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Original Research

Effects of sevoflurane inhalation anesthesia on IL-6, TNF-α and MMP-9 expression and hemodynamics in elderly patients undergoing lobectomy for lung cancer

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Abstract: Objective of current research was to investigate the effect of sevoflurane inhalation anesthesia on hemodynamics and inflammatory response in elderly patients with lung cancer lobectomy. Methods: A total of 168 patients with lung cancer who underwent lobectomy in our hospital from January 2019 to December 2019 were selected as the study subjects. The patients were divided into an observation group and control group according to the anesthesia program. In the control group, 1 mg/kg propofol intravenous pump induced anesthesia was maintained at 6mg/kg/h. In the observation group, 8% sevoflurane was used to induce anesthesia and 2% sevoflurane was used to maintain anesthesia. Mean artery pressure (MAP), heart rate (HR) and blood oxygen saturation (SpO_2) were monitored at the beginning of single-lung ventilation (t_1), when single-lung ventilation was changed to double-lung ventilation (t_2), and at 30 minutes after double-lung ventilation (t_3), respectively. Serum levels of interleukin-6 (IL-6), tumor necrosis factor (TNF-α), and matrix metalloproteinases (MMP-9) were measured using an enzyme-linked immunosorbent assay (ELISA) kit. Assess the patient's adverse reactions. Results: At time t_1 and time t_2, there was no significant difference in the three hemodynamic indicators between the two groups (P>0.05). However, at t_3, both MAP and HR in the observation group were significantly lower than those in the control group, while SpO_2 was significantly higher than those in the control group (P<0.05). At t_1 and t_2, there was no significant difference in IL-6 and TNF- levels between the two groups, but at t_3, IL-6 and TNF-α levels in the observation group were significantly lower than those in the control group (P<0.05). Compared with the control group, serum MMP-9 level was significantly decreased in the whole t_1 to t_3 stage (P<0.05). The incidence of complications in the observation group was significantly higher than that in the control group. It was calculated that Sevoflurane can significantly improve hemodynamics and inflammatory response in elderly patients with lung cancer lobectomy, but the incidence of complications is high.

Key words: Sevoflurane; Lung cancer; Hemodynamics; Inflammatory responses.

Introduction

Lung cancer is one of the most common malignant tumors in clinical practice, and the increasing air pollution leads to the increasing prevalence of lung cancer year by year (1,2). Surgical resection, radiotherapy, chemotherapy and molecular targeted therapy drugs are the main treatment methods for lung cancer patients. Unilateral lobectomy is the preferred treatment method for lung cancer patients, with the best curative effect, which is expected to achieve the goal of the radical cure of lung cancer and significantly improve the survival rate of patients (3). The trauma caused during the operation damages the physiological function of the patients, which often affects the surgical effect and postoperative quality of life of the patients, and seriously affects the prognosis of patients with lung cancer (4). In addition, perioperative mechanical ventilation and anesthesia can induce a series of systemic inflammatory reactions, among which lung injury is the most common. Lung injury is often manifested as pulmonary dysfunction such as shortness of breath, cough, chest tightness, and even acute respiratory distress syndrome in severe patients (5). Masato et al. (6) found that some anesthetic drugs can effectively reduce the intraoperative inflammatory response, reduce the damage to patients and improve the success rate of surgery. Therefore, it is of great significance to choose appropriate anesthetic drugs in lung cancer surgery. Cao et al. (7) found that propofol anesthesia can significantly reduce the impact of surgery on patients' cognitive function. Sevoflurane, as a new anesthetic, plays an anesthetic role by inhibiting the n-methyl-d-aspartic acid receptor, which has a good anesthetic effect on the elderly and children (8). In this study, the effects of propofol and sevoflurane on perioperative hemodynamics and inflammatory response were analyzed to evaluate the effects of propofol and sevoflurane on the anesthetic effect of lung cancer patients.

Materials and Methods

General information

168 lung cancer patients who underwent lobectomy in our hospital from January 2019 to December 2019 were selected as the study objects. According to the anesthesia scheme, the patients were divided into an

observation group (84 cases) and the control group (84 cases) respectively. There was no significant difference in general data between the two groups. All patients understood the study and signed informed consent.

Inclusion and exclusion criteria

Inclusion criteria: (A) lung cancer patients who met the indications of lobectomy; (B) lung cancer diagnosis criteria stipulated by the World Health Organization in 2007; (C) ASA anesthesia was classified as grade I or grade II. Exclusion criteria :(A) persons with mental disorders and unable to take care of themselves;(B) malignant tumor exists in other organs besides the lung;(C) severe diabetes, coronary heart disease, hypertension and other chronic diseases;(D) patients with primary liver and kidney dysfunction who cannot tolerate the operation.

Anesthesia method

All patients were intramuscular injected midazolam (Jiangsu Enhua pharmaceutical co., LTD.) 30 minutes before anesthesia. After the injection volume reached 0.1 mg/kg, 3μg/ kg fentanyl was injected intravenously. The multifunctional display (GE) was used to monitor various physiological indicators of patients. In the control group, 1 mg/kg propofol (Ligbon pharmaceutical co., LTD.) intravenous pump induced anesthesia was maintained at 6mg/kg/h.In the observation group, 8% sevoflurane (Lunambett pharmaceutical co., LTD.) was used to induce anesthesia and 2% sevoflurane was used to maintain anesthesia. After ventilation for 3 min, the trachea was intubated and the patient was mechanically ventilated by connecting the anesthesia machine. During the operation, the infusion speed was adjusted to make the patient's central venous pressure reach 5-10cm Hg. 30 minutes before the end of the operation, injection of muscle relaxant and use of anesthetics during the suture was stopped.

Hemodynamic index monitoring

Mean artery pressure (MAP), heart rate (HR) and blood oxygen saturation (SpO2) were monitored at the beginning of single-lung ventilation (t_1), when single-lung ventilation was changed to double-lung ventilation (t_2), and at 30 minutes after double-lung ventilation (t_3), respectively.

Inflammation monitoring

During the operation, anticoagulant blood vessels were used to collect 2ml arterial blood of each group. After centrifugation at 4000 rpm for 10 minutes, the supernatant was collected at 4 ℃ and stored at - 80 ℃ for standby. The levels of inflammatory factors in the serum of each group were detected by using the kit of Interleukin-6 (IL-6), tumor necrosis factor α (TNF – α) and metalloproteinase (MMP-9). The operation should be in strict accordance with the instructions of the ELISA kit.

Evaluation of adverse reactions

The adverse reactions were recorded in detail. The main adverse reactions were hypotension, bradycardia, nausea, vomiting and analgesia. Visual analog scale (VAS) was used to evaluate the pain index and analyze the patient's analgesia.

Data analysis

The data are expressed as mean ± standard deviation (x±SD) and SPSS 22.0 software (SPSS Inc., Armonk, NY, USA) is used for data processing. The t-test of independent samples and χ^2 test of counting data were used for comparison between groups. $P < 0.05$ was statistically significant.

Results

Comparison of general data between the two groups

Control group: 45 males and 39 females; age 56-78 (65.83 ± 8.35) years old; BMI 25.3 ± 1.8 kg / m2; course of the disease is 6 months-4 years (1.83 ± 0.73) years; ASA anesthesia grade: Grade I 43 cases, grade II 41 cases. Observation group: 44 males and 40 females; age 55-79 (66.39 ± 7.52) years; BMI (25.6 ± 2.4) kg / m2; course of the disease is 7 months-3 years (1.79 ± 0.54) years; ASA anesthesia grade: Grade I 39 cases, grade II 45 cases. There was no statistical difference between the two groups ($P > 0.05$) (Table 1).

Monitoring of patients' hemodynamic indexes

MAP, HR and SpO_2 were observed at t_0 to t_3. As shown in Table 2 and Figure 1, there was no significant difference between the two groups at t_1 and t_2 ($P > 0.05$). However, at t_3, the map and HR in the observation group were significantly lower than those in the control

Table 1. Comparison of general data of patients.

Group	Gender (Male/Female)	Age (Year)	BMI (kg/m²)	Course (Year)	ASA grade (I/II)
Control	45/39	65.83±8.35	25.3±1.8	1.83±0.73	43/41
Observation	44/40	66.39±7.52	25.6±2.4	1.79±0.54	39/45
t value	0.833	0.654	0.722	0.856	0.637
P value	>0.05	>0.05	>0.05	>0.05	>0.05

Table 2. Hemodynamic indexes of two groups at different times.

Group	MAP (p/mmHg)			HR (times/min)			SpO_2 (%)		
	t_1	t_2	t_3	t_1	t_2	t_3	t_1	t_2	t_3
Observation	88.79±3.25	76.76±4.07	76.57±3.97	68.74±6.57	71.49±4.73	70.25±4.19	98.66±3.89	95.27±3.56	94.06±3.25
Control	89.37±3.49	76.83±4.16	79.53±4.52	66.94±8.62	72.72±5.03	74.63±3.85	99.07±4.96	95.46±3.40	92.35±3.92
t value	0.97	0.13	4.52	1.52	0.99	3.22	1.56	0.39	4.10
P value	0.15	0.33	0.03	0.45	0.91	0.00	0.11	0.76	0.00

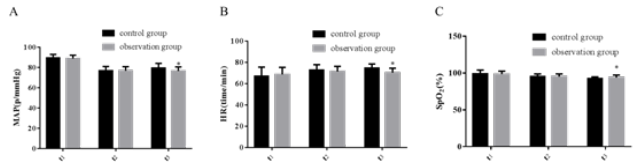

Figure 1. Hemodynamic index at a different time in the two groups. A: MAP. B: HR. C: SpO_2. * Compared with the control group, $P<0.05$.

group, while SpO_2 was significantly higher than that in the control group ($P < 0.05$).

Comparison of inflammatory reaction indexes between the two groups

As shown in Table 3 and Figure 2, there was no significant difference in the levels of IL-6 and TNF - α between the two groups at t_1 and t_2, but at t_3, the levels of IL-6 and TNF - α in the observation group were significantly lower than those in the control group ($P < 0.05$). In the whole stage of t_1 to t_3, compared with the control group, the serum mmp-9 level in the observation group was significantly reduced ($P<0.05$).

Comparison of complications between the two groups

As shown in Table 4 and 3, 9 patients in the observation group were hypotensive, 10 patients were nausea and vomiting, 10 patients were analgesia, and the incidence rate of complications was 33.33%, significantly higher than that of the control group. 16.67% cases were hypotension, 3 cases had bradycardia, 3 cases had nausea and vomiting, and 3 cases were pain relief.

Discussion

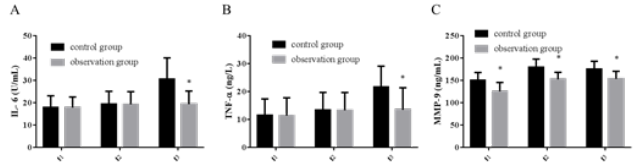

Figure 2. Evaluation of the inflammatory response. A, the concentration of IL-6 in serum; B, the concentration of TNF-α in serum; C, the concentration of MMP-9 in serum. * Compared with the control group, $P<0.05$.

Lung cancer is the leading cause of cancer death worldwide (10). With the improvement of screening technology, the number of peripheral lung small lesions significantly increased, and about 10% of the lesions were non-small cell lung cancer (11,12). Since 1995, the North American lung cancer research group has reported that lobectomy has a better survival rate than subaxillary pneumonectomy, and lobectomy with radical lymph node dissection is the preferred method for the treatment of stage I non-small cell lung cancer. Chen et al. (13,14) found that acute respiratory distress syn-

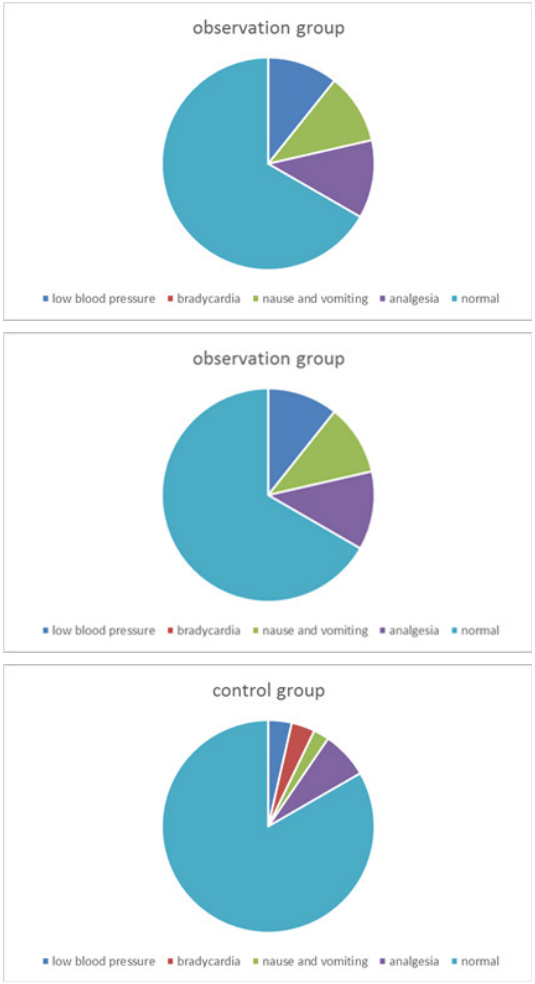

Figure 3. The incidence rate of adverse reactions of two groups of patients.

Table 3. Comparison of inflammatory response indicators between the two groups.

Group	IL- 6 (U/mL)			TNF-α (ng/L)			MMP-9 (ng/mL)		
	t_1	t_2	t_3	t_1	t_2	t_3	t_1	t_2	t_3
Observation	17.87±4.71	19.26±5.66	19.37±5.85	11.38±6.36	13.29±6.35	13.46±7.89	125.43±19.88	152.37±15.67	153.46±16.79
Control	17.94±5.15	19.42±5.68	30.60±9.46	11.46±5.89	13.36±6.33	21.64±7.43	150.18±17.35	179.36±18.22	175.53±17.29
t value	0.09	0.17	8.61	0.13	0.15	6.09	0.09	0.13	23.89
P value	0.95	0.87	0.00	0.90	0.88	0.00	0.01	0.02	0.00

Table 4. Comparison of complications between the two groups.

Group	hypotension (n)	bradycardia (n)	nausea and vomiting (n)	analgesia (n)	incidence rate (%)
Observation	9	0	10	10	33.33
Control	3	3	2	6	16.67
χ2 value					6.22
P-value					<0.013

drome caused by unilateral pneumonectomy in patients with lung cancer may be related to the injuries during the operation and one-lung ventilation. Hung et al. (15) found that lung tissue resection often leads to tissue damage, which seriously affects the prognosis. However, effective intravenous anesthetics can inhibit the inflammatory response and protect lung tissues and cells. Piegeler et al. (16) found that inhibiting the accumulation of neutrophils and the release of inflammatory factors and increasing the expression level of antioxidant proteins can effectively reduce the lung injury caused by unilateral lobectomies. Studies have found that sevoflurane can reduce systemic inflammation in rats compared with propofol (17). This study compared the effects of propofol and sevoflurane anesthesia on hemodynamics and inflammatory response in patients undergoing lung cancer resection.

Studies have found that lobectomy can lead to myocardial ischemia and hemodynamic disorders, especially in patients with coronary stenosis. The decrease of blood SpO2 caused by surgery is the direct cause of the hemodynamic disorder (18). In this study, sevoflurane increased blood SpO2 levels compared to propofol, which significantly improved hemodynamics in patients undergoing lobectomy. Studies have shown that normal high arterial blood pressure can effectively maintain normal vascular shear force and effectively reduce the occurrence of atherosclerosis, whereas elevated blood pressure can increase the risk of atherosclerosis and reduce blood flow velocity (19,20). In this study, sevoflurane reduced MAP in t_3 patients compared to propofol, suggesting that sevoflurane improved hemodynamics in patients undergoing lobectomy for lung cancer. In addition, patients in the observation group also experienced a significant reduction in heart rate at stage t_3 compared to the control group. Heart rate is closely related to cardiac output. The increase of heart rate in a certain range can keep the output of each beat unchanged, but if the heart rate is too fast and the diastolic period is shortened, the output of each beat will decrease, and the cardiac output will decrease instead (21,22). In this study, sevoflurane can better stabilize the heart rate and hemodynamics of patients undergoing surgery.

In addition, in this study, sevoflurane significantly reduced the levels of serum inflammatory factors IL-6, TNF - α and MMP-9 compared with the control group. Although sevoflurane has a different onset time for three inflammatory factors, the general trend is the same, which may be related to the onset time of inhalation anesthesia. It has been found that sevoflurane can play an anti-oxidation and anti-inflammatory role by increasing the concentration of heme oxygenase-1 in vivo (23). Heme oxygenase 1 is a key enzyme for heme degradation, which has anti-inflammatory, anti-apoptosis and anti-proliferation effects (24, 25). Zhao et al. Found that the concentration of MMP-9 in the serum of patients with pneumonia increased significantly (26). Mmp-9 can damage lung tissues by increasing the activity of elastase, promoting the adhesion of neutrophils and vascular endothelial cells, and hydrolytic adhesion proteins and connexins (27,28). In this study, sevoflurane can significantly reduce the concentration of serum mmp-9, so it can significantly improve the body's inflammatory response.

Although sevoflurane is effective in stabilizing hemodynamics and reducing levels of inflammatory factors in patients, its complications are numerous, mainly including hypotension, nausea and vomiting, and analgesia. In summary, sevoflurane in this study significantly improved hemodynamics and inflammatory response in elderly patients undergoing lobectomy for lung cancer, providing a reference for clinical surgery.

Today, for many common and deadly cancers, there are early methods of diagnosing the disease, and if diagnosed early, cancer treatment is very effective (29-33). Also, for its treatment, new methods based on genome editing can be effective in increasing the efficiency of diagnosis (34).

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