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Original Article

Study on the clinical efficacy, drug safety and prognosis of doxofylline combined with ceftazidime in patients with chronic obstructive emphysema complicated with infection

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Abstract: To investigate the effects of doxofylline combined with ceftazidime on the treatment of chronic obstructive emphysema complicated with infection, 450 patients admitted to Penglai Hospital of Traditional Chinese Medicine from January 2017 to December 2019 were investigated in this study. These patients were randomly separated into the observation group and the control group, with 225 individuals in each. The control group was treated with doxofylline, and the patients in the observation group were treated with ceftazidime in addition to doxofylline. Short-term efficacy, pulmonary ventilation function, patients' quality of life, peripheral blood TNF-α and PGDF-B levels, and adverse drug reactions were observed after two courses of treatment. We found that ceftazidime combined with doxofylline are more effective than doxofylline alone; the effective rates were 96.89% compared with 84%, respectively. The pulmonary ventilation function and quality of life of the observation group was greatly improved than the control group; and the levels of TNF-α and PDGF-B were also reduced in the observation group. Therefore, Doxofylline combined with ceftazidime is effective in the treatment of patients with chronic obstructive emphysema complicated with infection, which provides a reference for the clinical treatment of patients with chronic obstructive emphysema.

Keywords: Doxofylline, ceftazidime, chronic obstructive emphysema, infection

Introduction

Chronic obstructive emphysema is a chronic lung disease that mostly affects the elderly. Characterized by airway obstruction, the disease is usually caused by exposure to cigarette smoke, particulate and other noxious gases; clinical symptoms are chest stuffiness, cough, expectoration, dyspnea, etc. [1, 2]. As the fourth leading cause of death in the United States, chronic obstructive emphysema is expected to be the third leading cause of death worldwide by 2030 [3]. Elderly patients with weakened immunity and physical limitations are prone to suffer from complications of lung infection [4], and their conditions can easily be worsened. Therefore, it is vital to take timely and effective treatment to improve patients' health [5].

In general, improving airway symptoms is the priority of chronic obstructive emphysema treatment. Doxofylline is a derivative of methylxanthine, its main mechanism is relaxing the smooth muscle of the bronchus through the inhibition of phosphodiesterase (PDE) activities in smooth muscle cells. In consequence, it can alleviate cough and facilitate airway ventilation [6, 7]. Besides, compared to the traditional respiratory stimulant, it has a slighter side effect and can reduce impacts on nerve centers, the gastrointestinal system and cardiovascular system [8]. Cephalosporin antibiotics are spectrometric antibacterial agents that have been applied widely in the clinic. High resistance to acid, enzyme and bacteria makes them more and common in clinical application [9, 10].

Oxidative stress reactions and inflammatory mechanisms also play a vital role in the onset and development of chronic obstructive emphysema [11]. Platelet derived growth factor, PDGF-B, lies downstream of oxidative stress reaction; tumor necrosis factor-α, namely TNF-α, is an important factor that engages the inflammatory reaction. Clinical studies show that both PDGF-B and TNF-α play a vital role in the onset and development of chronic obstructive emphysema, and are of great significance in the progression and prognosis of the disease [12, 13].

In this study, 450 patients in the Penglai Hospital of Traditional Chinese Medicine for the treatment of chronic obstructive emphysema from January 2017 to December 2019 were studied. The aim was to investigate the effects of doxofylline combined with ceftazidime on the clinical efficacy, drug safety and prognosis of patients with chronic obstructive emphysema complicated with infection.

Materials and methods

Subjects

In this study, 450 patients admitted to Penglai Hospital of Traditional Chinese Medicine for the treatment of chronic obstructive emphysema from January 2017 to December 2019 were selected as research subjects. These patients were randomly separated into the observation group and the control group, with 225 individuals in each one. Patients in both groups were diagnosed with chronic obstructive emphysema after X-ray inspection or chest CT scanning. The present study was approved and supervised by Ethics Committee of Penglai Hospital of Traditional Chinese Medicine, and the patients were informed of the examination methods. All patients did not have history of drug allergy or nervous system disease and gave informed consent to be in this study.

Pathological inclusion and exclusion criteria

Inclusion criteria: (1) patients who met the diagnostic criteria for chronic obstructive emphysema [14]; (2) patients aged between 40-80; (3) patients who gave informed consent. Exclusion criteria: (1) those allergic to the medication in this study; (2) those with severe heart, liver and lung dysfunction; (3) those with malignant tumors or systemic immune diseases; (4) those with a recent history of surgery; (5) those under medication which is different from this study.

Treatment

(1) All patients received conventional treatment, including nutrition support, oxygen inhalation and fluid infusion, etc. (2) The control group was treated with doxofylline (A&Z Pharmaceutical Inc., SFDA approval number H200-52247). Treatment: 0.5 g doxofylline was dissolved in 250 ml glucose injection for intravenous injection once a day. (3) Patients in the observation group were treated with ceftazidime in addition to doxofylline. Therapy: 1 g ceftazidime (Shanghai New Asia Pharmaceutical Co., Ltd., SFDA approval number H200840-54) was dissolved in 250 ml glucose injection for intravenous injection once a day.

Observed indicators

Short-term efficacy: Short-term efficacy was observed after two courses of treatment, and the criteria for efficacy are: (1) Inefficacy: patients' clinical symptoms were not notably improved or aggravated after the treatment. (2) Efficacy: patients' clinical symptoms were notably improved but did not disappear after the treatment. (3) Marked efficacy: patients' clinical symptoms were notably improved or even disappeared after the treatment, having no impact on daily life.

Pulmonary ventilation function: The recovery of the pulmonary function of patients in the two groups was observed and compared, including the peak expiratory flow rate, maximal mid-expiratory flow curve and the volume of 1 second's forced respiration.

Patients' quality of life: Patients' quality of life, including physiological function, social function, role restriction and overall health, was collected and compared.

Peripheral blood TNF-α and PGDF-B levels: Fasting venous blood samples were collected in the early morning before treatment and after two courses of treatment. The samples were then centrifuged to get serum and the TNF-α and PGDF-B levels were tested with ELISA. Diagnostic kits were provided by Shanghai Jianglai Biotechnology Co., Ltd.

Table 1. General information comparison

Group	Case	Male (n, %)	Female (n, %)	Average age (year)	Average disease course (year)
Control Group	225	109 (48.44)	116 (51.56)	62.45 ± 11.02	10.57 ± 9.46
Observation Group	225	117 (52.00)	108 (48.00)	62.34 ± 10.87	10.66 ± 9.25
X^2 (t) Value		0.175		0.312	0.039
P Value		>0.05		>0.05	>0.05

Table 2. Efficacy comparison

Group	Case	Inefficacy (n, %)	Efficacy (n, %)	Marked efficacy (n, %)	Effective rate (n, %)
Observation group	225	7 (3.11)	83 (36.89)	135 (60)	218 (96.89)*
Control group	225	36 (16.00)	69 (39.67)	120 (53.33)	189 (84.00)

*compared to the control group, P<0.05.

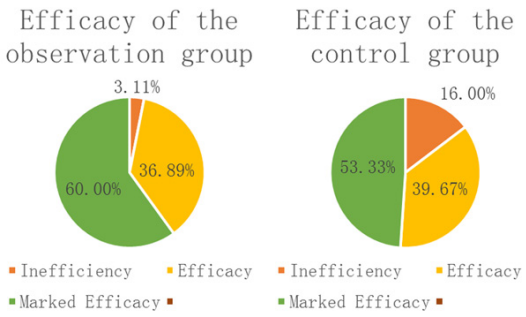

Figure 1. Efficacy comparison.

Adverse drug reactions: Adverse drug reactions of the two groups were collected and compared.

Statistical method

SPSS (version 19.0) was used for statistical analysis. Data represented as mean ± standard deviation and were analyzed by *t* test. The enumeration data represented by n (%) and was analyzed by chi-square test. P<0.05 was considered statistically significant.

Results

General data comparison

In the observation group, there were 117 male patients and 108 female patients with an average age of 62.34 ± 10.87 years and an average disease course of 10.66 ± 9.25 years. In the control group, there were 109 male patients and 116 female patients with an average age of 62.45 ± 11.02 years and an average disease course of 10.57 ± 9.46 years. No statistical significance was found in terms of gender, age, disease course and other general information when comparing the two groups (P>0.05, **Table 1**).

Efficacy comparison

Observing the short-term efficacy of the two groups, ceftazidime combined with doxofylline was more effective than doxofylline alone. The effective rates were 96.89% compared with 84%, respectively (x^2=5.997, *compared to the control group, P<0.05, **Table 2**; **Figure 1**).

Pulmonary function comparison

The peak expiratory flow rate of treated patients in the observation group was 0.54 ± 0.29 L/min; the volume of 1 second's forced respiration was 1.59 ± 0.68 L; the maximal mid-expiratory flow curve was 0.46 ± 0.30 ml/s. For treated patients in the control group, the peak expiratory flow rate was 0.28 ± 0.12 L/min, the volume of 1 second's forced respiration was 1.08 ± 0.37 L, and the maximal mid-expiratory flow curve was 0.19 ± 0.12 ml/s. The difference was statistically significant (P<0.05, **Table 3**).

Comparison of patients' quality of life

In the observation group, the physiological function score of treated patients was 76.10 ± 8.70; the social function score was 79.59 ± 10.49; the role restriction score was 79.99 ± 11.72 and the overall health score was 84.23 ± 11.89. In the control group, the physiological function score of treated patients was 63.28 ± 7.89; the social function score was 63.59 ±

Table 3. Pulmonary function comparison

Group	Case	The peak expiratory flow rate (L/min)	The volume of 1 second's forced respiration (L)	The maximal mid-expiratory flow curve (ml/s)
Observation group	225	0.54 ± 0.29	1.59 ± 0.68	0.46 ± 0.30
Control group	225	0.28 ± 0.12	1.08 ± 0.37	0.19 ± 0.12
t Value		4.678	4.339	5.327
P Value		<0.05	<0.05	<0.05

Table 4. Comparison of patients' quality of life

Group	Case	Physiological function	Social function	Role restriction	Overall health
Observation group	225	76.10 ± 8.70	79.59 ± 10.49	79.99 ± 11.72	84.23 ± 11.89
Control group	225	63.28 ± 7.89	63.59 ± 0.49	65.19 ± 11.37	65.87 ± 9.86
t Value		6.569	7.798	5.749	7.184
P Value		<0.05	<0.05	<0.05	<0.05

Table 5. Comparison of peripheral blood TNF-α and PGDF-B levels

Group	Case	TNF-α		PDGF-B	
		Before the treatment	After the treatment	Before the treatment	After the treatment
Observation group	225	53.72 ± 5.14	18.16 ± 2.45	525.78 ± 38.28	126.45 ± 11.63
Control group	225	55.05 ± 4.79	30.56 ± 3.88	519.45 ± 35.06	245.76 ± 17.00
t Value		1.178	20.067	0.351	38.652
P Value			<0.05		<0.05

Table 6. Comparison of adverse reactions

Group	Case	nausea	emesis	diarrhea	Adverse reaction rate
Observation group	225	5 (2.22)	10 (4.44)	10 (4.44)	25 (11.11)
Control group	225	3 (1.33)	9 (4.00)	9 (4.00)	21 (9.33)
X^2			0.100		
P			0.750		

0.49; the role restriction score was 65.19 ± 11.37 and the overall health score was 65.87 ± 9.86 (**Table 4**).

Comparison of peripheral blood TNF-α and PGDF-B levels

The peripheral blood TNF-α and PGDF-B levels of both groups have notably decreased after the treatment. Also, the levels of TNF-α and PDGF-B were lower in patients treated with both ceftazidime and doxofylline than treated with doxofylline alone (P<0.05, **Table 5**).

Adverse drug reactions

In the course of treatment, there were 5 cases of nausea, 10 cases of emesis and 10 cases of diarrhea in the observation group, the rate of adverse drug reactions being 11.11%. In the control group, there were 3 cases of nausea, 9 cases of emesis and 9 cases of diarrhea, the rate of adverse drug reactions being 9.33%. There was no significant difference between the rates (**Table 6**).

Discussion

Chronic obstructive emphysema is a respiratory disease with pathologic changes in the respiratory system; clinically, it includes localized obstructive emphysema and diffuse obstructive emphysema [15]. The main pathologic changes are increased residual volume and sustained expansion of pulmonary tissue on terminal bronchioles along with the destruction of the alveolar septum and reduced elasticity of pulmonary tissue, leading to increased volume [16-18]. Studies show that *Streptococcus pneumoniae*, *Hemophilus influenzae*, *Pseudomonas aeruginosa* and enterobacterium can all lead to chronic obstructive emphysema. In consequence, clinical treatment of chronic obstructive emphysema includes in-

fection control, ease of dyspnea and hypoxia improvement, etc. [19-21].

This study investigates the effects of doxofylline combined with ceftazidime on the clinical efficacy, drug safety and prognosis of patients with chronic obstructive emphysema complicated with infection. We found that the efficacy rate of doxofylline combined with ceftazidime in the treatment of patients with chronic obstructive emphysema was significantly higher than that of treatment with doxofylline. The rates of efficacy and marked efficacy of the observation group were significantly higher than those of the control group, indicating that the treatment of doxofylline combined with ceftazidime is more effective than the treatment of ceftazidime.

In general, improving airway symptoms is the priority of chronic obstructive emphysema treatment. Treated patients in the observation group witnessed a higher increase in the peak expiratory flow rate, maximal mid-expiratory flow curve and the volume of 1 second's forced respiration than those of the control group. The results further indicate that the treatment of doxofylline combined with ceftazidime is significantly more effective than the treatment of ceftazidime. Besides, the scores of patients' quality of life, including physiological function, social function, role restriction and overall health, indicate that the treatment of doxofylline combined with ceftazidime is significantly more effective than the treatment of ceftazidime. Patients with chronic obstructive emphysema usually suffer from long-term low oxygen levels and chronic inflammation, encouraging the secretion of inflammatory factors [22-25]. Furthermore, the findings show that the levels of TNF-α and PDGF-B were significantly lower in patients treated with both ceftazidime and doxofylline than treated with doxofylline alone. However, language fluency is one of limitations in this study, which brings about a hindrance in our research study. Moreover, some data in this study is self-reported, and some of these cannot be verified. More research needs to be conducted in the future in terms of fluent language and standardized data collection.

In conclusion, doxofylline combined with ceftazidime is effective in the treatment of patients with chronic obstructive emphysema complicated with infection, which provides a reference for the clinical treatment of patients with chronic obstructive emphysema.

Disclosure of conflict of interest

None.

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