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Original Article

Budesonide combined with ipratropium bromide in the treatment of bronchopneumonia and its efficacy on pulmonary function

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Abstract: Objective: To explore the clinical efficacy of budesonide combined with ipratropium bromide in the treatment of bronchopneumonia, and to analyze the pulmonary function changes. Methods: Eighty-two patients with bronchopneumonia were enrolled and randomly divided into a control group (41 cases, treated with conventional therapy) and a research group (41 cases, treated with budesonide and ipratropium bromide on the basis of conventional therapy). The clinical efficacy, symptom disappearance time, inflammatory factors (interleukin-6, IL-6), tumor necrosis factor-α (TNF-α), hypersensitive C-reactive protein (hs-CRP), adverse reactions, hospital stay and recurrence rate were compared. Results: The total effective rate in the research group was significantly higher than that in the control group (P<0.05). The disappearance time of rale, shortness of breath, cough, and hospital stay in the research group were significantly shorter than those in the control group (all P<0.05). The levels of IL-6, TNF-α, hs-CRP, incidence of adverse reactions and recurrence rate in the research group were significantly lower than those in the control group (all P<0.05). Conclusion: Budesonide combined with ipratropium bromide effectively reduces rale, shortness of breath, cough, and inflammatory reactions in patients with bronchopneumonia, as well as decreases adverse reactions and recurrence rate. Therefore, it achieves satisfying prognosis and is worthy of clinical application.

Keywords: Budesonide, ipratropium bromide, bronchopneumonia, clinical efficacy, pulmonary function

Introduction

Bronchopneumonia, a common clinical disease, is generally caused by virus and bacterial infection, ranking second in the incidence rate of respiratory diseases. It has a short course of disease (usually about 2-12 days) and is common in the elderly and children, with the clinical symptoms of pulmonary moist rale, fever, anhelation, and cough. With a high risk of death in severe bronchopneumonia, it has attracted great attention in clinical practice [1, 2]. At present, the conventional treatment for bronchopneumonia is mainly focused on prevention and treatment of complications, anti-heart failure, anti-fever, hypoxia correction, maintenance of airway patency, and infection control. However, it fails to meet the clinical needs without significantly improving symptoms including asthma and shortness of breath or good prognosis [3, 4]. The narrow bronchial mucosa caused by edema and congestion obstructs sputum in the respiratory tract and weakens ciliary movement. As a result, patients are incapable of removing the sputum autonomously and timely, which in turn triggers pulmonary atelectasis and respiratory obstruction. Eventually, there are serious adverse effects on the ventilation and breath, and obviously increased mortality rate of the patients [5, 6].

Therefore, timely and effective removal of sputum from patients' respiratory tract, improvement of pulmonary ventilation and exhalation functions, and enhancement of airway patency are the keys to the treatment of bronchopneumonia [7]. In the study of Sun et al., budesonide combined with ipratropium bromide can effectively shorten the treatment duration of patients with bronchiolitis and promote the remission of

stridor, wheezing and cough [8]. Budesonide and ipratropium bromide are commonly used drugs in the treatment of bronchopneumonia, and further the effectiveness and safety of their combination are currently highly concerned in clinical practice. In view of this, in our study, eighty-two patients with bronchopneumonia were selected to explore the clinical efficacy of budesonide combined with ipratropium bromide and to analyze the pulmonary function changes. The specific research results are reported as follows.

Materials and methods

Baseline data

The subjects included in the study were 82 patients with bronchopneumonia admitted to First Affiliated Hospital of Gannan Medical University from July 2016 to July 2018. They were divided into a control group (n=41) and a research group (n=41) using the random number table. There were 17 females and 24 males in the research group, aged 48-82 years with an average age of 68.5 ± 5.8 years, with a disease course of 2-10 days and an average disease duration of 6.06 ± 1.52 days. There were 19 females and 22 males in the control group, aged 49-80 years with an average age of 68.3 ± 5.6 years, with a disease course of 3-9 days and an average course of 6.08 ± 1.47 days.

This study was approved by the Ethics Committee of First Affiliated Hospital of Gannan Medical University. Patients and their families were informed about the study and signed the informed consent form.

Inclusion criteria were as follows: patients meeting the diagnostic criteria for bronchopneumonia described in Some Progresses of Respiration in 2012 [9]; patients diagnosed with pulmonary shadow by chest X-ray and with double pulmonary rales, cough and asthma in varying degrees; patients with no drug allergies and contraindications; patients with no history of drug allergy; patients with mental balance and good consciousness.

Exclusion criteria were as follows: patients with kidney and liver dysfunction; breast-feeding and pregnant women; patients with incomplete clinical data; patients with depression and schizophrenia; patients receiving relevant anti-infective treatment before the study; patients with other respiratory diseases; patients with malignant tumors.

Methods

Control group: symptomatic treatments, including antiviral, antitussive, anti-infective, phlegm-resolving, oxygen inhalation, nutritional support, were carried out. Ceftazidime (40-100 mg/(kg·d)) (Qilu Pharmaceutical Co., Ltd., China), an anti-infective drug, was dissolved in 150 mL of 9% glucose solution for intravenous drip, once a day. Banxia cough syrup (Guizhou Yibai Pharmaceutical Co., Ltd., Z52020502) was orally taken for antitussive and phlegm-resolving treatment, 20 mL each time and three times a day, for 7 consecutive days.

Research group: on the basis of the control group, budesonide combined with ipratropium bromide was inhaled. Together, 0.5-2 mL of budesonide (Shanghai Sine Promod Pharmaceutical Co., Ltd., China) and 1.25-2.50 mL of ipratropium bromide (Boehringer Ingelheim Pharma GmbH & Co. KG) were mixed with 20 mL of 0.9% sodium chloride solution, inhaled for 15 min after each meal, 2-3 times a day for 7 consecutive days.

Outcome measures and evaluation criteria

The clinical efficacy, disappearance time of symptoms (rales, shortness of breath, cough), inflammatory factors, adverse reactions (nausea and vomiting, facial flushing, rash), hospital stay, and recurrence rate were compared. (1) The evaluation of clinical efficacy diagnosed by Chest X-ray: markedly effective: pulmonary shadows disappeared, cough, rales, and asthma disappeared; Effective: pulmonary shadows disappeared by more than 50%, and cough, rales and asthma were significantly alleviated; Ineffective: pulmonary shadow changes were not obvious, cough, rales and asthma were not alleviated significantly or even aggravated. Total effective rate = (The number of markedly effective + effective)/the total number of cases [5, 6]. (2) Inflammatory factor detection: fasting venous blood (5 mL) was collected from all subjects to separate serum. The interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and hypersensitive C-reactive protein (hs-CRP) were detected using an automatic specific protein analyzer (Shenzhen Genrui Electronics Co., Ltd.) in strict accordance with relevant standards. (3) The patients were followed up for 3 months to count the recurrence of disease.

Table 1. General data ($\bar{x}$ ± sd)

Group	Research group (n=41)	Control group (n=41)	χ^2/t	P
Gender (male/female)	24/17	22/19	0.1980	0.6560
Average age (year)	68.5±5.8	68.3±5.6	0.1588	0.8742
Average course of disease (d)	6.06±1.52	6.08±1.47	6.0610	0.9520

Table 2. Clinical efficacy (n, %)

Group	Research group (n=41)	Control group (n=41)	χ^2	P
Markedly effective	15 (36.59)	10 (24.39)		
Effective	24 (58.54)	18 (43.90)		
Ineffective	2 (4.88)	13 (31.71)		
Total effective rate (%)	39 (95.12)	28 (68.29)	9.8726	0.0017

Table 3. Symptom disappearance time and hospital stay ($\bar{x}$ ± sd)

Group	Research group (n=41)	Control group (n=41)	t	P
Rales (d)	3.02±0.62	6.48±1.14	17.0725	0.000
Shortness of breath (d)	2.98±0.54	6.16±1.05	17.2454	0.000
Cough (d)	3.09±0.84	6.28±1.14	14.4246	0.000
Hospital stay (d)	6.05±1.05	7.92±1.84	5.6520	0.000

Table 4. Changes of inflammatory factors ($\bar{x}$ ± sd)

Group	Research group (n=41)	Control group (n=41)	t	P
IL-6 (pg/mL)				
Before treatment	98.25±10.25	98.33±10.21	0.0354	0.9718
After treatment	21.02±3.05	58.62±5.61	37.7038	0.0000
t	46.2414	21.8261		
P	0.0000	0.0000		
TNF-α (pg/mL)				
Before treatment	31.92±5.14	32.01±5.19	0.0789	0.9373
After treatment	8.06±0.52	16.13±1.05	44.1008	0.0000
t	29.5725	19.2028		
P	0.0000	0.0000		
hs-CRP (mg/L)				
Before treatment	13.98±1.52	13.96±1.46	0.0608	0.9517
After treatment	5.12±0.25	10.35±0.64	48.7390	0.0000
t	36.8287	14.5004		
P	0.0000	0.0000		

Note: IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; hs-CRP, hypersensitive C-reactive protein.

Statistical methods

The SPSS26.0 was used to process the collected data. The measurement data were expressed as mean ± standard deviation ($\bar{x}$ ± sd). The independent t test was used for inter-group comparison and paired t test for intra-group comparison. The counting data expressed as number of cases/percentage (n/%) were analyzed by χ^2 test. A value of P<0.05 was considered for statistically significant difference.

Results

Comparison of general data

There was no significant difference in gender, age and course of disease (P>0.05), as shown in **Table 1**.

Comparison of the clinical efficacy

The total effective rate in the research group was significantly higher than that in the control group (P<0.05), as shown in **Table 2**.

Comparison of the symptom disappearance time and hospital stay

The symptom disappearance time and hospital stay in the research group were significantly shorter than those in the control group (P<0.05), as shown in **Table 3**.

Comparison of the changes of inflammatory factors

Patients with running nose, cough and fever diagnosed with bronchopneumonia by bacteriological examination by lung puncture were determined to have the recurrence of disease.

Inter-group comparison: there was no significant difference in inflammatory factors between the two groups before treatment (P>0.05). After treatment, the factors in the

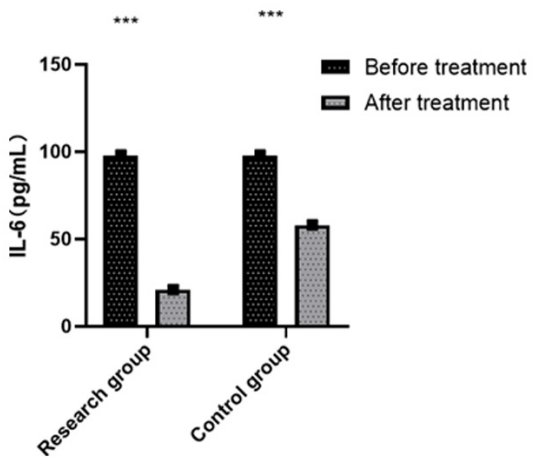

Figure 1. Comparison of IL-6. ***P<0.001. IL-6, interleukin-6.

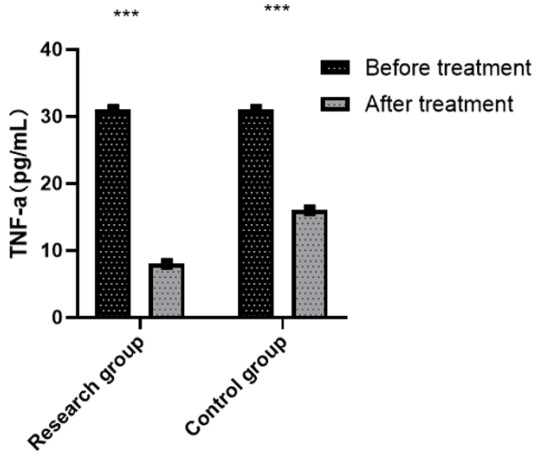

Figure 2. Comparison of TNF-α. ***P<0.001. TNF-α, tumor necrosis factor-α.

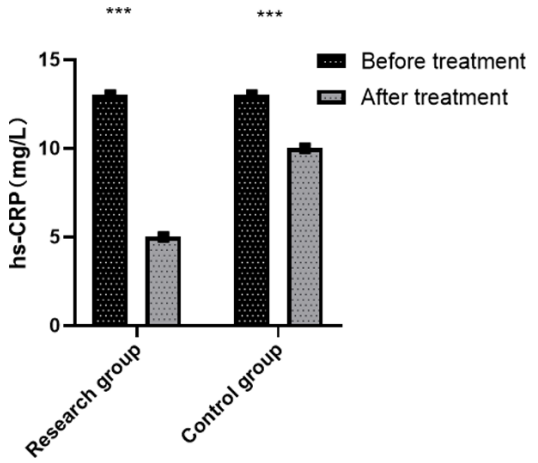

Figure 3. Comparison of hs-CRP. ***P<0.001. hs-CRP, hypersensitive C-reactive protein.

research group were significantly lower than those in the control group (P<0.05). Intra-group comparison: the inflammatory factors in both groups after treatment were significantly lower than those before treatment (P<0.05), as shown in **Table 4** and **Figures 1-3**.

Comparison of the incidence of adverse reactions

The incidence of adverse reactions in the research group was significantly lower than that in the control group (P<0.05), as shown in **Table 5**.

Comparison of the recurrence rate

The recurrence rate in the research group was significantly lower than that in the control group (P<0.05), as shown in **Table 6**.

Discussion

Bronchopneumonia mainly occurs in the alveoli near the bronchi. At present, its pathogenesis still remains unknown, but it is generally believed that the occurrence is closely related to drugs, allergy, immune injury, physical and chemical factors, and virus infection [7, 8]. IL-6 is a cytokine that plays an important role in autoimmune and inflammatory reactions and is highly expressed in acute inflammatory reactions [9, 10]. hs-CRP, a non-specific acute phase reaction protein, has a great correlation with inflammatory reaction and tissue damage. The level of hs-CRP is significantly increased in patients with inflammatory reactions [11, 12]. As an inflammatory medium, TNF-α participates in the pathophysiological reactions of inflammation, and its increase can easily trigger or aggravate inflammatory reactions [13, 14]. In this study, budesonide combined with ipratropium bromide was applied on the basis of antitussive, antiasthmatic, anti-infective, oxygen inhalation and other conventional treatments, which achieved significant therapeutic effects.

From the results of this study, it can be seen that the combination of budesonide and ipratropium bromide is of effectiveness and safety in the treatment of bronchopneumonia. First, budesonide belongs to glucocorticoid, which has significant inhibitory effect on immune response. It can effectively block antibody syn-

Table 5. Incidence of adverse reactions (n, %)

Group	Research group (n=41)	Control group (n=41)	χ^2	P
Nausea and vomiting	1 (2.44)	5 (12.20)	2.8772	0.0898
Facial flushing	1 (2.44)	2 (4.88)	0.3460	0.5564
Rash	0 (0.00)	3 (7.32)	3.1139	0.0776
Incidence of adverse reaction (%)	2 (4.88)	10 (24.39)	4.7833	0.0287

Table 6. The recurrence rate

Group	Research group (n=41)	Control group (n=41)	χ^2	P
Recurrence cases (n)	2	12		
Recurrence rate (%)	4.88	29.27	8.6134	0.0033

thesis, improve cell membrane stability, and reduce the release of histamine and other active substances, showing significant anti-allergic and anti-inflammatory effects [15-17]. Second, ipratropium bromide is a potent anticholinergic drug that plays a role in promoting bronchiectasis, reducing respiratory muscle spasm, decreasing mucus secretion, enhancing ciliary movement, promoting airway patency, and accelerating sputum excretion. It significantly improves the pulmonary function and the quality of life of patients [18, 19]. Last but not least, nebulized inhalation of budesonide combined with ipratropium bromide allows the drug to act directly on the lesion, accelerates sputum discharge, and increases the drug concentration in the lesion, thereby offering a significant anti-inflammatory effect. And the combination treatment can promote symptom regression and shorten the treatment duration significantly, which lowers the treatment costs and reduces the economic burden of patients and their families [20]. Zhang et al. found that, first, the total effective rate in the research group (97.78%) was significantly higher than that in the control group (81.40%), indicating the high effectiveness of budesonide combined with ipratropium bromide, which was similar to the results of this study [21]. Second, the incidence of adverse reactions in the research group (8.89%) was significantly lower than that in the control group (16.28%), suggesting that budesonide combined with ipratropium bromide had a high safety, which was also similar to the results of this study.

To sum up, due to the small sample size and short research period, the results lacks the universality and generality to some extent. Therefore, it is still necessary to further expand the sample size and extend the research period, in order to provide reference basis. In this study, for patients with bronchopneumonia, budesonide combined with ipratropium bromide effectively reduces pulmonary symptoms and inflammatory reactions, reduces the incidence of adverse reactions and recurrence rate, and greatly improves the prognosis of patients, thus making up for the deficiencies of clinical conventional treatment. It is believed that with the rapid development of medical technology in China, greater progress will be made in the treatment of bronchopneumonia.

Disclosure of conflict of interest

None.

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