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Effects of sevoflurane inhalation anesthesia on cognitive and immune function in elderly patients after abdominal operation

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Abstract. – OBJECTIVE: To observe the effects of sevoflurane inhalation anesthesia on cognitive and immune function in elderly patients after abdominal operation.

PATIENTS AND METHODS: 371 elderly patients who were diagnosed and received abdominal operation in the General Surgery Department of Jiangxi Provincial People's Hospital from January 2015 to December 2017 were retrospectively analyzed. 203 patients undergoing sevoflurane inhalation anesthesia were regarded as the sevoflurane group, and 168 patients anesthetized with propofol were taken as the propofol group. The Mini-Mental State Examination (MMSE) scores of patients at 1 d (T1) before the operation and at 1 d (T2), 3 d (T3), and 7 d (T4) after operation were recorded, and the levels of T lymphocyte subsets [cluster of differentiation (CD)3$^+$, CD4$^+$ and CD4$^+$/CD8$^+$] and natural killer (NK) cells in the patients' serum at each time point were determined and analyzed.

RESULTS: The MMSE scores at all time points after the operation in the sevoflurane group were remarkably higher than those in the propofol group (p<0.05), displaying statistically significant differences. The MMSE scores at T2, T3, and T4 were markedly decreased compared with that at T1 in the two groups (p<0.05). The levels of CD16$^+$/CD56$^+$ at T2 and T3 in the sevoflurane group were significantly increased compared with those in the propofol group (p<0.05). Compared with that at T1, the levels of CD16$^+$/CD56$^+$ at T2, T3, and T4 in the two groups declined, showing statistically significant differences (p<0.05). Compared with those at T1, the levels of CD3$^+$, CD4$^+$ and CD4$^+$/CD8$^+$ at T2 and T3 were markedly decreased in the two groups of patients (p<0.05).

CONCLUSIONS: Applying sevoflurane as an anesthetic for abdominal operation in elderly patients is a more effective method for alleviating perioperative cognitive dysfunction and improving immune function inhibition in elderly patients, so it is worthy of clinical promotion.

Key Words
Sevoflurane, Propofol, Abdominal operation in elderly patients, Cognitive function, Immune function.

Introduction

Since a variety of organs in the body of elderly patients experience different degrees of functional deterioration, the patients' demand for surgical operation is increasing[1]. As the degenerative weakening of the central nervous system in elderly patients leads in the function decline of neurotransmitters, a potential risk of anesthesia exists in elderly patients, and they are a high-risk group of adverse anesthesia reactions[2,3]. There is a large potential for elderly patients suffering from cognitive dysfunction after general anesthesia. Cognitive dysfunction is clinically manifested as cognition, memory and expression disorders and disturbances after anesthesia, thus affecting the quality of life and prognosis of elderly patients, and even resulting in permanent cognitive dysfunction in severe cases[4]. It was found in the study of Evered et al[5] that the occurrence rate of cognitive dysfunction in elderly patients after anesthesia is significantly higher than those in young and middle-aged patients, and the recovery period of elderly patients is longer than those of young and middle-aged patients. Therefore, searching for an anesthetic with little effect on cognitive function in elderly patients after the operation is of great clinical significance.

In clinical practice, propofol is frequently applied in general anesthesia during the operation. It is a highly lipid-soluble anesthetic, with advantages such as short-acting time, strong controllability and fast metabolism[6]. However, studies[7] have reported

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that adverse reactions (such as delirium, hallucination and hypotension) and even respiratory depression will occur after operation with propofol. However, sevoflurane, as a new inhalation anesthetic, is widely used currently. It can make hemodynamics and a variety of vital signs of patients more stable. Besides, its mode of administration is inhalation anesthesia, less stimulating the patients' respiratory tract, with a lower occurrence rate of postoperative adverse reactions[8]. The immune function of elderly patients is poor and further damaged by stresses such as operation, anesthesia and pain, thus affecting their recovery. Hence, adopting reasonable and safe anesthesia methods to stabilize the patients' immune function is especially important[9]. At present, the changes in immune function in elderly patients receiving abdominal operation with propofol and sevoflurane are rarely reported. In this study, the effects of sevoflurane and propofol anesthesia during abdominal operation on cognitive and immune function in elderly patients were analyzed, thus providing reference and guidance for the application of anesthetics in clinical abdominal operation in elderly patients.

Patients and Methods

Patients

A total of 371 elderly patients who were diagnosed and received abdominal operation in the General Surgery Department of Jiangxi Provincial People's Hospital from January 2015 to December 2017 were retrospectively analyzed. 203 patients undergoing sevoflurane inhalation anesthesia were regarded as the sevoflurane group, and 168 patients anesthetized with propofol were taken as the propofol group. There were 196 males and 175 females aged 60-82, with an average age of (72.16±5.68) years old. Inclusion criteria: patients who underwent the abdominal operation in the Jiangxi Provincial People's Hospital after definite diagnosis, older than 60 years old, had complete medical records and were not treated in other hospitals. Exclusion criteria: patients who had allergic reactions to the drugs used in this study, suffered from acute alimentary tract hemorrhage or other serious diseases, had communication dysfunction or cognitive dysfunction so that the Mini-Mental State Examination (MMSE) scoring could not be completed. All subjects and their family members signed the informed consent and cooperated with medical staff to complete relevant medical treatment.

Methods

Patients were asked to undergo liquid fasting for 4 h and solid fasting for 8 h before the operation. After entering the operating room, all patients were connected to the monitor (Wuhan Kaijin Medical Technology Co., Ltd., Wuhan, China) to detect changes in the levels of Blood Pressure (BP), Heart Rate (HR), Pulse Oxygen Saturation (SPO_2) and other indicators. Before the operation, the venous access of patients were routinely opened, and the patients inhaled oxygen with a mask for 10 min, followed by anesthesia induction using 0.03 mg/kg midazolam (Zhejiang Jiuxu Pharmaceutical Co., Ltd., NMPN: H20113433, Zhejiang, China), 1.5 mg/kg propofol (Beijing Fresenius Kabi Pharmaceutical Co., Ltd., NMPN: H20060086, Beijing, China), 0.6 mg/kg rocuronium bromide (Zhejiang Xianju Pharmaceutical Co., Ltd., NMPN: H20123188, Zhejiang, China) and 0.2 μg/kg sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd., NMPN: H20050580, Sichuan, China). After the patients were out of consciousness, the trachea was inserted with the intubation tube and connected to a ventilator [Philips Medical Devices (Suzhou) Co., Ltd., Jiangsu, China] for mechanical ventilation. The patients' mask was closed, with the ventilation frequency of 12 times/min and the oxygen flow rate of 1 L/kg, and 5 μg/(kg•h) rocuronium bromide and 0.1-0.2 V remifentanil [China National Pharmaceutical Industry (Langfang) Co., Ltd., NMPN: H20123422] were used. Anesthesia was maintained using 2.5%-3.5% sevoflurane (Shandong New Time Pharmaceutical Co., Ltd., National Drug Standard: H20080680, Shandong, China) for patients in the sevoflurane group and using propofol (Fresenius Kabi AB, NMPN: J20080023, Bad Homburg, Germany) in the propofol group, and 6 mg/(kg•h) propofol was then intravenously infused.

The cognitive function of the patients in the two groups was observed at 1 d (T1) before the operation and at 1 d (T2), 3 d (T3) and 7 d (T4) after the operation and evaluated using the Mini-Mental State Examination (MMSE) scale. The full score of this scale is 30 points. The score less than 24 points represents that patients are suspected of having cognitive dysfunction, and the lower the score is, the severer the cognitive dysfunction will be. The levels of T lymphocyte subsets [cluster of differentiation $(CD)3^+$, $CD4^+$ and $CD4^+/CD8^+$] and normal killer (NK) cells ($CD16^+/CD56^+$) in peripheral blood were measured and analyzed *via* a flow cytometer (Beckman Coulter Medical Devices, UK).

Statistical Analysis

Statistical Product and Service Solutions (SPSS) 17.4 software system (Bizinsight Information Technology Co., Ltd.) was used for statistical analysis, in which basic count data of patients were expressed as a percentage [n (%)] and differences between the two groups were detected using the χ^2-test. The operation time, intraoperative blood loss, cognitive function score and the expression levels of NK cells and T lymphocyte were expressed as (x±s), and the differences between the two groups were detected using the *t*-test. Differences in the expression levels at T1-T4 in the same group were analyzed by repeated measures analysis of variance. $p<0.05$ was considered statistically significant.

Results

Comparisons of Clinical Data of Patients

To make the experimental results accurate and credible, clinical data, including age, sex, body mass index (BMI), type of operation, operation time, American Society of Anesthesiologists (ASA) grade and intraoperative blood loss were compared between the two groups of patients. The results revealed that there were no significant differences in these indicators, proving that the two groups of patients were comparable ($p>0.05$) (Table I).

Comparisons of the MMSE Scores of Patients at Different Time Points Between the Sevoflurane Group and the Propofol Group

At T1, there was no significant difference in the MMSE score between the two groups ($p>0.05$). After reviving from anesthesia with different drugs, the MMSE score at each time point in the sevoflurane group was significantly higher than that in the propofol group, showing statistically significant differences ($p<0.05$). The MMSE scores at T2, T3, and T4 notably declined in the two groups compared with that at T1 ($p<0.05$) (Table II).

Changes in NK Cells in Patients at Different Time Points Between the Sevoflurane Group and the Propofol Group

At T1 and T4, there were no significant differences in the level of $CD16^+/CD56^+$ between the sevoflurane group and the propofol group ($p>0.05$). At T2 and T3, the level of $CD16^+/CD56^+$ in the sevoflurane group was significantly increased compared with those in the propofol group ($p<0.05$). Compared with that at T1, the levels of $CD16^+/CD56^+$ at T2, T3 and T4 were decreased in the two groups, and the differences were statistically significant ($p<0.05$), but the decrease degree in the sevoflurane group was lower (Table III).

Table I. Clinical data of 371 elderly patients undergoing abdominal operation [n (%)].

	Sevoflurane group (n=203)	Propofol group (n=168)	χ^2 or t	p
BMI (kg/m^2)	24.45±2.38	23.81±4.64	1.712	0.088
Sex			0.003	0.959
Male	107 (52.71)	89 (52.98)		
Female	96 (47.29)	79 (47.02)		
Age			0.120	0.729
<75	116 (57.14)	99 (58.93)		
≥75	87 (42.86)	69 (41.07)		
Type of operation			0.442	0.674
Acute appendicitis operation	91 (44.83)	75 (44.64)		
Cholecystitis operation	57 (28.08)	42 (25.00)		
Intestinal obstruction operation	36 (17.73)	35 (20.83)		
Gastrointestinal tumor operation	19 (9.36)	16 (9.52)		
ASA grade			0.865	0.478
Grade I	117 (57.64)	97 (57.74)		
Grade II	86 (42.36)	71 (42.26)		
Operation time (min)	71.37±4.23	71.34±3.65	0.072	0.942
Intraoperative blood loss (mL)	113.94±39.16	111.83±37.41	0.527	0.598

Table II. Comparisons of cognitive function at different time points between the two groups of patients.

	Sevoflurane group (n=203)	Propofol group (n=168)	*t*	*p*
T1	28.61±1.48	28.79±1.57	1.134	0.257
T2	23.79±1.54*	21.27±1.15*	17.540	<0.001
T3	25.56±1.08*	23.13±1.72*	16.570	<0.001
T4	26.62±2.01*	23.98±1.84*	13.080	<0.001
F	337.8	681.2		
p	<0.001	<0.001		

Note: * The difference is statistically significant compared with that at T1 ($p<0.05$).

Table III. Changes in the level of $CD16^+/CD56^+$ at different time points between the two groups of patients.

	Sevoflurane group (n=203)	Propofol group (n=168)	*t*	*p*
T1	221.72±78.72	223.81±81.64	0.250	0.803
T2	115.31±77.27*	78.34±46.53*	5.438	<0.001
T3	122.67±65.51*	85.12±44.27*	6.329	<0.001
T4	202.27±79.36*	191.57±66.59*	1.238	0.166
F	105.5	241.4		
p	<0.001	<0.001		

Note: * The difference is statistically significant compared with that at T1 ($p<0.05$).

Changes in T Lymphocytes in Patients at Different Time Points Between the Sevoflurane Group and the Propofol group

At T1 and T4, no significant differences were found in the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ between the sevoflurane group and the propofol group ($p>0.05$). At T2 and T3, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the sevoflurane group were significantly higher than those in the propofol group ($p<0.05$). Compared with that at T1, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ at T2 and T3 markedly declined in the two groups ($p<0.05$), but the decreases in the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ at T4 were not statistically significant ($p>0.05$), and the decline degree in the sevoflurane group was lower (Figures 1-3).

Discussion

With the gradual development of society into an aging society, the elderly population exhibits a progressively increasing trend, and the number of elderly patients needing operation is also increasing[10]. A variety of strong stress responses can result from perioperative pain and anesthesia in the body[11]. Excessive stress responses in the perioperative period can trigger stress complications such as cardiovascular disease in elderly patients with degenerated stress abili-

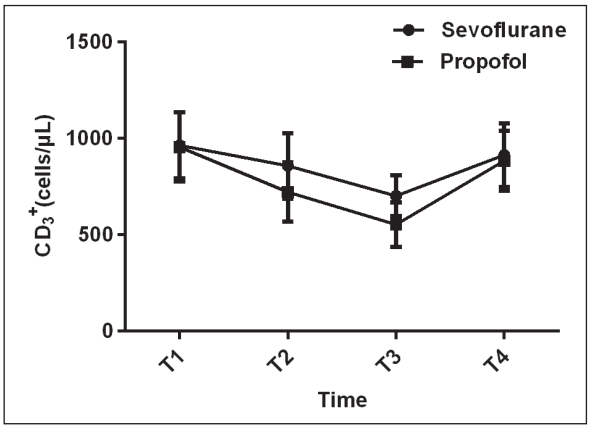

Figure 1. Changes in the level of $CD3^+$ in patients at different time points in the sevoflurane group and the propofol group. At T1 and T4, there are no significant differences in the levels of $CD3^+$ in patients between the sevoflurane group and the propofol group ($p>0.05$). At T2 and T3, the levels of $CD3^+$ in the sevoflurane group are significantly higher than those in the propofol group ($p<0.05$). Compared with that at T1, the levels of $CD3^+$ at T2 and T3 are remarkably decreased in both groups ($p<0.05$), but the decrease in the level of $CD3^+$ at T4 is not statistically significant ($p>0.05$), and the decrease degree in the sevoflurane group is lower. Note: * The difference is statistically significant compared with that at T1 ($p<0.05$).

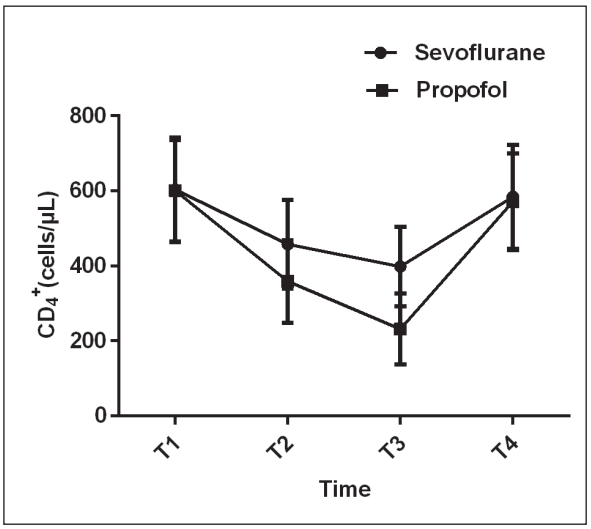

Figure 2. Changes in the level of $CD4^+$ in patients at different time points in the sevoflurane group and the propofol group. At T1 and T4, there are no significant differences in the levels of $CD4^+$ in patients between the sevoflurane group and the propofol group ($p>0.05$). At T2 and T3, the levels of $CD4^+$ in the sevoflurane group are significantly higher than those in the propofol group ($p<0.05$). Compared with that at T1, the levels of $CD4^+$ at T2 and T3 are markedly decreased in both groups ($p<0.05$), but the decrease in the level of $CD4^+$ at T4 is not statistically significant ($p>0.05$), and the decrease degree in the sevoflurane group is lower. Note: * The difference is statistically significant compared with that at T1 ($p<0.05$).

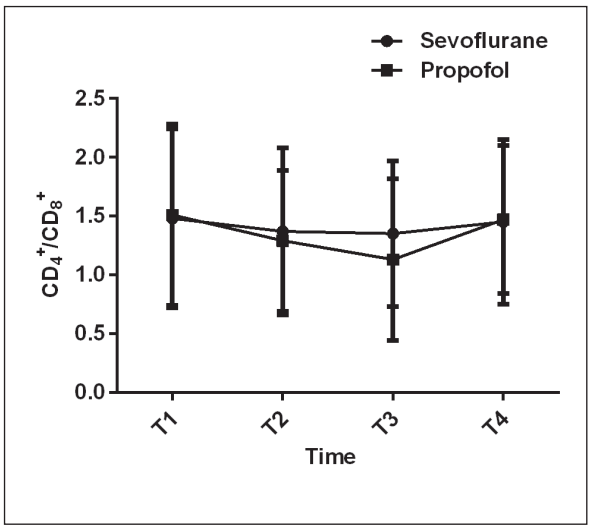

Figure 3. Changes in the level of $CD4^+/CD8^+$ in patients at different time points in the sevoflurane group and the propofol group. At T1 and T4, there are no significant differences in the levels of $CD4^+/CD8^+$ in patients between the sevoflurane group and the propofol group ($p>0.05$). At T2 and T3, the levels of $CD4^+/CD8^+$ in the sevoflurane group are significantly higher than those in the propofol group ($p<0.05$). Compared with that at T1, the levels of $CD4^+/CD8^+$ at T2 and T3 decline in both groups ($p<0.05$), but the decline in the level of $CD4^+/CD8^+$ at T4 is not statistically significant ($p>0.05$), and the decline degree in the sevoflurane group is lower. Note: * The difference is statistically significant compared with that at T1 ($p<0.05$).

ty and physiological function[12]. Reports[13] have pointed out that excessive stress responses in the perioperative period will increase the incidence rate of cognitive dysfunction after the operation. Postoperative cognitive dysfunction is one of the common complications in the central nervous system in patients after surgical anesthesia, and its incidence rate in elderly patients can be as high as over 45%[14]. Reversible mental disturbances and disorders in such aspects as memory, orientation and attention in the short term or long term are manifestations of postoperative cognitive dysfunction, which causes postoperative complications and increases the mortality rate on the one hand, and prolongs the recovery time and results in waste of medical resources on the other hand, thus posing serious impacts on patients and their family members[15]. In addition, as the surgical anesthesia in elderly patients increases the body's stress responses, soluble immunosuppressive factors will be produced in the body, which suppresses the immune function of elderly patients, thus decreasing the immune function level[16]. Meanwhile, the decreased number of T lymphocytes and NK cells in elderly patients and the slow-down cell-mediated immune responses reduce the immune function in patients[17]. Hence, applying effective methods for alleviating perioperative cognitive dysfunction and improving immune function inhibition in elderly patients and selecting suitable anesthetics are particularly important.

At present, propofol is generally applied in anesthesia maintenance, anesthesia induction and postoperative analgesia sedation in clinical practice. It is a new-type anesthetic with short-term effects[18], characterized by short-acting time in anesthesia induction and short recovery time[19]. However, the relatively low analgesic effect of propofol will lead to the reduced cerebral blood flow as well as lowered intracranial pressure and cerebral oxygen consumption, thereby causing respiratory depression and circulatory inhibition accompanied with temporary respiratory arrest and blood pressure reduction. Moreover, the occurrence rate of postoperative adverse reactions (such as nausea, vomiting, dizziness and headache) is higher[20]. Sevoflurane, as a new-type inhalation anesthetic frequently used in clinical practice with special pharmacological effects, achieves anes-

thetic efficacy by inhibiting N-methyl-D-aspartate receptors[21]. With good performance, sevoflurane has such characteristics as stable hemodynamics, a small amount of muscle relaxant and short postoperative recovery time. Additionally, sevoflurane is administrated through inhalation, and the occurrence rate of airway complications is low. Sevoflurane alleviates the stress responses in patients by limiting the inflammatory responses caused by endotoxins[22]. In this work, the effects of anesthesia on perioperative cognitive and immune function in elderly patients were observed by detecting the MMSE score as well as changes in the levels of T lymphocytes and NK cells in serum at each time point in elderly patients undergoing the abdominal operation.

We showed that at T1, there was no significant difference in the MMSE score between the two groups of patients ($p>0.05$). After patients woke up from anesthesia with different drugs, the MMSE scores at T2, T3, and T4 in the sevoflurane group were higher than those in the propofol group, displaying statistically significant differences ($p<0.05$). The MMSE scores at T2, T3 and T4 were markedly decreased compared with that at T1 in the two groups ($p<0.05$). According to recent studies[23], propofol can enhance the expression of cell synapses in the hippocampal CIA region of elderly patients, thus leading to cognitive dysfunction in elderly patients. During the operation, the body will produce inflammatory responses, and selecting an appropriate anesthetic will make the immune function in elderly patients more stable. There were no significant differences in the levels of $CD16^+/CD56^+$ at T1 and T4 between the sevoflurane group and the propofol group ($p>0.05$). The levels of $CD16^+/CD56^+$ at T2 and T3 in the sevoflurane group were markedly increased compared with those in the propofol group ($p<0.05$). Compared with that at T1, the levels of $CD16^+/CD56^+$ at T2 and T3 in the two groups declined, showing statistically significant differences ($p<0.05$); at T4, $CD16^+/CD56^+$ decreased in both groups, and the difference was statistically significant ($p<0.05$), but the decline degree in the sevoflurane group was lower. There were no statistically significant differences in the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ at T1 and T4 between the sevoflurane group and the propofol group ($p>0.05$). At T2 and T3, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ in the sevoflurane group were significantly higher than those in the propofol group ($p<0.05$). Compared with those at T1, the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ at T2 and T3 were markedly decreased in the two groups of patients ($p<0.05$), but the decreases in the levels of $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ at T4 were not statistically significant ($p>0.05$), and the decline degree in the sevoflurane group was lower. The results of this study are consistent with those of Sidiropoulou et al[24] on the effects of different anesthetics on the perioperative immune function in patients undergoing laparoscopic cholecystectomy. Sevoflurane is an anesthetic for abdominal operation in elderly patients, which can increase the levels of T lymphocytes and NK cells, so it is worthy of promotion and application in clinical practice.

In this experiment, the limited medical resources in Jiangxi Provincial People's Hospital and the small number of the selected subjects may lead to some contingency in the results. Besides, differences in responses after anesthesia caused by different genders or age grades were not excluded from this experiment. Therefore, longer-term follow-up investigations will be conducted for the research subjects, and our experiment will be continuously improved in the future to achieve the optimal experimental results.

Conclusions

We found that applying sevoflurane as an anesthetic for abdominal operation in elderly patients is a more effective method for alleviating perioperative cognitive dysfunction and improving immune function inhibition in elderly patients, so it is worthy of clinical promotion.

Conflict of Interests

The authors declare that they have no conflict of interest.

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