



Effect of bronchoscopic ambroxol lavage on inflammatory factors in lavage fluid of patients with bronchiectasis complicated by infection

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ABSTRACT

Objective: To study the effect of bronchoscopic ambroxol lavage on inflammatory factors in lavage fluid of patients with bronchiectasis complicated by infection. **Methods:** 100 patients with bronchiectasis complicated by infection who were treated in our hospital between May 2012 and January 2016 were divided into the control group ($n=54$) who received conventional treatment and the observation group ($n=46$) who received intravenous anti-infection combined with bronchoscopic ambroxol lavage after the therapies were reviewed. The contents of inflammatory factors, adhesion molecules and acute phase proteins in lavage fluid were compared between the two groups. **Results:** Before treatment, the differences in contents of inflammatory factors, adhesion molecules and acute phase proteins in lavage fluid were not statistically significant between two groups of patients. After treatment, inflammatory factors IL-4, IL-6, IL-10 and TNF- α contents in lavage fluid of observation group were lower than those of control group; adhesion molecules sICAM-1 and VCAM-1 contents in lavage fluid were lower than those of control group; acute phase proteins CRP, AAG, HPT and CER contents in lavage fluid were lower than those of control group. **Conclusion:** Bronchoscopic ambroxol lavage can reduce airway inflammation in patients with bronchiectasis complicated by infection.

1. Introduction

Bronchiectasis is the trachea wall structure destruction caused by purulent inflammation and fibrosis of bronchia and surrounding tissue, it can cause bronchial degeneration and persist dilation, and the patients are mainly characterized by chronic cough, expectoration and hemoptysis[1,2]. Repeated infection is the core in the occurrence and development of bronchiectasis, the anatomical changes of bronchial wall further increase the risk of local infection and increase the muscular and elastic tissue injury, acute infection in patients with bronchiectasis can even lead to serious ventilation/air exchange dysfunction, and early active treatment should be taken to control the disease[3,4]. Intravenous anti-infection is the most common therapy for patients with bronchiectasis complicated

by infection, but local drug concentration in lung lesions is low after intravenous drug use, the effect on controlling local infection is limited, and many scholars recommend joining adjuvant bronchoscopic therapy. Bronchoscopy is the common technique for clinical diagnosis and treatment at present, which applies sensitive drugs under direct vision, and can significantly enhance the clinical efficacy[5]. In the following studies, the effect of bronchoscopic ambroxol lavage on inflammatory factors in lavage fluid of patients with bronchiectasis complicated by infection was analyzed.

2. Information and methods

2.1 Case information

A total of 100 patients with bronchiectasis complicated by infection who were treated in Mianyang People's Hospital between May 2012 and January 2016 selected, and the patients or families were informed of the research items and signed consent form. After the therapies were reviewed, the enrolled patients were divided

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into the control group ($n=54$) who received conventional treatment and the observation group ($n=46$) who received intravenous anti-infection combined with bronchoscopic ambroxol lavage. Control group included 30 male cases and 24 female cases that were 49-78 years old, and with the course of bronchiectasis 5-19 years; observation group included 24 male cases and 22 female cases that were 47-80 years old, and with the course of bronchiectasis 6-18 years. The difference in general information between the two groups of patients was not statistically significant ($P>0.05$).

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) in accordance with the clinical diagnostic criteria for bronchiectasis; (2) associated with typical symptoms of infection such as fever and expectoration, and blood routine examination showing a large increase in white blood cell count; (3) without history of acute bronchiectasis attack or bronchoscopic treatment 6 months prior to admission. Exclusion criteria: (1) associated with asthma, chronic obstructive pulmonary disease, lung cancer and other lung diseases; (2) associated with the infectious diseases of other tissues and organs of the body; (3) associated with moderate-severe autoimmune diseases; (4) dropping out of treatment and with incomplete clinical data.

2.3 Therapy

Both groups of patients were given routine treatment such as anti-infection, reducing phlegm, dilating airway and so on, the observation group of patients reduced bronchoscopic ambroxol lavage on the basis of conventional treatment, and specific methods were as follows: they were fasting solids for 6-8 h and fasting for liquids for 4 h, 1% lidocaine was used before treatment for local nasal mucosa infiltration anesthesia, then bronchoscope (Olympus) was put into the lesion area and fully absorb the secreta, 90 mg of Ambroxol Hydrochloride Injection (Sinopharm Group Guorui Pharmaceutical Co., LTD, approved by H20113358) was added in 100 mL saline and used for pulmonary lavage by several times (about 20 mL each time for 15 min) until the secreta in lesions were completely removed, and the patient's vital signs should be closely observed during lavage treatment.

2.4 Observation indexes

Before and after treatment, 5.0 mL alveolar lavage fluid was collected from two groups of patients, placed in anticoagulant heparin sterile tube and centrifuged at low speed to get upper lavage fluid, which was frozen at -70°C low-temperature environment for test. Enzyme-linked immunosorbent assay (ELISA) was used to detect inflammatory factors interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10) and tumor necrosis factor (TNF- α) contents;

ELISA was used to determine the levels of adhesion molecules soluble intercellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in lavage fluid; automatic rate nephelometry was used to determine acute phase proteins C-reactive protein (CRP), 1-acidic protein (AAG), haptoglobin (HPT) and ceruloplasmin (CER).

2.5 Statistical processing

Data in the study were input in software SPSS 20.0, inflammatory factors, adhesion molecules, acute phase proteins and other measurement data were in terms of mean \pm standard deviation ($\bar{x}\pm s$), and comparison was by t test. $P<0.05$ meant statistical significance in differences.

3. Results

3.1 Inflammatory factors

Comparison of inflammatory factors IL-4, IL-6, IL-10 and TNF- α contents in lavage fluid between two groups of patients before and after treatment was as follows: before treatment, the differences in IL-4, IL-6, IL-10 and TNF- α contents in lavage fluid were not statistically significant between two groups of patients ($P>0.05$); after treatment, IL-4, IL-6, IL-10 and TNF- α contents in lavage fluid of both groups were lower than those before treatment, IL-4, IL-6, IL-10 and TNF- α contents in lavage fluid of observation group were lower than those of control group, and differences in contents of above inflammatory factors in lavage fluid were statistically significant within group before and after treatment as well as between groups after treatment ($P<0.05$), shown in Table 1.

3.2 Adhesion molecules

Comparison of adhesion molecules sICAM-1 and VCAM-1 contents in lavage fluid between two groups of patients before and after treatment was as follows: before treatment, the differences in sICAM-1 and VCAM-1 contents in lavage fluid were not statistically significant between two groups of patients ($P>0.05$); after treatment, sICAM-1 and VCAM-1 contents in lavage fluid of both groups were lower than those before treatment, sICAM-1 and VCAM-1 contents in lavage fluid of observation group were lower than those of control

Table 1.

Comparison of inflammatory factor contents in lavage fluid between two groups before and after treatment (pg/mL).

Groups	n	Time	IL-4	IL-6	IL-10	TNF- α
Control group	54	Before treatment	9.37 \pm 1.84	14.38 \pm 2.19	28.49 \pm 3.52	34.27 \pm 4.52
		After treatment	6.19 \pm 0.75*	8.19 \pm 0.95*	17.06 \pm 2.11*	20.63 \pm 3.58*
Observation group	46	Before treatment	9.31 \pm 1.79	14.57 \pm 2.08	28.76 \pm 3.41	34.19 \pm 4.37
		After treatment	3.42 \pm 0.45 [#]	4.23 \pm 0.56 [#]	8.53 \pm 0.94 [#]	9.73 \pm 1.05 [#]

Note: compared with same group before treatment, * $P<0.05$; compared with control group after treatment, [#] $P<0.05$.

Table 2.

Comparison of adhesion molecule contents in lavage fluid between two groups before and after treatment (ng/L).

Groups	n	Time	sICAM-1	VCAM-1
Control group	54	Before treatment	395.18±48.95	712.47±80.58
		After treatment	264.47±30.59*	452.47±54.72*
Observation group	46	Before treatment	392.64±45.18	709.66±82.31
		After treatment	171.53±20.42*#	214.33±30.69*#

Note: compared with same group before treatment, * $P<0.05$; compared with control group after treatment, # $P<0.05$.

group, and differences in contents of above adhesion molecules in lavage fluid were statistically significant within group before and after treatment as well as between groups after treatment ($P<0.05$), shown in Table 2.

3.3 Acute phase proteins

Comparison of acute phase proteins contents CRP, AAG, HPT and CER in lavage fluid between two groups of patients before and after treatment was as follows: before treatment, the differences in CRP, AAG, HPT and CER contents in lavage fluid were not statistically significant between two groups of patients ($P>0.05$); after treatment, CRP, AAG, HPT and CER contents in lavage fluid of both groups were lower than those before treatment, CRP, AAG, HPT and CER contents in lavage fluid of observation group were lower than those of control group, and differences in contents of above acute phase proteins in lavage fluid were statistically significant within group before and after treatment as well as between groups after treatment ($P<0.05$), shown in Table 3.

4. Discussion

Repeated infection has played an important role in occurrence and development process of bronchiectasis, the acute infection is the main cause of rapid disease aggravation and even respiratory failure in patients with bronchiectasis, and early positive treatment needs to be taken to control infection and suppress other viscera complications. Empirical intravenous antibiotic infusion is the most common treatment of bronchiectasis complicated by acute infection, related research also points out that the general use of antibiotics can't reach effective concentration in local area, and some patients may develop protracted course of disease and even ventilation dysfunction. With bronchoscope technology progression, the treatment of pulmonary lesions under direct vision is possible, bronchoalveolar lavage can on the one hand, directly remove the

airway secretions and help keep the airway unobstructed, and on the other hand, can obtain airway secretions for drug sensitive test, and then locally apply antibiotics according to the results of drug susceptibility, and it helps to control systemic inflammatory response in a short time[6]. Therefore, bronchoscopic alveolar lavage was used as an auxiliary therapy for patients with bronchiectasis complicated by infection in the study.

Local infections can lead to increased mucus secretion, and lead to local airway stenosis and difficult ventilation, so the local bronchial recanalization and effective ventilation restoration are the important processes for bronchiectasis with infection treatment. Ambroxol is a mucous solvent, which can effectively reduce the viscosity of the sputum, enhance the movement ability of the cilium and promote the discharge of sputum[7,8]. In this study, ambroxol lavage was applied in the observation group of patients in the study under direct vision of bronchoscope to dilute the local mucus and expel it from the body. Local and systemic inflammatory response is the foundation of bronchiectasis disease progression, massive secretion of numerous proinflammatory factors is a leading cause of increased bronchial mucus secretion, and bronchoscopic ambroxol lavage can not only remove local mucous, but can also take away a large number of inflammatory cytokines and reduce the degree of local inflammatory response[9,10]. IL-4, IL-6, IL-10 and TNF- α are the proinflammatory mediators that are commonly clinically studied and have been proven to participate in the local infection attack of the bronchiectasis[11,12]. In the study, the contents of these inflammatory factors in alveolar lavage fluid were compared between two groups of patients, and it was found that after treatment, IL-4, IL-6, IL-10 and TNF- α contents in lavage fluid of observation group were lower than those of control group, and it confirms that bronchoscopic ambroxol lavage can effectively reduce the local airway inflammation, which is mainly because that the dilution of sputum takes a large amount of inflammatory mediators out of the body.

Table 3.

Comparison of acute phase protein contents in lavage fluid between two groups before and after treatment (mg/L).

Groups	n	Time	CRP	AAG	HPT	CER
Control group	54	Before treatment	74.38±9.24	545.38±69.71	1 923.26±25.47	374.28±45.71
		After treatment	43.26±5.93*	311.29±35.84*	893.26±92.17*	179.46±22.53*
Observation group	46	Before treatment	73.19±9.45	549.29±64.63	1 915.42±23.58	371.64±48.32
		After treatment	20.36±2.74*#	173.27±20.57*#	403.74±58.63*#	74.32±9.15*#

Note: compared with same group before treatment, * $P<0.05$; compared with control group after treatment, # $P<0.05$.

Adhesion factors are the special inflammatory factors that are involved in the inflammatory process, and closely related to the degree of inflammatory response, the contents of sICAM-1, VCAM-1 and other adhesion molecules increase rapidly after the occurrence of local infection, they are mainly produced by the activated mononuclear cells, epithelial cells, T lymphocytes and so on, and they mediate the adhesion between leukocytes and endothelial cells, induce a large number of white blood cells to gather in the local bronchial intima, and increase the local inflammatory reaction[13,14]. The locally secreted sICAM-1 and VCAM-1 are well consistent with the process of inflammation. In the study, the analysis of sICAM-1 and VCAM-1 generation showed that after treatment, sICAM-1 and VCAM-1 contents in lavage fluid of observation group were lower than those of control group, indirectly confirming that bronchoscopic ambroxol lavage can effectively reduce the adhesion factor contents, and decrease their driving and adhesion to infection-related cells. Acute phase proteins are a class of proteins that are commonly studied at present and closely related to the inflammatory response, CRP is the most popular, and it is a sensitive inflammatory material that is massively secreted in the early infection and highly consistent with the infection degree[15,16]. AAG, HPT and CER are also the typical acute phase proteins that have been confirmed to be massively secreted in patients with acute septic shock and secondary infection of cirrhosis, and are speculated to be also directly related to the occurrence and progression of infection[17,18]. In the study, the contents of these acute phase proteins in lavage fluid were compared between two groups of patients, and it was found that after treatment, CRP, AAG, HPT and CER contents in lavage fluid of observation group were lower than those of control group, and this is another proof that bronchoscopic lavage relieves inflammation in patients.

Bronchoscopic ambroxol lavage can effectively relieve the local inflammatory response, and reduce the secretion of inflammatory factors, adhesion molecules and acute phase proteins in patients with bronchiectasis complicated by infection, and it is of positive clinical application value.

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