

Effects of Theophylline Sustained Release Tablets Combined with Erythromycin on Pulmonary Function and Inflammatory Factors in Elderly Patients with Severe Stable Chronic Obstructive Pulmonary Disease

Wujie Zhai ^{1,*}, Wenjie Zhai ²

¹ Hospital of China National Chemical Construction Corporation, 26 Yijing Street, Jinyuan District, 030021 Taiyuan, China

² Xi County Longquan Town Health Center, Xixian County, 1 Xi County South Street, 041399 Linfen, China

Keywords

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* Correspondence

Wujie Zhai
Hospital of China National Chemical
Construction Corporation, 26 Yijing Street,
Jinyuan District, 030021 Taiyuan, China
E-mail: zhaiwujie7322759@163.com

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Abstract

Objective: To investigate the effects of theophylline sustained release tablets combined with erythromycin on pulmonary function and inflammatory factors in elderly patients with severe stable chronic obstructive pulmonary disease (COPD). **Methods:** A total of 86 elderly patients with severe stable COPD in our hospital were selected from September 2016 to March 2018, and they were randomly divided into control group (n = 43) and observation group (n = 43) according to the random number table method, the control group was treated with erythromycin, the observation group was combined with theophylline sustained release tablets on the basis of the control group, Pulmonary function indexes, levels of inflammatory factors and adverse reactions were compared between the two groups before and after treatment. **Results:** After treatment, the forced expiratory volume/forced vital capacity in the first second (FEV1/FVC) and the percentage of forced expiratory volume in the first second (FEV1%Pred) of the two groups was significantly higher than those before treatment ($p < 0.05$), and the level of the above indicators in the observation group was significantly higher than those in the control group ($p < 0.05$); After treatment, the levels of c-reactive protein (CRP), interleukin (IL) -8 and tumor necrosis factor (TNF) - α in the two groups were significantly lower than those before treatment ($p < 0.05$), and the level of the above indicators in the observation group was significantly lower than those in the control group ($p < 0.05$); There was no significant difference in the incidence of adverse reactions between the two groups ($p > 0.05$). **Conclusion:** Theophylline sustained release tablet combined with erythromycin has a good effect in treating severe COPD, which can effectively improve lung function and reduce inflammatory factors in elderly patients.



1 Introduction

Chronic obstructive pulmonary disease (COPD) is one of common respiratory diseases in clinic, which mostly happens in elder patients. Pulmonary dysfunction is a major characteristic of the disease. Besides, patients with COPD usually perform systemic inflammatory response, aggravating the severity of the disease. Thus, anti-infection therapy is the key to alleviate the symptoms of COPD. Currently, macrolides like erythromycin is clinically used to control the inflammation induced by the disease, but its effect on patients with severe stable COPD is unsatisfactory. Hence, more effective drugs are needed. It has been demonstrated that theophylline sustained release tablets are able to continuously dilate the airways and its combination with macrolides can effectively improve the clinical symptoms of bronchiectasis [1], but there are few researches about its effect on severe stable COPD. Based on that, this work selected patients with severe stable COPD treated in our hospital as research objects, aiming to investigate the effects of theophylline sustained release tablets combined with erythromycin on pulmonary function and inflammatory factors in elderly patients with severe stable COPD.

2 Materials and methods

2.1 Research object

A total of 86 elderly patients with severe stable COPD treated in our hospital were from September 2016 to March 2018 were selected, and they were divided into control group (n = 43) and observation group (n = 43) according to the random number table method. The general information of each case including sex, age and course of disease was collected from patient records.

Control group: sex, 23 males and 23 females; average age, 67.42 ± 8.11 years old; average course of disease, 9.65 ± 1.87 years.

Observation group: sex, 25 males and 18 females; average age, 68.35 ± 7.62 years old; average course of disease, 10.34 ± 2.13 years.

Inclusion criteria: (1) Patients who met the diagnostic criteria of COPD in *Chronic obstructive pulmonary disease: diagnosis and management: summary of updated NICE guidance* [2]; (2) those with severe stable COPD; (3) those older than 65.

Exclusion criteria: (1) Patients with respiratory diseases; (2) those with severe diseases in other organs; (3) those with heart and brain diseases; (4) those with mental diseases; (5) those who had taken anti-infective agents such as macrolides and theophylline within two weeks.

The study was approved by the Ethics Committee of Sinochem No.2 Construction Group Hospital, with all patients volunteering for participation and signing the informed consent. There was no significant difference in general information between the two groups ($p > 0.05$), indicating the comparability between them.

2.2 Methods

Patients in the control group were treated with erythromycin (approval number of National Medical Products Administration (NMPA): H20057210, Yichang HEC Changjiang Pharmaceutical Co., Ltd., Hubei, China, <http://cj.hec.cn/>) 0.25 g/time and 3 times a day. On the basis of control group, while patients in the observation group were additionally treated with theophylline sustained release tablets (approval number of NMPA: H51021526, Sichuan Tongrentai Pharmaceutical Co. Ltd., Sichuan, China, <http://www.trtyy.com.cn/>) 0.1 g/time and twice a day. The treatment lasted for 6 months.

2.3 Observational indexes

Before and after treatment, pulmonary function was examined through Quark PFT Series Pulmonary Function Equipment (COSMED, Rome, Italy,

<https://www.cosmed.com/en/>), the indexes of which mainly contained forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) and percentage of predicted FEV1 (FEV1%Pred). Enzyme-linked immunosorbent assay (ELISA) was used to assess levels of C-reactive protein (CRP), interleukin (IL)-8 and tumor necrosis factor (TNF)-α in peripheral blood. Adverse reactions of all patients were viewed during the experiment.

2.4 Statistical analysis

Statistical analysis was operated by SPSS 20.0 (IBM, Armonk, NY, USA). The enumeration data were compared by X² test, while the measurement data presented as the means ± standard deviation were

contrasted through Student's t-test. A statistically significant difference was accepted when $\rho < 0.05$.

3 Results

3.1 Pulmonary function index level

FEV1/FVC and FEV1%Pred levels did not differ obviously between two groups before treatment (Table 1, $\rho > 0.05$), whereas after treatment, the levels of FEV1/FVC and FEV1%Pred in both groups were appreciably higher than those before treatment (Table 1, $\rho < 0.05$), with levels of indexes above after treatment in observation group dramatically rising in comparison with those in control group (Table 1, $\rho < 0.05$).

Table 1 Pulmonary function index level between two groups.

Group	n	FEV1/FVC		FEV1%Pred	
		Before	After	Before	After
Observation	43	54.65 ± 6.23	73.66 ± 6.59 *	61.24 ± 7.66	75.69 ± 5.31 *
Control	43	53.77 ± 5.96	65.42 ± 8.13 *	63.17 ± 6.41	68.42 ± 4.96 *
<i>t</i>		0.669	5.163	-1.267	6.561
ρ		0.505	0.000	0.209	0.000

Note: Compared with before treatment, * $\rho < 0.05$.

3.2 Inflammatory factor level

No marked difference in CRP, TNF-α and IL-8 levels between two groups was observed before treatment (Table 2, $\rho > 0.05$). After treatment, CRP, TNF-α and

IL-8 levels were decreased in both groups in contrast with before treatment (Table 2, $\rho < 0.05$), and the levels in observation group were notably lower than those in control group (Table 2, $\rho < 0.05$).

Table 2 Inflammatory factor level between two groups.

Group	n	CRP (ng/L)		TNF-α (ng/L)		IL-8 (ng/L)	
		Before	After	Before	After	Before	After
Observation	43	81.34 ± 6.59	48.54 ± 6.38 *	82.36 ± 5.79	38.26 ± 6.38 *	75.42 ± 5.33	43.37 ± 4.18 *
Control	43	79.53 ± 7.37	61.27 ± 5.96 *	83.68 ± 6.37	53.75 ± 5.19 *	76.89 ± 4.62	59.54 ± 6.57 *
<i>t</i>		1.201	-9.561	-1.006	-12.350	-1.367	-13.617
ρ		0.233	0.000	0.318	0.000	0.175	0.000

Note: Compared with before treatment, * $\rho < 0.05$.

3.3 Adverse reactions

There were 6 cases of adverse reactions comprising nausea and arrhythmia in observation group and the incidence of adverse reactions was 13.95%; 3 cases of

adverse reactions occurred in control group with the incidence of adverse reactions 6.98%. There was no significant difference in the incidence of adverse reactions between the two groups ($\rho > 0.05$).

4 Discussion

COPD is a frequent lung disease in clinic as well as a chronic disease prevalent in the elderly. The data exhibit that COPD possesses high morbidity and mortality and it is estimated that COPD will rank 5th disease affecting survival time and life quality of people worldwide [3]. Therefore, it is necessary to enhance the treatment effectiveness of the disease. At present, the pathogenesis of COPD remains unclear and clinicians generally adopt the corresponding therapeutic measures according to clinical manifestations. It has been reported that COPD is mainly characterized by systematic inflammatory response [4]. Clinically, it is speculated that harmful gas and particles enter the respiratory tract to cause production of inflammatory factors in large amount and block the airway so as to limit the exchange of gas between the lung and the external, thereby badly affecting pulmonary function. Thus, reduction of inflammatory response in the treatment of COPD is a crucial point for controlling the disease and ameliorating pulmonary function. Erythromycin realizes an effect on declining synthesis of inflammation factors, which has been widely utilized for controlling COPD-induced inflammation. However, patients with severe stable COPD develop serious condition, and the effect of erythromycin alone is not significant. Hence, drugs with better efficacy are urgently required. Theophylline sustained release tablets have been reported to continuously dilate the airways, which is extensively applied to multiple respiratory diseases in recent years. But there are few researches about its effect on severe stable COPD. In this work, we added the treatment of theophylline sustained release tablets on a basis of erythromycin treatment, trying to provide new reference for effective treatment of severe stable COPD.

The results of pulmonary function test helps to determine whether ventilation dysfunction exists, so

pulmonary function test is a basis of COPD severity evaluation. FEV1/FVC and FEV1%Pred are sensitive indexes of pulmonary function [5,6], whose levels indicate the airway obstruction, as the higher levels of them mean a better exchange of gas between the lung and the external environment as well as a better pulmonary function. Our research observed that after treatment, FEV1/FVC and FEV1%Pred levels in observation group were significantly higher than those in control group, implicating that theophylline sustained release tablets combined with erythromycin notably improved pulmonary function of COPD patients to mitigate the disease. Anhydrous theophylline, the active constituent of theophylline sustained release tablets, is a purine receptor blocker, which can effectively antagonize contraction of respiratory tract responding to adenine and dilate the airway through relaxation of airway smooth muscle, thereby ameliorating the ability of gas exchange between the lung and the external environment as well as pulmonary function.

Systemic inflammatory response is a typical extra-pulmonary feature after attack of COPD, and the inflammatory response in the body will activate the production of various inflammatory factors. CRP is a protein synthesized by hepatocytes when the body is influenced by inflammatory stimulation like microbial invasion. TNF- α and IL-8 are cytokines generated by macrophage stimulated by external stimulus, which play a vital part in inflammatory response. Currently, CRP, TNF- α and IL-8 are considered as clinical indexes of inflammatory response to judge the body infection [7-9]. In this study, levels of CRP, TNF- α and IL-8 in observation group were prominently lower than those in control group, which implied that theophylline sustained release tablets combined with erythromycin was able to effectively alleviate levels of inflammatory factors in COPD patients. It may attribute to anti-inflammatory effect of theophylline sustained release tablets and erythromycin: erythromycin can

elevate the activity of monocytes to decrease production of inflammatory factors; theophylline sustained release tablets fulfill the suppressive functions on adenosine receptor and transcription of nuclear factor kappa-B (NF-KB) so as to inhibit excessive release of inflammatory factors. The combination of the two drugs above strengthens the capability of the body against infection and dramatically reduces inflammatory factor levels. In addition, there was no marked difference in the incidence of adverse reactions between two groups, suggesting that theophylline sustained release tablets combined with erythromycin in the treatment of severe stable COPD possessed high safety and it could be a preferred solution for treatment of patients with severe stable COPD.

All in all, theophylline sustained release tablets combined with erythromycin had a remarkable effect on treating patients with severe stable COPD, which could effectively improve pulmonary function and decline inflammatory factor levels in elderly patients.

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Not applicable.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization, Wu.Z. and We.Z.; Data curation, Wu.Z.; Formal analysis, We.Z.; Methodology, Wu.Z.; Writing-original draft, Wu.Z. and We.Z.; Writing-review and editing, Wu.Z. and We.Z.; All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Sinochem No.2 Construction Group Hospital, with all

patients volunteering for participation and signing the informed consent.

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Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Materials

Not applicable.

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