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Efficacy of budesonide/formoterol and tiotropium combination for the treatment of Chinese patients with chronic obstructive pulmonary disease

Jun-fei Feng, MM[a], Guo-rong Ding, MM[b], Yan-zhong Xie, MM[b], Dejun Zhao, MM[c,*], Xuehui Wang, MD[d,*]

Abstract

This study investigated the efficacy and safety of budesonide/formoterol (B/F) and tiotropium combination in the management of chronic obstructive pulmonary disease (COPD) in Chinese patients.

Between January 2015 and November 2017, 113 eligible Chinese patients with COPD were included and divided into an intervention group and a control group. Sixty-three patients in the intervention group underwent B/F combined tiotropium, while 50 patients in the control group received tiotropium alone. The primary outcome was severity of dyspnea on exertion (DOE), measured by the 6-minute walk test (6MWT) scale. The secondary outcomes included lung function, measured by the forced expiratory volume in 1 second (FEV_1), quality of life, measured by the St. George's Respiratory Questionnaire (SGRQ), and adverse events. All outcomes were measured at the end of 12-week treatment.

B/F and tiotropium combination showed greater efficacy in DOE ($P < .01$), lung function ($P < .01$), and quality of life ($P < .01$), compared with tiotropium alone at the end of 12-week treatment. In addition, adverse events in both groups were similar and tolerable.

The findings suggest that B/F and tiotropium combination can be used as an effective treatment in Chinese patients with COPD.

Abbreviations: 6MWT = 6-minute walk test, B/F = budesonide/formoterol, COPD = chronic obstructive pulmonary disease, DOE = dyspnea on exertion, FEV_1 = forced expiratory volume in 1 second, GOLD = Global Initiative for Chronic Obstructive Lung Disease, LABA = long-acting β2-adrenergic agonist, SGRQ = St. George's Respiratory Questionnaire.

Keywords: budesonide, chronic obstructive pulmonary disease, efficacy, formoterol, tiotropium

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common progressing disease, which contributes to the leading cause of morbidity and mortality around the world.[1–3] It is estimated that 64 million people will suffer from COPD by 2030 according to the reports from World Health Organization.[4,5] It often brings a significant burden for individuals and society, and is often associated with poor quality of life in many patients.[6–8] Treatments for COPD often included long-acting β2-adrenergic agonists (LABAs), inhaled corticosteroid–LABA combinations, as well as the anticholinergic agents based on the recommendation of clinical guidelines.[9–14]

Budesonide/formoterol (B/F) intervention was approved and recommended for the maintenance treatment in patients with COPD.[15,16] It was used to improve airflow obstruction for COPD. In addition, tiotropium was also approved for treating patients with COPD. It was used as long-term, once-daily maintenance treatment, and was used to decrease COPD exacerbations.[17–19]

Presently, limited data are available to explore the efficacy and safety of B/F and tiotropium combination in the management of COPD among Chinese population. The objective of this retrospective study was to assess the efficacy and toxicity of B/F combined with tiotropium when compared with the tiotropium alone for a 6-month treatment in Chinese patients.

2. Methods and patients

2.1. Ethics

This study was approved by the Research Ethics Committee of Hangzhou Fuyang Hospital of Traditional Chinese Medicine, The People's Hospital of Fuyang, and the First Affiliated Hospital of Heilongjiang University of Chinese Medicine. All patients provided written informed consent according to the Declaration of Helsinki.

2.2. Study design

In this retrospective study, 113 Chinese patients with COPD were included between December 2014 and November 2017. They were divided into 2 groups according to the different therapies

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[a] Department of Respiratory Medicine, [b] Emergency Department, Hangzhou Fuyang Hospital of Traditional Chinese Medicine, [c] Department of Respiratory Medicine, The People's Hospital of Fuyang, Hangzhou, [d] Department of Respiratory Medicine, First Affiliated Hospital of Heilongjiang University of Chinese Medicine, Harbin, China.

[*] Correspondence: Dejun Zhao, Department of Respiratory Medicine, The People's Hospital of Fuyang, No. 400 Jinqiaobei Road, Hangzhou 311400, China (e-mail: Dejun19970@hotmail.com), Xuehui Wang, Department of Respiratory Medicine, First Affiliated Hospital of Heilongjiang University of Chinese Medicine, No. 24, Heping Road, Xiangfang District, Harbin 150040, China (e-mail: xuehuiwang2015@163.com).

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Table 1

Characteristics at baseline.

Characteristics	Intervention group (n = 63)	Control group (n = 50)	P
Mean age, y	64.9 (7.3)	66.2 (7.8)	.37
Race (Chinese)	63 (100.0%)	50 (100.0%)	–
Sex			
Male	49 (77.8%)	35 (70.0%)	.35
Female	14 (22.2%)	15 (30.0%)	.35
BMI, kg/m^2	21.8 (3.4)	21.6 (3.7)	.77
Smoking status, n			
Smokers	34 (54.0%)	26 (52.0%)	.84
Nonsmokers	29 (46.0%)	21 (48.0%)	.84
Brinkman index	1327.5 (547.1)	1368.4 (592.6)	.71
GOLD criteria			
II	15 (23.8%)	11 (22.0%)	.82
III	38 (60.3%)	33 (66.0%)	.54
IV	10 (15.9%)	6 (12.0%)	.56
GOLD stage	3.0 (0.7)	2.9 (0.8)	.49
Home oxygen therapy	18 (58.3%)	16 (50.0%)	.69
Anticholinergic	36 (83.3%)	33 (88.9%)	.34
Inhaled corticosteroid	15 (52.8%)	13 (58.3%)	.79
6MWT scale	4.7 (2.2)	4.9 (2.4)	.65
Pulmonary function			
FVC, L	2.8 (0.8)	2.7 (0.9)	.54
FEV_1,% predicted	45.1 (16.9)	44.3 (17.1)	.80

BMI = body mass index; 6MWT = 6-minute walk test; GOLD = Global Initiative for Chronic Obstructive Lung Disease; FEV_1 = forced expiratory volume in 1 s; FVC = forced vital capacity.

they received. Of them, 63 subjects underwent B/F combined tiotropium (intervention group), while 50 patients received tiotropium alone (control group). Patients in both groups were treated for a total of 12 weeks.

2.3. Eligibility

All patients were confirmed diagnosis as COPD (stage II, III, or IV)[4] without a history of infections or exacerbation of respiratory symptoms. In addition, they all had no signs of edema, ability to walk themselves. However, patients were excluded if they had severe cardiovascular disease, liver and renal failure, thyroid dysfunction, as well as severe mental disorder, which may affect the outcomes evaluation.

2.4. Intervention

Patients in both groups received tiotropium 18 μg once daily. In addition to the tiotropium, patients in the intervention group also underwent either B/F 160/4.5 mg, twice daily for a total dose of 320/9 mg. All medications were applied for a total of 12 weeks.

2.5. Outcome measurements

The primary outcome included severity of dyspnea on exertion (DOE), measured by the 6-minute walk test (6MWT).[20] This tool was a modified 10-point Borg category ratio scale with the higher scores, the more severe breath condition. The secondary outcomes consisted of lung function, measured by the forced expiratory volume in 1 second (FEV_1),[21] and quality of life, measured by the St. George's Respiratory Questionnaire (SGRQ).[22] In addition, any adverse events related to the treatments were also recorded. All outcomes were measured at baseline and at the end of 12-week treatment.

2.6. Statistical analysis

All data were analyzed by using SAS package (Version 9.1; SAS Institute Inc., Cary, NC). All the categorical data were analyzed by the Pearson Chi-square test or Fisher exact test. All the continuous data were analyzed by the *t* test or Mann–Whitney rank sum test. Statistical significant was defined as $P < .05$ (2 sides).

3. Results

The patient characteristics at baseline are summarized in Table 1. The 2 groups did not differ significantly in all the characteristics of age, sex, body mass index, smoking status, Brinkman index, Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, GOLD stage, home oxygen therapy, anticholinergic, inhaled corticosteroid, 6MWT scale, and lung function (Table 1).

At the end of 12-week treatment, B/F combined tiotropium showed greater efficacy in enhancing the severity of DOE ($P < .01$, Table 2), measured by the 6MWT, and lung function ($P < .01$, Table 2) compared with tiotropium alone. Moreover, B/F combined tiotropium also exhibited significant improvements in quality of life, measured by SGRQ scale, compared with tiotropium alone ($P < .01$, Table 2).

Adverse events are listed in Table 3. During the period of 12-week treatment, several adverse events were detected among patients in both groups (Table 3). These adverse events included severe COPD, nasopharyngitis, cough, myalgia, and pneumonia. However, no significant differences were found regarding these adverse events between the 2 groups ($P > .05$, Table 3). No death-related treatment occurred in both groups (Table 3).

Table 2

Outcome measurements at the end of 12-week treatment (change from baseline).

Outcome measurements	Intervention group (n = 63)	Control group (n = 50)	Difference	P
6MWT scale	−4.1 (−5.4, −1.9)	−1.9 (−3.2, −1.1)	−2.2 (−3.0, −1.4)	<.01
FVC, L	0.19 (0.11, 0.28)	0.06 (0.01 0.10)	0.14 (0.05, 0.22)	<.01
FEV_1, % predicted	3.4 (1.1, 4.7)	1.2 (0.4, 2.1)	2.2 (1.3, 3.1)	<.01
GRQ score				
Total	−14.9 (−20.2, −8.3)	−6.1 (−9.9, −2.7)	−8.8 (−11.2, −6.5)	<.01
Symptom	−22.6 (−30.4, −13.7)	−10.3 (−19.6, −3.4)	−12.4 (−18.9, −5.3)	<.01
Activity	−13.3 (−20.6, −4.5)	−4.2 (−9.4, −0.9)	−9.1 (−16.6, −4.2)	<.01
Impact	−12.8 (−19.5, −5.9)	−4.7 (−8.1, −1.0)	−8.2 (−13.3, −5.4)	<.01

6MWT = 6-minute walk test, FEV_1 = forced expiratory volume in 1 s, FVC = forced vital capacity, SGRQ score = St George Respiratory Questionnaire Scores.

Table 3

Adverse events.

Adverse events	Intervention group (n = 63)	Control group (n = 50)	*P*
Severe COPD	2 (3.2)	1 (2.0)	.70
Nasopharyngitis	4 (6.3)	2 (4.0)	.58
Cough	1 (1.6)	4 (8.0)	.14
Myalgia	3 (4.8)	1 (2.0)	.44
Pneumonia	2 (3.2)	1 (2.0)	.70
Death	0 (0)	0 (0)	–

COPD = chronic obstructive pulmonary disease.

4. Discussion

B/F is commonly used for the treatment of COPD. It has been found that budesonide, as a glucocorticoid, has an effect of inhibiting airway inflammation, and formoterol, a long-acting selective β2 agonist, has a long-lasting bronchodilatory effect.[23,24] Thus, the combination of both medications is reported to have a good coordination effect.[23,24] On the contrary, tiotropium bromide is a new type of long-acting anticholinergic drug with a dissociation half-life of up to 24 hours and a long duration of action.[25] The clinical evidence proved that tiotropium can improve the clinical symptoms of COPD patients and also the quality of life.[25]

This retrospective study specifically assessed the efficacy and safety of B/F combined tiotropium versus tiotropium alone in Chinese patients with COPD. Its results showed encouraging efficacy of B/F combined tiotropium compared with tiotropium alone, and were consistent with the results of previous studies.[26–28] The previous studies found that B/F combined tiotropium can manage the moderate-to-severe COPD by lung function enhancement, symptoms relief, and quality of life improvement, with well-tolerated adverse events.[26–28]

In this study, at the end of 12-week treatment, the 6MWT scores were significantly greater in the intervention group than that in the control group. Moreover, patients in the intervention group also showed higher improvement in DOE, lung function, as well as the quality of life, measured by the SGRQ scores, when compared with those in the control group. Thus, B/F combined tiotropium treatment appears to be promising efficacy for Chinese patient with COPD. In addition, the adverse events were acceptable in both groups.

This study has its own strengths and limitations. As for strengths, all patients belong to Chinese population, and thus, it cuts out the variability observed among different populations in the diagnosis and evaluation of the efficacy. When it comes to limitations, this study compared the efficacy and safety of B/F combined tiotropium versus tiotropium just based on the current available data of patients. Thus, it only evaluated the efficacy and safety at the end of 12-week treatment and did not consist of follow-up measurements after the treatment cessation.

5. Conclusion

The results of this retrospective study demonstrated that B/F combined tiotropium can either enhance DOE and lung function, or improve quality of life in Chinese patients with COPD.

Author contributions

Conceptualization: Dejun Zhao, Jun-fei Feng, Xue-hui Wang, Guo-rong Ding.
Data curation: Dejun Zhao, Jun-fei Feng, Xue-hui Wang, Guo-rong Ding.
Formal analysis: Xue-hui Wang.
Investigation: Xue-hui Wang.
Methodology: Xue-hui Wang.
Project administration: Jun-fei Feng, Yan-zhong Xie.
Resources: Dejun Zhao, Jun-fei Feng, Yan-zhong Xie.
Software: Yan-zhong Xie.
Supervision: Yan-zhong Xie.
Validation: Dejun Zhao, Guo-rong Ding.
Visualization: Guo-rong Ding.
Writing – original draft: Dejun Zhao, Jun-fei Feng, Xue-hui Wang, Guo-rong Ding, Yan-zhong Xie.
Writing – review & editing: Dejun Zhao, Jun-fei Feng, Xue-hui Wang, Guo-rong Ding, Yan-zhong Xie.

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