

## Original Article

# Effect of edaravone on serum SP-A and arterial blood gas in patients with lobectomy

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**Abstract:** Objective: To discuss the effect of edaravone on serum pulmonary surfactant protein A (SP-A) and arterial blood gas (ABG) in patients with thoracoscopic lobectomy. Methods: 40 lung cancer patients with right side of lobectomy were randomly divided into control group (group C, 20 cases) and edaravone group (group E, 20 cases). Group E was treated edaravone (1 mg/kg) between induction and skin incision, dropping within 30 min; group C was treated with equivalent normal saline. The venous and arterial blood were collected in both groups immediately before incision ( $T_0$ ), after 1 h of one-lung ventilation 1 h ( $T_1$ ) and in 1 h after lungs ventilation ( $T_2$ ) for ABG analysis and measurement of serum SP-A level. Results After OLV, serum SP-A levels were significantly increased in both groups ( $P < 0.05$ ); compared with group C, serum levels of SP-A were reduced ( $P < 0.05$ ) and ABG was significantly improved in group E. Conclusion: Edaravone can reduce serum SP-A levels in patients with lobectomy and alleviate acute lung injury to a certain extent in surgery.

**Keywords:** SP-A, lung ventilation, ABG analysis, edaravone

## Introduction

In recent years, with the increasing deterioration of the global air, the incidence and mortality of lung cancer show an increasing trend year by year [1]. Compared to traditional open surgery, thoracoscopic lobectomy showed the advantages of little trauma and rapid postoperative recovery [2], but due to technical subjects, OLV time is relatively extended in the surgery. The oxidative stress response in OLV would have some degree of damage to lung tissue, increasing epithelial cell apoptosis [3] and may inducing adverse postoperative complications [4]. Edaravone is a novel free radical scavenger; studies have shown that edaravone can reduce oxygen free radicals [5, 6] and inhibit perioperative systemic inflammatory response and oxidative stress response in patients with lung lobectomy, which is conducive to the prognosis of patients [7, 8]. This study observed the effect of preventive administration of edaravone on the serum SP-A in patients to explore its protective effect on acute lung injury in lobectomy and provide reference for clinical application.

## Material and methods

### General information

40 cases of lung cancer patients undergoing right side of thoracoscopic lobectomy in Affiliated Hospital of Qingdao University from August 2013 to January 2014 were all male, ASA I or II level, aged 45 to 65 years, with body mass index (BMI) between 18~26 kg/m<sup>2</sup>, without immune, endocrine and nervous system diseases, no serious cardiopulmonary dysfunction, no obvious abnormalities in liver and kidney functions. By random number table method, patients were randomly divided into two groups: control group (group C) and edaravone group (group E), respectively including 20 cases. All patients have signed informed consent.

### Anesthesia methods

All patients did not use drugs before surgery. After inter-room and opening venous access, catheterization was performed in side elbow vein, regularly monitoring blood pressure (BP), heart rate (HR) and oxygen saturation (SpO<sub>2</sub>);

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**Table 1.** Comparison of general information between two groups ( $\bar{x} \pm s$ )

Group	Cases	Age (Years)	BMI (kg/m <sup>2</sup> )	surgery duration (min)	OLV time (min)
Group C	20	51 ± 6	23.2 ± 3.2	210 ± 12	147 ± 12
Group E	20	49 ± 8	22.7 ± 2.8	225 ± 12	156 ± 10

under local anesthesia, radial artery catheterization was performed to monitor arterial blood pressure. Induction of anesthesia: in both groups, intravenous injections of sufentanil 0.1~0.2 µg/kg, propofol 1~2 mg/kg and rocuronium 0.6~0.8 mg/kg were performed in order; double-lumen endobronchial tube was intubated into the left side, using fiber bronchoscopy to adjust the position of the catheter, and then the anesthesia machine (Datex-Ohmeda Aestiva/7900) was connected for mechanical ventilation. Intraoperative ventilation parameters: for lung ventilation, preliminary tidal volume was 8 ml/kg, inspiratory to expiratory ratio was 1, respiratory rate was between 10 and 12 times/min, oxygen flow was 2 L/min; Oxygen concentration was 80%. For OLV, preliminary tidal volume was 6~8 ml/kg, respiratory rate was between 14 and 16 times/min, the other parameters were the same as above. Intraoperative respiratory parameters were adjusted based on the end-expiratory carbon dioxide partial pressure ( $P_{ET}CO_2$ ) and peak airway pressure (Peak).

After tracheal intubation, group E was treated with edaravone (1 mg/kg, solved in 100 ml saline), dripping within 30 min; group C was treated equivalent saline at the same time.

### Maintenance of anesthesia

Continually target-controlled infusion of sufentanil (plasma concentration of 0.2~0.3 ng/ml) and propofol (plasma concentrations of 2~3 µg/ml), and intermittent intravenous injection of cis-benzenesulfonic acid atracurium 0.5 mg/kg were performed to maintain muscle relaxation; maintain that intraoperative fluctuations in BP and HR did not exceed 20% of the preoperative base; intraoperative  $P_{ET}CO_2$  and Peak was monitored to maintain  $P_{ET}CO_2$  between 30 and 35 mmHg, Peak between 20 and 30 mmHg. Intraoperative crystalloid: colloid was infused with a rate of 1:1, following the principle of thoracic surgery transfusion. Excluding the patients with blood loss greater than 500 ml and blood transfusion patients, after post-

operative recovery of spontaneous breathing, the tidal volume > 6 ml/kg, respiratory rate > 10/min,  $P_{ET}CO_2$  between 35 and 45 mmHg; after awake, extubation was performed, and patients were observed in anesthesia recovery room.

### Specimen collection and index detection

operation time, OLV time, intraoperative fluid volume, urine volume and blood loss were recorded; 2 ml blood from the radial artery and 4 ml venous blood were respectively collected immediately before skin incision ( $T_0$ ), after 1 h of single-lung ventilation ( $T_1$ ), and after 1 h of lung ventilation ( $T_2$ ); ABG analysis of radial arterial blood samples was performed using the GEM Premier 3000 analyzer, measuring the arterial oxygen pressure ( $PaO_2$ ), carbon dioxide partial pressure ( $PaCO_2$ ) and arterial oxygen saturation index ( $SaO_2$ ), and calculating the alveolar-arterial oxygen difference ( $P_{A-a}O_2$ ), respiration index and oxygenation index. Venous blood samples were allowed to stand at 4°C for 30 min, and then the serum was separated and stored in -70°C refrigerator; ELISA method was used to detect the concentrations of SP-A (Wuhan Boster Biological Technology Co., Ltd.).

### Statistical analysis

SPSS 16.0 software was used for analysis. Measurement data were presented as mean±standard deviation ( $\bar{x} \pm s$ ); differences between groups and within groups were analyzed by t test; count data were compared using chi-square test.  $P < 0.05$  said the difference was statistically significant.

## Results

### Comparison of general information (Table 1)

Patients in C and E groups were all male, and the type of surgery was the right side of lobectomy. There were no statistically significant differences in the patients' age, body mass index and surgery duration between the two groups.

### Comparison of ABG indicators (Table 2)

The comparisons of arterial  $PaO_2$ ,  $PaCO_2$  and other related indicators at the time points of  $T_0$ ,  $T_1$  and  $T_2$  during lobectomy showed that: at  $T_0$ ,

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**Table 2.** Comparisons of ABG indicators between the two groups ( $\bar{x} \pm s$ )

Group	Cases	Indicators	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>
Group C	20	PaO <sub>2</sub> (mmHg)	302.02 ± 67.23	103.57 ± 31.17 <sup>a</sup>	207.29 ± 31.57 <sup>a</sup>
		P <sub>A-a</sub> O <sub>2</sub> (mmHg)	213.39 ± 24.12	100.43 ± 23.52 <sup>a</sup>	178.24 ± 14.14
		OI	335.39 ± 41.12	139.43 ± 32.52 <sup>a</sup>	232.24 ± 40.14 <sup>a</sup>
		RI	0.63 ± 0.11	0.96 ± 0.07 <sup>a</sup>	0.86 ± 0.13 <sup>a</sup>
Group E	20	PaO <sub>2</sub> (mmHg)	317.21 ± 58.57	159.84 ± 28.12 <sup>a,b</sup>	272.72 ± 29.81 <sup>a,b</sup>
		P <sub>A-a</sub> O <sub>2</sub> (mmHg)	206.45 ± 13.33	120.54 ± 13.76 <sup>a,b</sup>	200.45 ± 4.53 <sup>b</sup>
		OI	355.45 ± 3.33	178.54 ± 21.76 <sup>a,b</sup>	276.45 ± 34.53 <sup>a,b</sup>
		RI	0.65 ± 0.09	0.70 ± 0.05 <sup>b</sup>	0.66 ± 0.14 <sup>b</sup>

Note: Compared with T<sub>0</sub> in the same group, <sup>a</sup>P < 0.05; Compare with group C at the same time points, <sup>b</sup>P < 0.05.

**Table 3.** Comparisons of SP-A levels between the two groups (mg/L,  $\bar{x} \pm s$ )

Group	Cases	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>
C	20	17.23 ± 1.61	24.12 ± 2.11 <sup>a</sup>	20.82 ± 1.49 <sup>a</sup>
E	20	16.22 ± 1.96	20.05 ± 2.81 <sup>a,b</sup>	19.01 ± 1.21

Note: Compared with T<sub>0</sub> in the same group, <sup>a</sup>P < 0.05; Compare with group C at the same time points, <sup>b</sup>P < 0.05.

no significant difference was found between C and E groups in PaO<sub>2</sub>, P<sub>A-a</sub>O<sub>2</sub>, oxygenation index (OI), respiratory index (RI) and other arterial blood gas parameters. Compared to T<sub>0</sub>, PaO<sub>2</sub>, OI, and P<sub>A-a</sub>O<sub>2</sub> in group C significantly decreased at T<sub>1</sub>; although the same trend was also found in group E, the decline was significantly weaker than that of group C, and there were statistically significant difference in all observed indicators between the two groups at T<sub>1</sub> (P < 0.05). RI in group C at T<sub>1</sub> and T<sub>2</sub> was significantly increased compared to T<sub>0</sub>, while no significant increase had been found in group E; there also were significant differences in RI at T<sub>1</sub> and T<sub>2</sub> between the two groups (P < 0.05).

### SP-A Comparison (Table 3)

The comparisons of cubital vein serum levels of SP-A at the time points of T<sub>0</sub>, T<sub>1</sub> and T<sub>2</sub> during lobectomy showed that: at T<sub>0</sub>, SP-A levels were significantly increased both in group C and E, but the degree of increase in E group was significantly lower than that in group C; there was a significant difference between the two groups (P < 0.05). After T<sub>2</sub>, the levels of SP-A had a certain degree of recovery in two groups, and no significant difference had been found in the two groups.

### Discussion

In thoracoscopic lung surgery, the change of ventilation type could cause damage to lung tissue to some extent. In OLV stage, collapsed lung is in a hypoxic state, resulting in reflex contraction of pulmonary vascular, increased pulmonary shunt and imbalance of ventilation-perfusion ratio; at the same time, the contralateral lung bears the mechanical stretch injury caused by high airway pressure. In pulmonary reexpansion, collapsed lung experienced ischemia and hypoxia-reperfusion. The above process can cause inflammation and generation of oxygen free radical, resulting in acute lung cell damage, increased pulmonary capillary permeability, reduction in pulmonary surfactant [9, 10]; repeatedly collapse and reexpansion will aggravate the above inflammation reaction [11].

SP-A is mainly secreted by type II alveolar epithelial cells, involved in the formation of pulmonary surfactant, playing an important role in maintaining pulmonary blood-gas barrier, normal ventilation and diffusion function. Studies have shown that pulmonary surfactant protein A can inhibit the synthesis and release of inflammatory mediators through the down-regulation of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1B, MCP-1 and inhibition of NF- $\kappa$ B activity, such as to regulate local immune and inflammatory responses [12-14]; and its expression levels in the serum of patients with acute lung injury had a significant increase, which can be used as a serum marker of acute lung injury [15, 16]. In the present study, after one-lung ventilation, SP-A levels were significantly improved in the serum of patients, indicating

some degree of acute lung injury during OLV. The increased degree of SP-A in group E was smaller than that in group C, indicating that pre-injection of edaravone had a certain inhibition on the increased serum levels of SP-A caused by OLV.

ABG indicators, such as PaO<sub>2</sub>, P<sub>A-a</sub>O<sub>2</sub>, OI and RI, can reflect the gas diffusion and exchange capacity of alveolar membrane [17]. After OLV, PaO<sub>2</sub>, P<sub>A-a</sub>O<sub>2</sub> and OI decreased in both two groups, suggesting a decline in lung function in OLV compared with lung ventilation. Compared with group C, PaO<sub>2</sub>, P<sub>A-a</sub>O<sub>2</sub>, OI and RI had smaller degree of changes in group E, indicating that the capacity of lung ventilation and oxygen exchange was increased in group E, which was conducive to pulmonary oxygenation and tissue oxygen supply in surgery, reducing the incidence of hypoxemia and suggesting that pre-injection of edaravone had a protective effect on intraoperative lung function.

In summary, edaravone can inhibit the increase of serum SP-A levels caused by OLV-induced acute lung injury and improve ABG, with certain lung protection for patients with lobectomy.

### Disclosure of conflict of interest

None.

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