RESEARCH ARTICLE

Clinical effect of qingre bawei capsules combined with budesonide in the treatment of acute exacerbation of chronic obstructive pulmonary disease

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Abstract

Objective: To assess the clinical effect of Qingre Bawei capsules combined with budesonide in the treatment of acute exacerbation of chronic obstructive pulmonary disease.

Method: The retrospective study was conducted at the Baoding No.1 Central Hospital, China, and comprised data of patients with acute exacerbation of COPD admitted between June 1, 2020, and June 30, 2022. The patients were divided into two groups based on treatment methods. The group A had been treated with Qingre Bawei capsules in combination with budesonide, while the group B had been treated with budesonide alone. Both the groups had been treated for 2 consecutive weeks. The changes in blood gas indicators, inflammation indicators, and lung function indicators were compared between two groups of patients before and 24 hours after treatment. The time for clinical symptom disappearance and adverse reactions between the two groups of patients was also noted.

Results: Of the 120 patients, 60(50%) were in group A; 41(68.3%) males and 19(31.7%) females, with mean age 65.28±4.36 years (range: 47-78 years) and mean course of disease 31.22±4.75 hours (range: 6-65 hours). 60(50%) patients were in group B; 43(71.7%) males and 17(28.3%) females with mean age 65.31±4.31 years (range: 48-78 years) and mean course of disease 31.29±4.71 hours (range: 8-68 hours). The disappearance time of clinical symptoms in group A was better than group B ($p<0.05$). The levels of blood gas indicators, inflammation indicators, and lung function indicators in both groups significantly improved ($p<0.05$), but the degree of improvement in group A was better than group B ($p<0.05$); The total effective rate of group A was better than group B ($p<0.05$). None of the patients in either group experienced any significant adverse reaction.

Conclusion: Qingre Bawei capsules combined with budesonide had a significantly better therapeutic effect on cases of acute exacerbation of chronic obstructive pulmonary disease compared to budesonide alone.

Keywords: Qingre Bawei capsules, Budesonide, Acute exacerbation, Chronic obstructive pulmonary disease, Clinical effects. (JPMA 74: 1470; 2024) **DOI: https://doi.org/10.47391/JPMA.10244**

Introduction

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable chronic airway disease characterised by persistent airflow restriction and corresponding respiratory symptoms in clinical practice. Its pathogenesis commonly includes exposure to harmful gases or particles. such as smoke and cigarette. At present, COPD, similar to diabetes and hypertension, has been recognised to be a major chronic disease clinically, causing huge burden to society. In general, COPD is divided into stable and acute exacerbation stages according to the progression of the disease. In the early stage, patients with COPD may experience chronic inflammatory response in the airway, and then develop airway stenosis or occlusion gradually as the condition progresses, which may affect the ventilation function, and cause damage to pulmonary tissues to some extent. In terms of its clinical treatment using Western medicine at present, there is a lack of specific therapeutic options for acute exacerbation of COPD. Common therapies include bronchodilators, glucocorticoids and other drugs to alleviate patients' condition and improve their pulmonary function. However, owing to a rapid progression in the acute exacerbation stage and the resulting numerous complications, there may be a great challenge to treat this type of disease, and Western medicine alone is difficult to achieve an ideal therapeutic outcome.[1] In recent years, traditional Chinese medicine (TCM) has attracted clinical attention in the prevention and treatment of COPD. More importantly, it has been confirmed that compared to conventional medicine alone, TCM combined with conventional medicine can achieve a more significant effect in the treatment of acute exacerbation of COPD. Also, Chinese patent drugs have shown the advantage of convenient administration superior to TCM decoction.[2] Furthermore, according to TCM, the main pathological factors in the acute exacerbation of COPD are phlegm, heat and blood stasis, with phlegm-heat obstructing the lung as its important pathogenesis. Based on TCM therapeutic principle of treating symptoms in emergency, the therapeutic methods should be predominated by clearing away heat and toxic materials, resolving phlegm and

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reducing internal fire.[3] Qingre Bawei (QB) capsule is a traditional Mongolian medicine formula composed of eight TCMs, including safflower, sandalwood, corydalis bungeana, rhizoma picrorhizae, dianthus superbus, etc. It can clear away heat and toxic materials, and alleviate inflammation, which is commonly used for treating cough with lung heat, internal heat stagnation in the internal organs, etc.

The current study was planned to explore the clinical effect of QB capsules combined with budesonide in treating acute exacerbation of COPD.

Materials and Methods

The retrospective study was conducted at the Baoding No.1 Central Hospital, China, and comprised data of patients with acute exacerbation of COPD admitted between June 1, 2020, and June 30, 2022, the data was extracted on July 1, 2022. After approval from the institutional ethics review board, the sample size was calculated using the formula for comparing independent sample means of two groups: $N=[2\times(Z_\alpha+ Z_\beta)^2\times\sigma^2/(\mu_2-\mu_1)$.[2] Using the forced expiratory volume in the first second (FEV_1) as the main observation indicator in lung function,[4] $\alpha=0.05$, $\beta=0.10$, $Z_\alpha=1.96$, $Z_\beta=1.28$, $\sigma=0.5$, average FEV1 of control group $\mu_1=1.5$ FEV_1 after glucocorticoid treatment $\mu_2=1.9$, the minimum sample size for each group was 33 cases. The sample size was inflated by >80% to cover for dropouts.

The enrolled patients were divided into group A and B based on different treatment methods. The patients of group B were given inhalation therapy using budesonide pressurised inhalation solution 4mg once a day (National Medicine Permission No: HH20103795; Hubei Gedian Humanwell Pharmaceutical Co., Ltd.).

Patients in treatment group A were additionally provided with QB capsules (National Medicine Permission No: Z20063676; Inner Mongolia Aoteqi Mongolian Medicine Co., Ltd. [Jinshan] Mongolian Medicine Factory) at a dose of 3 capsules 2 times a day. Both the groups were treated continuously for 2 weeks.

Patients in both groups received routine symptomatic Western medicine treatment after admission, including continuous nasal catheter oxygen inhalation, atomisation using levosalbutamol hydrochloride nebuliser solution 0.63mg (National Medicine Permission No: H20205016, Shenzhen Taitai Pharmaceutical Industry Co., Ltd.) + acetylcysteine solution for inhalation 0.3g (National Medicine Permission No: H20183005; Hainan Star Pharmaceutical Co., Ltd.) twice a day, appropriate antibiotic treatment based on drug sensitivity test results in case of concomitant pulmonary infection, and active treatment of complications.

The Western medicine diagnosis of acute exacerbation of COPD was based on the Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease 2023,[5] which meant patients who had experienced events characterised by difficulty breathing or increased frequency of expectoration and cough within the preceding 14 days, accompanied possibly by tachycardia or shortness of breath, which might be explained by systemic and local inflammation caused by infection, airway damage, etc. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines were used for categorising the patients into grades 1-4[6] with grade 1 = $FEV_1\geq80\%$, grade 2=FEV1 50~79%, grade 3=FEV_1 30~49%, and grade 4=$FEV_1\leq29\%$. As for the TCM diagnosis, corresponding syndrome differentiation was determined to be the syndrome of phlegm-heat obstructing the lung according to the Diagnostic Criteria for Traditional Chinese Medicine Syndromes of Chronic Obstructive Pulmonary Disease (2011).[7] The main symptoms included cough, chest tightness, wheezing, shortness of breath, and excessive yellow or white sticky phlegm. The secondary symptoms were chest pain, fever, thirst, constipation, red tongue with yellow and thick coating of the tongue, and slippery and rapid pulse.

Those included were patients of either gender aged 45~80 years who met the diagnostic criteria for acute exacerbation of COPD, and had course of disease <72h, exhaled nitric oxide level ≥50ppb who had not used any Chinese patent drugs in the preceding 2 weeks, and had stable vital signs.

Those excluded were patients with concomitant diseases of pulmonary fibrosis, active pulmonary tuberculosis, severe bronchiectasis, and bronchial asthma, patients with severe liver and kidney function injury, cardio-cerebrovascular diseases and severe infectious diseases, patients with history of lung surgery, those in urgent need of mechanical ventilation, patients with communication problems, such as mental illness and dementia, and those who were allergic to TCM. Also excluded were patients who took other medications on their own during the study and affected the outcomes, patients with poor treatment compliance, and those who decided to withdraw from the study due to personal reasons.

Improvement in cough and expectoration, improvement in symptoms of suffocation, and disappearance of pulmonary rales were recorded for both the groups.

Extract 2 mL of radial artery blood before and 24 hours after treatment and using a blood gas analyser to detect the

levels of partial pressure of oxygen in arterial blood (PaO_2), arterial oxygen saturation (SaO_2), and partial arterial pressure of carbon dioxide ($PaCO_2$) in arterial blood.

Before and 24 hours after treatment, 5 ml fasting venous blood were collected from each patient and placed in an anticoagulant tube, after rapid centrifugation, use a fully automatic blood cell analyser to detect white blood cells (WBC) count, percentage of neutrophils (NE%), C-reactive protein (CRP) and procalcitonin (PCT) levels. FEV_1, forced vital capacity (FVC), and FEV_1/FVC ratio of patients before and 24 hours after treatment were measured using pulmonary function instruments.

In line with the Guiding Principle of Clinical Research on New Drugs of Traditional Chinese Medicines,[8] changes were recorded in TCM syndrome before and 24 hours after treatment in both groups. The clinical effect was then evaluated based on the difference in TCM syndrome scores before and after treatment.

Decrease in TCM syndrome scores by ≥90% was considered 'clinical control', by 70~89% was considered 'significant effective', by 30~69% was considered 'effective', and by 0~29% was considered 'ineffective'. The overall response was calculated according to the equation: case of clinical control+significant effective+effective/total casesx100=% response.[8]

Adverse reactions, like headache, palpitations, nausea, rash, etc., were recorded for patients in both the groups.

Data was analysed using SPSS 24. Data was found to have a normal distribution, and data was expressed as frequencies and percentages or as mean±standard deviation, as appropriate. Intragroup comparison was done using paired sample t-test, while intergroup comparison was done using two independent sample t-test. Chi-square test was used where necessary. P<0.05 was considered statistically significant.

Results

Of the 120 patients, 60(50%) were in group A; 41(68.3%) males and 19(31.7%) females, with mean age 65.28±4.36 years (range: 47-78 years) and mean course of disease 31.22±4.75 hours (range: 6-65 hours). 60(50%) patients were in group B; 43(71.7%) males and 17(28.3%) females with mean age 65.31±4.31 years (range: 48-78 years) and mean course of disease 31.29±4.71 hours (range: 8-68 hours). In treatment group A, there were 7(%) cases in GOLD grade 1, 29(%) in grade 2, 20(%) in grade 3, and 4(%) in grade 4. In control group B, there were 8(%) cases in GOLD grade 1, 30(%) in grade 2, 19(%) in grade 3, and 3(%) in grade 4. There was no significant intergroup difference in baseline parameters (p>0.05).

The disappearance time of clinical symptoms in group A was better than group B (Table 1). The levels of blood gas indicators, inflammation indicators, and lung function indicators in both groups significantly improved (p<0.05), but the degree of improvement in group A was better than group B (Table 2).

The overall response rate of group A was significantly better than that of group B (p=0.014) (Table 3).

Table-1: Intergroup comparison of the mean disappearance time of clinical symptoms.

Groups	Cases	Days of improvement in cough and expectoration	Days for improvement of symptoms of suffocation	Days for disappearance of pulmonary rales
Treatment group	60	6.22±0.45	5.47±0.42	5.82±0.51
Control group	60	11.30±0.67	9.87±0.69	9.57±0.59
t-value		48.565	41.992	37.075
p-value		<0.001	<0.001	<0.001

Table-2: Intergroup comparison of changes in mean values of blood gas indicators, inflammatory indicators and pulmonary function indices

Indicators	Observation points	Treatment group (n=60)	Control group (n=60)	*t*-test	*p*-value
Blood gas analysis					
PaO_2(mmHg)	Before treatment	62.30±4.15	62.19±4.17	0.145	0.885
	After treatment	82.59±4.18*	71.22±4.15*	14.957	<0.001
SaO_2(%)	Before treatment	85.97±2.31	85.41±2.35	1.317	0.190
	After treatment	95.56±1.36*	90.02±1.42*	21.841	<0.001
$PaCO_2$(mmHg)	Before treatment	52.36±3.35	52.48±3.32	0.197	0.844
	After treatment	37.11±2.23*	43.58±2.25*	15.807	<0.001
Inflammatory indicators					
WBC (10^9/L)	Before treatment	10.76±1.02	10.82±1.05	0.317	0.752
	After treatment	5.11±0.62*	6.30±0.68*	10.062	<0.001
NE% (%)	Before treatment	75.58±8.82	75.61±8.83	0.019	0.985
	After treatment	48.26±5.33*	63.31±5.51*	15.217	<0.001
CRP (mg/L)	Before treatment	15.15±2.21	15.18±2.23	0.074	0.941
	After treatment	2.49±0.35*	7.58±0.48*	65.882	<0.001
PCT (µg/L)	Before treatment	0.56±0.10	0.58±0.11	1.044	0.299
	After treatment	0.28±0.08*	0.39±0.09*	6.937	<0.001
Pulmonary function indexes					
FEV1(L)	Before treatment	1.78±0.45	1.69±0.41	1.143	0.255
	After treatment	2.56±0.49*	1.98±0.50*	6.386	<0.001
FVC(L)	Before treatment	2.15±0.38	2.15±0.35	0.000	1.000
	After treatment	2.58±0.41*	2.23±0.47*	4.361	<0.001
FEV1/FVC(%)	Before treatment	49.85±4.41	49.79±4.43	0.074	0.941
	After treatment	59.97±4.52*	54.49±4.49*	6.662	<0.001

Compared within the group before treatment, *p<0.05; PaO2: Partial pressure of oxygen in arterial blood, SaO_2: Arterial oxygen saturation, PaO_2: Partial pressure of oxygen in arterial blood, WBC: White blood cells, NE: Neutrophils elastase, CRP: C-reactive protein, PCT: Procalcitonin, FEV1: Forced expiratory volume in the first second, FVC: Forced vital capacity.

Table-3: Intergroup comparison of clinical effect.

Groups	Cases	Clinical control	Significant effective	Effective	Ineffective	Overall response rate
Treatment group	60	20(33.33)	24(40.0)	11(18.33)	5(8.33)	55(91.67)
Control group	60	12(20.0)	14(23.33)	19(31.67)	15(25.0)	45(75.0)
χ^2						6.000
p-value						0.014

None of the patients in either group experienced any significant adverse reaction.

Discussion

COPD is an affliction of the respiratory system which is a major non-communicable disease (NCD). COPD patients with acute exacerbation are mainly middle-aged and elderly. Studies have shown that COPD patients worldwide experience acute exacerbation about 0.5-3.5 times a year. In the absence of timely intervention, it can induce acute respiratory failure, which is closely related to patient survival and clinical prognosis.[9] COPD is often named "lung distension" in TCM, with the disease mainly located in the lungs and easily affecting the kidneys and spleen. The pathogenesis is always based on the principle of deficiency and excess. The acute exacerbation of COPD is mainly based on empirical evidence, with phlegm-heat obstructing the lungs being the most common syndrome type. Treatment should adopt the main treatment methods of clearing heat and detoxifying, resolving phlegm and relieving asthma. In the formula of QB capsules, sandalwood belongs to the lung and spleen meridians, and has good effects in regulating qi, regulating middle, promoting qi, and relieving pain. Safflower has the functions of promoting blood circulation, unblocking meridians, removing blood stasis, and relieving pain. Gypsum has the function of clearing heat and purging fire, which can effectively eliminate heat pathogens in the lungs and stomach. Kudi Ding has the functions of clearing heat, detoxifying, reducing swelling, and dispersing nodules. Qu Mai has the functions of promoting blood circulation and meridians, clearing heat and promoting diuresis. Hu Huanglian has the function of clearing heat and cooling blood, which can effectively clear excess fire in the lungs. Ophiopogon japonicus has the function of moistening the lungs, clearing the heart, nourishing yin, and generating fluids. Artificial bezoar has the functions of clearing heat, detoxifying, anti-inflammation, and resolving phlegm. The combination of various medicines plays a role in clearing heat, detoxifying, resolving phlegm, and relieving asthma. Niuhuang has sedative, analgesic, anti-inflammatory and antipyretic effects.[10-15]

In the current study, the combination of QB capsules and budesonide was used for the first time in the treatment of acute exacerbation of COPD. The results showed that the patients' cough, sputum production, and lung rales were alleviated more quickly, and lung function indicators improved more significantly than in those with budesonide alone. The clinical effective rate was also higher, and there were no significant adverse reactions during the treatment period, indicating that the combined treatment plan had a significant therapeutic effect and high treatment safety.

Blood routine has important diagnostic significance for acute exacerbation of COPD, as it can accurately detect levels of WBC, NE% and other indicators. These two indicators are clinically recognised infection indicators, and the higher their levels, the more severe is the infection in the patient's body.[16] CRP is a common inflammatory factor that can induce the aggregation of numerous inflammatory cells and participate in the pathological development of acute exacerbation of chronic obstructive pulmonary disease, PCT is a persistent protein that gets releases in large quantities when the body is severely infected and damaged.[17] In the current study, the levels of WBC, NE%, CRP and PCT in the treatment group were lower than those in the control group post-treatment, indicating that the combination of QB capsules and budesonide could reduce the levels of inflammatory factors and alleviate airway inflammation in cases of acute exacerbation of COPD. After treatment, the levels of PaO_2 and SaO_2 in the treatment group were higher than those in the control group, while the levels of $PaCO_2$ were lower than those in the control group, indicating that QB capsules combined with budesonide could effectively regulate blood gas indicators of patients with acute exacerbation of COPD.

Conclusion

The combination of QB capsules and budesonide has a significant therapeutic effect on the acute exacerbation of COPD. It can quickly alleviate clinical symptoms, alleviate airway inflammation, improve blood gas indicators, and enhance lung function.

Informed consent: This study obtained written informed consent from all participants.

Disclaimer: None.

Conflict of Interest: None.

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Author Contribution:

YS, HR: Design, preparation and responsible and accountable for the accuracy or integrity of the work and final approval.
XH, SY: Collected and analysed clinical data and final approval.
HA, XY: Revision and final approval.