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Original Article

Fluvastatin combined with corbrin capsule can improve depression and anxiety in the treatment of chronic obstructive pulmonary disease

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Abstract: Objective: To investigate the effect of fluvastatin (Flu) combined with corbrin capsule (CC) on the pulmonary function (PF) in patients with chronic obstructive pulmonary disease (COPD). Methods: Totally, 156 patients with COPD treated in our hospital were assigned: 86 patients in the research group (RG), who were treated with Flu plus CC, and 70 patients in the control group (CG), who were treated with CC plus conventional drugs. The changes in inflammatory factors, including interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α) and procalcitonin (PCT), of the two groups before and after treatment were compared. The complications, psychological status, quality of life (QOL) and recurrence rate of the two groups were analyzed. Results: The total effective rate in the RG was dramatically higher than that in the CG (P<0.05). Compared with the factors in the CG, the PF in the RG notably increased after treatment (P<0.05); the blood gas levels were noticeably better (P<0.05); and the level of inflammatory factors decreased (P<0.05). The incidence of complications in the RG was noticeably lower than that in the CG (P<0.05). The psychological status and QOL in the RG were remarkably better than those in the CG (P<0.05), and the recurrence rate within one year of diagnosis was lower than that in the CG (P<0.05). Conclusion: Flu combined with CC is effective and safe in the treatment of COPD and can effectively improve the PF and the QOL of patients.

Keywords: Flu combined with CC, chronic obstructive pulmonary disease, quality of life, pulmonary function

Introduction

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease in clinical practice [1]. Its main characteristics are progressive airflow limitation and certain inflammatory reactions, which can trigger a series of lesions in other tissues and organs and thus, cause great harm to patients [2]. Some studies have shown that the mortality of COPD is increasing due to multiple factors [3, 4], But the pathogenesis of COPD has not been clearly defined [5]. Studies have also demonstrated that both external factors, such as air and dust inhalation, and internal factors, including emphysema, may induce COPD [6, 7]. However, COPD may also be due to acute respiratory infection and cor pulmonale, which rleads to serious damage to cardiopulmonary function [8, 9]. Currently, conventional treatment measures, such as β2 adrenergic receptor agonists, antitussive phlegm, and oxygen therapy, which control clinical symptoms, are mainly used in the treatment of stable COPD [10] but still cannot fully meet patients' clinical needs. Therefore, understanding how to effectively diagnose and treat COPD is an important medical issue worldwide.

Fluvastatin (Flu) has been shown to greatly improve the inflammatory response and endothelial function and has been demonstrated to exert a good therapeutic effect on heart failure [11, 12]. More recent studies demonstrated that Flu can be used to effectively treat chronic cor pulmonale [13], but further experiments are needed to confirm this finding. Corbrin capsule (CC) has a strong tonic effect on human lungs and kidneys. CC has been clinically used as a common adjuvant therapy for chronic bron-

Table 1. General Information

Factors	The RG (n=86)	The CG (n=70)	F/X^2	P
Gender			3.192	0.9955
Male	40 (67.50%)	39 (67.44%)		
Female	46 (32.50%)	31 (32.56%)		
Age	57.3 ± 2.6	57.0 ± 2.4	0.5467	0.5861
Course of disease	11.6 ± 2.1	11.8 ± 2.1	0.3868	0.6999
WBC ($\times 10^9$/L)	17.68 ± 2.45	16.37 ± 2.97	1.844	0.068
CRP (mg/L)	29.38 ± 5.62	28.46 ± 6.03	0.863	0.390
Pulmonary auscultation				
Rale	17 (19.76%)	20 (28.57%)	1.550	0.213
Tubular breath sound	23 (26.74%)	23 (32.86%)		
Fever				
Yes	22 (25.58)	23 (32.86%)	0.118	0.894
No	64 (74.42%)	47 (67.14%)		
Asthma				
Yes	21 (52.5%)	23 (53.49%)	0.0001	0.976
No	19 (47.5%)	20 (46.51%)		

WBC: white blood cell count.

Table 2. Comparison of efficacy between the two groups

	RG (n=86)	CG (n=70)	χ^2	P
Markedly effective	65 (75.58)	36 (51.43)		
Effective	20 (23.26)	28 (40.00)		
Ineffective	1 (1.16)	6 (8.57)		
Total effective rate (%)	85 (98.84)	64 (91.43)	4.942	0.026

chitis [14]. In addition, CC combined with conventional drug therapy has been shown to improve pulmonary function (PF) and improve treatment efficacy in patients with COPD [15]. Here, we speculate that Flu combined with CC may have a good therapeutic effect on COPD. To verify our hypothesis, this study explored the role of Flu combined with CC in COPD.

Materials and methods

Research participant selection

The data of patients with COPD treated in our hospital from February 2016 to February 2018 were collected for prospective analysis. Totally 246 patients were enrolled in the study based on the following inclusion criteria: patients who were diagnosed with COPD and treated in our hospital after diagnosis, had complete case data, agreed to cooperate with the medical staff in our hospital to participate in the study, and signed or had their immediate family members sign the informed consent form. A total of 156 patients remained after applying the following exclusion criteria: patients with malignant tumors, multiple chronic diseases, other cardiovascular and cerebrovascular diseases, organ dysfunction or drug allergies; those with mental illness or physical disability that could not take care of themselves; or transferred patients. Of these 156 patients, 86 patients received Flu combined with CC and were grouped into research group (RG), and 70 patients received CC combined with conventional medication and were included in the control group (CG). This study was approved by People's Hospital of Xinjiang Uygur Autonomous Region (No. KY2018011869).

Treatment methods

After admission, patients in both groups were treated with antibiotics to control their infections and other agents to relieve asthma and phlegm and were provided with necessary nutritional support. In addition, CC (Hangzhou Zhongmei Huadong Medicine Co., Ltd., State Drug Approval Document Number: Z10910036) was administered as 10 tablets three times per day. The RG was treated with Flu (Beijing Novartis Pharmaceutical Co., Ltd., State Drug Approval Document Number: H20010518) at 20 mg/d. Both groups took these medications continuously for 8 weeks.

Outcome measures

Primary outcome measures: Clinical effectiveness was assessed with reference to the efficacy evaluation criteria of Wang et al. [16]. The PF (*i.e,* the FEV_1, MMEF, PEF and FVC) before and after treatment was measured using a PF meter (Jester, Japan, HI-801). The blood gas levels (i.e., the pre- and post-treatment PaO_2, SpO_2 and $PaCO_2$) of patients in the two groups were measured with a fully automated blood

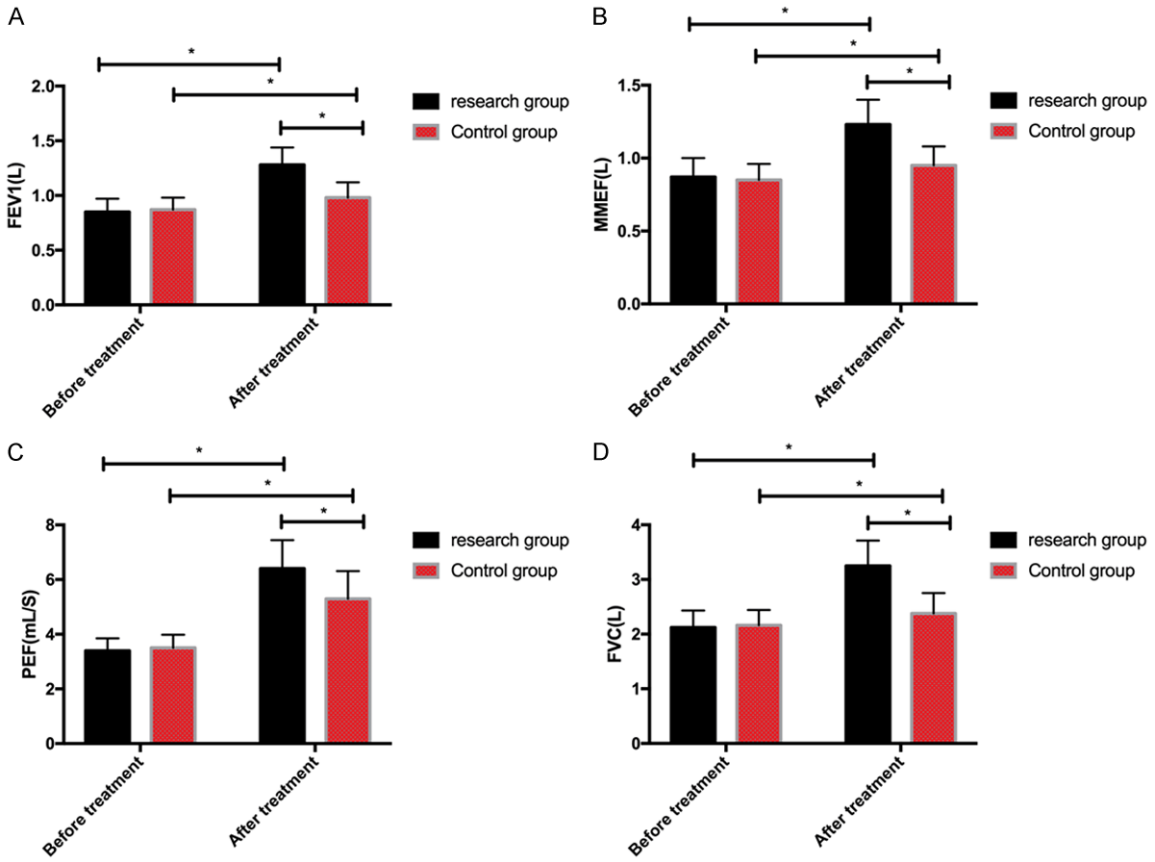

Figure 1. Comparison of PF between the two groups. A. Comparison of FEV_1 between the two groups before and after treatment. B. Comparison of MMEF between the two groups before and after treatment. C. Comparison of PEF between the two groups before and after treatment. D. Comparison of FVC between the two groups before and after treatment. *P<0.05.

gas analyzer (Rapidlabm 248, Bayer, British). The psychological status and QOL of patients were surveyed before and after treatment using the Hamilton Depression Scale (HAMD), Hamilton Anxiety Scale (HAMA), and St George's Respiratory Questionnaire. Recurrence was analyzed through hospital review within one year of diagnosis, and patients that experienced disease recurrence in the two groups were counted.

Secondary outcome measures: The inflammatory factors of: IL-6, IL-8, TNF-α and PCT were measured. Fasting venous blood (4 mL) was collected from patients, left at room temperature for 30 min, and then centrifuged for 10 min (500× g). The upper serum was obtained, and the IL-6, IL-8, TNF-α and PCT levels were detected by ELISA. The complications that occurred during treatment were recorded and compared.

Statistical methods

Statistical analysis of the collected data was performed using SPSS 22.0. Graphpad7 was used to visualize the graphs of the data results. Categorical data were expressed as the percentage and verified by the chi-square test. Continuous data were expressed as $\bar{x}\pm s$ and verified by the t test. Comparisons before and after treatment were performed using a paired t test. P<0.05 was considered to be statistically significant.

Results

General information

The data of patients with COPD treated in our hospital from February 2016 to February 2018 were collected for prospective analysis. Totally 246 patients were enrolled in the study based on the following inclusion criteria. Of these 156

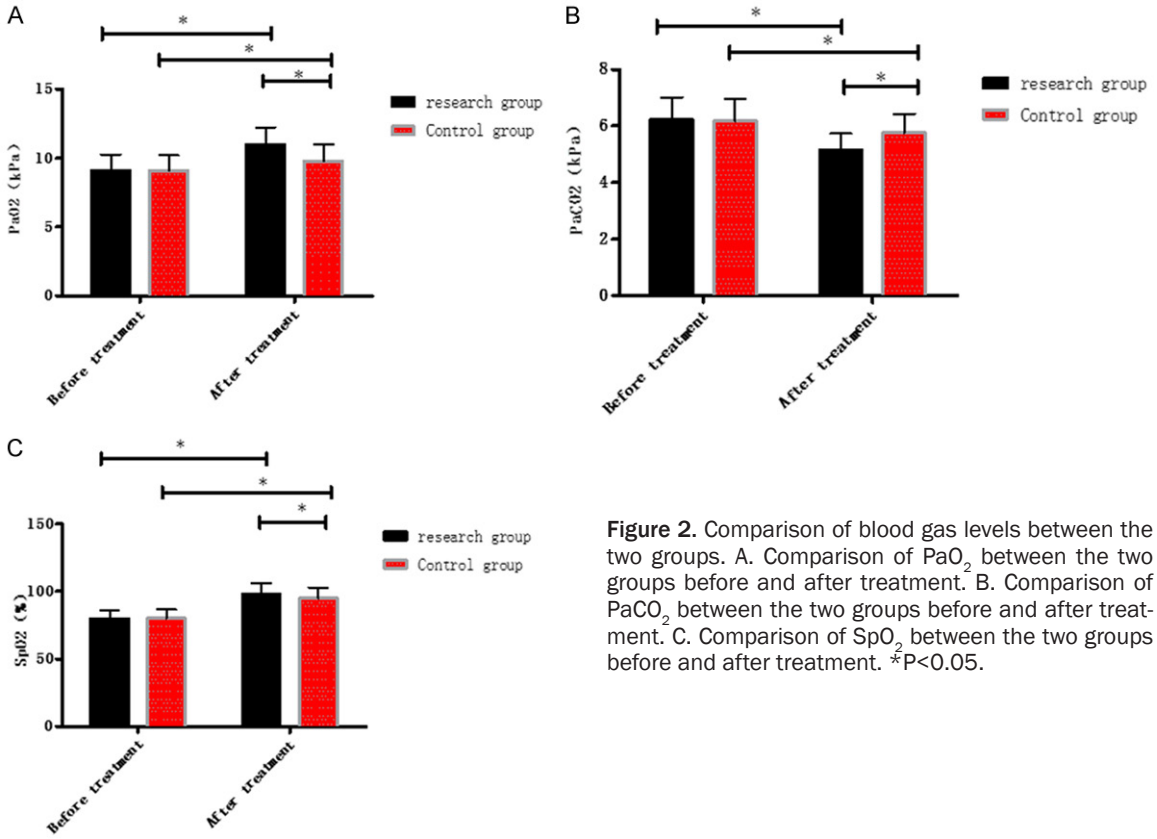

Figure 2. Comparison of blood gas levels between the two groups. A. Comparison of PaO_2 between the two groups before and after treatment. B. Comparison of $PaCO_2$ between the two groups before and after treatment. C. Comparison of SpO_2 between the two groups before and after treatment. *P<0.05.

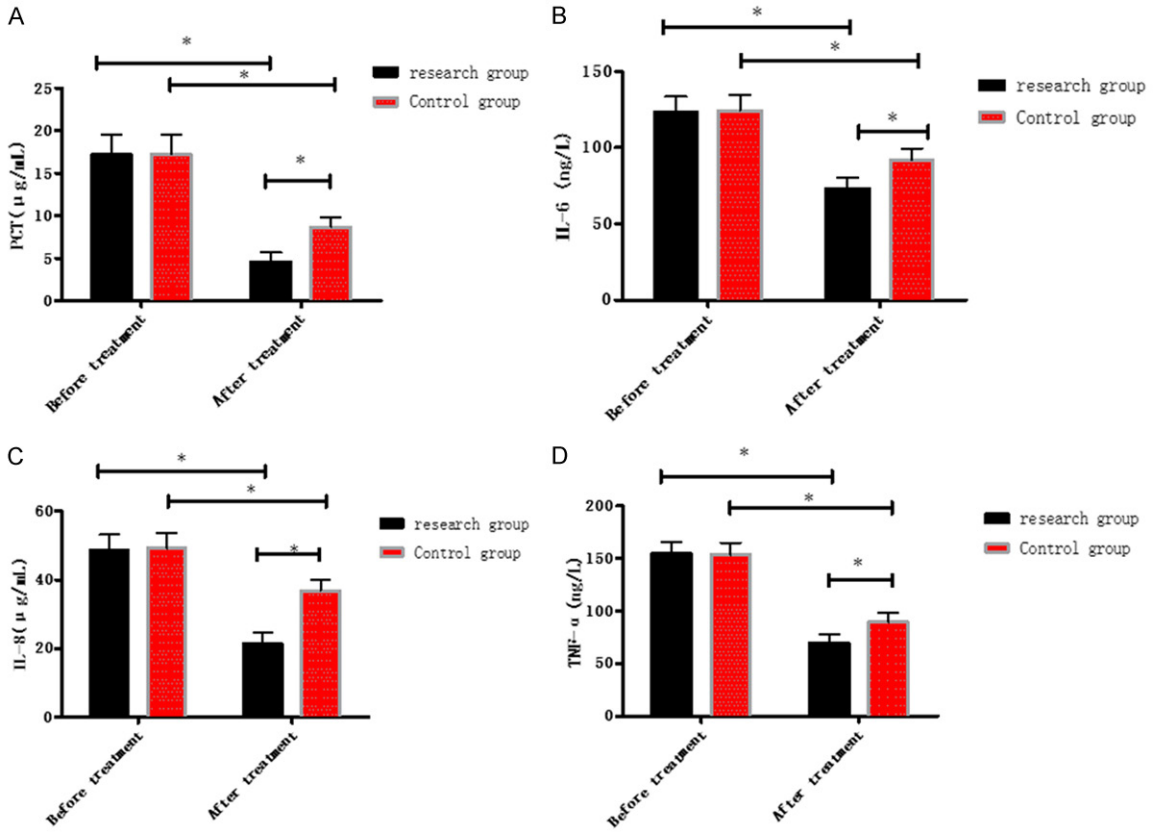

Figure 3. Changes in the levels of inflammatory factors in the two groups. A. Comparison of PCT levels between the two groups before and after treatment. B. Comparison of IL-6 levels between the two groups before and after treatment. C. Comparison of IL-8 levels between the two groups before and after treatment. D. Comparison of TNF-α levels between the two groups before and after treatment. *P<0.05.

Table 3. Complications in the two groups

	RG (n=86)	CG (n=70)	χ^2	p
Cough	2 (2.33)	4 (5.71)	2.170	0.142
Gasp for breath	2 (2.33)	3 (4.29)	1.914	0.167
Chest tightness	1 (1.16)	3 (4.29)	2.132	0.144
Night sweats	1 (1.16)	3 (4.29)	2.132	0.144
Total incidence (%)	6 (6.98)	13 (18.57)	3.861	0.049

patients, 86 patients received Flu combined with CC and were grouped into research group (RG), and 70 patients received CC combined with conventional medication and were included in the control group (CG). Although comparable, no significant difference was observed in the general information between the two groups (**Table 1**).

Patient efficacy

The total efficacy rate in the RG was 98.84%, which was higher than that in the CG (91.43%) (p<0.05, **Table 2**).

Comparison of PF

The both groups showed improved PF in after treatment, and the RG showed better improvement than the CG (P<0.05, **Figure 1**).

Comparison of blood gas levels

After treatment, the PaO_2 and SpO_2 increased, and the $PaCO_2$ decreased in both groups (P<0.05). The post-treatment blood gas levels in the RG were better than that in the CG (P<0.05, **Figure 2**).

Comparison of inflammatory factors

The levels of inflammatory factors decreased in both groups after treatment, and the levels of inflammatory factors in the RG were lower than those in the CG (P<0.05, **Figure 3**).

Complications

The incidence of complications in the RG was lower than that in the CG (P<0.05) (**Table 3**).

Psychological status and QOL

The psychological status and QOL scores decreased in both groups after treatment, and the scores in the RG were lower than those in the CG (P<0.05, **Figures 4** and **5**).

Recurrence

The RG showed significantly decreased recurrence rate compared with the CG (P<0.05, **Table 4**).

Discussion

The continuous decline in air quality may have contributed to the increasing incidence of COPD in these years [10, 17]. COPD is prone to being ignored or mistreated by patients in the early stage, as there are no specific clinical symptoms; as a result, the disease may have already progressed to relatively severe stages once patients are diagnosed, preventing optimal treatment timing [18]. Although much research has shown that conservative treatment can effectively improve the prognosis of COPD patients [19], the choice of drugs for treatment remains controversial. To better diagnose and treat COPD in future clinical practice, this study explored the PF and QOL of COPD patients treated with Flu plus CC, so as to provide a reliable theoretical basis for the clinical treatment of COPD in the future.

The results showed that the total efficacy rate of the RG was higher than that of the CG, suggesting that Flu combined with CC is more effective in the treatment of COPD. In addition, we tested the PF and blood gas levels of the two groups. The results showed that the FEV_1, MMEF, PEF, FVC, PaO_2, and SpO_2 in the RG were higher than those in the CG, while the $PaCO_2$ in RG was lower than that in the CG, suggesting that Flu combined with CC can significantly improve the PF of patients, alleviate the imbalance between oxygen supply and oxygen consumption, and reduce the hypoxia of tissue cell metabolism. Previous studies have demon-

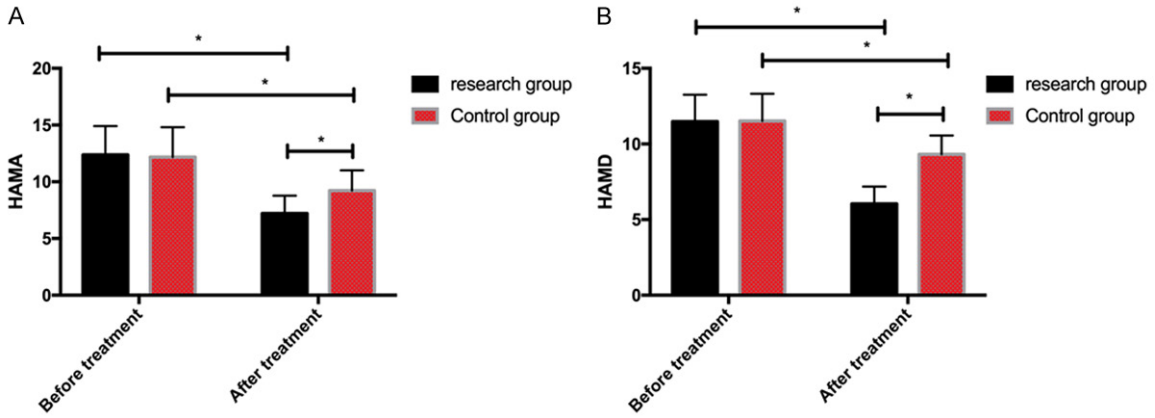

Figure 4. Psychological status of the patients in the two groups before and after treatment. A. Comparison of HAMA scores between the two groups before and after treatment. B. Comparison of HAMD scores between the two groups before and after treatment. *P<0.05.

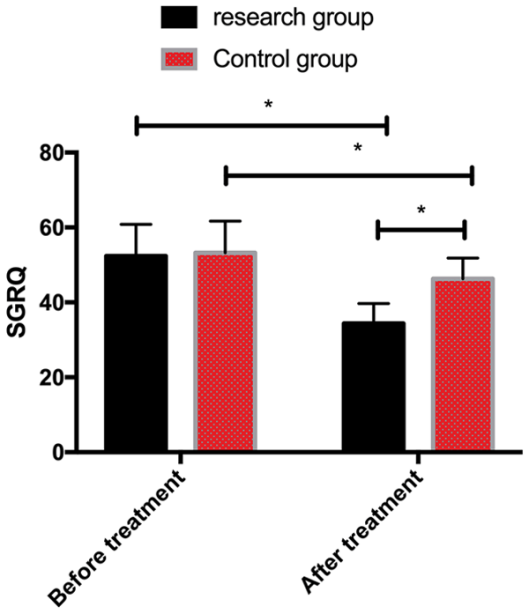

Figure 5. Comparison of improvement in QOL between the two groups before and after treatment. *P<0.05.

strated that CC boosted the body's immune function [20, 21]. A study by Liu et al. [22] showed that CC combined with respiratory rehabilitation training was clinically effective in patients with stable COPD. According to Wang et al. [23], statins had certain benefits in the treatment of COPD complicated with pulmonary hypertension, which can also confirm that Flu may have a great application in the treatment of COPD in the future. The response of inflammatory factors is also vital in the pathogenesis of COPD [24]. PCT, IL-6, IL-8 and TNF-α, as common indicators of inflammatory response, can elevate histamine levels in the peripheral blood to trigger an inflammatory response and activate macrophages to accelerate the development of inflammation [25-27]. Therefore, we detected the changes in serum levels of PCT, IL-6, IL-8 and TNF-α in the two groups and observed that their levels in the RG were noticeably lower than those in the CG after treatment, which also confirmed the strong inhibitory effect of Flu combined with CC on inflammatory factors. Moreover, the incidence of complications in the RG was lower, indicating that Flu combined with CC is safer, which further supports the above experimental results. The psychological status of patients in the RG was far better than that of patients in the CGwhich is reflected in the improvement of anxiety and depression in patients. In order to fundamentally solve the anxiety and depression of patients, the patient's condition must be significantly improved. In the above discussion, we proposed that COPD is a disease caused by multiple factors centering on inflammation. We speculated that the improvement of inflammatory factors in patients and the good therapeutic effect will play a great role in helping patients' nervous mood and QOL. The statistics of the QOL in the two groups validated our hypothesis (i.e., the QOL of the RG was indeed higher than that of the CG). Finally, we calculated the recurrence rate of patients in the two groups within one year of prognosis, and the recurrence rate of patients in the RG was lower than that in the CG after one year,

Table 4. Recurrence in the two groups within one year of prognosis

	RG (n=86)	CG (n=70)	χ^2	p
Recurrence	7 (8.14)	15 (20.29)	4.299	0.038
No recurrence	79 (91.86)	55 (79.71)	2.227	0.136

suggesting that Flu combined with CC was also beneficial in improving the prognosis of patients with COPD.

This study investigated the effects of Flu combined with CC on PF and QOL in patients with COPD, however, there are some limitations, as we did not conduct a comparative analysis on the dosage of the medication, which may affect the results and conclusions obtained. In addition, the experimental period of this study was relatively short. A more in-depth and comprehensive experimental analysis should help to obtain better experimental results.

In summary, Flu combined with CC has significant efficacy and safety in the treatment of COPD and can better improve patients' PF and blood gas levels, which may be related to the inhibition of inflammatory factors.

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Disclosure of conflict of interest

None.

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