

Effect of terbutaline combined with budesonide in treatment of bronchial asthma and rehabilitation nursing

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Abstract: Terbutaline aerosol and budesonide suspension are commonly used in the treatment of bronchial asthma, and budesonide suspension has local high efficiency and anti-inflammatory effects. In this paper, we selected 240 patients with bronchial asthma and randomly divided them into two groups. The experimental group was treated with atomization inhalation of terbutaline, after 5 minutes interval, nebulized inhalation of budesonide was performed. The control group was treated with atomized inhalation of mixed liquid as terbutaline and budesonide. After treatment, the cough scores of the two groups decreased, and the dyspnea score improved significantly compared with that before treatment ($P < 0.05$). After treatment, the levels of IL-6, BNP and CRP were decreased in the two groups. There was a significant difference between the two groups after treatment ($P < 0.05$). The incidence of adverse drug reactions was low. There were 2 cases of panic disorder and 8 cases of pharyngeal discomfort in the experimental group. The results show that the interval medication of terbutaline and budesonide in the treatment of bronchial asthma can achieve better clinical efficacy and can provide reference for clinical treatment. In addition, this method can effectively reduce the level of inflammatory factors in acute asthma patients, thereby reducing the damage of inflammatory factors to the body.

Keywords: Terbutaline, bronchial asthma, anti-inflammatory effect, budesonide suspensions.

INTRODUCTION

Bronchial asthma is one of the most common chronic diseases in the world (Zhu *et al.*, 2015). In recent years, the incidence of asthma is increasing year by year. The continuous severe asthma attacks can lead to pulmonary heart disease, severe respiratory failure and pneumothorax (Wang, 2016). The public health concerns have become a global concern. Because of repeated attacks and deferred condition, bronchial asthma requires a lot of time and money, and most of the patients are not well aware of the risk factors for asthma and have not really mastered how to control the attack, so many asthmatic patients have not been standardized, plus some grass-roots units (Yates, 2013; Nathan *et al.*, 2015). In addition, some primary medical staff is not fully aware of bronchial asthma, and is not properly prescribed according to medication guidelines, resulting in recurrent asthma attacks (Ghoneum *et al.*, 2015). At present, because most asthmatic patients can tolerate a series of clinical symptoms and signs of mild and moderate asthma acute attack, it is easy to ignore and fail to diagnose and treat in time, which leads to severe or even critical development, which seriously affects the treatment effect and prognosis of the patients (Yuan *et al.*, 2016). Therefore, how to control the symptoms of acute attack of bronchial asthma in time and how to prevent the recurrence and reduce the mortality have become the main problem that clinical workers face today. Because the inhalation of inhalation

can make the drug act directly on the bronchial mucosa and give full play to the local anti-inflammatory effect, it has become a new drug delivery method for the treatment of bronchial asthma, with high safety and easy operation when inhaling atomization, it is listed as the first choice for the treatment of asthma by WHO (Webster *et al.*, 2017).

Studies have shown that the main pathophysiological changes of bronchial asthma are airway inflammation and airway spasm, so the key to treating asthma is early anti-inflammatory and spasmolytic treatment (Yung *et al.*, 2015). The glucocorticoid has a strong local anti-inflammatory effect. It is considered to be the most effective drug to resist airway inflammation and control the acute symptoms of asthma (Kazani *et al.*, 2013). The budesonide suspension is the only glucocorticoid that is approved by the Food and Drug Administration (FDA) for atomization inhalation. Currently, the most commonly used bronchial dilator is β_2 -R agonist. It has become the preferred treatment for all asthmatic patients. The terbutaline atomization solution, as a quick effect β_2 -R agonist, can diastolic the smooth muscle of the bronchus very well, which is the first choice for the treatment of mild to moderate asthma (Kumaravel *et al.*, 2014). Compared with oral administration or intravenous administration, aerosol inhalation therapy can expand bronchi with less dosage, less side effects and faster expansion (Fitzpatrick *et al.*, 2016).

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The asthma group of the Chinese society of Chinese medicine proposed the treatment of moderate asthma, which recommended small dose of inhaled corticosteroids (ICS) combined with β_2 -R agonist, and the two had synergistic anti-inflammatory and antiasthmatic effects, which could effectively prevent asthma attacks (Caziuc *et al.*, 2015). However, most of the current clinical use of ICS and β_2 -R agonist atomization inhalation treatment, for the simultaneous use of inhaled bronchodilator and glucocorticoid treatment of asthma patients. The two kinds of inhalers should be separated from each other for a few minutes (Kazani *et al.*, 2013). It is suggested that the bronchodilator should be inhaled first and then inhaled in budesonide so as to increase the amount of drug entering the bronchus. At present, there are few studies on the treatment of acute attack of bronchial asthma by spaced nebulization inhalation of ICS and β_2 -R agonists. Most scholars focus on the observation and study of the curative effect of the mixture of inhalation and inhalation. There are few studies on the effect of inhaling ICS after inhaling bronchodilator for several minutes (Dobson *et al.*, 2015). Therefore, this study is intended to use oxygen to drive atomization inhalation. The first is to inhale two drugs in sequence, first inhaling terbutaline, and then inhaling budesonide after 5min. The second is simultaneous inhalation of budesonide and terbutaline mixture. The curative effects of these two models were compared, so as to provide reference for the treatment of patients with acute attack of bronchial asthma.

MATERIALS AND METHODS

Research object

The clinical manifestations of cough, chest tightness, asthma, double lung smelling and wheezing were found in 240 patients who were hospitalized in the respiratory department of our hospital in 2016-2017. All patients were approved by Ethics Committee of the Second Hospital of Dalian Medical University, ethical approval number as 2015SHDMUP2 and all patients signed on the informed consent.

Diagnostic criteria for asthma

Diagnostic criteria for asthma refer to guidelines for asthma prevention and treatment: (1) The patients were characterized by repeated episodes of wheezing, air urgency, chest tightness or coughing, which were related to contact allergens, cold air, physical or chemical stimulation, viral upper respiratory infection and exercise. (2) When the attack occurs, the lungs can be heard and disperse or diffuse, with the expiratory phase of the wheezing sound, and the expiratory phase lengthens. (3) The above symptoms and signs can be alleviated or relieved by treatment. (4) Wheezing, shortness of breath, chest tightness and cough caused by other diseases.

Inclusion and exclusion criteria

Inclusion criteria: (1) Sex is not limited, age is between 18-65 years old; (2) 1 month before admission, no systemic hormone was used. (3) There was no serious systemic infection within 2 weeks before admission, especially severe respiratory tract infection, fungal infection, tuberculosis and so on. (4) The history of no mental abnormality; (5) Allergic history of glucocorticoid and beta 2-R agonist. (6) Tell the patient to cooperate with this study.

Exclusion criteria: (1) The severity of the disease does not accord with the moderate diagnostic criteria for acute attack of bronchial asthma. (2) Women in pregnancy or lactation; (3) In the course of treatment, some factors aggravate the development of severe or severe asthma. (4) Combined with severe cardiopulmonary diseases (pneumothorax, COPD, cor pulmonale, bronchiectasis) or other systemic diseases. (5) There was contraindication of glucocorticoid and β_2 -R agonist or glucocorticoid dependence. (6) The need for ventilator assisted treatment. (7) The person who is not completed according to the research program.

Major reagents

Budesonide Suspension for Inhalation (specification 2ml: 1mg); terbutaline atomization fluid (specification 2ml: 5mg); human serum interleukin -6 Kit

Research method

According to the random number table method, 240 patients were divided into the experimental group and the control group, each of the 120 cases, and all the patients were told the atomization method and attention, and the nursing staff was trained by the special training.

In the experimental group, inhalation of terbutaline (terbutaline nebulizer 5 mg + 0.9% sodium chloride injection 3ml) on the basis of routine treatment was first inhaled. After the interval 5min, then the patients atomized budesonide (budesonide suspension 1mg+0.9% sodium chloride injection 3ml). On the basis of routine treatment, the control group was treated with atomization inhalation of bubutaline and budesonide mixture, in which the budesonide atomization solution 5mg+ budesonide suspension 1 mg + 0.9% sodium chloride injection 3ml was used. The two groups were treated for 7 days. By comparing the relevant indexes before and after treatment, the therapeutic effects of two ways on bronchial asthma were compared.

Detection index

Before taking medicine (before oxygen inhalation), Sa O₂ was drawn from the arterial blood. After treatment of 7D, the Sa O₂ was measured again. Before and after atomization inhalation, pulmonary function tests were performed to detect FEV₁%, PEF% and venous blood for WBC, EOS, BNP and CRP.

Cough score: score the cough frequency, cough intensity, daily activities or nocturnal sleep, divided into 0-3 points, 4 grades.

Dyspnea score: the British Medical Research Council (MRC) dyspnea scale was divided into 0-4 grades and 5 grades. Level 0: no obvious dyspnea (except for vigorous activity). Level 1: shortness of breath when walking or uphill. Level 2: because breathing difficulties are slower than walking of peers or walking on flat ground, they need to stop breathing. Level 3: walk on the ground for 100m or a few minutes and then stop breathing. Level 4 minutes: obviously breathing difficulties and not leaving the house or changing clothes.

Nursing intervention

Nursing staff should closely observe the patient's condition changes, mainly observe the patient's breathing depth and frequency and other changes, the patient is preferable to the seat or semi decubitus position, which helps the patient to rest better. According to the oxygen therapy of the patients, the respiratory condition was observed closely in the process of oxygen inhalation and the flow of oxygen was adjusted. Adjust 1 times every 30 minutes, and the occurrence of dyspnea was noted.

During the nursing process, we should help patients discharge sputum, maintain airway patency, improve ventilation function and suck sputum nursing intervention. In the remission period of bronchial asthma, pay attention to the environment of the patients in the ward, keep quiet, pay attention to the cleaning in the room, keep the flowers and feathers in the room, avoid the occurrence of asthma, and strictly prohibit smoking in the ward. The nursing staff asked for more rest in the remission period. In the process of nursing, according to the cause of the patient's bad mood, it helps the patient to relieve the bad mental mood, set up the patient's correct understanding of the disease, and improve the patient's coordination with the medical and nursing operation. Patients should be guided by medication so as to avoid taking non prescription drugs and avoiding self medication.

STATISTICAL ANALYSIS

The measurement data were expressed with mean standard deviation ($\bar{x} \pm s$). The statistical analysis was carried out by SPSS 18 software package. The group was compared with the t test of group design data. The paired t test was used in the two groups before and after treatment. The count data were expressed by frequency (%), and compared with the chi square test, $P < 0.05$ indicated that the difference was statistically significant.

RESULTS

General information

There were 120 cases in the experimental group,

including 67 males and 53 females, with an average age of 42.3 ± 7.15 years, with an average duration of 6.13 ± 2.65 years. The control group consisted of 120 patients, 62 males and 58 females, with an average age of 43.5 ± 6.14 years, with an average duration of 7.04 ± 3.17 years. There was no significant difference in general condition between the two groups ($P > 0.05$). As shown in table 1.

Comparison of clinical symptom scores

After treatment, the cough scores of the two groups were reduced, and there were statistical differences compared with those in the same group before treatment. There was no statistical difference between the two groups at seventh days after treatment ($P = 0.913$, $P > 0.05$), indicating that the degree of cough in the two groups was the same. The improvement of dyspnea score after treatment in the two groups was statistically significant compared with that before treatment ($P < 0.05$). Compared with the control group, the scores of dyspnea were more obvious in the two groups after treatment than in the control group, and the difference was statistically significant ($P = 0.025$, $P < 0.05$). The results are shown as shown in table 2

Comparison of pulmonary function

There was no significant difference in lung function index between the two groups before treatment (P value was 0.106, 0.054, $P > 0.05$). The two groups of lung function indexes were significantly improved ($P < 0.05$) after treatment ($P < 0.05$), and the difference between the two groups was statistically significant ($P = 0.000$, $P < 0.01$). It can be seen that the lung function of the experimental group is better than that of the control group. As shown in table 3

Comparison of experimental indexes

After treatment, the average of the two groups of IL-6 water decreased, and the difference between the two groups was statistically significant ($P = 0.002$, $P < 0.01$), and the experimental group was more significantly lower than the control group. After treatment, the level of BNP in the two groups was lower than that before treatment. The difference between the groups after treatment was statistically significant ($P = 0.004$, $P < 0.01$), and the level of the experimental group was more obvious than that of the control group. After treatment, the experimental group and the control group CRP were reduced, after treatment and before treatment, there was a statistical difference ($P < 0.05$). After treatment, the comparison between the two groups was significantly lower than that of the control group. The difference was statistically significant ($P = 0.003$, $P < 0.01$). As shown in table 4

Comparison of two groups of WBC and EOS

After treatment, the number of WBC and EOS in the two groups was lower than that before treatment. The difference between the two groups after treatment was statistically significant ($P < 0.05$). There was no statistical

difference between the two groups after treatment ($P=0.136$, $P>0.05$), and there was a statistical difference between the two groups ($P=0.001$, $P<0.01$). As shown in table 5

Adverse reaction

The incidence of adverse reactions in nebulized inhaled terbutaline and budesonide was low in this study. There were 2 cases of panic disorder and 8 cases of pharyngeal discomfort in the experimental group. Among them, electrocardiogram examination showed sinus rhythm, 1H's internal symptoms were relieved spontaneously, there was no other arrhythmia, and pharyngeal discomfort was better after gargling. In the control group, there were 1 case of slight finger tremor, 11 cases of pharyngeal discomfort, and 1 cases of oral mycotic infection. Among them, the finger microtremor disappeared spontaneously in 2H, and no special treatment was given. Pharynx discomfort was improved after corresponding intervention measures. Oral mold infection was fully explained and communicated to patients and gargle with 4% sodium bicarbonate solution, 1-2 times /d and 1-2min/ times, to keep the oral cavity alkaline environment and effectively inhibit the growth of mould. The symptoms improved after the above treatment, and did not affect the continued use of the original drugs. The results are shown as shown in table 6.

DISCUSSION

Bronchial asthma is a chronic inflammatory disease of the respiratory tract, its pathogenesis is complex and the specific etiology of individualization is not very clear (Brown, 2015). However, even if there are many kinds of drugs to control and prevent the attack of asthma at present, the incidence of the disease is increasing year by year because of the complexity of the pathogenesis, the constant change and increase of the allergens. Therefore, it has great importance to fully understand asthma and standardize medication according to medication guidelines for controlling asthma symptoms and treating asthma (Cingi *et al.*, 2015).

At present, it is agreed that the main method of treating bronchial asthma is still drug treatment; control asthma is mostly inhaled glucocorticoid (ICS), but generally it needs $>3d$ to play the effect of anti airway inflammation, so it is generally required to combine with bronchodilator (Caziuc *et al.*, 2015). For moderate patients with acute bronchial asthma, the key treatment is to quickly control acute symptoms to avoid continuous intensification, improve ventilation, and prevent hypoxemia (Chetna *et al.*, 2016). It is proved that atomization inhalation is one of the most effective methods to treat asthma at present. It is not only easy to operate and safe, but also can reduce the adverse reaction by reducing the dose of drug directly to the target organ. The oxygen driven atomization is the

use of oxygen as the power to use high speed oxygen flow to impact the drug into small droplets, and quickly enter the bronchi and alveoli with the patient's breathing, so as to expand the bronchus faster and relieve the bronchospasm, to reduce inflammation, antiasthmatic and expectorant, on the other hand, add atomization at the same time (Dai *et al.*, 2015). Inhaling oxygen can correct the symptoms of hypoxia and prevent the occurrence of hypoxic pulmonary vasoconstriction in patients with hypoxemia. At present, inhalation of small dose of glucocorticoid and β_2 -R agonist are recommended to treat asthma, and atomization inhalation of terbutaline atomization solution and budesonide suspension is a common drug for the treatment of bronchial asthma (Dobson *et al.*, 2015). The budesonide suspension has local high efficiency and anti-inflammatory effect and is the only adrenalin that can be inhaled by FDA batch. Corticosteroids, by reducing the synthesis of cytokines and preventing the proliferation of airway epithelial cells, reduce airway inflammation, plus its strong binding to glucocorticoid receptors. Atomization inhales can directly act on the airway and produce local anti-inflammatory effects. On the other hand, budesonide can also repair damaged airway inflammatory tissue, relieve airway edema and reduce sensitivity to external stimuli. Terbutaline is a highly selective, highly selective β_2 - R agonist with a starting time of about 5 min and a short duration of about 4-6 hours. It has been widely used as the most important bronchodilator in the treatment of bronchial asthma. At the same time, terbutaline can stimulate the relaxation of bronchial smooth muscle, relieve airway stenosis quickly, enhance the ability of bronchial mucociliary clearance of foreign body, and quickly reach the effect of antispasmodic and asthma. However, the study found that terbutaline had no significant effect on airway inflammation.

In this study, the experimental group was treated with atomizing inhalation of terbutaline atomization solution, followed by aerosolized inhalation of budesonide suspension after 5min interval (Dahlin *et al.*, 2016). The main basis is to consider the following points: The study found that β_2 - R can increase the displacement of glucocorticoid receptor into the nucleus in the cytoplasm, so that the biological effect of glucocorticoid can be amplified; It is reported that terbutaline can increase the contact area between budesonide and bronchial mucosa, which can lead to a higher concentration of drugs to direct the site of the lesion, which is beneficial to the full use of the drug, and the budesonide can also reduce the resistance of the bronchial smooth muscle to the terbutaline (Fitzpatrick *et al.*, 2016). Studies have shown that pre inhaled bronchodilator can prevent reflex bronchospasm caused by aerosol inhalation during persistent asthma (Ghoneum, 2015). The results of this study showed that the scores of dyspnea and pulmonary function indexes (FEV1%, PEF%) in the experimental

Table 1: General comparison of patients

Index	Experimental group (n=120)	Control group (n=120)	P value
Sex (male / female)	67/53	62/58	0.014
Age (age)	42.3±7.15	43.5±6.14	0.582
Course of disease (year)	6.13±2.65	7.04±3.17	0.16

Table 2: Score comparison

Group	Cough score		Dyspnea score	
	Before treatment	After treatment	Before treatment	After treatment
Experience group	1.82±0.72	0.71±0.66	2.01±1.24	0.63±0.71
Control group	1.79±0.4	0.88±0.4	2.35±1.12	0.91±0.86

Table 3: Pulmonary function index

Group	FEV1%		PEF%	
	Before treatment	After treatment	Before treatment	After treatment
Experience group	55.27±2.83	61.56±3.12	59.14±2.13	72.64±3.56
Control group	57.13±1.92	68.34±3.24	62.27±2.61	79.61±4.12

Table 4: Comparison of experimental indexes

Group	IL-6(ng/l)		BNP(pg/ml)		CRP(mg/l)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experience group	314.2±50.13	139.4±45.62	573.2±61.7	341.2±51.6	4.75±1.22	2.13±1.05
Control group	320.7±49.7	151.7±52.61	572.6±54.3	457.8±61.7	4.83±1.31	2.54±1.13

Table 5: Comparison of WBC and EOS

Group	WBC(10*9/L)		EOS(10*9/L)	
	Before treatment	After treatment	Before treatment	After treatment
Experience group	7.56±1.12	6.24±0.91	0.65±0.11	0.15±0.14
Control group	7.59±1.26	5.91±0.83	0.64±0.10	0.22±0.15

Table 6: Adverse reaction

Group	Flustered	Pharynx discomfort	Finger flutter	Fungal infection
Experience group	2	8	0	0
Control group	4	11	1	1

group were improved more significantly than those in the control group ($P<0.05$). It is suggested that inhalation of terbutaline first can give full play to the dilated bronchus and make budesonide more easy to reach the bronchial tree, improve the drug concentration and enhance the drug activity, effectively relieve the clinical symptoms and improve the lung function of the patients with acute asthma attack (Jonsson *et al.*, 2016).

IL-6 is mainly derived from lymphocytes and mononuclear macrophages. Some studies have found that some of the tumor cells and bone marrow cells can also be synthesized and secreted (Kazani *et al.*, 2013). At present, a number of cytokines are known to be associated with asthma, and IL-6 is an important proinflammatory cell factor involved in the inflammatory response of the

body (Kang *et al.*, 2003). The results of this study showed that the IL-6 levels of the two groups were significantly lower than those before treatment and the experimental group was significantly lower than that of the control group ($P<0.05$). It is reported that the symptoms and lung function of the patients with bronchial asthma affect the level of IL-6 and the level of serum IL-6 increases during the acute attack of asthma and decreases when the acute symptoms of asthma are controlled. Consistent with the results of this study, the level of cytokine interleukin-6 can be used as an indicator of acute attack of bronchial asthma (Kumaravel *et al.*, 2014). BNP is produced mainly by ventricular myocardium. It is produced when the volume of the ventricle increases and the pressure load is too large. It has a strong discharge of sodium, diuresis, reduction of pulmonary circulation and peripheral

vascular tension (Luo, 2015). The results showed that the levels of BNP in asthmatic patients of two groups were significantly lower than those before treatment, and the experimental group was significantly lower than that of the control group ($P<0.05$). The mechanism of BNP elevation is that when bronchial asthma is acute, hypoxia caused by bronchospasm causes pulmonary vasoconstriction and causes increased cardiac load to increase the release of BNP, so the serum BNP level can be used to evaluate the effective parameters of the severity of bronchial asthma (Liu *et al.*, 2015).

The content of CRP is very small in normal condition. It is mainly caused by the inflammatory mediators such as $il-6$ and $TNF-\alpha$ to stimulate the liver cells to produce a nonspecific acute phase protein (Oren *et al.*, 2017). The results of this study suggest that the level of serum CRP in the two groups decreased after treatment, and the two groups were statistically different ($P<0.05$). The results showed that C-reactive protein was involved in the acute attack of bronchial asthma (Nathan *et al.*, 2015). However, the current research indicates that the specific causes and mechanisms of the elevation of serum CRP in the acute attack of bronchial asthma are not very clear. The increase of CRP in the acute attack of bronchial asthma may be due to the ability of C reactive protein to identify foreign pathogens and injure cells, and to combine with the injured part and activate the complement system. It can eliminate foreign pathogens and damage cells, and promote the recovery of the body. At present, the exposure of respiratory tract infection and allergen is the two important cause of the acute attack of asthma (Shu *et al.*, 2016). The WBC count has the advantages of fast detection speed, only a few minutes to get the result, and the cheap patient is easy to accept. It is a commonly used index to judge the type and degree of infection and the curative effect in clinical. But the day changes of WBC are very large and there are many factors affecting WBC, such as individual difference, age, stress state, drug, exercise, pregnancy and other factors, so WBC count is limited to determine the type and effect of clinical infection. The white blood cells of the two groups improved compared with those in the same group before treatment, but there was no significant difference between the two groups after treatment ($P>0.05$).

Budesonide suspension into the lungs after inhalation was only 10%-20%, about 80% remained in the mouth and pharynx. The main adverse reactions were coughing, pharynx discomfort, hoarseness and oral *Candida albicans* infection and so on, considering the local deposition of the drug, the time of the laryngopharyngeal mucosa and the hormone contact (Webster *et al.*, 2017). It is concerned that the rate of local adverse reactions can be reduced by taking full mouthwash after use of drugs. The adverse reaction of terbutaline atomization solution is even tremor and palpitation, which is related to the

characteristic reaction of sympathetic amine, and it usually, does not need special treatment, but it can disappear spontaneously. In this study, the adverse reactions in the process of drug atomization inhalation were mild, and they were improved after the treatment, which did not affect the continued use of the original drug. In general, the adverse reaction rate of inhalation of terbutaline and budesonide in the treatment of bronchial asthma was low, and the safety was good.

CONCLUSION

To sum up, atomization inhalation is a new way to treat bronchial asthma at present. It has the characteristics of quick, simple, convenient, safe and less adverse reactions. The oxygen driven atomization inhalation is worth popularizing. Aerosol inhalation of glucocorticoid is the first choice. Budesonide is the most common therapy for improving the lung function of asthmatic patients. The results show that the inhalation of terbutaline and budesonide in the treatment of acute exacerbation of bronchial asthma is more effective and safe than the inhalation of budesonide and budesonide, which can provide a reference for clinical treatment. In addition, inhalation of terbutaline and budesonide at intervals can effectively reduce the levels of inflammatory factors in patients with acute asthma, and then reduce the damage to the body by inflammatory factors and control the symptoms of asthma in patients.

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