Original Article

A randomised trial on the therapeutic effectiveness of bronchoalveolar lavage under fiberoptic bronchoscopy in patients with severe lung infection living in the Tibetan plateau area

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Background: People living in plateau areas are prone to upper respiratory tract infections and secondary lung infections. The current study aimed to explore the effects of bronchoalveolar lavage under fiberoptic bronchoscope for the treatment of patients with severe pulmonary infection living in plateau areas.

Methods: 148 patients with severe lung infection admitted to the intensive care unit of Shigatse People's Hospital (Shigatse, Tibet Autonomous Region, China) between July 2019 and January 2021 were enrolled. Patients were randomly assigned to the observational group or the control group. For all patients, basic clinical data including sex, age, body mass index (BMI), blood pressure, diabetes history, stroke history, presence or absence of chronic obstructive pulmonary disease, lung infection (gram-positive bacterial infection, gram-negative bacterial infection, fungal infection, acute lung abscess), surgical history, and postoperative inhalation injury. were collected. The control group received conventional treatment, and the observational group received bronchoalveolar lavage under fiberoptic bronchoscopy. Pearson's correlation was used to analyze the correlations between bronchoalveolar lavage under fiberoptic bronchoscopy and inflammatory factors levels. Logistic regression was used to investigate the correlation between bronchoalveolar lavage under fiberoptic bronchoscopy and the effectiveness of the treatment.

Results: Before treatment, no significant difference existed in the basic data of the observational group and the control group. After treatment, the parameters of respiratory mechanics and inflammatory factors in the 2 groups were significantly improved compared with those before treatment ($P<0.05$). At the same time, in the observational group, the clinical parameters were significantly higher than those of the control group, and the levels of inflammatory factors were significantly lower than those of the control group (all $P<0.05$). After full adjustment for age, sex, BMI, gram-negative infection, diabetes, and acute lung abscess, compared with the control group, the therapeutic effectiveness in the observational group was increased by 23% (OR =1.23, 95% CI: 1.09–1.51, P=0.007).

Conclusions: For patients with severe lung infection who are resident in high altitude areas, compared with conventional treatments, bronchoalveolar lavage under fiberoptic bronchoscopy can significantly improve chest, lung, and total dynamic compliance, as well as reduce the levels of the inflammatory factors procalcitonin (PCT) and transforming growth factor-β, thus increasing the effectiveness of the treatment.

Keywords: Bronchoscopy; severe pulmonary infection; plateau area

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Introduction

Pulmonary infection is characterized by substantial inflammation of the alveolar cavity, the interstitium of the lungs, and terminal airways. It is mainly caused by virulent bacterial infection, including by drug-resistant bacteria, or infection with multiple bacteria simultaneously, with *Staphylococcus aureus* and *Streptococcus pneumoniae* being the most frequent culprit pathogens. The major clinical characteristics of pulmonary infection include cough, increased respiratory secretions, and weakness (1,2). The severe pulmonary infection is a serious lung illness accompanied by varying degrees of abnormal parameters of respiratory mechanics which can stimulate the overexpression of multiple inflammatory factors. Among these overexpressed inflammatory factors, procalcitonin (PCT) and transforming growth factor β (TGF-β) are the most significant. Therefore, measurement of the levels of these 2 growth factors can be used to evaluate the severity of pulmonary infection (3,4).

Year-round residents of plateau areas are prone to developing upper respiratory tract infections and secondary pulmonary infections. Long-term exposure to low oxygen, low air pressure, and cold can cause dryness and congestion of the upper respiratory tract, which is conducive to respiratory infections. If a severe pulmonary infection is complicated by a serious condition, a delay in treatment may even result in acute respiratory failure, which dramatically threatens the health and life of the patient (5,6). Timely control of the infected lesions is important for the effective treatment. At present, anti-infective treatment is still in a simple and systematic research stage. The effective concentration of drugs in the local lesions is often low; moreover, the application of broad-spectrum antibacterial drugs has led to an increase in drug-resistant strains, which makes constraining infections even more difficult to effectively accomplish (7). The key to treating a severe pulmonary infection is to support the patient to breathe smoothly so that the medicine can work more effectively. Increased lung secretions have been reported to lead to airway obstruction (8), increase the difficulty of expectoration, induce the accretion of irritating substances, and induce a series of cascade reactions. As a precision inspection method, fiberoptic bronchoscopy is widely used to diagnose and treat a variety of bronchial illnesses. It can eliminate sputum and visible inflammatory secretions, and can help to completely flush the patient's lesions, therefore allowing for better control of the pulmonary infection (9).

The purpose of the present research was to investigate the therapeutic effectiveness of bronchoalveolar lavage (BAL) under fiberoptic bronchoscopy in patients with severe pulmonary infection residing in the Tibetan plateau area, and to provide a clinical reference. We present the following article in accordance with the CONSORT reporting checklist (available at http://dx.doi.org/10.21037/apm-21-470).

Methods

Research participants

This study enrolled 148 patients with severe pneumonia of various causes who were admitted to the comprehensive intensive care unit of Shigatse People's Hospital (Shigatse, Tibet Autonomous Region, China) between July 2019 and January 2021. Patients were randomly assigned to the observational group or the control group. The criteria for patient inclusion were: (I) severe lung infection confirmed by laboratory examination and imaging examination; (II) bronchoscopy and treatment could be tolerated. Patients with mental illnesses were excluded, as were those with a tendency to severe bleeding or with blood coagulation mechanism disorders. All procedures in this study involving human participants were performed in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was taken from all the patients. The study protocol was approved by the ethics committee of Shanghai Ninth People's Hospital (No. 2021RSYLL001).

Study methods

Basic clinical data for all patients, including sex, age, body mass index (BMI), blood pressure, diabetes history, stroke history, presence or absence of chronic obstructive pulmonary disease, lung infection (gram-positive bacterial infection, gram-negative bacterial infection, fungal infection, acute lung abscess), surgical history, and postoperative inhalation injury were collected.

Control group patients received conventional treatment, such as anti-infective treatment, mechanical ventilation, and symptomatic treatment. In addition to the treatments received by the control group, patients in the observational group underwent BAL under fiberoptic bronchoscopy. Assess the patient's recovery after 1 month of treatment.

The specific operating procedures for BAL under fiberoptic bronchoscopy were as follows. The patient was given a subcutaneous injection of atropine 15 minutes before the operation. If the stress felt by the patient was too much, 10 mg diazepam would be injected 30 minutes before the operation. After that, the patient was anesthetized with lidocaine, delivered by inhalation. The trachea was then checked with a fiberoptic bronchoscope, the sputum was sucked, and a bacterial sputum culture was carried out. Following that, the fiberoptic bronchoscope front end was extended to the bronchial opening of the lung segment for lavage. The special catheter of the fiberoptic bronchoscope was inserted into the biopsy hole for lavage in stages. Sterile normal saline was used as the lavage fluid; the temperature of the saline was maintained at 37 ℃, and the volume of saline for each lavage was 10–15 mL, with the total volume being less than 200 mL. For each lung segment, lavage was performed 2 to 3 times. If a blood clot or spittoon was found during the procedure, it was crushed with a biopsy clip and sucked out. Finally, the fiberoptic bronchoscope was inserted into subsegments for the injection of amikacin, metronidazole, and amoxicillin. The injections were delivered over 5 to 10 minutes, once a day, for 1 week. Both the observational and control groups received the same comprehensive care during their treatment.

Statistical analysis

All data were expressed as the mean ± standard deviation or number of cases (percentage). Differences between groups were compared by *t*-test, and chi-square test was used to evaluate percentage differences. Pearson's correlation was used to analyze the correlations between bronchial lavage under fiberoptic bronchoscopy and the levels of inflammatory factors. Logistic regression was used to analyze the correlation between the bronchial lavage under fiberoptic bronchoscopy and the effectiveness of the treatment. Statistical analyses were performed with SAS version 9.4 software (North Carolina State University, United States, North Carolina), and differences were statistically significant when $P<0.05$.

Results

Basic information of the research participants

Of the 79 patients in the observational group, 58.2% were males. The average age was 52.4±5.3 years old, and the average BMI was 24.9±3.4 kg/m^2. The number of gram-positive bacterial, gram-negative bacterial, and fungal infections were 19 (24.1%), 49 (62.0%), and 11 (13.9%), respectively. Thirty (38.0%) and 19 (24.1%) patients in the observational group had diabetes and chronic obstructive pulmonary disease, respectively, and 30 (38.0%) patients had a history of surgery. Postoperative inhalation injury was reported in 17 (21.5%) patients.

Comparison of the basic patient information of the observational and control groups showed that the 2 groups were similar before treatment, and there were no statistically significant differences (*Table 1*).

Comparison of parameters of respiratory mechanics between the observational group and the control group after treatment

As shown in *Table 2*, a comparative analysis of the respiratory mechanics parameters (chest compliance, lung compliance, and total dynamic compliance) of the patients in the observational group and the control group before treatment showed that there was no significant difference between the groups with respect to chest compliance, lung compliance, and total dynamic compliance (all $P>0.05$). After treatment, the respiratory mechanics parameters in the 2 groups showed significant improvements compared with those before treatment (all $P<0.05$). Furthermore, the parameters in the observational group were significantly higher compared to the control group (chest compliance: 73.81±8.42 *vs.* 70.02±7.93 mL/cmH_2O; lung compliance: 42.64±5.47 *vs.* 35.88±5.31 mL/cmH_2O; total dynamic compliance: 42.41±4.28 *vs.* 33.76±3.09 mL/cmH_2O) ($P<0.05$).

Comparison of inflammatory factor levels between the observational group and control group after treatment

As shown in *Table 3*, a comparative analysis of the inflammatory factor levels (PCT and TGF-β) of the observational group and the control group before treatment showed no statistically significant difference in the levels of PCT or TGF-β (both $P>0.05$). After

Table 1 Comparison of basic data between the control group and the observational group

Variables	Control group (n=79)	Observational group (n=79)	P value
Age (year)	52.6±5.2	52.4±5.3	0.78
Male (n, %)	49 (62.0)	46 (58.2)	0.31
BMI (kg/m^2)	25.1±3.2	24.9±3.4	0.48
SBP (mmHg)	134±10.1	132±9.3	0.29
DBP (mmHg)	89±6.7	88±6.8	0.91
Heart rate (bpm)	93±8.1	92±7.7	0.63
Gram-positive infection (n, %)	16 (20.3)	19 (24.1)	0.42
Gram-negative infection (n, %)	53 (67.1)	49 (62.0)	0.33
Fungal infection (n, %)	10 (12.7)	11 (13.9)	0.17
Diabetes (n, %)	27 (34.2)	30 (38.0)	0.23
Chronic obstructive pulmonary disease (n, %)	22 (27.8)	19 (24.1)	0.08
Stroke (n, %)	14 (17.7)	16 (20.3)	0.76
Acute lung abscess (n, %)	11 (13.9)	8 (10.1)	0.17
History of surgery (n, %)	30 (38.0)	32 (41.0)	0.33
Postoperative inhalation injury (n, %)	17 (21.5)	19 (24.1)	0.09

n, the number of cases; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 2 Comparison of respiratory mechanics parameters between the control group and the observational group

Respiratory mechanics parameters	Observational group	Control group
Chest compliance (mL/cm H_2O)		
Pre treatment	55.32±7.42	56.62±6.46
Post treatment	73.81±8.42*#	70.02±7.93*
Lung compliance (mL/cm H_2O)		
Pre treatment	36.68±5.52	30.92±5.02
Post treatment	44.71±5.47*#	35.88±5.31*
Total dynamic compliance (mL/cm H_2O)		
Pre treatment	26.16±2.42	25.86±2.37
Post treatment	42.41±4.28*#	33.76±3.09*

*, P<0.05 compared with before treatment; #, P<0.05 compared with the control group.

Table 3 Comparison of inflammatory factor indexes between the patients in the control group and observational group

Inflammatory factors	Observational group	Control group
PCT (μg/L)		
Pre treatment	21.22±2.37	19.69±2.41
Post treatment	2.51±0.47*#	6.63±0.52
TGF-β (ng/L)		
Pre treatment	114.55±10.78	111.37±12.52
Post treatment	85.69±11.63*#	98.77±11.39

*, P<0.05 compared with the before treatment; #, P<0.05 compared with the control group. PCT, procalcitonin; TGF-β, transforming growth factor β.

treatment, the inflammatory factor indexes in both groups showed significant improvements compared with those before treatment (all P<0.05). Furthermore, the levels of inflammatory factors in the observational group were significantly lower than those in the control group (PCT: 2.51±0.47 *vs.* 6.63±0.52 μg/L; TGF-β: 85.69±11.63 *vs.* 98.77±11.39 ng/L) (all P<0.05).

Comparison of treatment effectiveness between the observational group and the control group

As shown in *Table 4*, the results of the logistic regression

Table 4 Comparison of treatment effectiveness in the observational group and control group

Models	OR	95% CI	P value
Model 1	1.54	1.15–1.68	<0.0001
Model 2	1.46	1.19–1.60	0.0009
Model 3	1.23	1.09–1.51	0.0070

OR, odds ratio; CI, confidence interval.

analysis showed that compared with the control group, without correction (model 1), the probability of the treatment in the observational group being effective was increased by 54% (OR =1.54, 95% CI: 1.15–1.68, P<0.0001). Compared with the control group, following adjustment for age and sex (model 2), the treatment effectiveness in the observational group was increased by 46% (OR =1.46, 95% CI: 1.19–1.60, P=0.0009). Compared with the control group, finally, when BMI, gram-negative infection, diabetes, and acute lung abscess were adjusted (model 3), the treatment effectiveness in the observational group was increased by 23% (OR =1.23, 95% CI: 1.09–1.51, P=0.007).

Discussion

This study showed that, under similar clinical conditions, BAL under fiberoptic bronchoscopy significantly improves chest compliance, lung compliance, and total dynamic compliance, and decreases the levels of inflammatory factors (PCT and TGF-β), compared with conventional treatment, thus increasing the effectiveness of treatment.

Patients with severe pulmonary infections have limited systemic activity and reduced ability to excrete sputum independently, which can result in thick sputum and the accumulation of secretions, and thus increases the risk of airway blockage (10,11). Studies have shown that the treatment of severe pulmonary infections should focus on fighting the infection, removing foreign bodies in the respiratory tract, and ensuring that the respiratory tract is clear of blockages (12). Studies have also found that current anti-infective treatments for severe pulmonary infections are not ideal. Recently, BAL under fiberoptic bronchoscopy has been gradually applied in clinical practice. Clinical experience has proved that fiberoptic bronchoscopy not only has the benefits of non-invasiveness and high efficacy, but that it can also reduce the impairment to airway mucosa (13,14). Research has shown that small-cavity fiber bronchoscopes can penetrate small lesions, enable accurate observation of lung lesions directly, and provide dynamic and clear bronchial images (15,16). These benefits are conducive to gaining an effective understanding of the progression of the disease, and to the clearing of respiratory secretions as well as foreign bodies, sputum, and blood clots, which can also help to alleviate bronchial obstructions in asthma and quickly enhance ventilation (17,18). A European study of 400 patients with severe lung infections showed that BAL has a significant effect on improving lung infections (19). Our research demonstrated that BAL under fiberoptic bronchoscopy shortened the duration of mechanical ventilation and reduced the use of antibiotics compared with the control treatment. Furthermore, the effects of the treatment with respect to respiratory failure correction, lowering body temperature, and recovering white blood cells were also significantly better in the observation than in the control group. Therefore, our findings suggest that BAL under fiberoptic bronchoscopy can effectively relieve heavy bleeding, small airway interference, restore breathing, increase the oxygen content in the blood, and help to reduce cerebral edema, thereby accelerate the recovery. At the same time, the effectiveness of treatment in the observational group was significantly compared to the control group, suggesting that BAL can effectively improve the treatment effectiveness, which is consistent with the conclusions of previous studies (20).

The pulmonary infection of severity may affect alveolar oxygenation because of airway hinderance, which can lead to a disorder of oxygen and carbon dioxide exchange as well as changes in the patient's respiratory mechanics parameters (21). The results of this study showed that the respiratory mechanics parameters of patients following BAL under fiberoptic bronchoscopy were significantly improved compared to those of conventionally treated patients, and the treatment also showed significantly greater effectiveness than conventional treatment. These findings suggest that BAL under fiberoptic bronchoscopy can improve the respiratory status of patients.

Severe pulmonary infections have been reported to induce systemic inflammation and cause the unrestrained release of pro-inflammatory factors (22). PCT consists of calcitonin and N-residues, which can inhibit the expression of the calcitonin gene when the host is not infected; therefore, in healthy people, the concentration of PCT is typically very low (23). However, during pathogenic infection, the expression of the calcitonin gene in the human body is up-regulated, which subsequently increases the level of PCT in the serum. Serum PCT can be used as a dependable index of severe infection to reveal the body's

condition. TGF-β is a polypeptide growth factor which is enriched in human kidney and lung tissues. It is typically released by lymphocytes and eosinophils, or by airway epithelial cells in the lungs (24). A variety of external stimuli can cause inflammation of the airways, thereby damaging the airway epithelium and increasing inflammation, as well as the secretion of TGF-β (25). In this study, the patients in both the observational and control groups had reduced levels of PCT and TGF-β postoperatively; however, the decrease in the observational group was more significant than that in the control group, which indicates that BAL under fiberoptic bronchoscopy can effectively improve the local microenvironment. Furthermore, when sensitive antibiotics were injected directly into the lesion under fiberoptic bronchoscopy, there was a higher concentration of antibiotics in the lesion than there was with intravenous delivery; thus, the former approach is more effective for achieving an anti-inflammatory effect than the latter. This study has certain limitations. First of all, the sample size of this study is small, and the conclusions of this study need to be verified in a larger study. Secondly, this study only included changes in PCT and TGF-β, and more inflammatory factors, such as IL-1β, IL-6, etc., need to be included for a more adequate assessment of changes in inflammation.

In summary, the application of BAL under fiberoptic bronchoscopy for the treatment of severe pulmonary infections can effectively alleviate symptoms, improve the respiratory mechanics parameters, enhance the clinical efficacy, reduce complications, and reduce the levels of PCT and TGF-β. Therefore, BAL under fiberoptic bronchoscopy is worthy of wider clinical application. However, BAL under fiberoptic bronchoscopy is an invasive treatment, which has a certain invasion risk, and carries the risk of complications such as hypoxemia and hemopneumothorax. In clinical practice, adequate anesthesia and intraoperative monitoring should be used to avoid adverse events as much as possible. Although none of the patients in the current research experienced these complications, this may have resulted from the limited sample size in the current study. Thus, the safety of the clinical application of BAL under fiberoptic bronchoscopy needs to be ascertained through the performance of large-scale, multi-center studies in the future.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures in this study involving human participants were performed in accordance with the Declaration of Helsinki (as revised in 2013). Informed consent was taken from all the patients. The study protocol was approved by the ethics committee of Shanghai Ninth People's Hospital (No. 2021RSYLL001).

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