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Original Article

Effect of bronchofibroscope bronchoalveolar lavage on respiratory mechanics, hemodynamics and inflammatory mediators in patients with severe pneumonia and mechanical ventilation in intensive care unit

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Abstract: Objective: To investigate the effect of bronchofibroscope bronchoalveolar lavage on respiratory mechanics, hemodynamics and inflammatory mediators in patients with severe pneumonia and mechanical ventilation in intensive care unit (ICU). Methods: Sixty ICU patients with severe pneumonia and mechanical ventilation were randomly divided into research group (30 cases, received bronchofibroscope bronchoalveolar lavage) and control group (30 cases, received sterile sputum suction). The clinical efficacy, mechanical ventilation time, duration of ICU stay, respiratory mechanics, hemodynamics, inflammatory mediators and adverse reactions were compared between the two groups. Results: Compared with the control group, the total effective treatment rate in the research group was higher, and the mechanical ventilation time and duration of ICU stay were shorter ($P<0.05$). Compared with the control group, there were lower levels of ventilatory work of breathing (WOBvent), peak airway pressure (PIP), airway resistance (RAW), C-reactive protein (CRP) and procalcitonin (PCT) in the research group after 1 week of treatment, but higher level of lung dynamic compliance (Cdyn) (all $P<0.05$). There was no significant difference in the total incidence of adverse reactions like vomiting, hoarseness, cyanosis and sinus tachycardia and levels of heart rate (HR), central venous pressure (CVP) and mean arterial pressure (MAP) after 1 week of treatment between the two groups ($P>0.05$). Conclusion: Compared with the therapy of sterile sputum suction, the treatment effect of bronchofibroscope bronchoalveolar lavage was more remarkable in ICU patients with severe pneumonia and mechanical ventilation. The therapy of bronchofibroscope bronchoalveolar lavage can improve lung compliance as well as respiratory mechanics and reduce inflammation, and there is no significant effect on hemodynamics.

Keywords: Intensive care unit, severe pneumonia, mechanical ventilation, bronchofibroscope, bronchoalveolar lavage, respiratory mechanics, hemodynamics, inflammatory mediator

Introduction

Severe pneumonia is a common respiratory infectious disease, which is characterized by rapid progression and severe illness. The patients with severe pneumonia have diffuse inflammation in the lungs and their main clinical symptoms are fever and expectoration. Their airways are often blocked due to difficulty in expectoration, which can cause dyspnea easily, further leading to ventilation dysfunction even respiratory failure, posing a serious threat to patient's life and health [1, 2]. Patients with severe pneumonia need endotracheal intubation or to be connected to a ventilator after tracheotomy to help ventilation due to respiratory failure. However, the cough reflex of patients will be decreased due to the use of sedatives, muscle relaxants and other drugs, and their airway secretions cannot be normally expelled from the body, which can cause the poor ventilation. The clearance of respiratory tract foreign bodies by sterile sputum suction was performed in clinic in the past, but the

effect was not obvious [3]. In recent years, with the development of fiberoptic bronchoscopy, bronchoalveolar lavage has been gradually applied to severe pneumonia in intensive care unit (ICU), which can effectively remove airway secretions [4]. The research by Guo et al showed that bronchofibroscope bronchoalveolar lavage can effectively improve the treatment effect of severe pneumonia in children, improve the blood gas levels and reduce the inflammation, and the total effective rate was as high as 95% [5]. Bronchofibroscope bronchoalveolar lavage can improve the effect of sputum suction. Some scholars have argued that sputum suction may has a certain impact on respiratory mechanics and hemodynamics of patients. However, there are few researches about the effect of sputum suction and it is still controversial. Based on this, our study enrolled 60 patients with severe pneumonia and mechanical ventilation in ICU and evaluated the effect of bronchofibroscope bronchoalveolar lavage on respiratory mechanics, hemodynamics and inflammatory mediators in them.

Materials and methods

General information

According to the random number table, 60 ICU patients with severe pneumonia and mechanical ventilation admitted to Kunshan Third People's Hospital from January 2017 to December 2019 were divided into control group (30 cases) and research group (30 cases). This study was approved by Ethics Committee of Kunshan Third People's Hospital.

Inclusion and exclusion criteria

Inclusion criteria: Patients who met the diagnostic criteria for severe pneumonia in "Chinese guideline for the diagnosis and treatment of adult community-acquired pneumonia" with diagnosis confirmed by CT scan of lungs [6]; patients with severe pneumonia caused by only bacterial infection; patients with mechanical ventilation by being connected to the ventilator after endotracheal intubation; patients with respiratory rate of >30 breaths/min; patients with PaO_2/FiO_2 ratio of <250; patients with inflammation involving multiple lung lobes; patients with leukopenia.

Exclusion criteria: Patients combined with tracheobronchial disease, chronic obstructive pulmonary disease and other respiratory disease; patients combined with severe diseases of other important organs such as heart and brain; patients combined with coagulation disorders or other diseases of blood system; patients with obvious electrolyte abnormality; patients with active tuberculosis and without treatment; patients with severe arrhythmia, heart failure and recent myocardial infarction; patients with acute respiratory failure; patients with severe pulmonary insufficiency.

Methods

All the patients in both groups received mechanical ventilation by being connected to a ventilator after endotracheal intubation. Besides, they all received conventional therapy, such as anti-infection, expectoration and bronchodilation. Patients in the control group received clearance of respiratory tract foreign bodies by sterile sputum suction tube. Patients in the research group received the therapy of bronchofibroscope bronchoalveolar lavage, and the detailed procedures are as the following: 10 minutes before lavage, the patients were given Midazolam 5 mg as sedative (Jiangsu Enhua Pharmaceutical Co., Ltd., Jiangsu, China). Then the patients were placed in the supine position and the fiberoptic bronchoscope was placed at the carina. After 5 ml lidocaine (Jiangsu Langer Pharmaceutical Co., Ltd., Jiangsu, China) was dripped into patients, suction of sputum under negative pressure was performed (the pressure was no more than 100 mmHg). The purulent discharge and mucus were aspirated fully from the airway of patients, then the secretion samples were collected for bacterial culture and drug susceptibility tests. During the whole process, the vital signs of patients were closely monitored such as the condition of bronchus, blood pressure, heart rate and so on. If any abnormalities occurred, the operation should be stopped immediately until the levels of blood oxygen saturation, heart rate and so on in patients returned to normal. If it was difficult to suck out purulent discharge and mucus in patient's airway, suction of sputum under negative pressure was performed after repeated washing with 5-10 ml of saline (Beijing Institute of Biological Products

Table 1. Comparison of baseline data between the two groups

Group	Control group (n=30)	Research group (n=30)	t/χ^2	P
Sex (Male/female)	18/12	17/13	0.069	0.793
Age (year)	40.8±5.2	40.6±5.3	0.148	0.883
Course of disease (d)	5.9±2.2	6.2±2.4	0.505	0.616
Respiratory rate (breaths/min)	29.34±7.34	28.94±7.82	0.204	0.839
White blood cell count ($\times10^9$/L)	13.94±4.56	14.03±4.62	0.076	0.940
Platelet count ($\times10^9$/L)	150.35±12.42	152.35±11.59	0.645	0.521
Oxygenation index (n, %)	134.56±27.32	136.38±28.13	0.254	0.800

Co., Ltd., Beijing, China). Bronchoalveolar lavage should be performed 1-2 times a day for 1 week according to the patient's condition.

Outcome measures

Efficacy evaluation: After 1 week of treatment, if there was no sputum in patient's basically, rales on lung auscultation disappeared basically, and lesions disappeared completely on CT scan, the treatment proved to be markedly effective; if the sputum and pulmonary rales decreased significantly, and lesions disappeared basically on CT scan, the treatment proved to be effective; patients who did not meet the above criteria were considered invalid [7]. Total efficiency was the combination of markedly effective rate and effective rate.

Treatment-related indicators: The duration of mechanical ventilation and ICU stay were compared between the two groups.

Respiratory mechanics: Ventilatory work of breathing (WOBvent), peak airway pressure (PIP), airway resistance (RAW) and lung dynamic compliance (Cdyn) in both groups were measured using the HAMILTON-G5 ventilator (purchased from Shanghai Jumu Medical Instrument Co., Ltd., China) before and 1 week after treatment.

Hemodynamics: Levels of heart rate (HR), central venous pressure (CVP) and mean arterial pressure (MAP) before and 1 week after treatment were recorded using the multi-parameter ECG monitor.

Inflammatory mediators: 2 mL of the patient's cubital blood were collected before and 1 week after treatment respectively, and the serum was separated by high-speed centrifugation. The serum levels of C-reactive protein (CRP) and procalcitonin (PCT) were determined by HF-120 automatic biochemical analyzer (purchased from Shenzhen Decca Precision Instrument Co., Ltd., China).

Adverse reactions: The incidences of adverse reactions such as cyanosis, vomiting and hoarseness were compared between the two groups. Incidence of adverse reactions = number of adverse reactions/total number of patients * 100%.

Statistical analysis

SPSS software 25.0 was used to process the data. The measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± sd). Independent sample t-test was used for comparison between groups, and a paired t-test was used to compare data before and after treatment in the same group. Enumeration data were expressed as number (n) and percentage (%) and analyzed by χ^2 test. $P<0.05$ was considered statistically significant.

Results

Baseline data

There was no significant difference in baseline data between the two groups ($P>0.05$). See **Table 1**.

Clinical efficacy

The total effective rate in the research group (96.67%) was higher than that in the control group (73.33%) ($P<0.05$), which suggested that bronchofibroscope bronchoalveolar lavage therapy cansignificantly improve the clinical efficacy of ICU patients with severe pneumonia and mechanical ventilation. See **Table 2**.

Table 2. Comparison of clinical efficacy between the two groups (n, %)

Group	Markedly effective	Effective	Invalid	Total effective rate
Control group (n=30)	7 (23.33)	15 (50.00)	8 (26.67)	22 (73.33)
Research group (n=30)	11 (36.67)	18 (60.00)	1 (3.33)	29 (96.67)
χ^2	1.270			6.405
P	0.260			0.011

Note: Total efficiency = markedly effective rate + effective rate.

Table 3. Comparison of treatment-related indicators between the two groups ($\bar{x} \pm sd$)

Group	Mechanical ventilation time (d)	Length of ICU stay (d)
Control group (n=30)	9.9±2.2	17.6±2.5
Research group (n=30)	8.5±2.1	14.8±2.4
t	2.521	4.425
P	0.015	0.000

Note: ICU: intensive care unit.

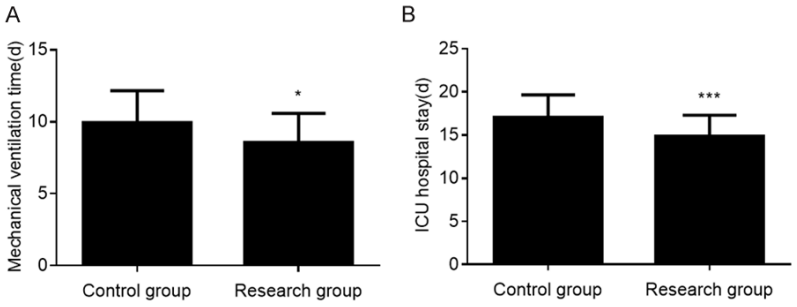

Figure 1. Comparison of treatment-related indicators between the two groups. A: Mechanical ventilation time; B: Duration of ICU stay. Compared with control group, *P<0.05, ***P<0.001. ICU: intensive care unit.

Treatment-related indicators

Compared with the control group, the mechanical ventilation time and duration of ICU stay in the research group were shorter (P<0.05), which suggested that bronchofibroscope bronchoalveolar lavage therapy can significantly shorten the duration of mechanical ventilation and ICU stay and promote patient's recovery. See **Table 3** and **Figure 1**.

Respiratory mechanics

Before treatment, there was no significant difference in levels of WOBvent, PIP, RAW and Cdyn between the two groups (P>0.05). Compared with before treatment, the levels of WOBvent, PIP, RAW and Cdyn in the two groups after treatment were significantly lower, but the level of Cdyn increased significantly (P< 0.05). Compared with the control group, there were lower levels of WOBvent, PIP, RAW but higher level of Cdyn in the research group after treatment (P<0.05), which suggested that bronchofibroscope bronchoalveolar lavage therapy can significantly improve indicators in respiratory mechanics of ICU patients with severe pneumonia and mechanical ventilation. See **Table 4** and **Figure 2**.

Hemodynamics

Before treatment, there was no significant difference in levels of HR, CVP and MAP between the two groups (P>0.05). Compared with before treatment, the improvement in levels of HR, CVP and MAP after treatment in both groups were not obvious (P>0.05). There was no significant difference in levels of HR, CVP and MAP after 1 week of treatment between the two groups (P>0.05), which suggested that bronchofibroscope bronchoalveolar lavage therapy has small impact on hemodynamics of ICU patients with severe pneumonia and mechanical ventilation. See **Table 5** and **Figure 3**.

Inflammatory mediators

Before treatment, there was no significant difference in serum levels of CRP and PCT between the two groups (P>0.05). Compared with before treatment, the levels of CRP and PCT after treatment in both groups were significantly lower (P<0.05). The serum levels of CRP and

Table 4. Comparison of indicators in respiratory mechanics between the two groups before and 1 week after treatment ($\bar{x} \pm sd$)

Group	Control group (n=30)	Research group (n=30)	t	P
WOBvent (J/L)				
Before treatment	0.80±0.45	0.85±0.51	0.403	0.688
After 1 week of treatment	0.61±0.26#	0.48±0.22##	2.091	0.041
PIP (cmH_2O)				
Before treatment	32.84±3.01	33.11±2.94	0.351	0.727
After 1 week of treatment	20.44±3.24###	17.90±3.18###	3.064	0.003
RAW (cmH_2O)				
Before treatment	16.58±0.90	16.92±0.81	1.538	0.129
After 1 week of treatment	11.71±0.70###	10.95±0.64###	4.389	0.000
Cdyn (mL/cmH_2O)				
Before treatment	20.18±5.54	19.83±5.67	0.242	0.810
After 1 week of treatment	34.11±7.21##	38.40±8.05##	2.174	0.034

Note: Compared with before treatment in the same group, #P<0.05, ##P<0.01, ###P<0.001. WOBvent: ventilatory work of breathing; PIP: peak airway pressure; RAW: airway resistance; Cdyn: lung dynamic compliance.

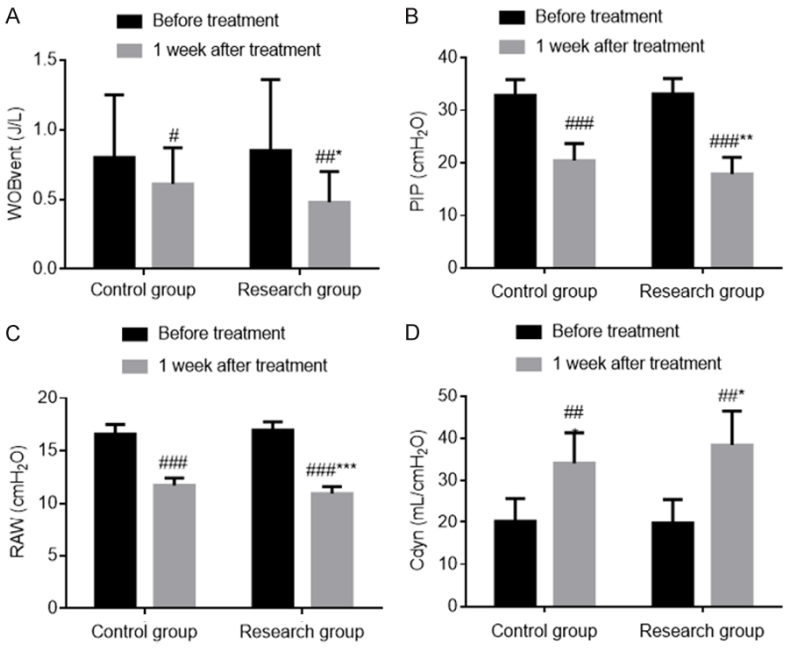

Figure 2. Comparison of indicators in respiratory mechanics between the two groups before and after 1 week of treatment. A: WOBvent; B: PIP; C: RAW; D: Cdyn. Compared with before treatment in the same group, #P<0.05, ##P<0.01, ###P<0.001; compared with the control group, *P<0.05, **P<0.01, ***P<0.001. WOBvent: ventilatory work of breathing; PIP: peak airway pressure; RAW: airway resistance; Cdyn: lung dynamic compliance.

PCT after 1 week of treatment in the research group were lower than those in the control group (P<0.05), which suggested that bronchofibroscope bronchoalveolar lavage therapy can significantly reduce the inflammation of ICU patients with severe pneumonia and mechanical ventilation. See **Table 6** and **Figure 4**.

Adverse reactions

There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05). See **Table 7**.

Discussion

Long-term mechanical ventilation is needed to provide life support with ICU patients with severe pneumonia. However, mechanical ventilation is an invasive procedure, which can cause damage to patient's airway and increase the risk of infection [8-10]. Moreover, ICU patients with severe pneumonia and mechanical ventilation need to stay in bed for a long time. On one hand, their airway secretions are very viscous; on the other hand, these secretions will move to the deep of airway under mechanical ventilation, so it is difficult to expel them for patients, causing the obstruction of the respiratory tract [11, 12]. In the past, sputum suction needed to be carried out by sputum suction tube repeatedly, which could easily aggravate the damage of respiratory mucosa [13]. In recent years, bronchofibroscope has become an essential equipment in ICU. It not only has a good effect of sputum suction, but also provides a new method for the treatment of ICU patients with severe pneumonia and mechanical ventilation [14]. The results of

Table 5. Comparison of hemodynamics before and after treatment ($\bar{x} \pm sd$)

Group	Control group (n=30)	Research group (n=30)	t	P
HR (beats/min)				
Before treatment	77.25±7.59	77.91±7.81	0.332	0.741
After 1 week of treatment	77.41±7.74	76.94±7.37	0.241	0.810
CVP (cmH_2O)				
Before treatment	8.06±1.30	7.99±1.38	0.202	0.841
After 1 week of treatment	8.11±1.40	7.96±1.33	0.425	0.672
MAP (mmHg)				
Before treatment	86.67±11.24	85.87±11.37	0.274	0.785
After 1 week of treatment	82.48±10.25	83.71±10.64	0.456	0.650

Note: HR: heart rate; CVP: central venous pressure; MAP: mean arterial pressure.

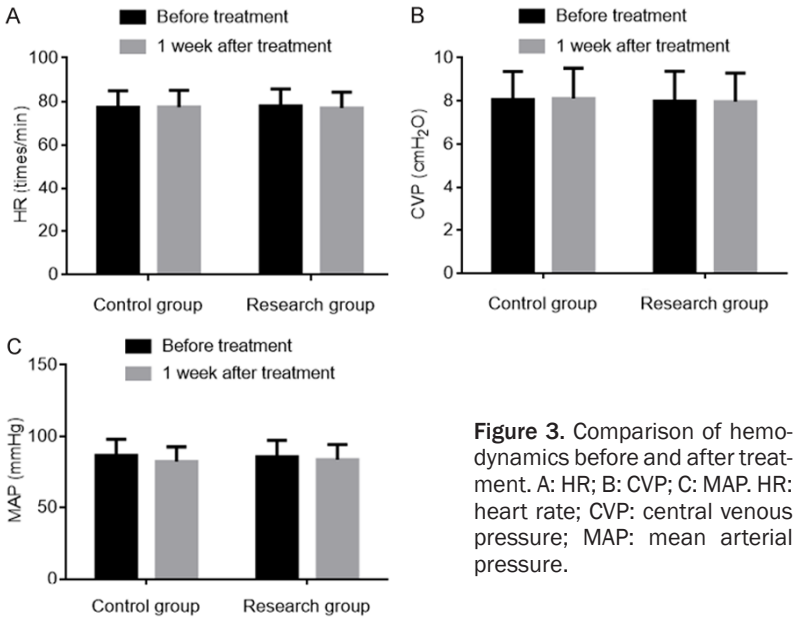

Figure 3. Comparison of hemodynamics before and after treatment. A: HR; B: CVP; C: MAP. HR: heart rate; CVP: central venous pressure; MAP: mean arterial pressure.

our study showed that patients in the research group had a higher total effective treatment rate, more sputum production and shorter duration of mechanical ventilation and ICU stay compared with those in the control group, which suggested that bronchofibroscope bronchoalveolar lavage can significantly improve the therapeutic effect of ICU patients with severe pneumonia and mechanical ventilation and shorten the overall treatment time. The reason is that bronchofibroscope bronchoalveolar lavage has the following advantages: First, it can be operated under direct vision, and this operation is more accurate. The secretions such as sputum can be fully sucked, so there is more sputum production and shorter mechanical ventilation time. Second, lavage can dilute the sputum embolus in the small airway and relieve the symptoms of bronchial mucosal edema and bronchospasm. Third, lavage can flush away the inflammatory mediators in the airway and reduce inflammation. Forth, sputum samples can be collected directly during lavage, which can provide evidence for antibiotic selection [15, 16]. Furthermore, the results of our study also showed that there were lower levels of WOBvent, PIP, RAW but higher level of Cdyn in the research group after treatment compared with the control group, which suggested that bronchofibroscope bronchoalveolar lavage therapy can significantly improve indicators in respiratory mechanics of ICU patients with severe pneumonia and mechanical ventilation. The reason is that bronchofibroscope bronchoalveolar lavage can keep the airway unobstructed by repeated washing of viscous sputum in the airway and expelling them from the airway, then lung recruitment can be realized. In addition, it can improve the ventilation function by improving lung compliance and reducing RAW [17, 18].

PCT, a glycoprotein with no hormonal activity, is a common inflammatory mediator. Under normal circumstances, the level of PCT in the body is very low, and it is difficult to be detected. However, when the body is infected, especially caused by bacteria, the expression level of PCT is abnormally elevated, and most of which are accompanied by abnormal body temperature and white blood cell count [19, 20]. When the level of PCT is too high, it is suggested that the inflammatory response is more serious, and antibiotic treatment should be given [21].

Table 6. Comparison of inflammatory mediators before and one week after treatment ($\bar{x} \pm sd$)

Group	Control group (n=30)	Research group (n=30)	t	P
CRP (mg/L)				
Before treatment	70.23±11.34	69.54±10.95	0.240	0.811
After 1 week of treatment	60.36±7.78	56.17±6.89	2.208	0.031
t	3.931	5.660		
P	<0.001	<0.001		
PCT (μg/L)				
Before treatment	28.43±3.56	28.15±3.47	0.308	0.759
After 1 week of treatment	25.53±3.03	23.86±2.88	2.188	0.033
t	3.398	5.211		
P	0.001	<0.001		

Note: CRP: C-reactive protein; PCT: procalcitonin.

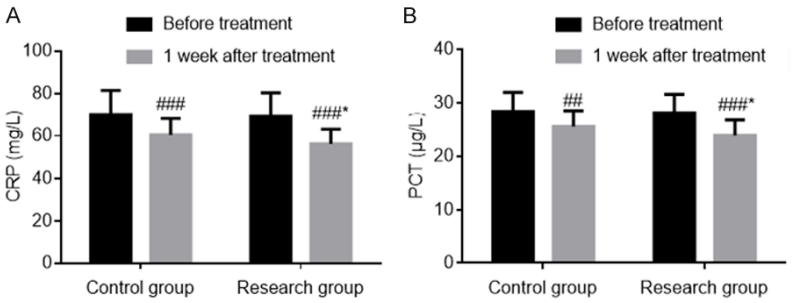

Figure 4. Comparison of inflammatory mediators before and after 1 week of treatment. A: CRP; B: PCT. Compared with before treatment, ##P<0.01, ###P<0.001; compared with control group, *P<0.05. CRP: C-reactive protein; PCT: procalcitonin.

CRP is a common high-sensitivity serum marker which can assess the degree of infection. Under normal circumstances, the level of CRP in human body is very low and it can keep stable for a long time. However, when the body is infected or injured, the level of CRP rises sharply, which can stimulate complement, enhance the activity of phagocytes and remove the invading pathogens [22]. When the body is placed under stress conditions, inflammatory factors such as IL-6, IL-1 and TNF-α can induce the synthesis of CRP [23]. The results of our study showed that the serum levels of CRP and PCT in the research group were lower than those in the control group after 1 week of treatment, suggesting that bronchofibroscope bronchoalveolar lavage therapy can effectively reduce the inflammation of ICU patients with severe pneumonia and mechanical ventilation. The reason as follows: First, the conditions of trachea and bronchus can be observed directly by bronchofibroscope. Second, local drug concentration can be increased to effective treatment concentration to exert antibacterial and anti-inflammatory effect by delivering the effective antibiotics to the indicated site directly through bronchofibroscope [24]. Third, normal saline needed to be used to wash the airway during lavage, which can effectively reduce the levels of local inflammatory factors [25]. The results of our study also showed that there was no significant difference in levels of HR, CVP, MAP and the incidence of adverse reactions after 1 week of treatment between the two groups, which suggested that bronchofibroscope bronchoalveolar lavage therapy for ICU patients with severe pneumonia and mechanical ventilation is very safe and has no significant effect on the hemodynamics of patients. It may be related to many factors such as too few samples and too short observation time in our study. Further study should be conducted by enlarging sample size and extending observation time.

In summary, the effect of bronchofibroscope bronchoalveolar lavage therapy for ICU patients with severe pneumonia and mechanical ventilation is obvious, which can shorten the overall treatment time, improve lung compliance and respiratory mechanics and reduce inflammation. Also, it has no significant effect on hemodynamics and produces few adverse reactions.

Disclosure of conflict of interest

None.

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Table 7. Comparison of adverse reactions between the two groups (n, %)

Group	Vomiting	Hoarseness	Cyanosis	Sinus tachycardia	Total incidence
Control group (n=30)	1 (3.33)	1 (3.33)	2 (6.67)	1 (3.33)	5 (16.67)
Research group (n=30)	2 (6.67)	0 (0)	1 (3.33)	1 (3.33)	4 (13.33)
t	0.351	1.017	0.351	0.000	0.131
P	0.554	0.313	0.554	1.000	0.718

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