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Clinical Efficacy and Safety of Mechanical Ventilation Combined with Fiberoptic Bronchoalveolar Lavage in Patients with Severe Pulmonary Infection

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to assess the clinical efficacy and safety of mechanical ventilation combined with fiberoptic bronchoalveolar lavage in patients with severe pulmonary infection.

Material/Methods: We randomly divided 81 patients with severe pulmonary infection into a control group (n=40) and an observation group (n=41). Both groups were treated using mechanical ventilation, and observation group additionally received assistive fiberoptic bronchoalveolar lavage.

Results: The cure rate and effectiveness rate in the observation group were higher than in the control group (P<0.05, χ^2=3.2), and the incidence of ventilator-associated pneumonia in the observation group was significantly lower than that in the control group (P<0.05, χ^2=9.4). The partial pressure of oxygen (PaO_2) and oxygen saturation (SaO_2) were higher in the observation group than in the control group (P<0.05, t=3.862, t=33.595), whereas the partial pressure of carbon dioxide ($PaCO_2$) and respiratory rate were lower in the observation group than in the control group (P<0.05, t=3.307, t=5.043). The levels of C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-8 (IL-8) in the 2 groups were lower after treatment than before treatment (all P<0.05), and the levels in the observation group were lower than those in the control group (all P<0.05). Hospital stay, infection control window appearance time, invasive mechanical ventilation time, and total mechanical ventilation time in the observation group were shorter than those in the control group (P<0.05, t=13.990, t=8.643, t=9.717, t=8.980).

Conclusions: Mechanical ventilation combined with fiberoptic bronchoalveolar lavage can effectively improve the curative effects and the blood gas and inflammation indicators in patients.

MeSH Keywords: Bronchoalveolar Lavage • Lung Diseases • Ventilation

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Background

Severe pulmonary infection is the most common form of severe pneumonia, which is serious because of its rapid development, long disease course, predisposition to cause respiratory failure, the involvement of many other organs, and its effects on the patient's quality of life [1,2]. The mortality rate of patients with severe pulmonary infection (approximately 20% to 50%) is the highest among those with infectious diseases. High-permeability edema, hyperemia, inflammatory exudation, and increased respiratory secretions in patients with severe pulmonary infection have a great effect on their respiratory function [3,4].

Mechanical ventilation is a very important assistive method in the treatment of patients with severe pulmonary infection, and can effectively improve pulmonary ventilation and gas exchange ability of patients [5,6]. However, owing to the serious condition of some patients and the poor therapeutic effect of mechanical ventilation, the mechanical ventilation time, incidence of ventilator-associated pneumonia, and mortality rate of patients have increased [7]. Fiberoptic bronchoalveolar lavage can allow clinicians to instantaneously evaluate the patients' lung conditions, sufficiently absorb airway excretions, restore airway smoothness, relieve bronchial obstruction, improve respiratory function, and more precisely determine the location of airway lesions; therefore, it is as an effective method for treatment of severe pneumonia [8]. Moreover, the microbiological analysis of alveolar lavage fluid can help identify pathogenic bacteria in the early clinical stage and facilitates targeted anti-microbial treatment [9]. Recently, some scholars have started preliminary explorations of whether mechanical ventilation combined with fiberoptic bronchoalveolar lavage can improve the curative effects in patients with severe pulmonary infection [10,11]. However, their findings have not been extensively verified by clinical experiments.

Therefore, we conducted a randomized controlled trial to study the clinical efficacy and safety of mechanical ventilation combined with fiberoptic bronchoalveolar lavage in patients with severe pulmonary infection.

Material and Methods

Study subjects

Eighty-one patients (ages 48–75 years) with severe pulmonary infection were selected from our hospital. They were randomly divided into a control group (n = 40) and an observation group (n=41). Both groups were treated using mechanical ventilation, and the patients in the observation group additionally received assistive fiberoptic bronchoalveolar lavage.

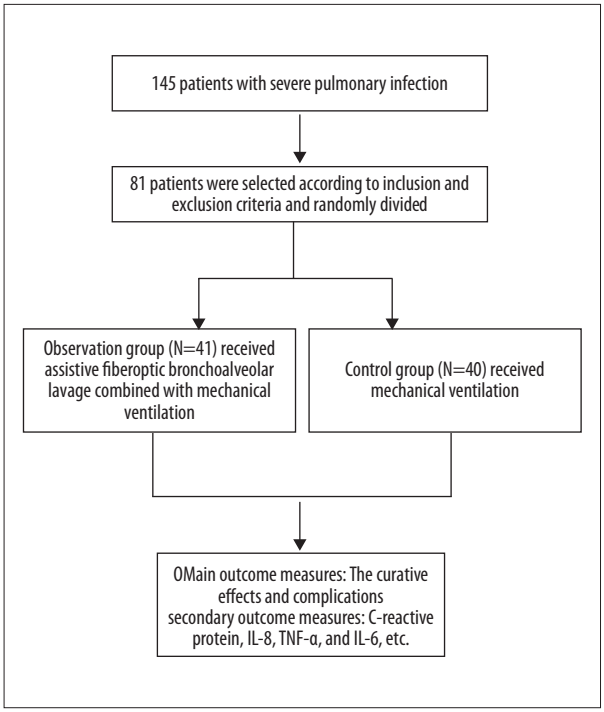

Figure 1. Flow chart of the study.

The inclusion criterion was that the study subjects meet the diagnostic criteria of the "Guidelines for the diagnosis and treatment of community-acquired pneumonia (CAP) for adults in China (2016 edition)." The exclusion criteria were as follows: patients with unstable coronary heart disease, patients with intermittent myocardial infarction, patients with severe pulmonary hypertension, patients with severe osteoarthritis or fracture, patients with concomitant liver and kidney dysfunction, patients with concomitant genetic and metabolic diseases, patients with concomitant endocrine system diseases, patients transferred midway, patients and relatives who do not co-operate with treatment, and patients with mental or learning dysfunctions (Figure 1). This study was approved by the Hospital Ethics Association, and informed consent forms were signed by the patients or their relatives (dated 13 September 2012).

Therapeutic methods

All patients received routine treatment, including spasmolytic and anti-asthmatic drugs, expectorants, broad-spectrum antibiotics, and anti-infective medications, as well as nutritional supplements. The artificial airway and tracheal intubation were established for invasive ventilation. The ventilation mode was synchronous intermittent forced ventilation combined with pressure support. After the control window of pulmonary infection appeared, tracheal intubation was discontinued and non-invasive ventilation was performed. The ventilator model used was BiPAP (Philips Respironics). The patients in the observation group underwent fiberoptic bronchoalveolar lavage

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as follows. The patients fasted and stopped drinking fluids 4 h before the operation. Thereafter, 3–5 mL of 2% lidocaine was administered through the tracheal tube for local anesthesia. Once anesthesia was induced, alveolar lavage was conducted using either an Olympus BF-3C30 or BF-P40 bronchofibroscope with 0.5–1 mL/kg of fluid collected each time, and the procedure was repeated 2–3 times. The alveolar lavage fluid was collected at 15-min intervals. During the course of fiberoptic bronchoalveolar lavage, an oxygen concentration of 30–50% and a negative pressure of no more than 200 mmHg were maintained.

Outcome measures

Main Outcome Measures: The curative effects and complications in the 2 groups were compared after 2 weeks of treatment.

Secondary Outcome Measures: The index changes in blood gas and blood routine indicators were observed. The levels of C-reactive protein (CRP), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) were compared between the 2 groups. The differences in hospital stay, infection control window appearance time, invasive mechanical ventilation time, and total mechanical ventilation time were also compared between the 2 groups.

Evaluation methods

The therapeutic effect evaluation criteria were as follows. Cured: The patients' lesions and symptoms disappeared completely, and the blood gas, blood routine, body temperature, and other physiological indicators returned to normal levels. Markedly effective: The patients' lesions and symptoms almost disappeared, body temperature returned to normal, and the blood gas, blood routine, and other indicators returned to almost normal levels. Ineffective: The patients' lesions did not decrease or even showed expansion; the symptoms were not alleviated or even showed aggravation; and the blood gas, blood routine, body temperature, and other physiological indicators did not improve. Effective rate=(number of cured+number of markedly effective)/total number of patients in the group×100%.

Blood gas and blood routine analyses were performed in the clinical laboratory of our hospital by using a fully automatic blood gas analyzer GEM3000 (Shanghai Yuyan Scientific Instrument Co.) and a fully automatic blood cell analyzer DS-580 (Xi'an Dongao Biological Technology Co.).

CRP, IL-8, TNF-α, and IL-6 were all detected using ELISA. The kits were purchased from Shanghai Jingkang Bioengineering Co. and their serial numbers were JK-EA00186, IC-IL8-p, JKSJ-1857, and JKSJ-2176, respectively. The tests were performed according to the manufacturer's instructions.

Statistical analysis

IBM SPSS Statistics for Windows/Macintosh, Version 19.0 (IBM Corp.) was used to process the data. Numerical data are expressed as [n (%)], and the rates were compared using χ^2 tests. Measurement data are expressed as x±sd. The independent-samples *t* test was used to compare the 2 groups, and the paired-samples *t* test was used for performing pre- and post-treatment comparisons. P<0.05 was considered to indicate statistical significance.

Results

Demographic data

The control group included 40 patients, ages 60.3±11.3 years, including 24 men (60.00%) and 16 women (40.00%). The observation group included 41 patients, aged 63.4±11.7 years, including 22 men (53.66%) and 19 women (46.34%). No significant difference was observed in sex and age between the 2 groups (P>0.05), and no significant difference was observed in other data, such as body temperature and respiratory frequency, between the 2 groups (P>0.05) (Table 1).

Curative effect evaluation

The cure rate and effective rate in the observation group were higher than those in the control group (P<0.05), and inefficiency was lower in the observation group than in the control group (P<0.05). No significant difference was observed in marked efficiency between the 2 groups (P>0.05) (Table 2).

Incidence of complications

The incidence of ventilator-associated pneumonia was 27.50% (11 cases) in the control group and 9.76% (6 cases) in the observation group. The incidence of ventilator-associated pneumonia in the observation group was significantly lower than that in the control group (P<0.05) (Figure 2).

Blood gas indicators detection results

No significant differences were observed in the PaO_2, $PaCO_2$, SaO_2, and respiratory rate between the 2 groups before treatment (P>0.05). After treatment, the PaO_2 and SaO_2 increased in both groups (P<0.05), and the $PaCO_2$ and respiratory rate decreased in both groups (P<0.05). The PaO_2 and SaO_2 in the observation group were higher than those in the control group (P<0.05), but the $PaCO_2$ and respiratory rate in the observation group were lower than those in the control group (P<0.05) (Table 3).

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Table 1. General data.

	Control group (n=40)	Observation group (n=41)	χ^2/t	P
Gender			0.332	0.565
Male	24 (60.00)	22 (53.66)		
Female	16 (40.00)	19 (46.34)		
Age (years)	60.3±11.3	63.4±11.7	1.213	0.229
Temperature (°C)	37.72±0.83	37.38±0.82	1.855	0.067
Respiratory rate (time/min)	29.13±8.96	28.46±9.31	0.330	0.742
Blood pH	7.23±0.06	7.25±0.07	1.379	0.172
$PaCO_2$ (mmHg)	58.63±11.75	56.42±11.86	0.842	0.402
Oxygenation index	132.14±28.67	139.71±28.46	0.193	0.237
Procalcitonin (ng/L)	1.65±1.38	1.43±1.04	0.812	0.420
CRP (mg/L)	117.28±43.82	116.43±34.85	0.097	0.923
White blood count (×10^9/L)	13.62±5.33	14.88±5.75	1.022	0.310
Platelet count (×10^9/L)	155.42±10.32	152.63±11.49	1.149	0.254
Mean arterial pressure (mmHg)	82.50±14.10	81.50±12.10	0.343	0.733

$PaCO_2$ – arterial partial pressure of carbon dioxide; CRP – C-reactive protein.

Table 2. Curative effect comparison.

	Control group (n=40)	Observation group (n=41)	χ^2/z	P
Cured	12 (30.00)	23 (56.10)	5.620	0.018
Marked effective	15 (37.50)	16 (39.02)	0.020	0.888
Ineffective	13 (32.50)	2 (4.88)	3.200	0.001
Effective rate	27 (67.50)	38 (92.68)	3.200	0.001

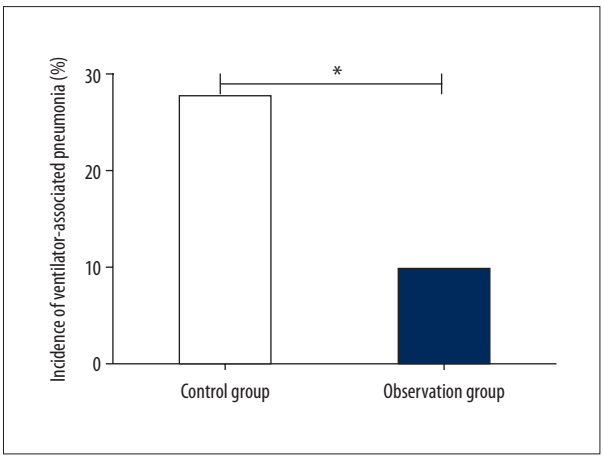

Figure 2. Incidence of ventilator-associated pneumonia. * P<0.05.

Routine blood indexes detection results

No significant difference was observed in the white blood cell count between the 2 groups before treatment (P>0.05). After treatment, the white blood cell count decreased in both groups (P<0.05), but no significant difference was observed between the observation group and the control group (P>0.05) (Figure 3).

Cytokines detection results

No significant differences were observed in the levels of CRP, TNF-α, IL-6, and IL-8 between the 2 groups before treatment (P>0.05). The levels of CRP, TNF-α, IL-6, and IL-8 in the 2 groups after treatment were lower than those before treatment (P<0.05). After treatment, the levels of CRP, TNF-α, IL-6, and IL-8 in the observation group were lower than those in the control group (P<0.05) (Table 4).

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Table 3. Detection results of blood gas indicators.

		Control group (n=40)	Observation group (n=41)	t	P
PaO_2 (mmHg)	Before treatment	51.13±14.32	51.26±14.27	0.041	0.928
	4 hours after the first treatment	70.16±13.22*	81.18±12.46*	3.862	
$PaCO_2$ (mmHg)	Before treatment	58.63±11.75	56.42±11.86	0.842	0.402
	4 hours after the first treatment	34.37±4.52*	31.14±4.27*	3.307	0.001
SaO_2 (%)	Before treatment	71.53±3.66	70.47±3.52	1.329	0.188
	4 hours after the first treatment	81.13±2.03*	93.68±1.25*	33.595	<0.001
Respiratory rate (time/min)	Before treatment	29.13±8.96	28.46±9.31	0.330	0.742
	4 hours after the first treatment	27.85±8.81*	20.39±3.44*	5.043	<0.001

* Shows that the P value was <0.05 compared with the same group after treatment. PaO_2 – arterial partial pressure of oxygen; $PaCO_2$ – arterial partial pressure of carbon dioxide; SaO_2 – blood oxygen saturation.

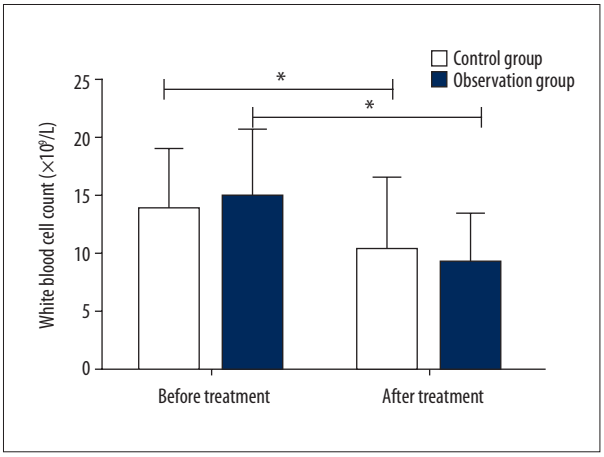

Figure 3. Changes in the white blood cell count before and after treatment in the 2 groups. * P<0.05.

Statistical results of the clinical indicators

Hospital stay, infection control window appearance time, invasive mechanical ventilation time, and total mechanical ventilation time in the observation group were shorter than those in the control group (P<0.05) (Table 5).

Discussion

The mortality rate of patients with severe pulmonary infection is very high. Moreover, the condition is serious because of its rapid development, long disease course, predisposition to cause respiratory failure, the involvement of many other organs, and its effects on the quality of life and prognosis of patients [12,13]. Mechanical ventilation is an indispensable

Table 4. Detection results of cytokines.

		Control group (n=40)	Observation group (n=41)	t	P
CRP (mg/L)	Before treatment	117.28±43.82	116.43±34.85	0.097	0.923
	After treatment	27.49±8.25*	13.62±1.73*	10.532	<0.001
TNF-α (ng/L)	Before treatment	45.76±14.54	46.38±14.29	0.194	0.847
	After treatment	26.63±8.22*	13.36±3.26*	9.594	<0.001
IL-6 (ng/L)	Before treatment	94.04±25.43	93.57±22.56	0.088	0.930
	After treatment	33.28±9.13*	11.15±3.27*	14.593	<0.001
IL-8 (ng/L)	Before treatment	309.24±79.59	317.29±81.27	0.450	0.654
	After treatment	83.16±21.16*	20.14±4.75*	18.5999	<0.001

* Shows that the P value was <0.05 compared with the same group after treatment. CRP – C-reactive protein; IL-8 – interleukin-8; TNF-α – tumor necrosis factor-α; IL-6 – interleukin-6.

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Table 5. Statistical results of clinical indicators (days).

	Control group (n=40)	Observation group (n=41)	t	P
Hospital stay	25.53±2.54	19.24±1.31	13.990	0.000
Infection control window appearance time	9.17±2.41	5.41±1.38	8.643	<0.001
Invasive mechanical ventilation time	15.33±3.26	9.35±2.18	9.717	<0.001
Total mechanical ventilation time	9.21±2.31	4.66±2.25	8.980	<0.001

assistive method for the treatment of severe pneumonia, but it can easily cause lung injury or bacterial infection, and can prolong the mechanical ventilation time, which in turn affects the weaning and prognosis of patients. Since the first report of alveolar lavage in 1974 and the continuous improvements in bronchofibroscopy, fiberoptic bronchoalveolar lavage has become widely used in clinical practice. The reduction in the diameter of the bronchofibroscope and advancements in its application technology have enabled its synchronous use with mechanical ventilation [14,15]. Recent studies have reported the efficacy and promising results of mechanical ventilation combined with fiberoptic bronchoalveolar lavage in the treatment of severe pneumonia [16,17]. However, these findings have not been extensively evaluated in the clinical setting. Therefore, this study re-validated the application of mechanical ventilation combined with fiberoptic bronchoalveolar lavage in patients with severe pulmonary infection to provide a reference for the clinical treatment of severe pulmonary infection.

This retrospective study included 81 patients with severe pulmonary infection. The findings showed no statistically significant difference in the general data between the 2 groups, suggesting that they were comparable and that the results of the study are credible. The curative effect analysis of the 2 treatment methods showed that the curative effect of mechanical ventilation combined with fiberoptic bronchoalveolar lavage was significantly better than that of mechanical ventilation alone, and the cure rate of the observation group was significantly higher than that of the control group. The analysis of blood gas indicators also showed that the improvement in PaO_2, $PaCO_2$, SaO_2, and respiratory rate was significantly better in the observation group than in the control group at 4 h after the first treatment.

Physical expectoration, wetting expectoration, and drug expectoration are common methods of expectoration applied during mechanical ventilation for patients, and include techniques such as turning the patient over and patting the back as well as aerosol inhalation of a wetting solution containing expectorant drugs. However, these methods often present difficulties in clinical application. Physical expectoration is not effective in patients with severe disease, and wetting expectoration has the risk of burning the respiratory tract mucosa and causing laryngospasms [18,19]. Drug expectoration is an ideal method, but compared to conventional aerosol inhalation or oral administration, bronchofibroscopy can help more accurately administer drugs locally to airway lesions and can increase the drug concentration in a shorter time. Moreover, fiberoptic bronchoalveolar lavage can thoroughly remove bronchiolar and alveolar excretions, including viscous sputum and sputum bolt. Studies have also shown that physical expectoration is more difficult to achieve [16,20]. This may be why the curative effects in the observation group were better than those in the control group.

Compared with the control group, the observation group had significantly shorter time of invasive mechanical ventilation and total mechanical ventilation. The mechanical ventilation time was the main cause of ventilator-associated pneumonia [21]. Our results showed that the incidence of ventilator-associated pneumonia in the observation group was significantly lower than that in the control group, which was an important reason for the better curative effect in the observation group. During bacterial and other pathogenic infections, the immune response of patients with severe pulmonary infection was stimulated, and a variety of inflammatory factors were secreted [22]. CRP, TNF-α, IL-6, and IL-8 are the important proinflammatory factors secreted during the process of inflammation. The detection of these factors can help accurately evaluate the degree of inflammation reaction and infection control. Our results showed that the improvement in CRP, TNF-α, IL-6, and IL-8 levels after treatment was significantly better in the observation group than in the control group. Some studies have also reported that detecting the expression of inflammatory factors in the bronchoalveolar lavage fluid can help identify bacterial infection, viral infection, and mixed infection [23], and this is very important in designing clinical treatment, because mixed infection and bacterial infection have a more serious impact on the prognosis of the patients [24].

The advantages of mechanical ventilation combined with fiberoptic bronchoalveolar lavage in the treatment of patients with severe pulmonary infections were reflected in our results [25]. However, owing to the retrospective nature of this study, there were some limitations, such as small sample size as well as the sputum expectoration method used in the control group and the inadequate control of the initial cause of severe pulmonary infection, which may lead to a bias in the

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results. In addition, from an economic perspective, fiberoptic bronchoalveolar lavage will increase medical costs. Although our results showed that the hospital stay of patients in the observation group was significantly shorter than that of patients in the control group, it is uncertain whether the reduced medical costs can make up for the treatment costs of fiberoptic bronchoalveolar lavage. We plan to further control the experimental conditions and increase the sample size in future multicenter randomized controlled trials. One study has reported that IL-33 can bind to ST2L on the surface of inflammatory cells, activate various biochemical pathways such as mitogen-activated protein kinase, and finally activate nuclear factor-κB kinase complex to exert the proinflammatory effect of nuclear factor-κB. There is a relationship between the immune system cells, cytokines, and the ST2 expression. IL-6 produced by antigen-presenting cells can promote the expression of ST2 during Th2 differentiation [26]. Whether ST2 could be treated as potential targets should be explored further as well.

Conclusions

In conclusion, mechanical ventilation combined with fiberoptic bronchoalveolar lavage can effectively improve the therapeutic effect and the blood gas and inflammatory indicators in patients, while reducing the incidence of ventilator-associated pneumonia, mechanical ventilation time, and hospital stay, thereby making this technique worthy of clinical promotion.

Conflict of interest

None.

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