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The Efficacy of Budesonide-formoterol in Patients with Acute Attacks of Mild-to-moderate Bronchial Asthma: An Observational Study

Yutong Li, Weitong Zeng, Qinyong Lu, Weimou Yin, Shiting Huang, Hanyi Wei, Longxiong Liao, Jiajiang Zhong, and Xuejun Qin

Department of Respiratory and Critical Care Medicine, Liuzhou People's Hospital, Guangxi, China

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ABSTRACT

To assess the impact of budesonide-formoterol on pulmonary ventilation function and prognosis in patients with mild-to-moderate acute exacerbations of bronchial asthma.

A retrospective analysis was conducted on clinical data from 232 patients with acute exacerbations of bronchial asthma. These patients were divided into 2 groups based on their treatment: a control group (n=104) receiving budesonide dry powder inhalation and an observation group (n=107) receiving budesonide-formoterol dry powder inhalation. Clinical efficacy and safety indicators were compared.

The results showed that the total treatment effectiveness rate in the observation group was significantly higher than that in the control group. Following treatment, the observation group exhibited significantly higher scores in the Asthma Quality of Life Questionnaire (AQLQ), as well as improved levels of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF), compared to the control group. Moreover, levels of tumor necrosis factor-alpha, interleukin-6, and C-reactive protein were significantly lower in the observation group. The incidence of adverse reactions between groups was comparable.

Based on these findings, the application of budesonide-formoterol demonstrated significant effectiveness in patients with mild-to-moderate acute exacerbations of bronchial asthma. The combination therapy led to improved clinical outcomes, including enhanced pulmonary ventilation function and reduced inflammatory markers. Importantly, the safety profile of budesonide-formoterol was comparable to that of budesonide monotherapy. These results highlight the potential benefits of using budesonide-formoterol as an alternative treatment option for patients experiencing acute exacerbations of mild-to-moderate bronchial asthma.

Keywords: Acute exacerbation; Bronchial asthma; Budesonide; Combination therapy; Formoterol; Pulmonary ventilation function; Treatment efficacy

INTRODUCTION

Bronchial asthma, a prevalent chronic inflammatory disorder characterized by airway inflammation, reduced airway patency, airway hyperresponsiveness, and airway remodeling,[1] frequently manifests as acute

Corresponding Author: Xuejun Qin, PhD;
Department of Respiratory and Critical Care Medicine, Liuzhou People's Hospital, Guangxi, China. Tel: (+86 137) 8840 8308, Email: qinxuejun886@163.com

exacerbations, which can be life-threatening in severe cases.[2] Glucocorticoids currently serve as the primary treatment modality for acute exacerbations of bronchial asthma, and budesonide, a glucocorticoid, is commonly used in asthma management.[3] However, the efficacy of glucocorticoid monotherapy may be insufficient, leading to recurrent exacerbations and worsening airway inflammation in some instances.[4] Consequently, there is a pressing need to investigate more effective therapeutic strategies.

Budesonide-formoterol combination therapy, delivered via dry powder inhalation, represents an innovative approach that harnesses the dual mechanisms of action conferred by glucocorticoids and long-acting β2-agonists.[5] Previous studies,[6] have indicated that budesonide-formoterol combination therapy exhibits superior control over airway inflammation and improved lung function compared to monotherapy. Nevertheless, comprehensive investigations into the efficacy of this approach during acute exacerbations, particularly in the context of mild-to-moderate cases, remain relatively limited. Therefore, the objective of this study is to evaluate the impact of budesonide-formoterol combination therapy on treatment effectiveness, pulmonary ventilation function, and prognosis in patients experiencing mild-to-moderate acute exacerbations of bronchial asthma. The aim is to provide clinicians with more tailored and individualized therapeutic options, potentially introducing novel strategies to enhance the management of acute exacerbations in bronchial asthma patients. Furthermore, exploring the mechanisms and safety profile of budesonide-formoterol combination therapy may serve as a crucial reference for future drug development and treatment strategies.

To accomplish this, we conducted a retrospective analysis of clinical data from hospitalized patients with mild-to-moderate acute exacerbations of bronchial asthma, divided into control and observation groups, receiving budesonide or budesonide-formoterol treatments, respectively. The anticipated outcomes of this study include a more comprehensive understanding of the treatment efficacy, pulmonary ventilation function improvements, and prognosis associated with budesonide-formoterol combination therapy in this specific patient population. The findings will provide valuable insights to guide clinical decision-making and potentially revolutionize the management of acute exacerbations in bronchial asthma patients. Additionally, elucidating the underlying mechanisms and evaluating the safety profile of budesonide-formoterol combination therapy will contribute to the advancement of future therapeutic approaches and optimize patient outcomes.

MATERIALS AND METHODS

Study Subjects

A retrospective analysis was conducted on the clinical data of 232 patients presenting with mild-to-moderate acute exacerbation of bronchial asthma who were admitted to our hospital between August 2020 and July 2023. Following stringent criteria, 21 cases were excluded, resulting in a final cohort of 211 patients meeting the comprehensive inclusion and exclusion criteria. The inclusion criteria included adult patients (>18 years) of any gender, with complete and reliable clinical data available for meticulous analysis, diagnosed with mild-to-moderate bronchial asthma based on rigorous clinical assessments as per the established grading criteria:[7] those who achieved complete control after the first- or second-level treatment were classified as having mild asthma, while those who achieved complete control after third-level treatment were classified as having moderate asthma. The exclusion criteria consisted of concurrent autoimmune diseases, neoplastic diseases, cardiovascular diseases, infectious diseases, organ dysfunction, and similar conditions, concomitant other pulmonary and respiratory system diseases; having received interventions (such as corticosteroids) that could potentially introduce confounding variables within the preceding 6 months, allergic reactions or relevant contraindications to the drugs or interventions employed in this study patients and their families, and concurrent mental disorders or impaired consciousness. Based on the treatment interventions received, patients were meticulously classified into a control group (n=104) and an observation group (n=107). The control group received beclomethasone inhalation therapy, while the observation group received beclomethasone-formoterol inhalation therapy.

Control Group

Control Group: Patients in the control group were administered budesonide dry powder inhalation therapy with Pulmicort Turbuhaler, manufactured by AstraZeneca AB (Approval Number: H20130322, Specification: 200 doses/inhaler). The treatment

regimen consisted of 1 to 2 inhalations (each containing 100 μg of budesonide) per administration, twice daily. Patients were instructed to promptly rinse their oral cavities with water after each inhalation to eliminate any residual medication.

Observation Group

Patients in the observation group received budesonide-formoterol dry powder inhalation therapy using Symbicort Turbuhaler, manufactured by AstraZeneca AB (Registration Number: H20140458, Specification: 200 doses/inhaler). The treatment regimen comprised 1 to 2 inhalations (each containing 160 μg of budesonide and 4.5 μg of formoterol) per administration, twice daily, considering the severity of the condition. Similar to the control group, patients were advised to rinse their mouths with water immediately after each inhalation to eliminate any oral residue. Both groups underwent treatment evaluation to assess efficacy after 5 days of treatment.

Outcomes

Clinical Treatment Effects

Clinical treatment effects were evaluated based on the 2021 Global Initiative for Asthma (GINA) guidelines for asthma management and prevention.[8] The treatment effects were classified as complete control, partial control, or uncontrolled, aligning with the objectives of asthma symptom control. Complete control and partial control were grouped as treatment effectiveness, and the total effective rate was calculated using the following formula: Total Effective Rate=(Number of complete control cases + Number of partial control cases)/Total number of cases×100%.

Asthma Quality of Life Questionnaire Scores

The prognosis of patients was assessed by measuring the Asthma Quality of Life Questionnaire (AQLQ) scores[9] before and after treatment. The AQLQ score scale consists of the 2 dimensions of symptoms and emotions and comprises a total of 11 items. Scores on this scale range from 1 to 7, with higher scores indicating better prognostic outcomes.

Pulmonary Ventilation Function Indicators

Pulmonary function indicators, including forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and peak expiratory flow rate (PEF), were measured before and after treatment using the Master Screen Diffusi-type fully automatic pulmonary function detector (Germany Jaeger).

Inflammatory Factor Indicator Levels

Fasting venous blood samples of 5 mL were collected from each patient before and after treatment. The serum was obtained through centrifugation, and the levels of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP) were measured using enzyme-linked immunosorbent assay (ELISA) (Quantikine, R&D Systems Europe, Oxon, UK) and high sensitivity particle-enhanced immunonephelometry (Cardiophase; BN systems, Dade Behring, Newark, NJ, USA).

Occurrence of Adverse Reactions

Adverse reactions observed in this study included dizziness, headache, muscle tremors, palpitations, hoarseness, insomnia, and fatigue. The occurrence of these adverse reactions was uniformly recorded by relevant medical staff at our institution.

Statistical Analysis

GraphPad Prism 8 software was used for data visualization, while SPSS 22.0 was employed for data analysis. Continuous variables were described using mean and standard deviation, and statistical analysis was conducted using the *t*-test. Categorical data were described using frequencies and percentages, and the chi-square test was used for statistical analysis. Differences were considered statistically significant at a significance level of $p<0.05$.

RESULTS

Comparison of Baseline Characteristics

The baseline characteristics of the 2 patient groups were comparable, demonstrating no significant differences ($p>0.05$; Table 1).

Comparison of Clinical Treatment Effects

The total effective rate in the control group was 77.88%, whereas in the observation group, it reached 92.53%. The observation group exhibited a significantly higher total effective rate compared to the control group ($p=0.002$; Table 2).

AQLQ Score Comparison

Figure 1 illustrates the AQLQ scores before and after treatment in both the control and observation groups. In the control group, the scores were (2.46±0.43) before treatment and (4.63±0.84) after treatment. In the observation group, the scores were (2.51±0.41) before treatment and (5.59±0.76) after treatment. Before treatment, there was no significant difference in AQLQ scores between the 2 groups (p>0.05). However, after treatment, the AQLQ scores in the observation group were significantly higher than those in the control group (p=0.023).

Table 1. Comparison of Basic Information

	Control (n=104)	Observation (n=107)	t/χ^2	p
Gender			0.424	0.514
Male	61	58		
Female	43	49		
Age (years)	46.37±14.57	46.52±14.35	0.075	0.940
Body mass index (kg/m²)	24.83±3.27	24.65±3.44	0.389	0.697
Duration of illness (years)	2.83±1.26	2.79±1.31	0.226	0.821
Duration of attacks (days)	1.37±3.52	1.43±3.49	0.124	0.901
Smoking			0.003	0.954
Yes	55	57		
No	49	50		
Severity of condition			0.831	0.361
Mild	45	53		
Moderate	59	54		
Exercise habits	-	-	0.189	0.663
Yes	32	30	-	-
No	72	77	-	-

Table 2. Comparison of Clinical Treatment Effects

Group	n	Complete Control	Partial Control	Uncontrolled	Total Effective Rate (%)
Control	104	27	54	23	77.88%
Observation	107	38	61	8	92.53%
χ^2	-	-	-	-	9.017
P	-	-	-	-	0.002

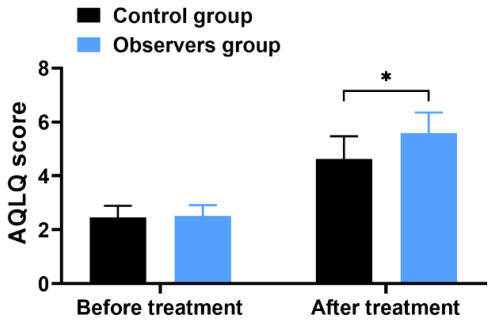

Figure 1. Asthma Quality of Life Questionnaire (AQLQ) score comparison. This figure compares the AQLQ scores between the observation group and the control group. The AQLQ scores provide an assessment of the impact of treatment on the quality of life of patients with acute mild-to-moderate bronchial asthma exacerbations. Higher AQLQ scores indicate better quality of life and improved asthma control. * p<0.05.

Pulmonary Ventilation Function Index Comparison

Figure 2 presents the comparison of FEV1, FVC, and PEF before and after treatment in both the control and observation groups. In the control group, the values were (65.43±3.02) and (81.65±6.97) for FEV1, (3.01±0.35) and (3.07±0.43) for FVC, and (3.34±0.39) and (3.54±0.42) for PEF before and after treatment, respectively. In the observation group, the values were (64.92±3.27) and (84.31±5.85) for FEV1, (2.98±0.34) and (3.32±0.45) for FVC, and (3.32±0.36) and (3.97±0.52) for PEF before and after treatment, respectively. Before treatment, no significant differences were observed in FEV1, FVC, and PEF levels between the 2 groups (p>0.05). However, after treatment, the levels of FEV1, FVC, and PEF in the observation group were significantly higher than those in the control group (p=0.032, 0.041, and 0.027, respectively).

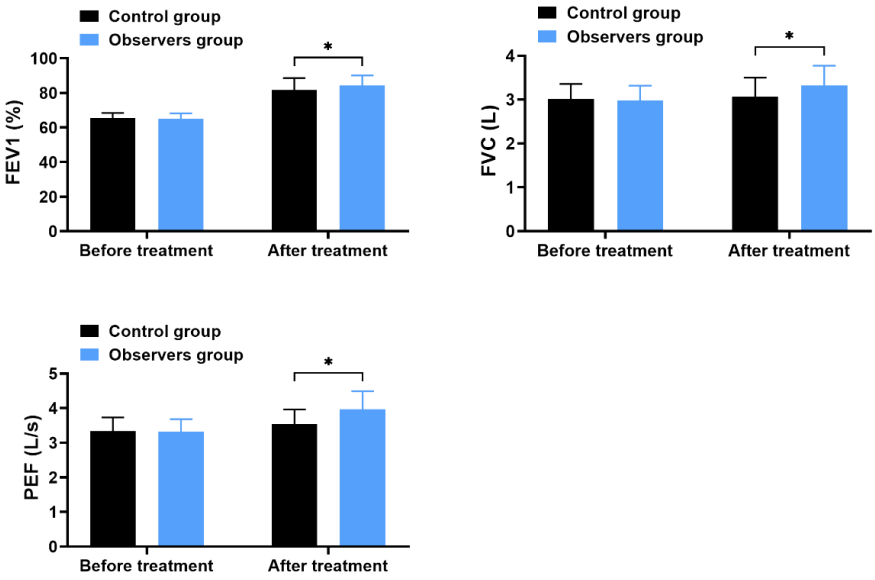

Figure 2. Pulmonary ventilation function index comparison. This figure compares the pulmonary ventilation function indices between the observation group and the control group. The indices, such as forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and peak expiratory flow (PEF), reflect the lung function and airflow in patients with acute mild-to-moderate bronchial asthma exacerbations. Higher values indicate improved pulmonary ventilation function and better respiratory capacity. * p<0.05.

Inflammatory Factor Index Comparison

Figure 3 presents the comparison of TNF-α, IL-6, and CRP levels before and after treatment in both the control and observation groups. In the control group, the levels were (322.47±78.76) and (310.24±51.69) for TNF-α, (34.79±9.86) and (31.86±6.89) for IL-6, and (16.07±9.43) and (13.74±7.56) for CRP before and after treatment, respectively. In the observation group, the levels were (319.96±75.87) and (258.16±45.97) for TNF-α, (35.12±10.14) and (28.63±5.72) for IL-6, and (16.15±9.29) and (11.38±6.35) for CRP before and after treatment, respectively. Before treatment, no significant differences were observed in TNF-α, IL-6, and CRP levels (p>0.05). However, after treatment, the levels of TNF-α, IL-6, and CRP in the observation group were significantly lower than those in the control group (p=0.04, 0.043, and 0.033, respectively).

Comparison of Adverse Reaction Incidence

The incidence of adverse reactions in the control group was 7.69%, while in the observation group, it was 9.35%. The comparison of adverse reaction incidence showed no significant difference between the 2 groups (p=0.667; Table 3).

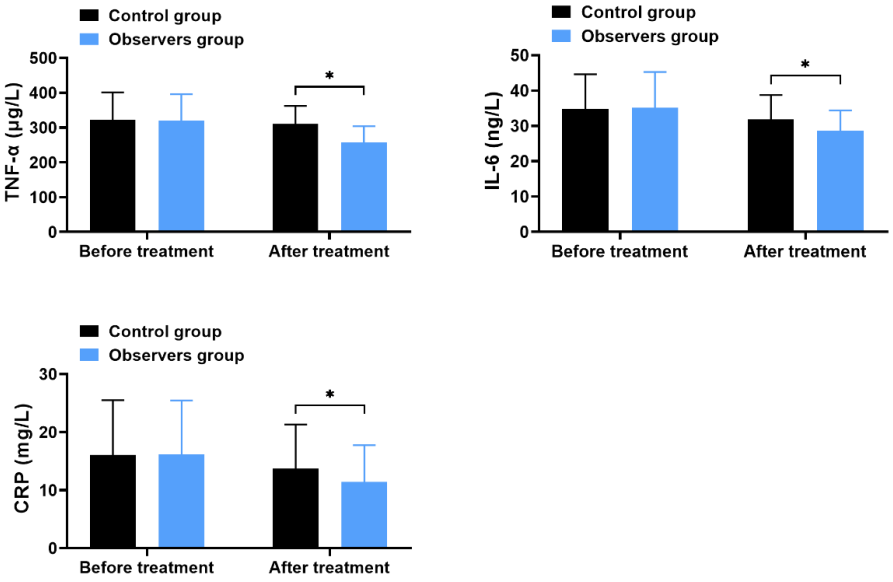

Figure 3. Inflammatory factor index comparison. This figure compares the levels of inflammatory factors between the observation group and the control group. The inflammatory factors, such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), are markers of airway inflammation in patients with acute mild-to-moderate bronchial asthma exacerbations. Lower levels indicate reduced inflammation and improved control of the inflammatory response. *p<0.05.

Table 3. Comparison of Adverse Reaction Incidence

Adverse Reaction	Control (n=104)	Observation (n=107)	x^2	p
Dizziness, headache	2	4	-	-
Muscle tremor	1	0	-	-
Palpitations, hoarseness	2	2	-	-
Insomnia, fatigue	3	4	-	-
Total Incidence (%)	7.69%	9.35%	0.184	0.667

DISCUSSION

The present study aimed to investigate the impact of budesonide-formoterol on the treatment effectiveness, pulmonary ventilation function, and prognosis of patients experiencing mild-to-moderate acute exacerbations of bronchial asthma. The results of this retrospective analysis provide valuable insights into the use of budesonide-formoterol combination therapy as a potential treatment option for these patients.

The findings of this study demonstrated that budesonide-formoterol dry powder inhalation treatment was associated with a significantly higher total effective rate compared to budesonide dry powder inhalation treatment alone. This indicates that the combination therapy of budesonide and formoterol has a more pronounced therapeutic effect in managing acute exacerbations of bronchial asthma. Moreover, the observation group showed significantly improved asthma-related indicators, including higher AQLQ scores, FEV1, FVC, and PEF levels, compared to the control group. These improvements in pulmonary ventilation function suggest that budesonide-formoterol combination therapy effectively alleviates airway obstruction and improves lung function in patients experiencing acute asthma attacks.

Furthermore, the observation group exhibited significantly lower levels of inflammatory markers, including TNF-α, IL-6, and CRP, compared to the control group. This indicates that budesonide-formoterol therapy has a beneficial effect on reducing airway inflammation, which is a key pathological feature of bronchial asthma. By targeting both airway inflammation and bronchodilation, the dual-action mechanism of budesonide-formoterol combination therapy may contribute to its superior efficacy in controlling acute exacerbations of bronchial asthma compared to glucocorticoid monotherapy.

Importantly, the incidence of adverse reactions was comparable between the observation and control groups, suggesting that budesonide-formoterol therapy is well-tolerated and safe for patients with mild-to-moderate acute exacerbations of bronchial asthma. This finding supports the use of budesonide-formoterol as a viable treatment option in clinical practice.

The superior clinical efficacy of budesonide-formoterol combination therapy compared to glucocorticoid monotherapy can be attributed to the dual-action mechanism of the two drugs. Budesonide, as a glucocorticoid, exerts anti-inflammatory effects by suppressing the production of pro-inflammatory cytokines, such as TNF-α and IL-6. This action helps to reduce airway inflammation, a key pathological feature of bronchial asthma.[10-12] By targeting the underlying inflammatory processes, budesonide mitigates the airway hyperresponsiveness and remodeling associated with acute exacerbations. Formoterol, on the other hand, is a long-acting β2-agonist that acts as a bronchodilator. It binds to β2-adrenergic receptors on smooth muscle cells in the airways, leading to relaxation and bronchial dilation.[13] This bronchodilatory effect improves airflow and alleviates airway obstruction, resulting in improved pulmonary ventilation function.[14] By combining the anti-inflammatory properties of budesonide with the bronchodilatory effects of formoterol, the budesonide-formoterol combination therapy effectively addresses both the underlying inflammation and the bronchoconstriction associated with acute exacerbations.[15-17]

The observed reduction in inflammatory markers, such as TNF-α, IL-6, and CRP, in the observation group compared to the control group further supports the anti-inflammatory effects of budesonide-formoterol therapy. By suppressing the production of these inflammatory mediators, budesonide-formoterol therapy helps to normalize the immune response in the airways, reducing the severity of inflammation and its associated symptoms.[18-20] The improved clinical outcomes and pulmonary function parameters observed in the observation group can be attributed to the synergistic effects of budesonide and formoterol. Budesonide reduces airway inflammation, allowing for improved airway patency and decreased airway hyperresponsiveness.[21] Simultaneously, formoterol acts as a bronchodilator, relaxing the smooth muscles in the airways and improving airflow. Together, these mechanisms contribute to the observed improvements in symptoms, lung function, and overall treatment effectiveness.[22]

The comparable incidence of adverse reactions between the observation and control groups suggests that budesonide-formoterol therapy is well-tolerated and safe for patients with mild-to-moderate acute exacerbations of bronchial asthma. This is consistent with the known safety profiles of budesonide and formoterol when used individually. The combination therapy does not appear to increase the risk of adverse events beyond what is expected with glucocorticoid monotherapy.[23] The results of this study contribute to the

growing body of evidence supporting the effectiveness of budesonide-formoterol combination therapy in managing acute exacerbations of bronchial asthma.[24] The findings highlight the potential of this treatment approach to improve symptoms, enhance pulmonary function, and reduce airway inflammation in patients experiencing mild-to-moderate asthma attacks.

However, it is important to acknowledge certain limitations of this study. Firstly, this was a retrospective analysis, which may be susceptible to inherent biases and confounding factors. Prospective randomized controlled trials are warranted to further validate these findings. Additionally, the study sample size was relatively small, and the follow-up period was limited. Future studies with larger sample sizes and longer follow-up durations would provide more robust evidence regarding the long-term efficacy and safety of budesonide-formoterol combination therapy.

Hence, ongoing studies concerning the following aspects are encouraged. 1) Comparative and prospective studies: further comparative studies are needed to compare the effectiveness of budesonide-formoterol combination therapy with other standard treatment regimens, such as glucocorticoid monotherapy or other combination therapies, and should consider prospective randomized controlled trials to minimize these limitations and provide more robust evidence. This would help in determining the optimal treatment strategy for patients with acute exacerbations of bronchial asthma. 2) Long-term outcomes: future research should investigate the long-term outcomes of budesonide-formoterol therapy, including its impact on disease progression, frequency of exacerbations, and quality of life. Longitudinal studies with extended follow-up periods would provide valuable insights into the sustained benefits and safety of this treatment approach. 3) Mechanistic studies: in-depth mechanistic studies are warranted to understand the specific cellular and molecular mechanisms underlying the synergistic effects of budesonide and formoterol. This could involve investigating the modulation of inflammatory mediators, signaling pathways, and gene expression patterns associated with the combination therapy. 4) Subgroup analysis: further exploration through subgroup analysis based on patient characteristics, such as age, gender, disease severity, and comorbidities, may reveal potential variations in treatment response and help identify specific patient populations that would benefit the most from budesonide-formoterol therapy.

In conclusion, the findings of this study support the use of budesonide-formoterol combination therapy as an effective treatment option for patients experiencing mild-to-moderate acute exacerbations of bronchial asthma. The combination therapy demonstrated superior clinical efficacy, improved pulmonary ventilation function, and reduced airway inflammation compared to glucocorticoid monotherapy. These results have important implications for optimizing the management of acute exacerbations in bronchial asthma patients and may guide the development of novel treatment strategies in the future. Further research is encouraged to corroborate these findings and explore the long-term benefits of budesonide-formoterol therapy in a larger patient population.

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

STATEMENT OF ETHICS

The protocol was approved by the Ethics Committee of Liuzhou People's Hospital (Approval number: 2020-381-01). The study was conducted in accordance with the Declaration of Helsinki, Written Informed consent was obtained from patients involved in the study.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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