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Effects of Doxofylline Combined with Ceftazidime on Clinical Efficacy, Drug Safety, and Prognosis in Patients with Chronic Obstructive Pulmonary Disease Complicated with Infection

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Background: The aim of this study was to investigate the effects of doxofylline combined with ceftazidime on clinical efficacy, drug safety, and prognosis in patients with COPD complicated with infection.

Material/Methods: A total of 450 patients admitted to the Inner Mongolia BaoGang Hospital for treatment of COPD from January 2017 to December 2019 were selected to participate. All patients were randomly divided into control and observation groups, with 225 patients in each group. In addition, patients with COPD in the remission stage were matched by sex and age for a blank control group. The control group was treated with doxofylline, and the observation group was treated with ceftazidime and doxofylline. No drug intervention was given to the blank control group. Short-term efficacy, pulmonary ventilation function, patient quality of life, peripheral blood TNF-α and PGDF-B levels, and adverse drug reactions were observed.

Results: The effective treatment rate in the observation group was 96.89%, which was significantly higher than that in the control group (84.00%). Measures of pulmonary ventilation function and patient quality of life in the observation group were significantly higher than those in the control group. Levels of TNF-α and PDGF-B in the observation group were significantly lower than those in the control group. There were no significant differences in the above indicators between the blank control group and the observation group.

Conclusions: Doxofylline combined with ceftazidime effectively treated patients with COPD complicated with infection. These results provide a reference for clinical treatment.

Keywords: Adenophorea Infections • Ceftazidime • Pulmonary Emphysema

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Background

Chronic obstructive pulmonary disease (COPD) is a chronic lung disease that mostly affects the elderly. Characterized by airway obstruction, COPD is usually caused by exposure to cigarette smoke, particulates, and other noxious gases. The clinical symptoms include chest congestion, cough, expectoration, and dyspnea [1,2]. As the fourth leading cause of death currently in the United States, COPD is expected to be the third leading cause of death worldwide by 2030 [3]. Patients who are elderly and have weakened immunity and physical limitations are prone to have complications of lung infection [4], and their condition can easily worsen. Therefore, timely and effective treatment of patients with COPD and lung infection is vital to improving patients' health [5].

In general, improving airway symptoms is the priority of COPD treatment. Doxofylline is a derivative of methylxanthine, and its main mechanism is relaxing the smooth muscle of the bronchus through the inhibition of phosphodiesterase activities in smooth muscle cells. Consequently, doxofylline can alleviate cough and facilitate airway ventilation [6,7]. Also, compared with traditional respiratory stimulants, doxofylline has fewer adverse effects and reduces the impact on the nervous, gastrointestinal, and cardiovascular systems [8]. Cephalosporin antibiotics are spectrometric antibacterial agents that have been applied widely clinically. Their high resistance to acids, enzymes, and bacteria makes cephalosporin antibiotics increasingly common in clinical application [9].

The oxidative stress reaction and inflammatory mechanism play vital roles in the onset and development of COPD [11]. Platelet-derived growth factor (PDGF-B) lies downstream of the oxidative stress reaction, and tumor necrosis factor-α (TNF-α) is an important factor in the inflammatory reaction. Clinical studies show that PDGF-B and TNF-α play critical roles in the onset and development of COPD and are of great significance in the progression and prognosis of the disease [12,13].

In this study, 450 patients admitted to the Inner Mongolia BaoGang Hospital for the treatment of COPD from January 2017 to December 2019 were selected as research participants. The aim of this study was to investigate the effects of doxofylline combined with ceftazidime on clinical efficacy, drug safety, and prognosis in patients with COPD complicated with infection.

Material and Methods

General Patient Information

In this study, 450 patients admitted to the Inner Mongolia BaoGang Hospital for treatment of COPD from January 2017 to December 2019 were selected to participate. All 450 patients were randomly allocated into an observation group or control group, with 225 patients in each group. In addition, patients with COPD in the remission stage, with matching sex and age, were selected as a blank control group. There were no significant differences in sex, age, disease course, and other general information among these 3 groups ($P>0.05$, **Table 1**). Patients in all groups were diagnosed with COPD after X-ray or chest computed tomography (CT) scanning. No patients had a history of drug allergy or nervous system disease. All patients gave their informed consent to participate in the study.

Pathological Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) patients who met the diagnostic criteria of COPD [14]; (2) patients aged between 40 and 80 years; and (3) patients who gave informed consent. The exclusion criteria were as follows: (1) patients with allergy to the medication used in this study; (2) patients with severe heart, liver, or lung dysfunction; (3) patients with malignant tumors or systemic immune diseases; (4) patients with a recent history of surgery; and (5) patients taking medication that was different from the study medication.

Treatment

Patients in the observation group and control group received conventional COPD treatment including nutrition support,

Table 1. Comparison of patients' general information.

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
Blank group	50	33 (66.00)	27 (54.00)	60.28±8.31	9.17±7.39
χ^2/F value		1.053		0.883	0.563
P value		0.591		0.414	0.570

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Table 2. Comparison of efficacy.

Group	Case	Inefficacy (n, %)	Efficacy (n, %)	Marked efficacy (n, %)	Effective rate (n, %)
Observation group	225	7 (3.11)	83 (36.89)	135 (60.00)	218 (96.89)*
Control group	225	36 (16.00)	69 (39.67)	120 (53.33)	189 (84.00)

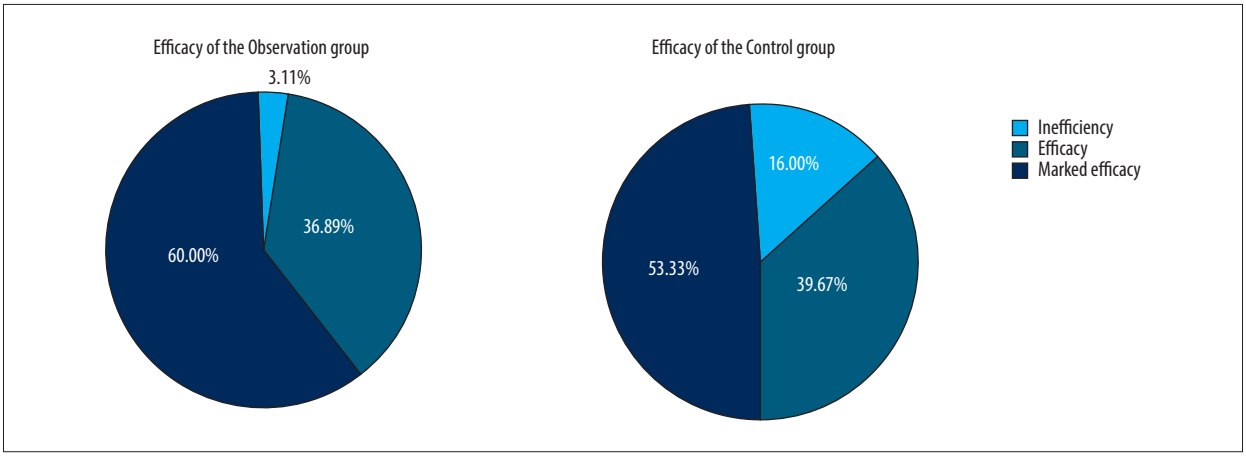

Figure 1. Efficacy comparison.

oxygen inhalation, and fluid infusion. No drug intervention was given to the blank control group. The patients in the control group were treated with doxofylline (A&Z Pharmaceutical Inc., SFDA approval no. H20052247) as follows: 0.5 g doxofylline was dissolved in 250 mL glucose for intravenous injection once per day. The patients in the observation group were treated with doxofylline, as above, combined with ceftazidime with 1 g ceftazidime (Shanghai New Asia Pharmaceutical Co., Ltd., SFDA approval no. H20084054) dissolved in 250 mL glucose injection for intravenous injection once per day.

Measurement of Short-Term Efficacy

Short-term efficacy was observed after 2 courses of treatment, and the criteria for efficacy were as follows: (1) inefficacy: patients' clinical symptoms were not notably improved or were aggravated after treatment; (2) efficacy: patients' clinical symptoms were notably improved but did not resolve after treatment; and (3) marked efficacy: patients' clinical symptoms were notably improved or even resolved after treatment and had no further impact on daily life.

Measurement of Pulmonary Ventilation Function

The recovery of the pulmonary function of patients in the observation and control groups was observed and compared, including the peak expiratory flow rate, maximal mid-expiratory flow curve, and the forced expiratory volume in 1 s.

Measurement of Patients' Quality of Life

Data on patients' quality of life, including physiological function, social function, role restriction, and overall health, were collected, and the scores were compared between the groups.

Measurement of Peripheral Blood TNF-α and PGDF-B Levels

Fasting venous blood samples were collected in the early morning before the treatment and after 2 courses of treatment. The samples were then centrifuged to separate the serum, and the TNF-α and PGDF-B levels were tested by enzyme-linked immunosorbent assay. The diagnostic kits were provided by Shanghai Jianglai Biotechnology Co., Ltd.

Measurement of Adverse Drug Reactions

Data on the adverse drug reactions between the observation and control groups were collected and compared.

Statistical Analysis

In this study, all experimental data were statistically analyzed and processed by SPSS software version 19.0. The measurement data were tested by the *t* test and expressed as mean±standard deviation, and categorical data were tested using the chi-squared test and expressed by n (%). When $P<0.05$, the difference between groups was considered statistically significant.

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Table 3. Comparison of pulmonary function.

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
Blank group	50	0.55±0.14	1.61±0.53	0.47±0.22
F value		91.6	54.84	88.25
P value		<0.05	<0.05	<0.05

* Represented compared with Control group P<0.05; # represented compared with Blank group, P>0.05.

Table 4. Comparison of patients' quality-of-life scores.

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±9.37	65.19±11.37	65.87±9.86
Blank group	50	77.19±8.21	81.58±11.27	82.18±12.29	85.28±13.94
t value		152.7	163.7	106.5	168.2
P value		<0.001	<0.001	<0.001	<0.001

* Represented compared with Control group P<0.05; # represented compared with Blank group, P>0.05.

Results

Comparison of Efficacy

Results of measurements on the short-term efficacy of the observation and control groups showed the effective rate of treatment in the observation group was 96.89%, which was significantly higher than that in the control group (84.00%). The difference was statistically significant (chi-square=5.997, *P*<0.05) (**Table 2, Figure 1**).

Comparison of Pulmonary Function

In the observation group, the peak expiratory flow rate was 0.54±0.29L/min; the volume of 1 s forced expiratory respiration was 1.59±0.68 L; and the maximal mid-expiratory flow curve was 0.46±0.30 mL/s. In the control group, the peak expiratory flow rate was 0.28±0.12 L/min; the volume of 1 s forced expiratory respiration was 1.08±0.37 L; and the maximal mid-expiratory flow curve was 0.19±0.12 mL/s. The differences between the observation and control groups were statistically significant for the 3 variables (*P*<0.05, **Table 3**). In the blank control group, the peak expiratory flow rate was 0.55±0.14 L/min; the volume of 1 s forced expiratory respiration was 1.61±0.53 L; and the maximal mid-expiratory flow curve was 0.47±0.22 mL/s. There were no significant differences between the blank control group and the observation group (*P*>0.05, **Table 3**).

Comparison of Patient 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 was 63.28±7.89; the social function score was 63.59±0.49; the role restriction score was 65.19±11.37; and the overall health score was 65.87±9.86. The above indicators in the blank group were 77.19±8.21; 81.58±11.27; 82.18±12.29; and 85.28±13.94, respectively, and there were no statistically significant differences between the blank group and the observation group (**Table 4**).

Comparison of Peripheral Blood TNF-α and PGDF-B Levels

The peripheral blood TNF-α and PGDF-B levels of the observation and control groups were significantly lower after treatment. Also, the levels of TNF-α and PDGF-B in the observation group were significantly lower than those in the control group after treatment (*P*<0.05). TNF-α and PGDF-B levels in the blank group were 17.78±2.36 and 123.89±16.28, respectively, and there was no statistically significant difference between the blank group and the observation group after treatment (*P*>0.05, **Table 5**).

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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	54.05±4.79	30.56±3.88	519.45±35.06	245.76±17.00
Blank group	50	–	17.78±2.36	–	123.89±16.28
t/F value		0.705	958.5	1.829	4085
P value		0.482	<0.001	0.068	<0.001

* Represented compared with Control group P<0.05; # represented compared with Blank group, P>0.05.

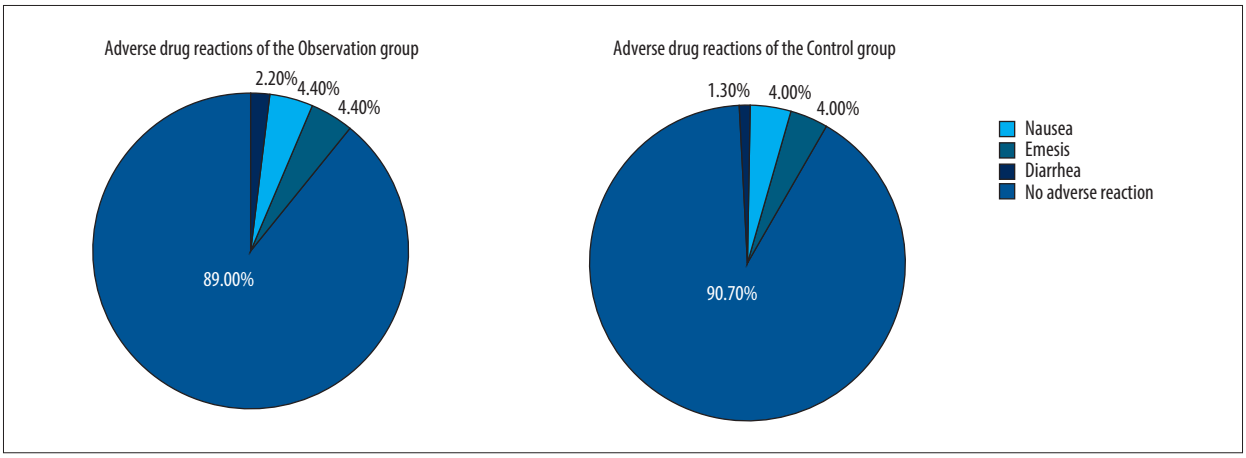

Figure 2. Adverse drug reactions in the observation and control groups.

Comparison of 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, with a rate of adverse drug reactions of 11.11%. In the control group, there were 3 cases of nausea, 9 cases of emesis, and 9 cases of diarrhea, with a rate of adverse drug reactions of 9.33%. There was no significant difference between the groups (chi-square=0.10, *P*=0.750, **Figure 2**).

Discussion

COPD is a respiratory disease characterized by 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 have shown that *Streptococcus pneumoniae*, *Hemophilus influenzae*, *Pseudomonas aeruginosa*, and *Enterobacterium* can lead to COPD. Therefore, the clinical treatment of COPD includes infection control, easing of dyspnea, and improvement of hypoxia [19-21]. The statistics on antimicrobial resistance in China from 2014 to 2019 show that the proportion of gram-positive bacteria was 28.5% to 29.7% and gram-negative bacteria was 70.3% to 71.5%. The top 5 gram-positive bacteria were *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, and *Enterococcus faecium*. The gram-positive *Staphylococcus epidermidis* and *Coccus faecalis* showed a downward trend. The top 5 gram-negative bacteria were *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Enterobacter cloacae*. Among them, *Haemophilus influenzae* is one of the important pathogens causing community-acquired pneumonia. The resistance rates of ampicillin, ampicillin/sulbactam, cefaclor, cefuroxime, and azithromycin have all increased, with the resistance rate of ampicillin increasing from 48.1% to 69.0%. Therefore, slow resistance to drug therapy and effective antibiotics for patients with COPD play a pivotal role in their treatment.

This study investigated the effects of doxofylline combined with ceftazidime on the clinical efficacy, drug safety, and prognosis of patients with COPD complicated with infection.

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It showed that the efficacy rate of doxofylline combined with ceftazidime was significantly higher than that of treatment with doxofylline alone. The rates of efficacy and marked efficacy in the observation group were significantly higher than that in the control group, indicating that treatment using doxofylline combined with ceftazidime was more effective than treatment with doxofylline alone.

In general, improving airway symptoms is the priority of COPD treatment. In the present study, the treated patients in the observation group had larger increases in peak expiratory flow rate, maximal mid-expiratory flow curve, and forced expiratory respiration volume of 1 s than did the control group, and there were no significant differences between the observation group and the blank control group. The results further indicated that treatment using doxofylline combined with ceftazidime was significantly more effective than the treatment using doxofylline alone. Also, the quality-of-life scores, including physiological function, social function, role restriction, and overall health, indicated that the treatment using doxofylline combined with ceftazidime was significantly more effective than the treatment of doxofylline. There were no significant differences in quality-of-life scores in the blank control group. Patients with COPD usually have long-term low oxygen levels and chronic inflammation, which encourage the secretion of inflammatory factors [22-25]. Our results showed that the levels of TNF-α and PDGF-B in the observation group were significantly lower those in the control group, and there were no significant differences in levels between the observation group and the blank control group.

Conclusions

In this study, doxofylline combined with ceftazidime effectively treated patients with COPD complicated with infection. The results of this study provide a reference for the clinical treatment of COPD.

Conflicts of Interest

None.

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