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Effect of Propofol and Isoflurane on Postoperative Cognitive Dysfunction Following Elective Laminectomy Surgery in Adult Elderly Patients: A Randomized Controlled Trial Study

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Abstract

Background: Postoperative cognitive dysfunction (POCD) is a significant complication, especially prevalent among elderly individuals following major surgical procedures.

Objectives: This study aims to compare the impact of isoflurane and propofol on the occurrence of POCD in patients undergoing elective laminectomy surgery under general anesthesia.

Methods: This randomized, double-blind clinical trial took place at Shariati Hospital in Tehran. Patients scheduled for elective laminectomy between December 2020 and November 2021 were enrolled in the study and randomized into 2 groups. Patients in Group P received a Propofol infusion, while patients in Group I were administered isoflurane. Cognitive function assessments were conducted using the Mini-Mental State Examination (MMSE) at 3-time points: Twelve hours before surgery and 6 and 24 hours after surgery.

Results: The MMSE scores demonstrated a significant increase in the Propofol group compared to the Isoflurane group at the 6-hour and 24-hour post-surgery time points. However, no significant difference was observed at baseline before surgery ($P = 0.04$, $P = 0.005$, and $P = 0.2$, respectively).

Conclusions: These findings suggest that the use of propofol for general anesthesia may be a favorable choice for surgical procedures in elderly patients.

Keywords: Isoflurane, Propofpl, POCD

1. Background

Postoperative cognitive dysfunction (POCD) has garnered substantial attention in recent years as a significant complication arising from major surgery. Its consequences encompass escalated medical care expenses, heightened morbidity and mortality rates, as well as profound alterations in an individual's quality of life and work capacity (1, 2).

Elderly patients, in particular, are susceptible to experiencing cognitive decline following surgery, with some still exhibiting impaired cognitive function at least one year post-noncardiac surgical procedure. Nonetheless, certain healthcare professionals have questioned the significance of POCD due to its elusive nature and uncertain long-term effects (3, 4).

Recent studies have revealed that approximately 40% of individuals aged 60 and above, hospitalized for surgical interventions, manifest POCD upon discharge, and around 10% continue to exhibit POCD three months after the procedure (5).

The administration of anesthetics can contribute to the development of POCD by affecting various types of receptors in the brain (6). POCD is frequently a subtle change but may leave patients less able to live independently and at their expected quality of life. The current understanding of the pathophysiology of POCD is thought to be cholinergic dysfunction in response to neuroinflammation and synaptic impairment. It may be caused by the body's inflammatory response to surgery, stress hormone release during surgery, ischemia, or hypoxemia (3, 5, 6). This raises concerns regarding

the use of isoflurane and propofol, which are commonly employed for maintaining general anesthesia.

2. Objectives

The current study aims to compare the impact of isoflurane and propofol on the occurrence of POCD in patients undergoing elective laminectomy surgery under general anesthesia.

3. Methods

This study was designed as a prospective, randomized, double-blind clinical trial conducted at Shariati Hospital in Tehran. All patients enrolled in this study between December 2020 and November 2021 were scheduled for elective laminectomy surgery and provided written consent to participate. The study adhered to the principles of the Declaration of Helsinki and followed good clinical practices in accordance with the International Conference on Harmonization guidelines. Ethical approval for the study was obtained from the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.NI.REC.1400.056). Clinical trial registration code is IRCT20211023052849N3.

Inclusion criteria encompassed patients aged 18 to 70 years with an American Society of Anesthesiologists score of I-III, possessing adequate cognitive abilities to complete the required tests, and being candidates for elective non-emergent/urgent laminectomy surgery.

Exclusion criteria included a history of psychotropic drug usage, previous diagnoses of dementia or schizophrenia, known mental dysfunction, recent cerebral surgery or cerebrovascular events, chronic alcohol or opioid dependency, advanced renal or liver failure, and advanced atrioventricular conduction abnormalities.

After carefully matching patients based on age, gender, and underlying medical conditions, patients were randomized using 4-block methods into 2 groups. Patient monitoring in charge, data collectors, and statistical analysis were blind to this study's aims. Group P received a Propofol infusion, while Group I received isoflurane. Prior to commencing anesthesia and upon the patient's arrival in the operating room, all individuals underwent standard monitoring, including electrocardiography, monitoring of oxyhemoglobin saturation (SpO_2), and non-invasive blood pressure measurement. Furthermore, all patients received crystalloid fluid in accordance with their physiological requirements. A single anesthesiologist oversaw the administration of anesthesia, and patients were preoxygenated with 100% oxygen for 3 minutes.

After administering premedication with Midazolam and Fentanyl, anesthesia induction was accomplished using Sodium Thiopental (3 mg/kg) and Atracurium (0.3 mg/kg). Following intubation, patients in Group P received a Propofol infusion (50 - 150 mcg/kg/min), while patients in Group I were administered isoflurane (1 - 1.5 minimum alveolar concentration [MAC]). Fentanyl (50 mcg) was administered to all patients at 30-minute intervals.

The depth of anesthesia was continuously monitored using the BIS (Bispectral Index). The concentrations of propofol and isoflurane were adjusted to maintain BIS levels within the range of 40 - 60. Post-intubation, ventilation parameters were set as follows: tidal volume of 8 mL/kg, respiratory rate of 10 - 12/min, the fraction of inspiratory oxygen between 50 - 80%, and adjustment of end-tidal CO_2 partial pressure to 40 - 50 mmHg.

Anesthetic agents were gradually reduced toward the end of surgery, and neuromuscular blockade was reversed using neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg). Extubation was performed once the BIS reading exceeded 80, and spontaneous breathing was observed.

Following surgery, all patients were transferred to the post-anesthesia care unit and closely monitored. If patients were able to maintain SpO_2 levels above 96% in room air and displayed stable hemodynamics, they were discharged from the post-anesthesia care unit to the ward.

Cognitive function assessments were conducted using the Mini-Mental State Examination (MMSE) at 3-time points: Twelve hours prior to surgery and then at 6 and 24 hours post-surgery, respectively. These tests were conducted between 10 AM to 2 PM and 4 PM to 8 PM, with a trained individual administering the MMSE under the supervision of a psychologist. The MMSE validation and ability to compare the results is proved on different studies (7, 8).

4. Results

A total of 160 patients initially participated in the study, with 30 patients subsequently excluded based on the predefined exclusion criteria. This resulted in a final study cohort of 130 patients, equally divided into 2 groups, each comprising 65 patients.

The mean age of patients in the Propofol group was 62 ± 3.2 years, while in the Isoflurane group, it was 61 ± 2.5 years (P = 0.08). Gender distribution indicated that 40% of the Propofol group and 49% of the Isoflurane group were male (P = 0.1). Notably, there were no significant differences in baseline demographic characteristics observed between the two groups.

The timing of data collection did not yield any significant impact on the study results, as evidenced by a lack of significance (P = 0.3).

As shown in Table 1, the Mini-Mental State Examination scores demonstrated a significant increase in the Propofol group compared to the Isoflurane group at the 6-hour and 24-hour post-surgery intervals, although no significant difference was observed at the baseline assessment before surgery.

Table 1. Preoperative and Postoperative Mini-Mental State Examination Scores

Pocd Groups	Preoperative	6 Hours After Surgery	24 Hours After Surgery
Isoflurane	27.38 ± 3.4	24.76 ± 5.7	25.89 ± 4.9
Propofol	28.89 ± 2.7	27.81 ± 4.6	28.26 ± 3.9
P-value	0.2	0.04	0.005

5. Discussion

POCD is a common complication observed in patients undergoing anesthesia and surgery, presenting challenges to anesthesiologists specializing in perioperative medicine. This study revealed a noteworthy reduction in POCD incidence at both 6 and 24 hours post-surgery in patients who received isoflurane during elective laminectomy, as compared to those who were administered propofol. Furthermore, it was observed that the incidence of POCD significantly decreased in patients receiving propofol compared to those receiving isoflurane for anesthesia maintenance at the same time intervals.

Consistent findings in our study align with certain prior investigations. For instance, a study conducted in China reported that propofol anesthesia was linked to a lower incidence of early POCD in adult patients when compared to inhalation anesthesia (9). Another study demonstrated a significant reduction in postoperative cognitive dysfunction among patients who received propofol in contrast to those administered isoflurane, with the lowest occurrence observed in the sevoflurane group (10). Some studies have postulated that the antioxidant properties of propofol may contribute to improved cognitive status relative to volatile anesthetics like isoflurane or sevoflurane (11). Furthermore, propofol has been noted for its neuroprotective effects without compromising blood supply to affected regions, a characteristic that sets it apart from isoflurane.

However, it is worth noting that certain studies have produced conflicting results. In a study by Schoen et al. (12), patients maintained on volatile anesthetics exhibited better postoperative cognitive status than those receiving propofol.

The Mini-Mental State Examination can serve as a valuable tool in routine clinical practice to identify preoperative and subclinical dementia, which places patients at a higher risk for developing POCD (13, 14). Additionally, assessing anxiety and depression, which can also influence cognitive performance, should be considered, though this practice is not currently widespread. To date, no definitive evidence supports the hypothesis that anesthesia itself leads to prolonged POCD (15). Instead, POCD due to anesthesia may arise from direct toxic effects, systemic inflammatory responses secondary to surgical trauma, age-related suppression of neuronal stem cell function, and the acceleration of ongoing endogenous neurodegenerative processes (16, 17).

A study parallel to ours that presents particular challenges is Millar et al. (18) study on pediatrics. In this study, cognitive impairment and recovery in children after general anesthesia with propofol and isoflurane were assessed. Their findings indicated impairment of visual memory to an equivalent degree by both propofol and isoflurane. However, they observed selective impairment of verbal memory due to propofol. While both propofol and isoflurane exhibited a marginal decline in immediate verbal recall during the predischarge period, propofol demonstrated selective impairment under delayed recall conditions (19). This suggests that material encoded under propofol may become relatively less accessible when recall is delayed, potentially affecting long-term memory retention. Further evaluation is necessary to fully understand the implications of these findings beyond the assessed periods.

In conclusion, the incidence of POCD was significantly reduced in the postoperative period at 6 and 24 hours after surgery in adult elderly patients undergoing elective laminectomy administered propofol compared to patients administered inhaled volatile isoflurane anesthetic. These data suggest that general anesthesia with propofol could be a proper option for surgery in elderly patients. It should be mentioned that although a significant difference in MMSE between the Propofol and Isoflurane groups is reported in the 6th and 24th hour after awakening from anesthesia, the clinical difference may not be meaningful as in both groups, the average MMSE score is more than 21/30 which represents normal or mild cognitive impairment.

These data are in accordance with those from a previous study but require further investigation due to the small sample size. Furthermore, monitoring the long-term outcome of patients can determine the

long-term prognosis of patients anesthetized with propofol and volatile anesthetics.

Due to limitations for long-term post-surgical follow-up, the research team could collect data from patients during hospital admission. Many patients are referred to this center from different parts of the country, so it is not easy to conduct regular follow-ups as some of them never come back to this center again. On the other hand, checking mental and cognitive state could not be made by phone calls or available remote methods, and these problems were the most remarkable challenge and limitation of the study.

Footnotes

Authors' Contribution: Arash Heroabadi developed the original idea and the protocol, abstracted and analyzed data, wrote the manuscript, and is a guarantor. Shirin Motaghian, Keyvan Teymourei Khanesari, Reza Atef Yekta, Khalil Pestei and Mojtaba Marashi contributed to the development of the protocol, abstracted data, and prepared the manuscript.

Clinical Trial Registration Code: Code: IRCT20211023052849N3.

Conflict of Interests: Authors have no conflicts of interest to declare.

Data Reproducibility: The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to study restrictions.

Ethical Approval: This study was approved by the ethics committee of the Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.NI.REC.1400.056).

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Informed Consent: All patients enrolled in this study between December 2020 and November 2021 were scheduled for elective laminectomy surgery and provided written consent to participate.

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