

The Effect of Propofol and Gas Anesthesia on Postoperative Cognitive Dysfunction in Elderly Patients

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ABSTRACT

Objective: The study aimed to investigate the effect of propofol and gas anesthesia (xenon, sevoflurane, isoflurane) on the incidence of postoperative cognitive dysfunction in elderly patients. **Methods:** The literature about the comparing of the effect of propofol and inhalation anesthesia on the incidence of early postoperative cognitive dysfunction were collected by searching the Pubmed, Cochrane library, CBM, CNKI, wanfang data and vip database within October 2012. The literature were carefully browsed and data were quality extracted, evaluated. Then all the data were assessed by Stata 12.0 program. **Results:** There were 753 cases of patients and 13 randomized controlled trials including 2 of comparing propofol with xenon, 7 of comparing propofol with sevoflurane and 4 of comparing propofol with isoflurane. The ratio of the incidence of postoperative cognitive dysfunction between patients with propofol anesthesia and those with xenon anesthesia, sevoflurane anesthesia and isoflurane anesthesia were 1.62 (95% CI 0.81-3.23, $p=0.533$), 0.67 (95% CI 0.39-1.14, $p=0.833$) and 0.20 (95% CI 0.08-0.50, $p=0.925$) respectively. In conclusion, the ratio of the incidence of early POCD was 0.68 (95% CI 0.47-0.98, $p=0.189$) for propofol anesthesia compared with inhalation anesthesia. The Egger's test showed that there was a publication bias ($p=0.011$). **Conclusion:** Compared with inhalation anesthesia, propofol anesthesia had lower incidence of early POCD in elderly patients, but the conclusion needs to be further verified by well-designed large-scale experiments.

Keywords: Anesthesia, Propofol, Gas anesthesia, Postoperative cognitive dysfunction, Incidence rate, Meta-analysis

INTRODUCTION*

Postoperative cognitive dysfunction is a common neurological complication in older patients, which is often expressed as the change of mental activity, social activity and cognitive ability [1]. It includes memory barrier, directional obstacle, language barrier, and the decrease of computational power [2]. This complication not only affects the patient's self-management ability, but also makes a great burden on family and society. In recent years, with the development of our country

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into the aging society, there was a growing number of elderly patients receiving surgery. Therefore, POCD is also getting more and more important. There was study reported that the incidence rate of POCD for elderly patients up to 25.8%. Study also showed that the incidence of POCD was associated with anesthesia, age, surgical method, and the use of anti-cholinergic drugs [3]. Mason's study showed the general anesthesia was more easily to result in POCD than the non-general anesthesia. However, the clinical trial about the effect of general anesthesia and the gas general anesthesia on the incidence of POCD was coincident. So,

in this study, we aimed to clarify the effect of propofol and gas anesthesia (xenon, sevofurane, isoflurane) on the incidence of postoperative cognitive dysfunction in elderly patients.

MATERIALS AND METHODS

Standards

Study type

The randomized controlled trials include comparing the effects of propofol and gas anesthesia (atmosphere, sevofurane, isoflurane) on the incidence of early postoperative cognitive dysfunction in elderly patients undergoing non-cardiac surgeries.

Research object

Requirement: First: age>60 Second, the patients had no heart, lung and kidney disease, endocrine disease, and neurological history of mental illness; Third, the patients occurred POCD within 7d after accepting surgeries . Exclusion condition:(1) The maintenance of mixed general anesthesia during operation;(2) Heart surgery (3) Neurosurgery operation

Intervention study

Treatment group: Intravenous anesthesia of propofol Control group: gas anesthesia (atmosphere, sevofurane, isoflurane)

Detection index

The incidence rate of early POCD

Search methods

Pubmed, Cochrane library, CBM, CNKI, wanfang data and vip database within October 2012 were searched. The english search terms include propofol, postoperat, anaesth, neurocogniti, cogniti, neuropsychology, neurobehaviour, decline, dysfunction, impairment, disorder, deficit, effect, outcome, function. The chinese search terms include propofol, phenol, and post cognition. There were no time and language restrictions, but the restricted document type is "randomized controlled trials". The retrieved references which met the criteria were studied.

Data extraction and quality evaluation

Data extraction and quality evaluation were performed for the obtained literature by two reviewers independently. In case of a different opinion, the third person was invited to assess the results. Data extraction:(1) The general information, such as the first author and published years; (2) Research Methods, such as random, blind method; (3) The general information of the research object, such as age, gender, grade, etc; (4) The processing of research object, including specific methods of anesthesia, drug dosage, etc;(5) The research results: the evaluation method and results (four grid data) of the study etc.

Quality evaluation: According to modified Mason method-Jadad method to evaluate the study (1): Random, random allocation or similar words are used in this study. +1 represents the method is sufficient, such as the generation of random number; -1 represents the method is not sufficient, such as the date of surgery(2) blind method: +1 represents the assessors are blind, -1 represents the assessors are not blind(3) the accuracy of the results: +1 represents the objective measurement method has been mentioned, -1 represents measurement method is not sufficient and could not be replicated(4) The equivalence of treatment for each group: +1 represents the clinical characteristics are detail and there were no significant difference between each group, -1 represents the characteristics of cases were not mentioned. Taking 3 points as the boundary, if the value >3, it is considered as the high quality literature. In contrast, it is considered to low quality literature.

Statistical analysis

All data were assessed by Stata 12.0 program. The data were analyzed by sub group analysis, and the homogeneity of $p>0.1$ was analyzed. If there is no heterogeneity, the fixed effects model is used, and the random effects model is adopted for the presence of heterogeneity.

Table 1: characteristics and quality assessment of the included RCTs

Reference	Gender	Age	ASA	Induce drug	Maintenance drugs	Surgery	Detect	Score
Hocker 2009	22:79	65-83	I-III	Etomidate 0.2-0.4mg/kg	Propofol 2-4ug/kg xenon 60%	Abdominal or Urology operation	RAVLT,STROOP,TMT,Digits Pan,DSST,PBT,VFT	4
Rohan 2005	7:23	65-86	N	Propofol or Sevoflurane	Propofol or Sevoflurane	Urology or gynecological operation	MMSE, STROOP, MODIFIED WORD RECALL TEST	3
rasmussen	26:13	63-79	I-III	Propofol 2mg/kg Bupivacaine 15mg Spinal anesthesia	Propofol3-5mg/kg/h xenon 65%	Knee arthroplasty	VVL, CST, Stroop colour word interference test, LDC, number of correct answers in letter digit coding test	5
Lanyinglin 2011	N	65-75	I-II	Propofol or Sevoflurane	Propofol or Sevoflurane	Radical gastrectomy for gastric cancer	MMSE	3
Tuanxucui 2011	N	>65	N	Midazolam 3mg Fentanyl 0.1mg	Propofol50-150ug/kg/min or Sevoflurane 0.8%-2%	Femoral head replacement	MMSE	3
Rong tan 2009	N	60-81	I-II	Propofol1.5-2.0 mg/kg	Propofol 100-150 ug/kg / min Isoflurane 1%-2%	Upper abdominal operation	MMSE	1
Haixiashi 2009	16:24	65-75	I-II	Etomidate 0.25-0.3mg/kg	Propofol or Sevoflurane	Abdominal tumor operation	MMSE	1
Guohuicao 2009	N	60-81	I-II	Propofol1mg/kg	Propofol 5mg/kg/h Isoflurane 1.1%-1.7%	Upper abdominal operation	MMSE	2
You gan 2001	20:40	65-78	I-II	Propofol 3ug/kg or Sevoflurane 7%	Propofol2ug/kg or Sevoflurane 7%	Radical gastrectomy for gastric cancer	MMSE, WMS, WAIS	0
Shunvcui 2011	60:0	65-80	I-III	Propofol 1.5-2.0 mg/kg or Sevoflurane 8%	Propofol6-10mg/kg/hor Sevoflurane	Improved breast cancer	MMSE	3
Ronghui-gan 2011	29:41	>60	I-II	Etomidate 0.3mg/kg	Propofol3-6mg/kg/h or Isoflurane 1-2MAC	Abdominal surgery	MMSE	3
Hongye-zhang 2011	24:56	65-83	I-III	Propofol 1.5mg/kg	Propofol3-6mg/kg/min or Sevoflurane	Thoracic operation	MMSE	0
Zhiwenzeng 2011	27:33	65-87	I-II	Etomidate 0.2mg/kg	Propofol 6mg/kg/min or Isoflurane 1.5%-2.5%	Laparoscopic cholecystectomy	MMSE, WMS, WAIS	2

OR value or 95% CI was used for the evaluation of count data. Egger's test was used to detect the publication bias of the RCTs retrieved and differences were considered to be statistically significant at $p < 0.05$.

RESULTS

The characteristics and quality evaluation of the involved references

There were 309 literature involved in this study, it main included PubMed(80), Cochrane library(11), CBM(23), CNKI(101), wanfang data(73) and vip database(21). The literature was carefully browsed and data were quality extracted and evaluated. Finally, 13 randomized controlled trials were involved in this study which include 2 of comparing propofol with xenon [4], 7 of comparing propofol with sevoflurane and 4 of comparing propofol with isoflurane [5]. The characteristics and quality evaluation of the involved references were shown in table1. Among this, 7 literatures were considered of high quality and 3 were thought to be low quality.

The results of Meta-analysis

The heterogeneity results of the 13 studies showed no statistical significance ($p > 0.05$). So, the data was merged with fixed model. The results were shown in Fig.1. The Meta-analysis results showed that the ratio of the incidence of postoperative cognitive dysfunction between patients with propofol anesthesia and those with xenon anesthesia, sevoflurane anesthesia were separately 1.62(95% CI 0.81-3.23) and 0.67(95% CI 0.39-1.14) which indicated there was no significantly difference. However, the ratio between patients with propofol anesthesia and isoflurane anesthesia was 0.20(95% CI 0.08-0.50) and had significantly difference. In conclusion, the ratio of the incidence of

early POCD was 0.68(95% CI 0.47-0.98) for propofol anesthesia compared with inhalation anesthesia. Compared with inhalation anesthesia, the Egger's test (Fig 2) revealed propofol anesthesia had lower incidence of early POCD in elderly patients but there was a publication bias ($p = 0.011$).

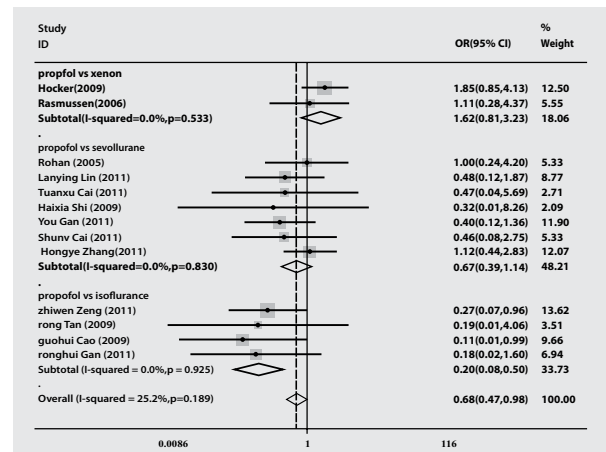


Fig 1. Comparison of the incidence of POCD between propofol and inhalation anesthesia.

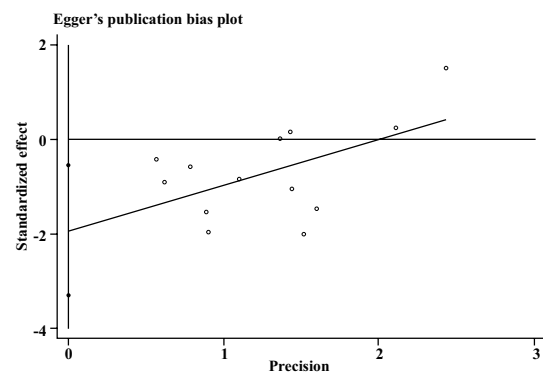


Fig. 2 The results of Egger's test

Sensitivity analysis

Changing model, removing the maximum weight and the removal of the minimum weight were used to analysis the sensitivity and results were shown in Table 2. The results showed that the OR value stand still after the modification. So, the study was stable and reliable.

Table 2 Sensitivity analysis

Method	Heterogeneity test	Effect model	OR(95% CL)
Change of effect model	P=0.189	random	0.63(0.39,1.02)
Removal of maximum weight	P=0.262	fixed	0.75(0.51,1.10)
Removal of minimum weight	P=0.149	fixed	0.69(0.48,1.00)

DISCUSSION

The incidence of early postoperative cognitive dysfunction in the elderly patients was high [6]. In this study, the total incidence rate of cognitive dysfunction in early patients undergoing noncardiac surgeries was 23.9%. The results were close to the Moller's report which revealed the incidence rate of POCD was 25.8% [7].

POCD could increase the postoperative complications, prolong the hospitalization time of the patients and increase the social medical care [8]. Therefore, the doctor should pay enough attention to the incidence of POCD. However, the pathogenesis of POCD is not clear now, it may be related to the patient's age, hand surgery and anesthesia, etc.

The mechanisms of POCD induced by general anesthetics are not clear. It might enhance the activation of GABAA receptors to activate the CL-pathway or directly activate GABAA receptors which would enhance the inhibition of the potential of the burst and antagonist the effect of NMDA (Chonchubhair and O'Keeffe, 1998). GABA and NMDA receptors are closely related to the formation of cognitive functions in learning and memory. The clinical study showed that propofol anesthesia and inhalation anesthesia could cause early postoperative cognitive dysfunction in the elderly patients after cardiac surgery, but the incidence rate of POCD was different [9].

In this paper, we compared the effect of propofol and gas anesthesia (atmosphere, sevofurane, isoflurane) on the incidence of postoperative cognitive dysfunction in elderly patients. The results showed that the ratio of the incidence

of postoperative cognitive dysfunction between patients with propofol anesthesia and those with xenon anesthesia, sevoflurane anesthesia had no significantly difference. However, propofol anesthesia had lower incidence of early POCD in elderly patients compared with isoflurane anesthesia. Acetylcholine is a neurotransmitter closely related with learning and memory [10], but isoflurane could inhibit the uptake of choline which limited the synthesis of choline. In addition, isoflurane can induce A β protein, increase the cytotoxicity and promote apoptosis of nerve cells [11]. A β is the main component of senile dementia, which can directly increase the accumulation of free radicals in the cells and damage the recognition and memory function [12]. Propofol is a high liposolubility intravenous anesthetic, it had many advantages such as rapid onset, short duration, quick and complete consciousness etc. [13]. The previous study showed that propofol had the effect of enhancing the GABA receptor function and inhibiting the long term potentiation of the synapse of the hippocampus which resulted in the influences of the learning, memory and other cognitive functions [14,15]. Propofol or gas anesthesia may cause postoperative cognitive dysfunction in the elderly, but the specific mechanism need to be further explored. The comprehensive evaluation showed that the incidence of POCD in elderly patients with propofol anesthesia was slightly lower than that of gas anesthesia, suggesting that propofol may be more suitable for the clinical use of anesthesia for elderly people. This analysis showed that there was a publication bias which may be related to the low quality of the study method and the minor sample size. Besides, because there was no

uniform definition and diagnostic criteria for current international, individual differences in the results of the evaluation and assessment scales may also be present embodiment bias and measurement bias. So, we should be careful with the result that propofol anesthesia had lower incidence of early POCD in elderly patients and more large samples and high quality randomized controlled trials need to be designed to demonstrate the results.

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