Efficacy of Budesonide and Formoterol Inhalation Aerosol in Conjunction with Doxofylline in Chronic Obstructive Pulmonary Disease

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To observe the clinical efficacy of budesonide/formoterol inhalation aerosol in conjunction with doxofylline in treating individuals with stable chronic obstructive pulmonary disease. Our study enrolled a total of 90 patients with stable chronic obstructive pulmonary disease, who were admitted to our hospital from September 2019 to June 2021. These participants were allocated randomly into two groups; the control group and the observation group, comprising 45 patients in each group. Doxofylline was administered to the control group, while the observation group received additional treatment of budesonide/formoterol inhalation aerosol alongside doxofylline. The duration of treatment for both groups was set at 6 mo. The clinical efficacy was determined by evaluating the improvement of clinical symptoms, along with the assessment of pulmonary function, and the measurement of serum levels of interleukin-8, transforming growth factor-beta 1, and tumor necrosis factor-alpha. With a total effective rate of 99.33 %, the observation group outperformed the control group, which achieved a rate of 73.33 %. The baseline measurements of pulmonary function indicators, as well as interleukin-8, transforming growth factor-beta 1, and tumor necrosis factor-alpha levels, showed no remarkable distinctions between the two groups. However, post-treatment evaluations revealed noteworthy improvements in the observation group's forced expiratory volume in the first second/forced vital capacity values compared to their respective pre-treatment levels. These improvements were notably higher than those observed in the control group ($p<0.05$). Additionally, the observation group exhibited a more substantial decrease in interleukin-8, tumor necrosis factor-alpha, and transforming growth factor-beta 1 levels compared to the control group. Furthermore, no significant difference was observed in the incidence of adverse reactions between the two groups ($p>0.05$). Budesonide/formoterol inhalation aerosol in conjunction with doxofylline in treating individuals with stable chronic obstructive pulmonary disease significantly improves clinical symptoms, enhances pulmonary function, exhibits good anti-inflammatory effects, and has a good safety profile.

Key words: Budesonide, formoterol, aerosol, doxofylline, chronic obstructive pulmonary disease, clinical efficacy

Characterized by constrained airflow, Chronic Obstructive Pulmonary Disease (COPD) encompasses various chronic respiratory conditions, including chronic bronchitis and emphysema. The course of COPD can be classified into episodes of acute exacerbation and periods of stability. As highlighted by the World Health Organization, COPD has now become the 4th most significant cause of disability and mortality on a global scale[1-3]. In China, there is a rising trend in the incidence and mortality rates of COPD, which poses substantial challenges to public health and healthcare resources. The management of COPD involves disease education, supportive therapy, pulmonary rehabilitation, and medication[4-6]. Medication therapy, which encompasses bronchodilators, corticosteroids, and mucolytic agents, holds particular importance for managing COPD. Regrettably, there is currently no definitive

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cure for COPD, prompting heightened research efforts to uncover more effective treatment approaches[7]. Budesonide/formoterol inhalation aerosol, a potent blend of inhaled corticosteroids and long-acting β2-agonists, has found extensive application in the management of COPD. Through diminishing airway inflammation, suppressing bronchial constriction, and optimizing airway patency, this inhalation aerosol significantly alleviates symptoms, improves pulmonary function, and fosters an improved quality of life for individuals with COPD. Doxofylline, widely employed in the treatment of COPD, acts as a potent bronchodilator with broad-spectrum effects. This medication relaxes bronchial smooth muscles and promotes increased expiratory flow by targeting phosphodiesterase and adenosine receptors[8-11]. The concurrent use of budesonide/formoterol inhalation aerosol and doxofylline holds the potential for synergistic effects, thereby enhancing the therapeutic efficacy in patients with COPD. This study seeks to examine the clinical efficacy of combining budesonide/formoterol inhalation aerosol with doxofylline in managing stable COPD patients. It also aims to explore the effects of this treatment approach on clinical symptoms and lung function. The findings from this study are anticipated to offer novel perspectives and empirical evidence for the management of COPD, ultimately fostering better health outcomes and enhancing the life quality for individuals with COPD. Our study enrolled a total of 90 patients with stable COPD, who were admitted to our hospital from September 2019 to June 2021. These participants were allocated randomly into two groups; the control group and the observation group, comprising 45 patients in each group. The control group included 24 females and 21 males, with an age range of 50 y to 76 y and an average age of (59.35±10.12) y. Conversely, the observation group consisted of 22 females and 23 males, aged between 49 y and 77 y, with an average age of (60.11±10.24) y. In terms of general characteristics, there were no noteworthy disparities between the two groups ($p>0.05$), suggesting comparability. The inclusion criteria for participant selection encompassed the following; clinical diagnosis of COPD during a stable phase[12-14]; sustained consciousness; complete availability of data; age ≥49 y and informed consent obtained from either the patient or their family member. Exclusion criteria excludes incomplete data; pregnancy; allergies to the study drugs; diagnosis of malignant tumors; critical medical conditions and presence of mental abnormalities. The Hospital Ethics Committee granted approval for the implementation of this study. Both groups of patients received routine treatment including expectorants, oxygen therapy, and anti-infection measures. Additionally, patients were assisted and guided to perform pulmonary rehabilitation training, including abdominal breathing and pursed-lip breathing. The control group received doxofylline (Zhejiang Anglikang Pharmaceutical Co., Ltd., National Medical Products Administration License H20000011, specifications: 0.2 g/tablet) treatment, 1 tablet per dose, twice a day. As part of their treatment, the observation group received budesonide/formoterol inhalation aerosol (Manufacturer: Astrazeneca Dunkerque Production, Approval Number: H20190062) in conjunction with the therapeutic regimen administered to the control group. The dosing consisted of 1 inhalation per dose, twice daily. Both groups of patients were treated for 6 mo. Complete disappearance of lung wheezing and significant improvement in abnormal signs are considered as marked improvement; improvement in lung wheezing and breath sounds, with mild clinical symptoms that do not affect daily life, is considered improvement and no significant improvement in symptoms is considered ineffectiveness[15-17]. Overall effectiveness rate=(marked improvement cases+improvement cases)/total cases×100 %. Utilizing the Cosmed pulmonary function testing instrument from Italy, measurements of Forced Expiratory Volume in 1 s (FEV_1) and the ratio of FEV_1 to Forced Vital Capacity (FVC) were acquired. Larger values for these indices correspond to improved lung function. Venous blood samples (5 ml) were collected from the patient's elbow veins both prior to treatment initiation and upon completion. Subsequent to high-speed centrifugation, the resultant supernatant was extracted to quantify the levels of Tumor Necrosis Factor-Alpha (TNF-α), serum Interleukin-8 (IL-8), and Transforming Growth Factor-Beta 1 (TGF-β1). The records were kept of any adverse reactions experienced by patients in both groups throughout the course of treatment. Statistical Package for the Social Sciences (SPSS) 25.0 will be employed to perform the statistical analysis in this research. Continuous variables will be presented as means and standard deviation, and their analysis will be conducted using t-test. Categorical variables, on the other hand, will be expressed as frequencies and percentages (n (%))

and assessed using Chi-square (χ^2) tests. To establish statistical significance, a threshold of $p<0.05$ will be utilized. According to the findings presented in Table 1, a remarkable contrast is observed in the total effective rate between the observation group (99.33 %) and the control group (73.33 %) ($p<0.05$). The comparison of FEV1 and FEV1/FVC between the two groups before treatment did not yield any noteworthy difference ($p>0.05$). However, post-treatment, both groups experienced an increase in FEV1 and FEV1/FVC values compared to their respective pre-treatment values. Remarkably, the observation group exhibited a notable improvement as opposed to the control group ($p<0.05$) (Table 2). Prior to treatment, there were no remarkable differences observed in the levels of IL-8, TNF-α, and TGF-β1 between the two groups ($p>0.05$). Following treatment, both groups experienced a decrease in the levels of IL-8, TNF-α, and TGF-β1 compared to their respective pre-treatment values. Notably, the observation group displayed a substantially greater decrease as opposed to the control group ($p<0.05$) (Table 3). Throughout the treatment period, adverse reactions including dry mouth, nausea, headache, and sore throat were reported by patients in both groups. The overall incidence rates of these reactions were 15.56 % and 20.00 % in the respective groups. Nevertheless, the incidence rates between the two groups did not exhibit a notable difference ($p>0.05$), as depicted in Table 4. Due to recurrent acute exacerbations, COPD can result in disease progression and a subsequent decline in lung function. Therefore, the management of COPD should prioritize not only the treatment of critical conditions but also the stabilization of symptoms during non-acute periods. This approach aims to prevent exacerbations, slow the decline of lung function, enhance life quality, and reduce mortality rates. The treatment during the stable phase of COPD should be a key focus in clinical management. This study sought to assess the clinical efficacy of budesonide/formoterol inhalation aerosol in conjunction with doxofylline for the management of individuals with stable COPD. Furthermore, it sought to compare the influence of this combination therapy on clinical symptoms, lung function, and inflammatory markers. The study findings exhibited a noteworthy disparity in the total effective rate between the observation group and the control group, with the former demonstrating a substantially higher rate. Moreover, both groups demonstrated improvements in lung function, with the observation group displaying a greater degree of improvement. Furthermore, a notable reduction in the levels of inflammatory markers IL-8, TNF-α, and TGF-β1 was observed in both groups. Remarkably, the decrease observed in the observation group was more significant than that in the control group. Additionally, notable disparities were identified in the incidence rates of adverse reactions between groups. The results indicate that the combination of budesonide/formoterol inhalation aerosol and doxofylline can effectively ameliorate clinical symptoms and improve lung function in patients with stable COPD. Furthermore, this combination treatment demonstrates a beneficial effect on regulating inflammatory markers. These findings are consistent with previous research, further confirming the effectiveness of this combination therapy. Throughout the treatment period, adverse reactions commonly associated with medication use, including dry mouth, nausea, headache, and sore throat, were observed in both groups. Most adverse reactions were mild and reversible, consistent with the known safety profile of budesonide/formoterol inhalation aerosol and doxofylline. Physicians should actively monitor and manage adverse reactions to ensure patient safety. This study does have several limitations. The study was conducted at a solitary center, and the sample size was comparatively limited. Consequently, this may introduce some potential selection bias. Additionally, the study's evaluation of treatment efficacy was limited to the short term, highlighting the necessity for more comprehensive data to effectively assess the long-term efficacy and safety of the treatment approach. In order to further confirm the effectiveness and safety of this combination therapy, future research should focus on conducting multicenter studies with larger sample sizes and implementing long-term follow-up. In summary, the utilization of budesonide/formoterol inhalation aerosol in conjunction with doxofylline generates considerable enhancements in clinical symptoms, lung function, and exhibits significant anti-inflammatory effects in individuals with stable COPD. It offers a novel therapeutic alternative for COPD patients, contributing to an improved quality of life and offering prospects for better disease prognosis. However, further research is needed to refine the application guidelines and promotion strategies for this combination therapy.

TABLE 1: CURATIVE EFFECT

Group (n=45)	Marked improvement	Improvement	Ineffectiveness	Overall effective rate
Observation	24 (53.33)	18 (40.00)	3 (6.67)	42 (93.33)
Control	17 (37.77)	16 (35.56)	12 (26.67)	33 (73.33)
χ^2		-		6.480
p		-		0.011

TABLE 2: PULMONARY FUNCTION INDEX

Group (n=45)	FEV1 (L)		FEV1/FVC	
	Before	After	Before	After
Observation	1.54±0.29	2.16±0.45*	36.90±8.64	50.87±10.71*
Control	1.46±0.28	1.81±0.34*	36.74±7.31	39.44±12.43*
t	-1.247	-4.152	-0.098	-4.677
p	0.216	0.000	0.922	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 3: PERIPHERAL BLOOD RELATED INDEX

Group (n=45)	IL-8		TNF-α		TGF-β1	
	Before	After	Before	After	Before	After
Observation	23.82±6.12	11.79±3.24*	34.58±8.20	16.82±4.92*	4.83±1.15	2.30±0.82*
Control	23.62±6.07	16.86±4.99*	37.69±7.06	22.13±6.55*	4.58±1.18	3.47±1.23*
t	-0.155	5.718	1.928	4.349	-0.99	5.286
p	0.877	0.000	0.057	0.000	0.325	0.000

Note: (*): Indicates noteworthy difference following treatment compared with prior to treatment

TABLE 4: ADVERSE REACTIONS n (%)

Group (n=45)	Dry mouth	Nausea	Headache	Sore throat	Overall incidence
Observation	3 (6.67)	2 (4.44)	0 (0.00)	2 (4.44)	7 (15.56)
Control	2 (4.44)	3 (6.67)	1 (2.22)	3 (6.67)	9 (20.00)
χ^2		-			0.304
p		-			0.581

Author's contributions:

Yanling Jiang and Qingming Meng have contributed equally to this work.

Conflict of interests:

The authors declared no conflict of interests.

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