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Original Article

Effect of fiberoptic bronchoscope combined with ambroxol alveolar lavage on the treatment of pulmonary atelectasis in severe pneumonia and its influences on systemic inflammatory response and respiratory mechanics

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Abstract: Objective: To explore the efficacy of fiberoptic bronchoscope combined with ambroxol alveolar lavage on patients with both severe pneumonia and pulmonary atelectasis and its effects on their systemic inflammatory response and respiratory mechanical indexes. Methods: A total of 60 patients diagnosed with both severe pneumonia and pulmonary atelectasis from May 2018 to May 2019 were enrolled and studied, and they were randomly assigned to a control group and an observation group (each n=30). The control group was treated with fiberoptic bronchoscopic lavage, while the observation group was treated with fiberoptic bronchoscope combined with ambroxol alveolar lavage. After 2 weeks of intervention, the efficacy and complications were compared between the two groups, and the following aspects of the two groups before and after treatment and at 6-month follow-up were analyzed: Serum inflammatory indexes including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) and respiratory mechanical indexes including forced expiratory volume in 1 second (FEV1)% and FEV1/forced vital capacity (FVC), arterial oxygen partial pressure (PaO_2), arterial partial pressure of carbon dioxide (PCO_2), and oxygen saturation. Results: The total effective rate of the observation group was significantly higher than that of the control group (P<0.05), and no serious complications occurred in either of the two groups. After treatment, both groups showed a decrease in the levels of CRP, IL-6, and TNF-α and PCO_2 and an increase in FEV1%, FEV1/FVC, PaO_2, and oxygen saturation, and the improvement of the observation group in those aspects was more significant than that of the control group (all P<0.05). In addition, at the 6-month follow-up, there was no significant difference in CRP, IL-6, and TNF-α levels, FEV1%, FEV1/FVC, PaO_2, PCO_2, and oxygen saturation between the two groups (all P>0.05). Conclusion: Fiberoptic bronchoscope combined with ambroxol alveolar lavage is relatively safe and effective in treating patients with both severe pneumonia and pulmonary atelectasis, and can effectively improve the systemic inflammatory response and respiratory mechanical indexes of the patients, with long-lasting improvement effects on the pulmonary function.

Keywords: Fiberoptic bronchoscope, ambroxol, alveolar lavage, severe pneumonia, pulmonary atelectasis, inflammatory response, respiratory mechanics

Introduction

Severe pneumonia is one of the major fatal diseases found in intensive care units. Advanced age, long-term bed rest, diabetes mellitus, stroke, chronic obstructive pulmonary disease, kidney dialysis, and immunosuppressive therapy are high-risk factors for severe pneumonia [1], and the main pathogenic bacteria are Gram-negative bacteria. With the non-standard usage of antibiotics, the generation rate of drug-resistant bacteria is increasing, leading to the failure of antibacterial therapy [2]. Severe pneumonia mainly manifests as pulmonary infection, pulmonary function decline, secondary sepsis, pulmonary atelectasis, and pleural effusion, and even consciousness disorders and multiple organ dysfunction syndrome or death [3]. Therefore, it is crucial to find an effective and reasonable treatment.

Fiberoptic bronchoscope can directly reach the lower airway to provide a direct vision and focus on tissues and help to locally inject antibiotics into the airways and alveoli and flush blocked airways and alveoli, which can more effectively increase the concentration of antibiotics in the airway [4-6]. At present, there are no specific drugs for severe pneumonia comorbid with pulmonary atelectasis used in clinical practice, and this disease is often treated by antibiotics under fiberoptic bronchoscope, which is prone to bring about drug resistance and it cannot meet the clinical treatment demands [7]. Ambroxol can effectively inhibit the secretion of mucus in the airways, dilute the mucus, and promote the excretion of mucus, and it can also effectively inhibit airway inflammatory reactions and increase the body's immune function and anti-infection ability; so it plays a crucial role in the treatment of various respiratory diseases [8-11]. However, there are few related studies on lavage therapy with ambroxol hydrochloride with administration by fiberoptic bronchoscope. On the basis of previous studies, this study retrospectively analyzed the general clinical data of 60 patients with both severe pneumonia and pulmonary atelectasis and explored the clinical efficacy of different treatment methods and their effects on inflammatory factors and respiratory mechanical indexes, with the goal of providing a basis for clinical treatment of the disease. The results are reported as follows.

Participants and methods

Data about participants

A total of 60 patients with both severe pneumonia and pulmonary atelectasis admitted to Xuzhou Central Hospital from May 2018 to May 2019 were enrolled and studied. The inclusion criteria of the study: Patients between 18 and 75 years old, patients meeting the diagnostic criteria of severe pneumonia and pulmonary atelectasis [12], and patients who signed informed consent forms. The exclusion criteria of the study: Patients with comorbid lung tumors or severe pulmonary dysfunction, patients with severe heart, liver or kidney dysfunction or antibiotic resistance, patients with contraindications to bronchial lavage, and those unable to cooperate with the treatment and follow-up. The included patients were assigned to a control group and an observation group with 30 cases in each group according to the even and odd admission date.

Research methods

After admission, all patients received relevant examinations, including CT imaging of the lung, bronchoscope and examinations of pulmonary function, routine blood work, liver and kidney function, coagulation function, etc., and they were told about the main steps and precautions of bronchoalveolar lavage. Each patient signed a consent form, and his/her nervousness was relieved. In addition, regular rescue instrument and drugs were prepared. Patients in the two groups were given routine clinical treatment, including administration of enough broad-spectrum antibiotics in the early stage, appropriate amount of infusions, and respiratory support treatment when necessary. Blood and sputum were sampled from each patient for bacterial culture, and antibiotic types and schemes were adjusted according to a drug sensitivity test.

Patients in the control group were treated through the fiberoptic bronchoscopic lavage, and patients in the observation group were treated through fiberoptic bronchoscope (Olympus Corporation, PENTAX EB-1575K) combined with ambroxol (EMIS, Shandong, China) alveolar lavage as follows: the patients were asked to fast from solids for 12 h and from liquids for 4 h before operation, and then their airway was locally anesthetized with 2% lidocaine (Cisen Pharmaceutical Co., Ltd., Shandong, China) in a supine position. Afterwards, a fiberoptic bronchoscope was inserted through a tracheal intubation according to imaging results to gradually aspirate the secretions in the airway, and bacterial culture and drug sensitivity tests were conducted to analyze the infected site.

Different groups were given different lavage drugs. Each patient in the control group was rapidly injected with 37°C sterilized saline through biopsy holes, 20-50 mL each time and 60-120 mL in total. Finally, they were given 50-100 mmHg negative pressure to suck out the lavage fluid (the recovery of the lavage fluid was guaranteed to be more than 30%). In contrast, each patient in the observation group was injected with 15 mg ambroxol dis-

solved in 20 mL normal saline several times, 20-50 mL each time and 60-120 mL in total, and they were given 50-100 mmHg negative pressure to suck out the lavage fluid (the recovery of the lavage fluid was guaranteed to be more than 30%). Patients in both groups were treated 2-3 times per week for 2 weeks, and finally the mucus was filtered with double-layer sterile gauze and transferred to a silicon plastic bottle for inspection. Bacterial culture and drug sensitivity test were conducted.

Outcome measures and detection indexes

After 2 weeks of intervention, the efficacy and complications were compared between the two groups, and the following aspects of the two groups before and after treatment and at 6-month follow-up were analyzed: Serum inflammatory indexes including C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α) and respiratory mechanical indexes including forced expiratory volume in 1 second (FEV1)% and FEV1/forced vital capacity (FVC), arterial oxygen partial pressure (PaO_2), arterial partial pressure of carbon dioxide (PCO_2), and oxygen saturation.

The clinical efficacy was classified into four types according to the guiding opinion for the treatment of pulmonary infection [12]: recuperative, markedly effective, effective, and ineffective. Treatment with the following outcomes was considered as recuperative: the Chest X-ray and CT showed that the pneumonia and pulmonary atelectasis disappeared, and all vital signs returned to normal. Treatment with the following outcomes was considered as markedly effective: pneumonia and pulmonary atelectasis were alleviated significantly according to imaging, and all vital signs gradually returned to normal. Treatment with the following outcomes was considered as effective: pneumonia and pulmonary atelectasis were alleviated according to imaging, and all vital signs were improved. Treatment with the following outcomes was considered as ineffective: pneumonia and pulmonary atelectasis were not alleviated or even aggravated. The total effective rate = (the number of patients with recuperative efficacy + the number of patients with markedly effective efficacy + the number of patients with effective efficacy)/the total number of patients. The complications mainly included sepsis, multiple organ dysfunction syndrome, consciousness disorders, and death.

Fasting peripheral venous blood (10 mL) was sampled from each patient in the morning, placed in anticoagulant tubes, and centrifuged at 2,500 r/min for 10 min, and the collected upper serum was stored at -70°C for later analysis. CRP, IL-6 and TNF-α in the serum were detected using an enzyme-linked immuno-sorbent assay (ELISA) with corresponding ELISA kits from Sigma in the United States (item numbers: 2018121312, 2018165549, and 2018356497) in strict accordance with kit instructions. FVC and FEV1 of the patients were detected by a skilled examination physician independently with an Italian MIR III portable pulmonary function apparatus. After being guided to perform effective and accurate respiratory movements, each patient was examined two times at an interval of 25 min, and the obtained results were averaged. In addition, the PaO_2, PCO_2, and oxygen saturation of the patients in a clam state were determined using a domestic finger-clip-pattern pulse oximeter according to instructions, three times and the results were averaged.

Statistical analysis

The data were processed statistically using SPSS 19.0. Measurement data in normal distribution are expressed as the ($\bar{x} \pm$ sd), and compared between groups using the independent-samples t test. Enumeration data were analyzed using the χ^2 test, and ranked data were analyzed using the Mann-Whitney U rank sum test. α=0.05 was taken as the test criteria. $P<0.05$ indicated significance.

Results

General data

There was no significant difference between the two groups in sex, age, body mass index (BMI), strain, and pulmonary atelectasis ratio (all $P>0.05$), which were comparable. See **Table 1**.

Comparison of clinical efficacy and complications between the two groups

The total effective rate of the observation group was significantly higher than that of the control group (χ^2=4.812, P=0.028), and no serious complications occurred in the two groups. See **Table 2**.

Table 1. Comparison of general data

Group	Number of cases	Male/Female	Age (years)	Body mass index (kg/m^2)	G-/G+ strain infection	Pulmonary atelectasis ratio (%)
Control group	30	18/12	58.9±6.5	24.5±2.3	17/13	12.3±3.6
Observation group	30	16/14	59.6±6.8	24.8±2.6	18/12	13.5±3.9
t/χ^2		0.271	0.563	0.329	0.069	0.196
P		0.602	0.524	0.627	0.793	0.852

Table 2. Comparison of clinical efficacy and complications (n, %)

Group	Number of cases	Recuperative	Markedly effective	Effective	Ineffective	Total effective
Control group	30	6 (20.0)	5 (16.7)	9 (30.0)	10 (33.3)	20 (66.7)
Observation group	30	11 (36.7)	9 (30.0)	7 (23.3)	3 (10.0)	27 (90.0)
χ^2						4.812
P						0.028

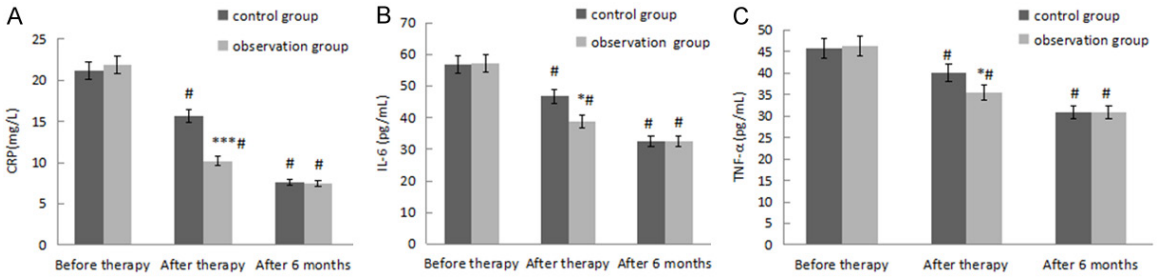

Figure 1. Comparison of serum CRP, IL-6, and TNF-α levels between the two groups before and after treatment. A: Comparison of serum CRP before and after treatment; B: Comparison of serum IL-6 before and after treatment; C: Comparison of serum TNF-α before and after treatment. Compared to control group, *P<0.05, compared to control group, ***P<0.001, compared to before the treatment, #P<0.05. CRP: C-reactive protein; IL-6: interleukin6; TNF-α: tumor necrosis factor α.

Comparison of serum CRP, IL-6, and TNF-α levels between the two groups before and after treatment

After treatment, both groups showed a decrease in the levels of CRP, IL-6, and TNF-α, and the observation group showed a more significant improvement in those aspects than the control group (t=10.358, 11.022, 9.614, respectively; P=0.000, 0.012, 0.023, respectively). In addition, at the 6-month follow-up, there was no significant difference in CRP, IL-6 and TNF-α levels between the two groups (t=1.247, 0.981, 0.659, respectively; P=1.652, 2.327, 3.644, respectively). See **Figure 1**.

Comparison of pulmonary function between the two groups before and after treatment

After treatment, both groups showed an increase in FEV1% and FEV1/FVC (both P<0.05), and the improvement of the observation group in these aspect was more significant than that of the control group (t=4.757, 4.622, respectively; P=0.044, 0.041, respectively). At the 6-month follow-up, there was no significant difference in FEV1% and FEV1/FVC between the two groups (t=0.884, 0.685, respectively; P=1.243, 1.184, respectively). See **Figure 2**.

Comparison of blood oxygen indexes between the two groups before and after treatment

After treatment, both groups showed an increase in PaO_2 and oxygen saturation (both *P*<0.05) and a decrease in PCO_2, and the observation group showed a more significant improvement than the control group (t=8.613, 9.482, 7.668, respectively; P=0.041, 0.042, 0.044, respectively). At 6-month follow-up, there was no significant difference in PaO_2, PCO_2, and oxygen saturation between the two groups (t=0.474, 0.388, 0.404, respectively;

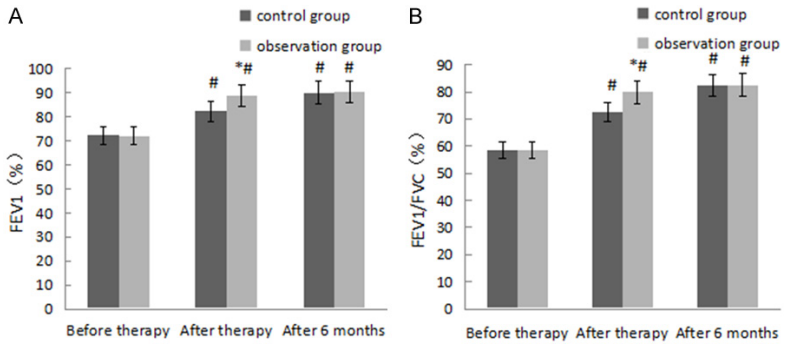

Figure 2. Comparison of pulmonary function before and after treatment. A: Comparison of FEV1% before and after treatment; B: Comparison of FEV1/FVC before and after treatment. Compared to control group, *P<0.05; compared to before the treatment, #P<0.05. FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity.

P=2.66, 1.976, 2.253, respectively). See **Figure 3**.

Discussion

Severe pneumonia is often complicated with pulmonary atelectasis, which increases the difficulty of anti-infection and respiratory support treatment and is an important adverse factor of clinical death [13]. The increase of pathogenic bacteria in the airway causes epithelial cells to release a large amounts of mucus and inflammatory factors, inducing the aggregation of inflammatory cells and mediators, increasing tissue edema, blocking the airway and alveolar tissues, and finally resulting in dyspnea, ventilation disorder, alveolar oxygenation disorder, and more severe tissue hypoxia [14]. In addition, due to the increase, a large amount of mucus in the airway cannot be discharged, which aggravates pulmonary atelectasis. Antibiotics and ambroxol applied systemically cannot efficiently accumulate in the airway, which may prolong drug use time and increase mortality and complications.

One study has shown that fiberoptic bronchoscope combined with ambroxol alveolar lavage can strongly alleviate the neurological deficit of patients with cerebral infarction complicated with severe pneumonia and pulmonary atelectasis and can lower the influence of inflammatory factors in the patients and improve the treatment effect and recovery of patients [15]. This study explored fiberoptic bronchoscope combined with ambroxol alveolar lavage, finding that the total clinical effective rate of the observation group was significantly higher than that of the control group, and no serious complications occurred in the two groups, which implied that fiberoptic bronchoscope combined with ambroxol alveolar lavage was more effective in the treatment of severe pneumonia comorbid with pulmonary atelectasis than normal saline under bronchoscope delivery. It may be due to the fact that under the direct vision of bronchi, ambroxol could be focused more accurately, and could effectively accumulate at the site with mucus secretions in the airway, strongly inhibit the secretion of airway mucus, dilute mucus, and promote the excretion of mucus, and it could also effectively inhibit airway inflammatory reactions, and increase the body's immune function and anti-infection ability, and alveolar lavage could reduce airway inflammation and mucus secretion and restore airway physiological function.

One study by Chen et al. has pointed out that IL-6 in bronchoalveolar lavage fluid can be used as a useful indicator for the severity of acute severe pneumonia in children [16]. Some studies have shown that patients with severe pneumonia, stimulated by inflammatory factors and antigenic substances, secrete a large number of inflammatory factors such as high sensitivity C-reactive protein (hs-CRP), TNF-α, IL-6, and procalcitonin (PCT) that participate in the disease progression [17]. In this study, after treatment, the observation group showed decreased serum CRP, IL-6, and TNF-α levels, increased FEV1% and FEV1/FVC, PaO_2, and oxygen saturation, and decreased PCO_2 compared with the control group, and the differences between the two groups in CRP, IL-6, and TNF-α levels, PaO_2, PCO_2, and oxygen saturation were insignificant. CRP, IL-6, and TNF-α are sensitive indicators, quantitatively reflecting the severity of pulmonary infection, which have a correlation with the severity of the disease and clinical prognosis [18]. One study by Guan et al. [19] has revealed that ambroxol is effective in the treatment of adults with severe pneumonia and can significantly ameliorate the

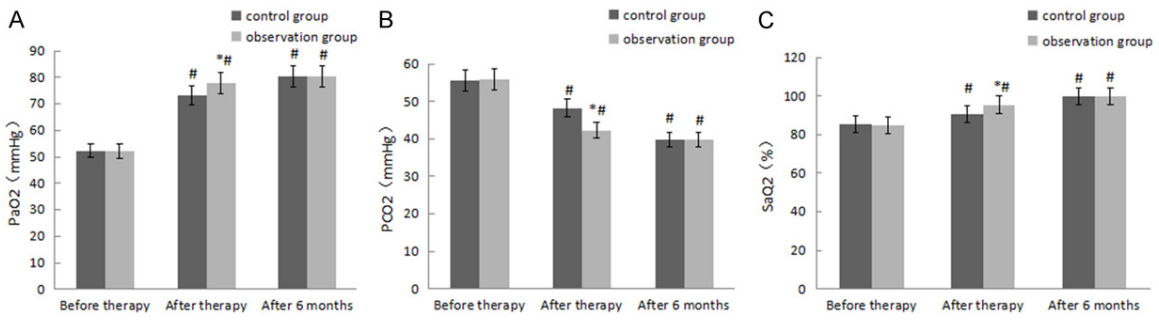

Figure 3. Comparison of blood oxygen indexes between the two groups before and after treatment. A: Comparison of PaO_2 between the two groups before and after treatment; B: Comparison of PCO_2 between the two groups before and after treatment; C: Comparison of SaO_2 between the two groups before and after treatment. Compared to control group, $^*P<0.05$, compared to before the treatment, $^\#P<0.05$. PaO_2: arterial oxygen partial pressure; PCO_2: arterial partial pressure of carbon dioxide; SaO_2: oxygen saturation.

clinical symptoms of patients and reduce the inflammatory reaction of patients, which further verifies the research results of this study. FEV1% and FEV1/FVC, as the main indexes reflecting the pulmonary function, can provide a high accuracy in judging lung oxygenation ability [20]. It suggests that bronchoscope combined with ambroxol alveolar lavage can strongly inhibit the inflammatory reaction of the body and improve the pulmonary function and oxygenation function.

We believe that fiberoptic bronchoscope combined with ambroxol alveolar lavage is a relatively safe clinical scheme and has favorable application effects on various lung diseases. By increasing the concentration of local ambroxol in the airway, fiberoptic bronchoscope combined with ambroxol alveolar lavage further exerts its functions of diluting sputum, inhibiting inflammatory reactions, enhancing immune function, and remodeling airway physiological function. It is worth noting that it is necessary to strictly screen patients who are suitable for bronchoscopy and alveolar lavage and to determine the scope of lung diseases before operation and whether there is an exact lavage scope. In addition, it is also necessary to determine the insertion point of bronchoscope, understand the lavage times, and accurately evaluate the clinical symptoms of patients. Anti-infection and respiratory support is the basis of all treatments [21].

There are some deficiencies in this study. For example, the number of cases enrolled in this study is small, and the patients were not followed up for long term prognosis. In the future, we will increase the sample size and prolong the follow-up time to further clarify the curative effect of fiberoptic bronchoscope combined with ambroxol alveolar lavage.

To sum up, fiberoptic bronchoscope combined with ambroxol alveolar lavage is relatively safe and effective in treating patients with both severe pneumonia and pulmonary atelectasis and can strongly improve the recent systemic inflammatory response and respiratory mechanical indexes of the patients, with long-lasting improvement effects on the pulmonary function.

Disclosure of conflict of interest

None.

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