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Anesthetics and Postoperative Delirium in Elderly after Elective Surgery: A Retrospective Comparison between Sevoflurane and Propofol

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Abstract

Background: Postoperative delirium (POD) in elderly subjects is an important health issue as it is associated with high morbidity and mortality. Anesthetic agents are associated factors for the development of POD. However, the results of previous studies are heterogeneous. The current work aimed to determine the incidence and associated factors of POD after sevoflurane or propofol general anesthesia.

Methods: This was a retrospective study, where data were collected from the medical records of 200 subjects scheduled for elective surgery under general anesthesia. One hundred received sevoflurane, and the other 100 received propofol. The collected data included patient characteristics and preoperative and operative data. In addition, POD and any complications developed after surgery are also included. Mean and standard deviation were used to summarize quantitative variables, while frequency and percentages were used to express categorical data. The independent sample's student test was used to compare two means, and Chi-Square was used to calculate associations between categorical parameters. Risk estimate was determined by calculation of odds ratios. *P* value<0.05 was considered significant.

Results: Operative time was significantly shorter in sevoflurane than in propofol groups (249.91±45.41 vs 264.60±45.78 minutes, respectively). Otherwise, no significant differences were recorded for preoperative and operative data. The incidence of POD was significantly higher after propofol than sevoflurane (30.0% vs 14.0%). The POD was significantly associated with higher ASA-class physical status, diabetes mellitus, and type of anesthetic agent. ASA-III was 34.1% and 10.3% in patients with delirium than without delirium. Diabetes recorded 65.9% for the group with delirium compared to 10.3% for those without delirium.

Conclusion: POD was higher after propofol than sevoflurane anesthesia. It is associated with ASA physical status, diabetes, and the type of anesthetic agent used.

Keywords: Propofol, Intravenous Anesthesia, Inhalational Anesthesia, Elderly, Delirium

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Introduction

With the development of the healthcare s ystem, the number of elderly above 65 years is increasing. Many of them underwent different surgical procedures (1, 2).

Postoperative delirium is one of the common complications of anesthesia and surgery in elderly subjects. Its incidence ranges between 4% and 41% of patients undergoing

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↑What is "already known" in this topic:
Postoperative delirium (POD) in elderly subjects is associated with high morbidity and mortality. It usually attributed to the anesthetic agents. However, other factors are linked to development of POD. In addition, the results about anesthetic agents-associated delirium and results of previous studies are heterogeneous.

→What this article adds:
Postoperative delirium seems to be higher after propofol than sevoflurane. This is an interesting finding, as the most of previous literature reported higher incidence of POD after sevoflurane. This raised the need to future large-scale studies comparing those two agents to validate known results. The POD linked to the presence of comorbid chronic disease (e.g., Diabetes mellitus). The type of anesthetic agent was the main determinant factor for POD.

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spine surgery (3, 4), and from 12 to 56% after hip fracture surgery (5).

In addition, there is a piece of evidence that demonstrates that the same surgery under different anesthetics may have different incidences of postoperative comorbid conditions (e.g., neurocognitive disorders) (6-8).

Postoperative delirium (POD) is associated with a significant increase in morbidity and mortality. Specifically, there is an increase in the duration of hospital stay, impairment of cognition, and development of dementia or Alzheimer's disease. However, the pathophysiological mechanisms of POD are poorly understood and may be multifactorial. POD may be affected by the anesthetics, as the main target of anesthetic is the brain (9-12).

General anesthesia is usually maintained by intravenous (e.g., propofol) or inhalational (sevoflurane) anesthetics. However, their effects on the brain remain unclear (13). Some studies indicated that sevoflurane is a neuroprotection (14, 15), and others showed it has a neurotoxicity (16, 17) .

In the current work, we evaluated the incidence of POD after sevoflurane and propofol anesthesia in elderly subjects undergoing major elective surgery.

Methods

This was a retrospective study, where data of elderly patients (older than 65 years of age) who submitted to elective major surgery were collected. Specifically, patients operated under general anesthesia with sevoflurane (n=100) or propofol (n=100). Patients were selected from Al-Azhar University Hospitals (Cairo and Damietta). The data was collected for patients who underwent surgery from the first of February 2020 to the first of February 2024.

The exclusion criteria were incomplete records, the presence of preoperative delirium, psychiatric disorders, renal or hepatic chronic diseases, need for mechanical ventilation (MV) after surgery, recent surgery (within 6 months before the study), or the use of combined anesthetics for maintenance were excluded. However, patients submitted to major elective abdominal, orthopedic, or spinal surgery were included.

Anesthesia was maintained by inhalation anesthesia (sevoflurane, group 1) or total intravenous anesthesia (propofol, group 2). The choice of anesthetic agent was totally based on the anesthesiologist's preferences. As a standard protocol, 1–2 mg midazolam was administered preoperatively as a premedication.

In all subjects, a continuous infusion of remifentanil or propofol boluses was used for intraoperative analgesia. The anesthetic depth was measured by the bi-spectral index (BIS), and values above or equal to 40 and lower than 60 were guaranteed. The dose of propofol was reduced before the end of surgery earlier than sevoflurane to permit proper awakening. The standard intraoperative monitoring was applied (e.g., electrocardiogram, blood pressure, and oxygen saturation).

The collected data included patient demographics (e.g., age, sex, weight, height, and body mass index were calculated), ASA physical state, smoking habit, and comorbid conditions. In addition, perioperative data were collected. These included type of surgery (abdominal, orthopedic, or spinal), duration of surgery, duration of anesthesia, intraoperative BIS, estimated blood loss, amount of fluids infused during surgery and blood transfusion (either intra-or post-operative), the severity of pain (using numerical rating scale), use of opioids for postoperative analgesia, incidence of POD, duration of hospital stay and postoperative complications (during hospitalized or shortly after discharge, till the end of the postoperative 30 days).

The postoperative complication comprised cardiovascular (e.g., angina or infarction), cerebrovascular (e.g., stroke or transient ischemic attacks), respiratory (e.g., pneumonia), deep vein thrombosis, and acute kidney injury (AKI).

The diagnosis of POD delirium is passed into two phases. The first included screening carried out by a trained nurse using the Nursing Delirium Screening Scale (NDSS) during hospital stay. The scale included (disorientation, inappropriate behavior, inappropriate communication, hallucination, and psychomotor retardation), as described by Hargrave et al. (18). The second phase carried by an expert psychiatrist, where any patient with one of the manifestations of NDSS was referred to the expert for proper diagnosis and initiation of treatment. The incidence of POD was based on the diagnosis by a psychiatrist.

The primary outcome of the current work was the development of POD after surgery during the hospital stay. However, secondary outcomes included postoperative complications, length of stay, and associated demographic or surgery criteria with POD.

Statistical analysis: the collected data were fed to an Excel sheet (Microsoft Office, 2019). Then, it was transferred to the statistical package for social sciences (SPSS) for Windows, version 20 (IBM®, Armonk, USA). Arithmetic means, and standard deviations (SD) were used as primary values of continuous, normally distributed data. Otherwise, relative frequencies and percentages were used to express qualitative data. The independent sample's student test was used to compare two means, and Chi-Square was used to calculate associations between categorical parameters. Risk estimate was determined by calculation of odds ratios. P value < 0.05 was considered significant from the statistical point of view.

Results

Both groups (sevoflurane and propofol) were comparable (showed non-significant differences) regarding patient demographics, ASA physical status, pre-operative pain, and comorbid conditions. The majority of patients were in their seventies, with increased males in sevoflurane and females in the propofol group. No one was obese in the current work. However, overweight was reported. The commonest ASA class was class–II, and the most common comorbid condition was hypertension, followed by cardiovascular events and diabetes mellitus (Table 1).

The operative data revealed that abdominal injury was the commonest, followed by orthopedic and final spinal surgeries. The mean duration of surgery was around 200 minutes, and the bispectral index was above 40. The mean estimated blood loss increased by 500 ml and infused fluids

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Table 1. Patient demographics and preoperative data among study groups

Variable		Sevoflurane (n=100)	Propofol (n=100)	Test	*P*
Age (years)		70.29±2.94	70.24±2.71	0.13	0.902
Gender	Male	47	42	0.51	0.484
(n)	Female	43	48		
BMI (kg/m^2)		26.12±1.27	26.21±1.26	0.48	0.632
ASA	I	28	24	0.42	0.811
	II	58	61		
	III	14	15		
Smoking (n)		33	25	1.55	0.212
Comorbidities	Hypertension	53	45	1.28	0.261
(n)	DM	24	21	0.26	0.613
	Cerebrovascular	9	7	0.27	0.603
	Cardiovascular	27	22	0.68	0.414
Preoperative NRS		3.78±0.96	3.59±0.82	1.51	0.132

Table 2. Operative data among study groups

Variable		Sevoflurane (n=100)	Propofol (n=100)	Test	*P*
Surgery	Spinal	30	28	0.82	0.673
	Orthopedics	31	37		
	Abdominal	39	35		
Duration of surgery (minute)		194.91±45.41	206.53±45.75	1.80	0.073
Anesthesia duration (minute)		249.91±45.41	264.60±45.78	2.28	0.0241*
Bispectral index		42.48±2.38	42.22±2.16	0.81	0.424
Estimated blood loss (ml)		643.50±106.76	661.50±112.78	1.16	0.253
Infused fluids (ml)		2100.00±402.02	2075.00±416.67	0.43	0.671
Perioperative transfusion		13	19	1.34	0.252

above 2000 ml. Thirty patients in sevoflurane and 19 patients in the propofol group needed perioperative blood transfusion, with no significant difference between groups. However, the duration of anesthesia was significantly shorter in sevoflurane than in the propofol group (249.91±45.41 vs 264.60± 45.78 minutes, respectively) (Table 2).

The incidence of PO delirium was reported in 14% and 30% in the sevoflurane and propofol groups, respectively, with a significant increase in the propofol group. Otherwise, there were no significant differences between groups regarding postoperative pain, the need for opioids, and postoperative complications. The commonest complications were respiratory, followed by wound infection and AKI (Table 3).

The significant associations for the development of delirium included ASA class, diabetes mellitus, and type of anesthesia, where patients who developed delirium were of higher ASA class (Class III, was reported in 34.1% vs. 9.1%), increased diabetes (65.9% vs. 10.3%) and propofol anesthesia (62.8% and 44.9%) in those developed delirium than those without delirium respectively (Table 4).

Running multiple logistic regression analyses for significant association, diabetes, ASA-III class, and propofol anesthesia remain significant predictors for the development of POD (Table 5).

Discussion

Different anesthetic substances usually target the inhibitory gamma-aminobutyric acid type-A receptors (19). However, the exact mechanism of action of sevoflurane and propofol (for example) has not been clearly identified. Thus, their pathophysiology in the development and incidence of POD is widely different and controversial (20, 21). Thus, it is of crucial importance to explore the incidence of POD and its associated factors among different ethnic groups.

Table 3. Postoperative data among study groups

Variable		Sevoflurane (n=100)	Propofol (n=100)	Test	*P*
PO delirium		14	30	7.45	0.006*
Postoperative NRS		4.09±1.27	4.28±1.14	1.11	0.273
Postoperative opioids		48	43	0.50	0.483
Postoperative hospital stay (days)		11.30±3.49	12.04±3.14	1.58	0.124
Postoperative	None	74	73	3.81	0.582
complications	Cardiovascular	0	3		
	Respiratory	11	10		
	DVT	4	2		
	AKI	5	6		
	Wound infection	6	6		

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Table 4. Associations between delirium and studied variables

Variable		Delirium (44)	No delirium (156)	Test	*P*
Age		70.86±3.13	70.09±2.72	1.60	0.111
BMI		25.99±1.39	26.20±1.22	0.98	0.328
Duration of surgery (min)		195.72±44.94	202.12±46.13	0.82	0.415
Anesthesia duration (min)		254.88±45.28	257.92±46.40	0.38	0.700
BIS		42.40±2.17	42.33±2.30	0.19	0.846
Estimated blood loss (ml)		645.45±108.80	654.48±110.47	0.48	0.631
Infused fluids (ml)		2034.09±423.13	2102.56±404.48	0.98	0.327
Preoperative NRS		3.75±1.01	3.67±0.86	0.54	0.586
Postoperative NRS		4.34±1.31	4.14±1.77	0.97	0.333
Duration of hospital stay		11.11±2.92	11.83±3.42	1.25	0.210
Age group	>=70	17(38.6%)	76(48.7%)	1.40	0.233
Gender	Male	18(40.9%)	71(45.5%)	0.29	0.582
ASA-Class	I	10(22.7%)	42(26.9%)	17.68	<0.001*
	II	19(43.2%)	100(64.1%)		
	III	15(34.1%)	14(9.0%)		
Smoking		14(31.8%)	44(28.2%)	0.21	0.642
Comorbidities	Hypertension	24(54.5%)	74(47.4%)	0.69	0.401
	Diabetes	29(65.9%)	16(10.3%)	60.95	<0.001*
	Cerebrovascular disease	3(6.8%)	13(8.3%)	0.11	0.742
	Cardiovascular	14(31.8%)	35(22.4%)	1.63	0.203
IOP transfusion		8(18.2%)	24(15.4%)	0.20	0.652
Type of surgery	Spinal	10(22.7%)	48(30.8%)	5.07	0.412
	Orthopedic	16(36.4%)	52(33.3%)		
	Abdominal	18(40.9%)	56(35.9%)		
Anesthesia	Sevoflurane	14(31.8%)	86(55.1%)	7.45	0.006*
	Propofol	30(68.2%)	70(44.9%)		

Table 5. Risk estimate by multiple logistic regression among study groups

	Estimate (odds)	95% CI	*P* value
Diabetes	6.42	3.85-10.70	<0.001*
ASA-III	3.79	1.98-7.25	<0.001*
Propofol /Sevoflurane	1.52	1.16-1.98	0.006*

The current work is designed as a retrospective one to estimate the incidence of POD after anesthesia using inhalation (sevoflurane) or total intravenous (propofol) agents. Results showed that the total incidence of POD was 22% (44 out of 200 subjects). It was significantly increased in propofol than sevoflurane anesthesia (30% vs 14%). The duration of anesthesia was significantly shorter with sevoflurane than with propofol. The development of POD was significantly associated with higher ASA-class (III vs. I and II), the presence of diabetes, and the anesthetic agent. These variables remain significantly associated with the development of POD in multivariate regression.

The overall reported incidence of POD is higher than that reported in the study of Chang et al. (13), who reported an incidence of 10.3% and within the overall reported POD incidence (between 4 and 41%) reported in others (3, 4). However, our results are in contradiction to those reported by Chang et al. (13), who reported that POD was lower with propofol than sevoflurane (5% vs 15.7%). In addition, it is different from Ishii et al. (20), who reported that the incidence was lower with propofol than sevoflurane (6.9% vs 26.7%, respectively) after gastrointestinal surgery. In addition, Nishikawa et al. (22) reported a non-significant difference among the elderly after laparoscopic surgery. Mei X, et al. (21) also reported a non-significant difference between propofol and sevoflurane-based anesthesia regarding the development of POD. However, the days with delirium were longer with Propofol than sevoflurane.

Different researchers reported that POD is associated with different factors (e.g., patient age, ASA physical status, diabetes mellitus, intraoperative blood loss and transfusion, electrolyte disturbances, perioperative pain, and surgery duration) (3, 23, 24). The current work was able to detect three associated factors (ASA, diabetes, and the type of anesthetic agent). Thus, it is partially consistent with previous studies.

Although the exact mechanism linking POD to sevoflurane and propofol is poorly understood, it was reported that sevoflurane protects the brain from ischemic injury (14, 15), while propofol had neurotoxic effects on the brain (25, 26).

Mei X, et al. (21) reported that POD incidence is 33% with propofol and 23.3% with sevoflurane. However, the difference did not reach a statistically significant difference. However, the days of delirium/patient were significantly longer with propofol than sevoflurane, as noted above.

The lower incidence of POD with sevoflurane than propofol in the current work was not completely understood. However, many factors may play a role. For example, the use of premedication and its interaction with sevoflurane or propofol, the type and duration of surgery, which may increase the risk of stress and associated chemical response and mediators. In addition, the screening tool used to elucidate POD and the time of diagnosis may be associated factors (27, 28).

The use of midazolam as a premedication may be responsible for the increased incidence of delirium with propofol than sevoflurane.

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Kim et al. (29) reported that midazolam had no effect on POD with propofol anesthesia but reduced POD incidence of patients undergoing dental surgery under sevoflurane anesthesia (30). This hypothesis needs further validation in future studies. However, the higher incidence of POD after sevoflurane than propofol reported in the study of Chang et al. (13) may support this hypothesis, as they did not use midazolam as premedication. In addition, the longer duration of propofol clearance when compared to sevoflurane may be responsible for the increased incidence of POD after propofol anesthesia (31, 32). This, with the action of midazolam premedication, may partially explain the higher incidence of POD after propofol than sevoflurane observed in the current work and in the work of Mei X, et al. (21)

Limitations

The current work had some limitations, including its retrospective nature and small sample size. Thus, results need future validation. However, the study explored the POD incidence among Egyptians after different surgeries, which represents a strength point of the current study.

Conclusion

In conclusion, the current work revealed a higher incidence of POD after propofol than sevoflurane anesthesia. It is associated with ASA physical status, diabetes, and the type of anesthetic agent used.

Authors' Contributions

Authors contributed equally in this work.

Ethical Considerations

No applicable.

Acknowledgment

Not applicabale.

Conflict of Interests

The authors declare that they have no competing interests.

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