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Original contribution

Effect of propofol, sevoflurane, and isoflurane on postoperative cognitive dysfunction following laparoscopic cholecystectomy in elderly patients: A randomized controlled trial

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ABSTRACT

Study objective: To compare the incidence of postoperative cognitive dysfunction (POCD) in elderly surgical patients (>60 years) receiving different anesthetics (propofol, sevoflurane, or isoflurane) and to identify potential biomarkers of POCD in this patient population.
Design: Prospective, randomized, double-blind clinical trial.
Setting: University-affiliated teaching hospital.
Patients: One hundred and fifty elderly patients scheduled for laparoscopic cholecystectomy.
Interventions: Elderly patients undergoing laparoscopic cholecystectomy were randomly assigned to receive propofol, sevoflurane, or isoflurane anesthesia. Measurements: Cognitive function was assessed using neuropsychological tests at baseline (1 day before surgery [D0]), and on postoperative day 1 (D1) and day 3 (D3). Plasma S-100β and $A\beta_{1-40}$ protein, IL-1β, IL-6 and TNF-α concentrations were assessed before induction of anesthesia (T0), after extubation (T1), and 1 h (T2) and 24 h (T3) postoperatively.
Main results: The incidence of POCD was significantly lower in the propofol group compared to the isoflurane group and the sevoflurane group at D1 and D3 (propofol vs. isoflurane: D1 and D3, $P < 0.001$; propofol vs. sevoflurane: D1, $P = 0.012$; D3, $P = 0.013$). The incidence of POCD was significantly lower in the sevoflurane group compared to the isoflurane group at D1 ($P = 0.041$), but not at D3. Postoperatively, plasma S-100β and $A\beta_{1-40}$ protein, IL-1β, IL-6, and TNF-α concentrations were significantly decreased in the propofol group compared to the isoflurane group.
Conclusions: Propofol anesthesia may be an option for elderly surgical patients.

1. Introduction

Postoperative cognitive dysfunction (POCD) affects 15–25% of surgical patients, the majority of whom are elderly. POCD causes substantial morbidity and mortality. Patients affected by POCD experience impairments in recent memory, concentration, language comprehension, and social integration [1]. Morbidity associated with POCD is most severe in patients >60 years of age [2,3]. The 5-year mortality rate due to POCD is estimated to be 70% [4]. POCD results in a substantial health care burden, including a prolonged length of hospital stay and increased health care costs [5].

The occurrence of POCD has been related to surgical trauma and general anesthetics [6,7]. Surgical procedures may activate nuclear factor (NF)-κB and the release of cytokines, which impair the integrity of the blood–brain barrier. Anesthetics may have detrimental effects on cognitive function through the cholinergic system, including the nicotinic acetylcholine receptors M1 and M3, which play an important role in cognitive tasks, learning, and memory [7–10].

Several studies suggest that intravenous and inhaled anesthetics are neuroprotective in cerebral injury [11–17]. Evidence indicating that anesthetic exposure impairs neurocognitive performance in older individuals is controversial [18–23]. However, such information is necessary to guide clinical anesthesia, increase safety, and improve outcomes in elderly surgical patients. Propofol, isoflurane, and sevoflurane are commonly used in clinical anesthesia. In a previous report, Qiao and colleagues found that inhaled anesthetics aggravated POCD compared to propofol in elderly patients that underwent resection of esophageal carcinoma [24]. This study was based on patients undergoing long duration surgeries during which the target concentrations of propofol and sevoflurane were not constant. Furthermore, isoflurane was not included in the study, even though isoflurane is commonly used in the clinic.

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Currently, the comparative effect of propofol, isoflurane, and sevoflurane on postoperative cognitive function in elderly patients undergoing short duration surgeries is unknown. We hypothesized that propofol may provide better neurological and physiological outcomes than constant levels of inhaled anesthetics in this patient population. The objectives of this randomized clinical trial were to compare the incidence of POCD in elderly surgical patients receiving different anesthetics and to identify potential biomarkers of POCD in this patient population.

2. Materials and methods

2.1. Study population

Patients scheduled for laparoscopic cholecystectomy between December 2010 and June 2011 were enrolled in this prospective, randomized, double-blind clinical trial (ChiCTR-OCC-11001411). Anesthesia on all patients was performed by one anesthesiologist, and a second anesthesiologist, who was blinded to the randomization, evaluated patients' cognitive scores and collected peripheral blood. A third anesthesiologist allocated included patients to 3 groups according to a computer-generated random number table.

Inclusion criteria were: patients with American Society of Anesthesiologists score of II–III, age ≥ 65 years, and a sufficient level of education to be capable of completing neuropsychological tests. Exclusion criteria were: a history of allergy to anesthetics; dialysis-dependent renal failure; liver transaminase level < 1.5 times the normal value; Mini-Mental State Examination score ≤ 26; preexisting diagnosis of schizophrenia or dementia; recent stroke; known disorder affecting cognition; mental dysfunction; history of cerebral surgery; severe anxiety; recent history of alcohol abuse; or history of chronic opioid or other

Table 1
Baseline demographic and clinical characteristics ($n = 50$ patients in each group).

	Isoflurane	Propofol	Sevoflurane	*P* value
Male *n* (%)	18 (36%)	20 (40%)	22 (44%)	0.41
Body mass index	23.97 ± 2.10	24.37 ± 2.34	24.06 ± 2.23	0.87
Education *n* (%)				
No education	6 (12)	5 (10)	5 (10)	0.86
Elementary school	8 (16)	7 (14)	6 (16)	0.94
Junior school	20 (40)	22 (44)	21 (40)	0.92
High school	12 (24)	11 (22)	15 (26)	0.63
University	4 (8)	5 (10)	3(10)	0.76
Smoking, *n* (%)	18 (36)	15 (30)	14 (28)	0.66
Alcohol, *n* (%)	10 (20)	8 (16)	11 (22)	0.74
American Society of Anesthesiologists score, *n* (%)				0.70
II	33 (66)	35 (70)	31 (62)	
III	17 (34)	15 (30)	19 (38)	
Comorbidities				
Hypertension, *n* (%)	11(22)	12 (24)	14 (28)	0.77
Coronary arterial disease, *n* (%)	8 (16)	9 (18)	12 (24)	0.57
Diabetes *n* (%)	7 (14)	5 (10)	8 (16)	0.67

The data were presented with number (%) and mean ± SD.

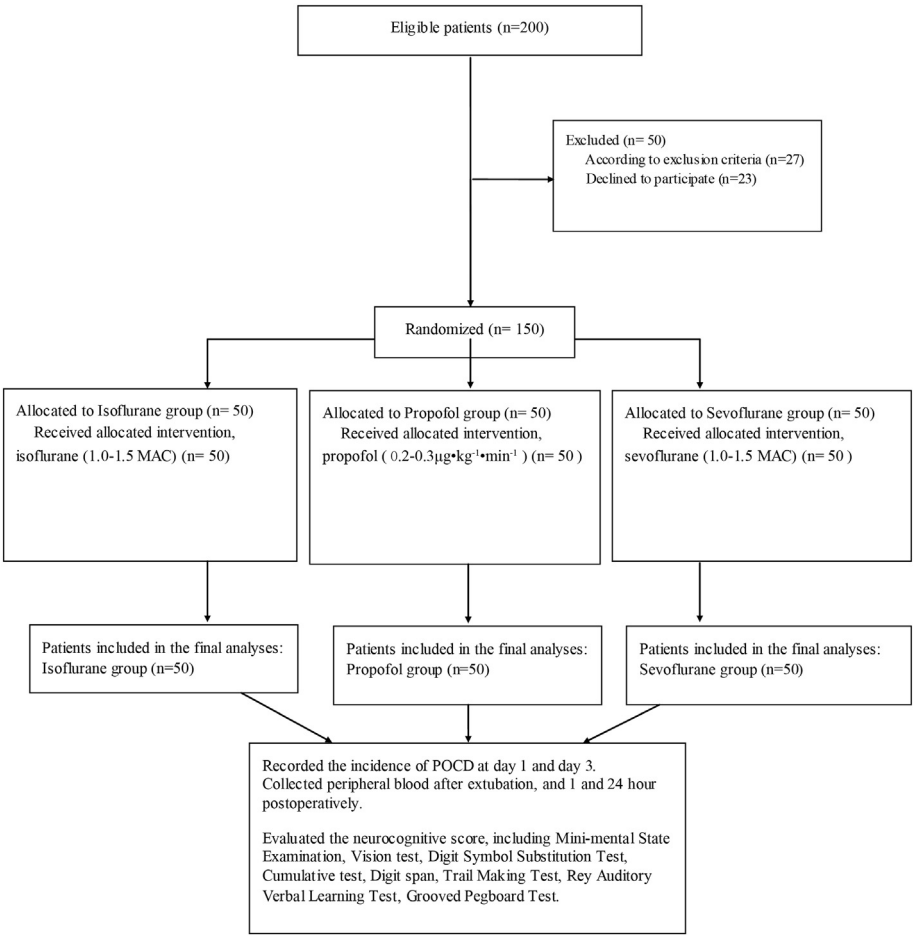

Fig. 1. Flow diagram of enrolled patients.