunction—that manifest after anaesthesia and surgery, typically within days to weeks, and may persist for months or even permanently in vulnerable individuals [1]. POCD is associated with decreased quality of life, delayed recovery, loss of independence, increased risk of dementia, and higher mortality rates [2]. With the increasing number of elderly individuals undergoing surgical procedures due to rising life expectancy and medical advancements, mitigating the risk of POCD has become a priority in perioperative care.

The etiology of POCD is multifactorial and still not fully understood, but age-related neuronal vulnerability, systemic inflammation, neuroinflammation, disruption of the blood-brain barrier, and anaesthetic neurotoxicity are considered important contributors [3]. Among these, the choice of anaesthetic agent has gained attention as a modifiable perioperative factor that could influence neurocognitive outcomes.

Propofol and sevoflurane are two widely used agents in general anaesthesia, each with distinct pharmacological profiles. Sevoflurane is a volatile halogenated ether that is favored for its rapid onset and smooth induction and recovery. However, animal and human studies have raised concerns about its neurotoxicity, particularly in the aging brain. Experimental evidence suggests that sevoflurane may increase neuroinflammation, apoptosis, and deposition of amyloid-beta and phosphorylated tau—pathological hallmarks associated with Alzheimer's disease and cognitive decline [4,5]. Moreover, sevoflurane exposure has been linked to increased levels of proinflammatory cytokines such as IL-6 and TNF-α in the central nervous system, which are known to contribute to neuronal dysfunction and cognitive impairment [6].

On the other hand, propofol, an intravenous anaesthetic agent, has demonstrated neuroprotective effects in various preclinical and clinical studies. Propofol modulates GABAergic neurotransmission and possesses potent antioxidant and anti-inflammatory properties. It has been shown to inhibit the release of inflammatory mediators, attenuate oxidative stress, and reduce neuronal apoptosis in the hippocampus—an area crucial for memory and learning [7,8]. In clinical settings, propofol has been associated with faster recovery of

cognitive function, lower incidence of delirium, and improved postoperative neurocognitive outcomes compared to inhalational agents like sevoflurane [9,10,11,12].

Several comparative studies have explored the impact of anaesthetic technique on postoperative cognitive outcomes. Chen et al. reported better recovery profiles in elderly patients receiving propofol compared to inhalational anaesthetics [13,14,15,16]. In a randomized controlled trial, Silbert et al. found that elderly patients undergoing major non-cardiac surgery had a significantly lower incidence of POCD with propofol-based total intravenous anaesthesia (TIVA) than with sevoflurane-based anaesthesia [17,18,]. These findings suggest that propofol may offer a neuroprotective advantage in the geriatric population.[19,20]

Given the growing concern over cognitive complications after surgery and the potential influence of anaesthetic choice, it is imperative to evaluate and compare the neurocognitive outcomes associated with propofol and sevoflurane in older adults. This study aims to investigate whether propofol-based general anaesthesia is associated with a lower incidence of POCD compared to sevoflurane, thereby contributing to evidence-based strategies for safer anaesthetic management in the elderly.

MATERIAL AND METHODS

This was a prospective, randomized controlled trial conducted in the Department of Anaesthesiology at a tertiary care teaching hospital in duration of 6 month and written informed consent was obtained from all participants or their legally authorized representatives.Patients aged ≥65 years scheduled to undergo elective non-cardiac, non-neurosurgical surgeries under general anaesthesia were screened for eligibility. The study aimed to compare the incidence of postoperative cognitive dysfunction (POCD) between two anaesthetic techniques: propofol-based and sevoflurane-based general anaesthesia.

Inclusion Criteria:

- Age ≥ 65 years
- ASA physical status I–III
- Duration of surgery between 1 and 3 hours
- MMSE score ≥ 24 at baseline
- Ability to provide informed consent

Exclusion Criteria:

- Pre-existing cognitive dysfunction (MMSE < 24)
- History of neurological, psychiatric, or neurodegenerative disease
- Recent use of sedatives or antipsychotics
- Significant sensory impairments affecting cognitive testing
- Intraoperative complications requiring ICU admission
- Randomization and Group Allocation
- Participants were randomly allocated into two groups using a computer-generated randomization list:
- Group P (Propofol group): Patients received total intravenous anaesthesia (TIVA) using propofol.
- Group S (Sevoflurane group): Patients received inhalational anaesthesia with sevoflurane.

Randomization was concealed using sealed opaque envelopes. Cognitive assessments were conducted by an assessor blinded to group allocation.

Anaesthesia Protocol

All patients were premedicated with intravenous midazolam (0.02 mg/kg) and glycopyrrolate (0.2 mg) 30 minutes before induction.

Group P (Propofol-based TIVA):

- Induction: Propofol 2 mg/kg + fentanyl 2 µg/kg IV
- Maintenance: Propofol infusion at 100–150 µg/kg/min + fentanyl boluses as needed
- Group S (Sevoflurane-based):
- Induction: Propofol 2 mg/kg + fentanyl 2 µg/kg IV
- Maintenance: Sevoflurane in 50% air/oxygen to maintain MAC of 1.0–1.2

Neuromuscular blockade was achieved using atracurium 0.5 mg/kg, with maintenance dosing as needed in both groups. Depth of anaesthesia was monitored using Bispectral Index (BIS) to maintain levels between 40 and 60.

Cognitive Assessment

Cognitive function was assessed using the following tools:

- Mini-Mental State Examination (MMSE)
- Montreal Cognitive Assessment (MoCA)
- Digit Span Test (Forward and Backward)
- Trail Making Test Part A and B (TMT-A and TMT-B)

Testing was conducted at three time points:

1. Preoperatively (Baseline)
2. Postoperative Day 1 (POD1)
3. Postoperative Day 7 (POD7)

Definition of POCD

POCD was defined as a decline of ≥1 standard deviation from baseline performance in two or more tests on POD7, adjusted for age and education norms. Standardized z-scores were calculated for each test.

Outcome Measures

• Primary Outcome: Incidence of POCD on postoperative day 7

• Secondary Outcomes: Early cognitive decline (POD1), intraoperative haemodynamic parameters, anaesthesia duration, and length of hospital stay

Statistical Analysis

All data were analyzed using SPSS software version [Insert Version]. Continuous variables were expressed as mean ± standard deviation (SD) and analyzed using independent t-test or Mann–Whitney U test. Categorical variables were analyzed using the Chi-square test or Fisher's exact test. Multivariate logistic regression was used to control for confounding variables. A p-value < 0.05 was considered statistically significant.

Sample Size Calculation

Assuming a 40% incidence of POCD in the sevoflurane group and a 20% incidence in the propofol group, with α = 0.05 and power of 80%, the calculated sample size was 90 patients (45 per group). Accounting for 10% loss to follow-up, 100 patients were enrolled.

RESULTS AND OBSERVATIONS:

A total of 100 patients were enrolled and randomized equally into two groups:

- Group P (Propofol-based anaesthesia): n = 50
- Group S (Sevoflurane-based anaesthesia): n = 50

All participants completed the study and underwent cognitive assessment at baseline, POD1, and POD7.

Table 1: Baseline Demographic and Clinical Characteristics

Variable	Group P (n=50)	Group S (n=50)	p-value
Age (years, mean ± SD)	69.8 ± 4.2	70.3 ± 5.1	0.51
Gender (M/F)	28 / 22	26 / 24	0.68
Education (years)	11.5 ± 2.3	11.1 ± 2.5	0.45
ASA Class I/II/III	12 / 28 / 10	14 / 26 / 10	0.91
Baseline MMSE Score	27.2 ± 1.4	27.0 ± 1.5	0.59

As shown in Table 1, no statistically significant differences were observed between the two groups at baseline in terms of age, gender, ASA class, education, or baseline MMSE scores, indicating comparability.

Table 2: Intraoperative Parameters

Parameter	Group P	Group S	p-value
Anaesthesia duration (min)	108.5 ± 14.2	110.1 ± 13.7	0.48
Surgery duration (min)	95.7 ± 12.4	97.3 ± 12.1	0.43
BIS range maintained	42–58	40–60	NS
Episodes of hypotension (%)	12%	24%	0.12

As shown in Table 2, both groups had similar intraoperative anaesthesia and surgical durations, and depth of anaesthesia was adequately maintained. Hypotension was slightly more common in the sevoflurane group but not statistically significant.

Table 3: Postoperative MMSE Scores

Time Point	Group P (mean ± SD)	Group S (mean ± SD)	p-value
Preoperative	27.2 ± 1.4	27.0 ± 1.5	0.59
POD1	25.5 ± 1.7	23.8 ± 2.1	0.002*
POD7	26.8 ± 1.3	25.1 ± 1.6	0.001*

As shown in Table 3, both groups showed a transient decline in MMSE postoperatively, but the sevoflurane group had significantly lower scores on POD1 and POD7, indicating greater cognitive decline.

Table 4: Incidence of POCD on Postoperative Day 7

POCD Incidence	Group P (n=50)	Group S (n=50)	p-value
Present	**6 (12%)**	**17 (34%)**	**0.01***
Absent	**44 (88%)**	**33 (66%)**	

As shown in Table 4, the incidence of POCD on POD7 was significantly lower in the propofol group compared to the sevoflurane group (p = 0.01), supporting the neuroprotective effect of propofol.

Table 5: Neurocognitive Test Scores (Trail Making and Digit Span Tests)

Test	Time Point	Group P (Mean ± SD)	Group S (Mean ± SD)	p-value
TMT-A (sec)	POD7	43.2 ± 6.1	49.8 ± 7.2	0.001*
TMT-B (sec)	POD7	87.1 ± 9.3	94.6 ± 10.4	0.005*
Digit Span (total)	POD7	10.2 ± 1.4	8.9 ± 1.7	0.002*

As shown in Table 5, patients in the propofol group performed significantly better in attention, executive function, and memory tasks, as indicated by superior Trail Making and Digit Span test scores.

Table 6: Length of Hospital Stay and Recovery Profile

Parameter	Group P	Group S	p-value
Time to orientation (min)	12.4 ± 3.2	17.6 ± 4.1	<0.001*
Time to ambulation (hrs)	15.3 ± 2.6	18.1 ± 3.2	0.004*
Length of hospital stay (days)	4.6 ± 1.2	5.3 ± 1.4	0.03*

As shown in Table 6, the propofol group demonstrated faster recovery, earlier ambulation, and shorter hospital stays, suggesting better postoperative outcomes overall.

Table 7: Multivariate Logistic Regression for Predictors of POCD

Variable	Odds Ratio (95% CI)	p-value
Age > 70 years	1.62 (0.85–3.24)	0.14
ASA III	1.95 (0.92–3.89)	0.09
Sevoflurane use	3.41 (1.39–8.31)	0.007*
Education < 10 years	2.22 (1.01–5.32)	0.04*

As shown in Table 7, use of sevoflurane and lower educational status were independently associated with increased risk of POCD. Age and ASA class showed trends but were not statistically significant.

DISCUSSION

Postoperative cognitive dysfunction (POCD) is increasingly recognized as a significant complication in older adults undergoing surgery under general anaesthesia. It is associated with adverse outcomes including delayed recovery, reduced independence, and increased long-term mortality [1]. In this study, we found that propofol-based anaesthesia was associated with a significantly lower incidence of POCD compared to sevoflurane-based anaesthesia in elderly patients undergoing elective, non-cardiac surgeries.

On postoperative day 7, the incidence of POCD in the propofol group was 12%, significantly lower than the 34% observed in the sevoflurane group (p = 0.01). This is consistent with findings from Silbert et al., who reported that propofol resulted in fewer cognitive impairments compared to sevoflurane after non-cardiac surgery in patients aged 60 years and above [2]. Similarly, Zhang et al. demonstrated that patients receiving propofol exhibited better performance in memory and attention tasks postoperatively than those receiving sevoflurane [3].

One of the key mechanisms proposed to explain this difference lies in the neuroprotective properties of propofol, which include anti-inflammatory and antioxidant effects, as well as inhibition of neuronal apoptosis [4,5]. In contrast, volatile anaesthetics such as sevoflurane have been shown in both animal and human studies to induce neuroinflammation, tau phosphorylation, and amyloid-beta aggregation, which may contribute to postoperative cognitive impairment [6,7].

Our findings also align with those of Chen et al., who found that patients receiving desflurane or sevoflurane exhibited slower postoperative recovery of cognitive function compared to those who received total intravenous anaesthesia (TIVA) with propofol [8]. Additionally, our study observed significantly better MMSE, Digit Span, and Trail Making Test scores in the propofol group, which further supports the hypothesis that propofol may help preserve cognitive domains such as attention, memory, and executive function in the early postoperative period.

Another important observation in our study was the shorter time to orientation, earlier ambulation, and reduced hospital stay in the propofol group. These findings are clinically relevant, especially in the elderly, where prolonged recovery can lead to functional decline, delirium, and loss of independence. The rapid clearance of propofol and its favorable recovery profile likely contribute to these benefits [9].

Multivariate regression in our study identified the use of sevoflurane and lower educational level as independent predictors of POCD, which is consistent with earlier studies emphasizing cognitive reserve as a protective factor [10]. Although older age and higher ASA class showed trends toward higher POCD incidence, they were not statistically significant in our cohort, possibly due to our exclusion of patients with major comorbidities.

It is worth noting that while sevoflurane remains a preferred inhalational agent for its hemodynamic stability and ease of titration, its effects on the aging brain require careful consideration. In high-risk elderly patients, TIVA with propofol may be a more suitable alternative when the goal is to minimize postoperative neurocognitive complications.

Limitations

Despite its strengths, this study has certain limitations. It was conducted in a single tertiary care center with a relatively small sample size, which may limit generalizability. The study followed patients up to postoperative day 7, and longer-term cognitive outcomes were not assessed. Additionally, although validated neurocognitive tools were used, learning effects and individual variability in cognitive performance may have influenced the results.

CONCLUSION

In conclusion, our study adds to the growing body of evidence suggesting that propofol-based general anaesthesia is associated with a lower incidence of postoperative cognitive dysfunction in older adults compared to sevoflurane. The findings support the consideration of TIVA with propofol as a preferred anaesthetic technique in the elderly, particularly those at risk for cognitive impairment. Further multicentric trials with longer follow-up are recommended to validate these findings and guide clinical practice.

Conflict of Interest

None.

Source of Funding

None.

Authorship Contribution Statement

Thej Kiran Namburi: experimentation and Writing-original draft, U.G.Thirumaaran, Vishak Manikandan M, Vigneshwaran& K, Chandru E: Review and editing, T. Arun Prasath: Conceptualization and supervision

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