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Analysis of comparative anesthetic effects of sevoflurane and propofol on lung and cognitive functions

Yuan Zhiguo[*1], Zhou Nanxiang[2] and Man Jinyu[1]
[1]Department of Anesthesiology, Jiangsu Taizhou People's Hospital, Taizhou, Jiangsu, PR China
[2]Department of Rehabilitation, Jiangsu Taizhou People's Hospital, Taizhou, Jiangsu, PR China

Abstract: This study was designed to compare the effects of TIVA (total intravenous anesthesia) by propofol and sevoflurane inhalation on perioperative inflammatory response, pulmonary function and postoperative cognitive function in patients with lung cancer resection. A total of 98 patients were randomly divided into study and control group with 49 cases in each group. The study group was given total intravenous anesthesia with propofol while the control group underwent simple inhalation anesthesia with sevoflurane. A-aDO2 (Alveolar-arterial oxygen partial pressure difference), RI (respiratory index), Qs/Qt (intrapulmonary shunt), MMP-9 (serum matrix metalloproteinase-9) and MDA (malondialdehyde) concentrations were compared between the two groups respectively at T0 (immediately before anesthesia induction), T1 (immediately at the beginning of OLV), T2 (immediately at the end of OLV), T3 (immediately before, immediately after closure of thoracic incision) and T4 (24h after operation). The MMSE score of two groups were compared before operation at 6, 24, 72 h and 7 d after operation. The A-aDO2, RI and Qs/Qt of two groups were significantly higher at T3 -T4 than at T0 and T3 the concentrations of MMP-9 and MDA were markedly increased. Compared with the control group, the concentrations of A-aDO2, MMP-9 and MDA at T3, the RI at T2-T3 and the Qs/Qt at T1-T3 all were lower in the study group. The MMSE (Mini Mental State Scale) score of the control group was higher than study group at 24 and 72 h after operation. The anesthesia with propofol can significantly reduce the perioperative inflammatory response and peroxidation with fewer damages on lung function.

Keywords: Propofol, sevoflurane, cognitive functions.

INTRODUCTION

With the urban industrialization and modernization, environmental pollution and the increasing number of smokers, lung cancer has recently become the cancer with highest mortality rate in China. The patients with lung cancer are often accompanied by immune deficiency and the poor control of immune function can affect the prognosis of patients (Jin *et al*., 2014). Any anesthesia for surgery can change the state of autoimmunity and also stimulate severe complications in patients. Patient's body function is being weakened with the central nervous system being sensitive to intravenous anesthetics, likely to cause serious adverse drug reactions (Guo *et al*., 2014). And in some patients the compensation of cardiovascular system is decreased and reserves of important organs are significantly reduced, easily giving rise to decompensation of some important functions during anesthesia (Harris and Simpson, 2010). The ideal depth of anesthesia should ensure no pain and consciousness in patients, hemodynamic stability, good anesthesia recovery and no postoperative recall (Kumar *et al*., 2015). Propofol is currently the main drug for inducing and maintaining intravenous anesthesia. It leads to rapid and stable recovery with quick onset and short action time (Mahli *et al*., 2010). However, it has been reported that large doses of propofol may result in postoperative cognitive dysfunction in patients undergoing cardiac surgery. Therefore, the effect of propofol on cognitive function remains to be further investigated (Olivier *et al*., 2009). Sevoflurane is a new inhalational anesthetics developed in clinical trials. It has stable physical and chemical property and is not easy to be dissolved or absorbed by tissues and blood, making it easy to control the depth of anesthesia and shortening the recovery time of patients (Kashifard *et al*., 2011). At present, there are few reports about the effects of total intravenous anesthesia with propofol and sevoflurane inhalation anesthesia on perioperative inflammatory response, pulmonary function and postoperative cognitive function in patients with lung cancer resection. In view of this, the research has carried out thorough analysis with the details now reported as follows.

MATERIALS AND METHODS

General data

A total of 98 patients treated with simple resection of lower lobe of left lung at Taizhou People's Hospital, Taizhou, China from June 2015 to September -2017 were randomly divided into study group and control group with 49 cases in each group. In the study group there were 30 males and 19 females at the age of (58.4±2.3) years, and with the body mass index of (24.5±2.1) kg/m^2, including ASA I in 38 cases and ASA II in 12 cases. In the control group there were 31 males and 18 females, at the age of

**Corresponding author:* e-mail: xerrng2335@163.com

(58.2±2.5) years, and with the body mass index of (24.7±2.2)kg/m^2, including ASA I in39 cases, and ASAII in 10 cases.

Treatment Protocol

Patients were injected with midazolam (0.1mg/k) 30min before operation followed by entering operation room, then under local anesthesia they were given radial artery puncture and right internal jugular vein puncture with the monitoring instrument connected for close monitoring of patient electrocardiogram, blood oxygen saturation, invasive arterial blood pressure, central venous pressure, cardiac output and partial pressure of end-tidal CO_2 during surgical operations.

The control group were given anesthesia induction by 6-8% sevoflurane inhalation simultaneously with 0.1mg/kg vecuronium, 4-6μg//kg fentanyl and the continuous inhalation of 1-3% sevoflurane; the study group underwent the anesthesia induction by 2mg/kg propofol, 0.1mg/kg vecuronium, 4-6 μg//kg fentanyl and the continuous infusion of propofol 6-10mg/ (kg·h).Operation was started 1 hour after the induction of anesthesia and patients in the two groups were treated by the same group of doctors with the same surgical plan.

Observation index

The arterial blood was collected for blood gas analysis respectively at the time points of "immediately before anesthesia induction (referred as T0), immediately at the beginning of one-lung ventilation, OLV (T1), immediately at the end of OLV(T2) immediately before, immediately after closure of thoracic incision (T3) and 24h after operation(T4)", and alveolar-arterial oxygen partial pressure difference(A-aDO_2), respiratory index (RI) as well as intrapulmonary shunt (Qs/Qt) were calculated; and the concentrations of serum matrix metalloproteinase-9(MMP-9) and malondialdehyde (MDA) were detected at T0, T3 and T4 respectively. The calculation methods:(1) A-aDO_2=fraction of inspired oxygen(FiO_2)×713 - 5/4 × partial pressure of carbon dioxide (PaCO2) - partial pressure of oxygen (PAO_2); (2) RI=A - aDO_2/PaO_2; (3) Qs/Qt=pulmonary capillary oxygen content(CcO_2) - arterial oxygen content (CaO2) / (CcO_2- venous oxygen content,CvO_2).

The Mini Mental State Scale (MMSE) score was compared between the two groups before operation and at 6, 24, 72 h and 7 d after operation, which is composed of such 7 items as orientation to time, orientation to place, immediate memory, attention and computational power, delayed memory, language and visual space, having the advantages of good sensitivity and easy operation. Postoperative cognitive dysfunction (POCD) diagnostic criteria: the MMSE score was under 23 with a total score of 30 and with 27~30 scores as the normal.

Ethical approval

This study was approved by the institutional ethical committee of Taizhou People's Hospital, Taizhou, China. Helsinki's declaration was followed during experimentation. The reference is 0098/IEC/TH-PRC/2015.

STATISTICAL ANALYSIS

SPSS 21 statistical software was used for data analysis. The measurement data were expressed by mean±standard deviation and assessed by t test, chi-square test with count data. $P<0.05$ suggested that there was statistically significant difference.

RESULTS

Comparison of perioperative A-aDO2, RI and Qs/Qt

The A-aDO2, RI and Qs/Qt of the two groups were significantly higher at T3 -T4 than at T0 ($P<0.05$) and compared with the control group, the concentrations of A-aDO2at T3, the RI at T2-T3 and the Qs/Qt at T1-T3 all were significantly lower in the study group ($P<0.05$), with the differences being statistically significant ($P<0.05$) (table 1).

Comparison of perioperative MMP-9 and MDA concentrations

The concentrations of MMP-9 and MDA in the two groups were significantly higher at T3 than at T0 and compared with the control group, the levels of MMP-9 and MDA at T3 were significantly lower in the study group with the differences being statistically significant ($P<0.05$) (table 2).

Comparison of postoperative MMSE scores

The MMSE scores of the control group were higher than those of the study group at 24h and 72 h after operation ($P<0.05$) with no significant difference in between at 6 h and 7d after operation ($P<0.05$), as shown in table 3.

DISCUSSION

At present, clinical studies suggest that (Yamagishi *et al*., 2000) Jin *et al*., 2013) A-aDO2 and RI are important indicators that can directly reflect pulmonary diffusion function and evaluate the extent of lung injury. The higher the values of A-aDO2 and RI, the more serious the lung injury. It is revealed in the study that during one lung ventilation the levels of A-aDO2 and RI were significantly increased in the two groups, especially in the control group, suggesting that the patients with sevoflurane anesthesia had more serious injury of lung function and more significant decrease of lung elasticity during the surgery, which affects the diffusion of oxygen in the lung. It may be related to the aggravated lung edema and reduced pulmonary surfactant activity induced by sevoflurane.

Table 1: Comparison of perioperative A-aDO2, RI and Qs/Qt between the two groups (n=49)

Index	T_0	T_1	T_2	T_3	T_4
A-aDO_2(mmHg)	24. 6±1. 3	213.7±25.2*	426.2±41.6*	247. 9±30. 2*	26.2±1.6
	24. 5±1. 2	206.2±23.8*	411.8±41.4*	218. 3±32. $8^{*\Delta}$	25.4±1 5
RI	0.27±0.02	0.52±0.12*	2. 06±0.27*	0. 84±0. 17*	0.32±0.05
	0.27±0.03	0.50±0.11*	1.83±0.28$^{*\Delta}$	0. 71±0. $16^{*\Delta}$	0.33±0.08
Qs /Qt(%)	8.8±1.6	12.7±1.4*	25.6±3.4*	15. 2±1. 5*	9.5±1.4
	8.7±1.7	10. 8±1.5$^{*\Delta}$	21. 3±2. $9^{*\Delta}$	13. 3±1. $9^{*\Delta}$	9.4±1.5

Compared with T0, $P < 0.05$; $^{\Delta}$compared with the control group, $P < 0.05$

Table 2: Comparison of perioperative MMP-9 and MDA levels between the two groups (n=49)

Group	MMP-9(ng /ml)			MDA(nmol /L)		
	T_0	T_3	T_4	T_0	T_3	T_4
Control	100. 3±12. 6	184. 2±14. 8*	111. 5±17. 3	6. 5±0. 5	9. 8±1. 2*	7. 3±0. 6
Study	101. 5±13. 1	165. 5±11. 3*	109. 3±16. 2	6. 7±0.9	8. 4±1. 1*	7. 2±0. 4
t	0. 562	4. 793	0. 971	0. 453	4. 955	0. 208
P	>0. 05	<0. 05	>0. 05	>0. 05	<0. 05	>0. 05

*Compared with T0, $P < 0.05$

Table 3: Comparison of postoperative MMSE scores between the two groups (n=49)

Group	at 6 h after operation	at 24h	at 72 h	at 7d
Control	21.45 ± 1.87	25.62± 1.56	27.44±2.03	28.07± 1.61
Study	21.43 ± 1.95	22.05 ± 1.13	23.02 ± 1.96	27.54 ± 1.48
t	1.073	5.059	5.147	0.912
p	>0. 05	<0. 05	<0. 05	>0. 05

Qs/Qt includes functional shunt and anatomical shunt in which the former is closely related to the imbalance of V/Q, while the latter is caused by pulmonary artery blood's flowing into pulmonary vein due to anatomy defects. Studies have shown that hypoxic pulmonary vasoconstriction (HPV) is one of important protective mechanisms of the pulmonary circulation system on ischemia and hypoxia conditions, and plays an important role during single lung ventilation (Fuchs *et al*., 2010) (Young and Joon *et al*., 2013). It can make non-ventilated pulmonary arteriole contract, pulmonary vascular resistance increase significantly, and Qs/Qt decline, which is of essential significance in the prevention of hypoxia. A research has indicated that (Schwarzkopf *et al*., 2003) volatile anesthetic inhibits HPV with dose dependence manner, resulting in a rise in Qs/Qt. Therefore, we believe that inhalational anesthetics like sevoflurane have the potential risk of aggravating hypoxia during single lung ventilation.

MMP-9 is a proteolytic enzyme released by neutrophils and can activate a variety of inflammatory cells as well as inflammatory mediators in the lung, and it acts on basement membrane of the pulmonary capillary to increase the permeability and ultimately cause pulmonary edema (Ardi *et al*., 2009). In this study, the level of MMP-9 was obviously increased in the two groups with more significant elevation in the control group. These results suggest that inflammatory response of the lung tissue during operation is more severe in the control group, which may be related to the release of some inflammatory mediators or induced up-expression of proinflammatory cytokine after inhalation of sevoflurane. Studies have shown that (Kotani *et al*., 1999) after anesthetics inhalation, both the releases of some inflammatory mediators and the expression of proinflammatory cytokine increase, exacerbating lung injury in patients. MDA belongs to a decomposition product of lipid peroxide and its level can reflect the severity of tissue and cell injury by oxygen free radicals attacks. In the study, the perioperative MDA level was significantly increased in the two groups, especially in the control group, indicating that lipid peroxidation is stronger during anesthesia with sevoflurane. It is worth noting that in this study the levels of MMP-9, MDA, A-aDO2, RI and Qs/Qt in the two groups of patients recovered to normal range after surgery, indicating that the two drugs will not adversely affect the recovery of patients with lung cancer surgery.

In addition to sedative and hypnotic effects, anesthetic drugs used for clinical surgery also have the function of amnesia, which is one of important reasons leading to POCD (Wang *et al*., 2012). At present, there is no unified

evaluation method and diagnostic standard for POCD, which is basically assessed through Questionnaires and neuropsychological tests on the prospective of changes in intelligence and personality before and after operation. MMSE is the most commonly used scale for cognitive function testing in clinic. This study found that both sevoflurane and propofol can affect the early cognitive function of patients after radical resection of lung cancer. Compared with propofol, sevoflurane leads to lower incidence of POCD, faster recovery and better MMSE scores at 24 and 72 h after operation. A research suggests that (Annecke *et al*., 2012) sevoflurane can reduce the brain damage caused by hypoxia with a strong effect of brain protection. Obvious brain protection effects will be seen in Hippocampal neurons within 30 min after being treated with sevoflurane, and hippocampus is closely related to cognitive function. Therefore, it is suggested that sevoflurane can reduce the occurrence of POCD.

CONCLUSION

As a conclusion the findings suggest, compared with sevoflurane in patients undergoing lung cancer resection surgery the anesthesia with propofol can significantly reduce the perioperative inflammatory response and peroxidation with less damages on lung function but leads to relatively higher incidence of cognitive dysfunction.

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