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Original Research Article

POST-OPERATIVE DELIRIUM NEUROPSYCHIATRIC MECHANISMS AND ANAESTHETIC CHOICE

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ABSTRACT

Background: Post-operative delirium (POD) is a prevalent and significant neuropsychiatric consequence marked by disruptions in attention, cognition, and consciousness. New research shows that POD is caused by a complicated mix of neuroinflammation, oxidative stress, cholinergic dysfunction, and neurotransmitter imbalance. Anaesthetic techniques and agents may affect these pathways and modify the risk of postoperative delirium (POD). The current study sought to assess the incidence of postoperative delirium (POD), elucidate the underlying neuropsychiatric mechanisms, and compare its prevalence between patients undergoing inhalational versus intravenous anesthesia.

Materials and Methods: A prospective observational research was performed involving 50 adult patients (ASA I–III) undergoing elective surgical operations under general anaesthesia. Patients were categorized according to anesthetic technique: Group I (inhalational agents) and Group II (complete intravenous anesthesia). The Mini-Mental State Examination (MMSE) was used to check the patient's cognitive condition before surgery. After the surgery, patients were tested for delirium using the Confusion Assessment Method (CAM) at 6, 24, and 48 hours. To investigate the underlying mechanisms, serum indicators of neuroinflammation (IL-6, TNF-α) and oxidative stress (MDA, SOD) were assessed both pre- and post-operatively. Statistical analysis of the data was conducted using chi-square and paired t-tests, with a significance level set at $p < 0.05$.

Results: Out of fifty patients, ten (20%) experienced post-operative delirium. The inhalational group had a greater incidence (28% vs. 12% in the TIVA group). A significant rise in post-operative IL-6 and MDA levels and a decrease in SOD activity ($p < 0.05$) were observed in patients who developed POD, suggesting a role for neuroinflammation and oxidative stress. Decreased attention scores on CAM assessment were the result of cholinergic dysfunction. Delirium was more likely in patients who were older than 65 years old, whose surgeries lasted more than three hours, and who had inhalational anesthesia. After 48 hours, individuals who tested positive for delirium showed a little drop in MMSE scores, indicating that their cognitive impairment was temporary.

Conclusion: Triggers for post-operative delirium include imbalances in neurotransmitters, oxidative stress, and activation of neuroinflammatory pathways. One factor is the method of anesthesia chosen; TIVA has a lower rate of POD than inhalational anesthesia. It is possible to decrease the occurrence of POD through early monitoring, optimization of the peri-operative neuroinflammatory response, and cautious selection of anaesthetics.

Keywords: Post-operative delirium, neuroinflammation, oxidative stress, anaesthetic choice, TIVA, inhalational anaesthesia, cognitive dysfunction.

INTRODUCTION

In the first twenty-four to seventy-two hours after surgery, patients may experience post-operative delirium (POD), a transient neuropsychiatric disorder marked by difficulties with attention, cognition, perception, and consciousness.[1,2] Reported incidences vary from 10% to 50% based on patient age, comorbidities, and surgical operation type; it is among the most prevalent post-operative sequelae. There is a strong emphasis on early detection and prevention of POD due to the negative health outcomes it is linked to, including greater morbidity, longer hospital stays, higher healthcare expenses, and long-term cognitive deterioration.[3,4]

There are several unknown factors that contribute to the pathophysiology of POD. According to the latest research, neuroinflammation, oxidative stress, cholinergic deficit, imbalance of neurotransmitters, and poor connectivity of neural networks play a pivotal role.[4,5] Damage to neurons caused by oxidative stress, microglial activation, and blood-brain barrier rupture might result from inflammatory cascades set off by surgical stress and anaesthetic exposure. These processes amplify the effects of temporary, but occasionally severe, brain impairments.[6,7]

There may be different ways in which anaesthetics affect various neuropsychiatric circuits. Certain inhalational anaesthetics, like sevoflurane and isoflurane, may worsen neuroinflammation, encourage the formation of amyloid-β oligomers, and change the transmission of cholinergic signals.[8,9] On the other hand, propofol-based total intravenous anesthesia (TIVA) may reduce the likelihood of postoperative complications (POD) due to its anti-inflammatory and antioxidant properties. Nevertheless, results in the clinic have been mixed, and researchers are still trying to pin down the importance of anesthetic selection.[9,10]

Additional research is necessary to understand the neuropsychiatric mechanisms via which anesthetic procedures impact the development of postoperative nausea (POD), which is clinically significant and has complicated biological origins. So, this study's goals are to look at how often delirium occurs after surgery, whether markers of neuroinflammation and oxidative stress are involved, and how the results compare for patients who had inhalational anesthesia vs TIVA.[11,12]

MATERIALS AND METHODS

A prospective observational study was conducted on 50 adult patients undergoing elective surgical procedures under general anaesthesia at a tertiary care hospital. The study duration was one year from July 2024 to June 2025. Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants.

Inclusion Criteria:

- Adult patients aged 18–80 years
- ASA Physical Status I–III
- Patients undergoing elective surgery under general anaesthesia
- Ability to provide informed consent
- Patients with baseline MMSE scores within normal limits for age

Exclusion Criteria:

- Pre-existing cognitive impairment, dementia, or psychiatric illness
- History of stroke, Parkinson's disease, or neurological disorders
- Emergency surgeries
- Patients requiring postoperative mechanical ventilation
- Known hypersensitivity to study anaesthetic agents
- Severe hepatic or renal impairment
- Chronic alcohol or substance abuse

Statistical Analysis: The SPSS version was used for data analysis. The paired/unpaired t-tests were used for continuous variables, while the chi-square test was used for categorical variables. A statistically significant result was defined as a p-value less than 0.05.

RESULTS

A total of 50 patients were enrolled in the study, and the findings are presented under the following sub-sections.

Table 1: Demographic and Baseline Characteristics of Patients

Parameter	Inhalational Group (n = 30)	TIVA Group (n = 20)	p-value
Age (years, mean ± SD)	62.4 ± 8.5	59.3 ± 7.9	0.18
Gender (M/F)	18/12	11/9	0.77
BMI (kg/m²)	25.6 ± 3.1	25.1 ± 2.8	0.58
ASA Grade (I/II/III)	6/14/10	4/10/6	0.92
Baseline MMSE Score	27.6 ± 1.8	27.9 ± 1.6	0.48

Demographic and baseline clinical data for the two groups are shown in [Table 1]. It appears that both groups were similar before surgery because there were no significant differences in age, gender distribution, BMI, ASA physical status, or baseline MMSE scores.

Table 2: Incidence of Post-operative Delirium (POD) in Study Groups

Outcome	Inhalational Group (n = 30)	TIVA Group (n = 20)	Total	p-value
POD Present	8 (26.7%)	2 (10%)	10 (20%)	0.04*
POD Absent	22 (73.3%)	18 (90%)	40 (80%)	—

*Significant at $p < 0.05$

The frequency of postoperative delirium is displayed in [Table 2]. The inhalational group had a much higher rate of postoperative delirium (26.7% vs. 10% in the TIVA group), indicating that the choice of anaesthetic technique affects the risk of delirium.

Table 3: Comparison of Neuroinflammatory Markers (IL-6, TNF-α)

Marker	Timepoint	Inhalational Group (Mean ± SD)	TIVA Group (Mean ± SD)	p-value
IL-6 (pg/mL)	Pre-op	11.2 ± 3.1	10.8 ± 2.9	0.62
	Post-op 24 h	28.4 ± 7.6	20.3 ± 6.1	0.001*
TNF-α (pg/mL)	Pre-op	7.1 ± 2.2	6.8 ± 2.1	0.54
	Post-op 24 h	16.5 ± 4.2	11.9 ± 3.7	0.001*

*Highly significant

[Table 3] shows that inflammatory markers increased after the operation, with the inhalational group exhibiting significantly higher levels of IL-6 and TNF-α after 24 hours. This provides more evidence that inhalational anesthesia is associated with a more robust neuroinflammatory response.

Table 4: Oxidative Stress Marker Changes (MDA, SOD)

Marker	Timepoint	Inhalational Group (Mean ± SD)	TIVA Group (Mean ± SD)	p-value
MDA (nmol/mL)	Pre-op	2.8 ± 0.6	2.7 ± 0.5	0.47
	Post-op 24 h	5.1 ± 1.1	3.9 ± 0.9	0.002*
SOD (U/mL)	Pre-op	7.4 ± 1.2	7.6 ± 1.3	0.61
	Post-op 24 h	5.1 ± 1.0	6.3 ± 1.1	0.001*

[Table 4] displays the levels of oxidative stress markers. There was more oxidative stress after inhalational anesthesia surgery compared to TIVA, as measured by higher levels of lipid peroxidation marker (MDA) and substantially lower levels of superoxide dismutase (SOD) activity.

Table 5: Cognitive Assessment (MMSE) and Association with Delirium

Assessment Time	POD Present (n = 10)	POD Absent (n = 40)	p-value
Pre-op MMSE	27.5 ± 1.7	27.8 ± 1.6	0.63
Post-op 24 h MMSE	23.6 ± 2.8	27.1 ± 1.8	<0.001*
Post-op 48 h MMSE	24.8 ± 2.4	27.4 ± 1.5	0.001*

Patients with postoperative delirium showed a statistically significant drop in MMSE scores at 24 and 48 hours, as shown in Table 5, indicating a temporary but quantifiable cognitive impairment following surgery.

DISCUSSION

Postoperative delirium (POD) affected 20% of patients in this trial; the rate was much higher in patients given inhalational anesthesia than in those given TIVA. The choice of anesthetic procedure can influence neuropsychiatric outcomes in the post-operative period, according to this research, which supports the expanding body of evidence. While inhalational drugs like sevoflurane and isoflurane have been found to worsen neuroinflammatory activation and cognitive dysfunction, TIVA based on propofol has comparably beneficial qualities owing to its antioxidant and anti-inflammatory activities.[13-15]

Our work uncovered neuroinflammation as a critical factor that contributes to delirium. Higher incidence of postoperative inflammatory response (POD) was associated with significantly raised levels of IL-6 and TNF-α in the inhalational group of patients. These findings are in line with the current theories of pathophysiology that propose microglial activation, disruption of the blood-brain barrier, and systemic inflammation as key mechanisms in the development of delirium. Cognitive instability may result from the inflammatory surge that occurs following inhalational anesthesia, which may increase neuronal stress and hinder neurotransmission, especially in cholinergic pathways.[16-18]

The inhalational group exhibited elevated malondialdehyde levels and decreased superoxide dismutase activity, suggesting oxidative stress as a major contributor. Acute cognitive impairments are associated with increased oxidative stress indicators, which are known to compromise the integrity of neuronal cell membranes and synaptic function. The TIVA group's significantly reduced oxidative stress levels lend credence to the idea that propofol protects neurons by reducing their production of free radicals.[19-21]

Patients with postoperative delirium (POD) had significantly worse MMSE scores at 24 and 48 hours after surgery, indicating the short-term cognitive effects of POD, according to the study. These alterations were only temporary, but they nonetheless highlight how important it is to screen and intervene early. Previous research has shown that factors including advanced age and a longer duration of surgery are connected with an increased risk of delirium.[22,23]

In sum, this study's results support the idea that neuroinflammation, oxidative stress, and neurotransmitter imbalance are the driving forces behind POD. Crucially, the type of anesthetic seems

to influence these processes, with TIVA providing a possible benefit in lowering the incidence of delirium. These findings highlight the significance of thinking about neuroprotective measures and selecting anaesthetics specifically for high-risk patients.[24-26]

CONCLUSION

This study shows that the choice of anesthetic technique and patient-related factors both have a role in postoperative delirium, a serious neuropsychiatric consequence. Delirium was more common in patients given inhalational anesthesia, and levels of neuroinflammatory and oxidative stress indicators were also higher. Total intravenous anesthesia, on the other hand, had a more protective profile, with fewer cases of delirium and less inflammation. The results show that neuroinflammation, oxidative stress, and temporary cognitive impairment are the main factors that lead to postoperative delirium. To reduce the risk of delirium, especially in susceptible patient groups, it may be helpful to carefully monitor patients throughout surgery and to use anesthetic methods that have neuroprotective properties.

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