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2025 Volume 10, Issue 3
Journal of Medicines Development Sciences
ISSN: 2382-6371(Online) ISSN: 2382-6363(Print)

A Study on the Long-Term Efficacy and Safety of Budesonide-Formoterol Versus Montelukast in the Treatment of Seasonal Asthma

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Abstract: *Objective:* To compare the long-term efficacy and safety of budesonide-formoterol and montelukast in patients with seasonal asthma. *Methods:* A total of 270 outpatient asthma patients with seasonal exacerbation characteristics were selected from our hospital from March 2022 to September 2025 and randomly divided into three groups (A, B, and C), with 90 patients in each group. All patients received asthma health education. Patients in Group A inhaled budesonide-formoterol inhalation powder, patients in Group B took oral montelukast sodium tablets, and patients in Group C did not use any asthma control medications but only used salbutamol aerosol for symptomatic treatment during acute exacerbations. All patients were followed up for more than 2 years, and ACT scores, lung function indicators, and safety were compared. *Results:* (1) The ACT scores of Groups A and B were higher than those before treatment at 3, 6, 12, and 30 months of treatment ($P<0.05$), and continued to increase with the prolongation of treatment time, while there was no significant change in Group C ($P>0.05$). When comparing between groups, the ACT scores of Groups A and B were higher than those of Group C at 3, 6, 12, and 30 months of treatment ($P<0.05$), and Group A was significantly higher than Group B at 6, 12, and 30 months ($P<0.05$). (2) The FEV1 and FEV1/FVC of Groups A and B were higher than those before treatment at 3, 6, 12, and 30 months of treatment ($P<0.05$), while there was no significant change in Group C ($P>0.05$). When comparing between groups, the FEV1/FVC of Groups A and B were higher than those of Group C at 3, 6, 12, and 30 months of treatment ($P<0.05$), and Group A was significantly higher than Group B at 6, 12, and 30 months ($P<0.05$). (3) During the treatment period, there was no significant difference in the incidence of adverse reactions between Group A and Group B ($P > 0.05$). During the follow-up period, Group C experienced a total of 15 cases of asthma exacerbation complicated by other conditions, including 14 cases of pulmonary infection and 1 case of respiratory failure. All patients improved after symptomatic treatment, and no deaths occurred due to complications. *Conclusion:* Implementing preventive treatment for patients with seasonal asthma is of utmost importance. Both budesonide-formoterol and montelukast therapies can effectively alleviate patients' symptoms and exhibit comparable safety profiles. However, budesonide-formoterol demonstrates superior performance in long-term symptom control and lung function improvement. Clinical decision-making should comprehensively consider the specific conditions and treatment responses of patients to develop suitable individualized treatment plans.

Keywords: Seasonal asthma; Budesonide; Formoterol; Montelukast sodium; ACT score; Lung function; Safety

Online publication: September 26, 2025

1. Introduction

Seasonal asthma is a common subtype of bronchial asthma, closely associated with climatic changes or seasonal allergens such as pollen and mold spores. It predominantly affects children, the elderly, and individuals with allergic predispositions. The typical symptoms of this condition include mucosal edema and increased secretions triggered by airway hyperresponsiveness, accompanied by recurrent episodes of wheezing, shortness of breath, chest tightness, and coughing. Patients generally experience worsening symptoms at night and in the early morning, which, in severe cases, can induce acute respiratory insufficiency and significantly diminish their quality of life [1]. Epidemiological surveys indicate an increasing annual prevalence of asthma globally, making it a significant public health concern [2].

According to the "2025 GINA Global Strategy for Asthma Management and Prevention," the key treatment strategies for asthma involve controlling airway inflammation and alleviating bronchial spasm [3]. Currently, commonly used clinical medications include inhaled corticosteroids (ICS), long-acting beta-agonists (LABA), and leukotriene receptor antagonists (LTRA), among others. Budesonide-formoterol dry powder inhaler is widely used in the long-term management of bronchial asthma. It is a combination formulation of ICS/LABA, in which budesonide can inhibit airway inflammation, reduce the aggregation of inflammatory cells and the release of inflammatory mediators, and decrease airway hyperresponsiveness [4]; formoterol, on the other hand, can activate the β2 receptors on the airway smooth muscle cell membrane, relax the bronchial smooth muscle, and thereby alleviate airway spasms [5]. Montelukast sodium, as an LTRA, reduces allergen-induced airway constriction and inflammation by inhibiting cysteinyl leukotriene receptors [6]. Although these two drugs have been widely used in the clinical treatment of asthma, research data on the comparison of their efficacy and safety in the long-term management of seasonal asthma remain relatively limited. This study aims to provide a more sufficient theoretical basis for clinical rational drug use by comparing the long-term efficacy and safety of budesonide-formoterol and montelukast in patients with seasonal asthma.

2. Materials and Methods

2.1. General Information

A total of 270 outpatient asthma patients with seasonal onset characteristics were selected from our hospital from March 2022 to September 2025 and randomly divided into three groups (A, B, and C), with 90 patients in each group. Among them, there were 119 males and 151 females, aged between 17 and 56 years, with a disease duration of 5-11 years, a body mass index (BMI) of 20-28 kg/m², and an Asthma Control Test (ACT) score of 16-24 points. The general information of the three groups was comparable, with no statistically significant differences ($P > 0.05$) (see **Table 1**).

Table 1. Comparison of General Information Among the Three Groups

Indicator	Group A	Group B	Group C	F/ χ^2 value	P-value
Gender (n, Male/Female)	38/52	40/50	41/49	0.210	0.900
Age (Mean ± SD, years)	35.79 ± 5.01	36.33 ± 5.24	36.61 ± 4.98	0.606	0.546
Disease Duration (Mean ± SD, years)	6.02 ± 1.17	5.94 ± 1.33	5.81 ± 1.41	0.592	0.554
BMI (Mean ± SD, kg/m²)	23.24 ± 1.81	23.06 ± 1.79	23.19 ± 1.84	0.236	0.790
ACT Score (Mean ± SD, points)	19.32 ± 2.76	20.01 ± 2.09	19.94 ± 2.31	2.248	0.108

2.2. Inclusion and Exclusion Criteria

Inclusion criteria: (1) Patients primarily presented with recurrent symptoms such as wheezing, dyspnea, chest tightness, or coughing, and during episodes, scattered or diffuse wheezing sounds predominantly in the expiratory phase could be auscultated in both lungs, with prolonged expiration; (2) The symptoms of acute exacerbation improved after

treatment with antiasthmatic drugs; (3) Outpatient visits ruled out wheezing, shortness of breath, chest tightness, or coughing caused by other diseases; (4) At least one of the following three criteria is positive: a positive bronchial provocation test or exercise test; a positive bronchodilation test; a diurnal PEF variation rate greater than 20%. After meeting the diagnostic criteria for bronchial asthma, patients still need to meet the inclusion criteria, including seasonal exacerbations occurring from April to May and August to September each year; (5) No acute exacerbations of bronchial asthma in the past three months and no maintenance treatment with any medications.

Exclusion criteria: (1) Recent (within the past month) onset of upper respiratory tract infections or other diseases; (2) Concomitant diagnosis of other respiratory system diseases; (3) Current smoking, alcohol consumption, or consumption of beverages containing caffeine; (4) Allergy to the medications used in this study; (5) Breastfeeding and pregnant women; (6) Inability to cooperate and complete this study or withdrawal midway.

2.3. Methods

All three groups of patients received asthma health education, including avoidance of allergens, proper use of inhalation devices, and identification and pre-treatment of acute exacerbations. On this basis:

Group A: Inhaled budesonide/formoterol fumarate inhalation powder (AstraZeneca AB, National Medical Products Administration Approval Number: H20140458, specification: 60 inhalations per device, each inhalation containing 160 μg budesonide and 4.5 μg formoterol fumarate), 1 inhalation per dose, twice daily, with rinsing of the mouth with water after inhalation; Group B: Oral montelukast sodium tablets (Hangzhou MSD Pharmaceutical Co., Ltd., National Medical Products Administration Approval Number: J20130047, specification: 10 mg), 10 mg once nightly; Group C: No asthma control medications were used, and only salbutamol aerosol was used for symptomatic treatment during acute exacerbations. The start date for preventive medication was from March 1st to April 1st and August 1st to September 1st each year.

All three groups of patients were treated and followed up for 30 months. During this period, a WeChat group for patients was established, and follow-up was conducted once every four weeks through on-site visits, video calls, and phone calls. During the follow-up period, patients conducted regular peak expiratory flow rate measurements at home and filled out asthma diaries based on their actual conditions. Regular medication administration and dynamic monitoring continued until the occurrence of an acute exacerbation. For patients without acute exacerbations, preventive medication was administered until September 31, 2025, after which their diaries were collected.

2.4. Observation Indicators

(1) Comparison of ACT Scores Among the Three Groups: ACT scores were assessed at 3 months, 6 months, 12 months, and 30 months of treatment. The total score for this test is 25 points, with 25 points indicating complete control, 20-24 points indicating good control, and <20 points indicating inadequate control.

(2) Comparison of Pulmonary Function Indicators Among the Three Groups: Pulmonary function indicators, including Forced Expiratory Volume in One Second (FEV1) and the ratio of FEV1 to Forced Vital Capacity (FEV1/FVC), were measured using a spirometer at 3 months, 6 months, 12 months, and 30 months of treatment. Prior to testing, patients were required to sit quietly for 15 minutes. Each measurement was repeated three times, and the best value was recorded.

(3) Safety Analysis: Adverse drug reactions occurring during preventive treatment in Groups A and B were recorded, including throat discomfort, gastrointestinal reactions, headaches, allergic reactions, palpitations, etc. The incidence of complications during the study period in Group C patients, such as pulmonary infections and respiratory failure, was also recorded.

2.5. Statistical Methods

Data were processed using SPSS 26.0 statistical software. Continuous variables were expressed as “Mean±SD” and

analyzed using the t-test. Categorical variables were expressed as (n,%) and analyzed using the chi-square (X^2) test. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Comparison of ACT Scores Among the Three Groups

After 3 months, 6 months, 12 months, and 30 months of treatment, the ACT scores of Groups A and B were higher than those before treatment ($P < 0.05$), and they continued to increase with the prolongation of treatment duration. In contrast, Group C showed no significant change ($P > 0.05$). In inter-group comparisons, the ACT scores of Groups A and B were higher than those of Group C at 3 months, 6 months, 12 months, and 30 months of treatment ($P < 0.05$). Furthermore, at 6 months, 12 months, and 30 months, Group A had significantly higher scores than Group B ($P < 0.05$). See **Table 2**.

Table 2. Comparison of ACT Scores Before and After Intervention Among the Three Groups (Mean±SD, points)

Time Point	Group A	Group B	Group C	F-value	P-value
Before Treatment	19.32 ± 2.76	20.01 ± 2.09	19.94 ± 2.31	2.248	0.108
3 Months	20.51 ± 1.94	20.82 ± 2.04	19.87 ± 1.61	6.027	0.003
6 Months	23.51 ± 2.01	21.30 ± 2.11	19.90 ± 2.41	62.546	<0.001
12 Months	24.21 ± 1.54	22.15 ± 1.75	20.10 ± 2.22	110.030	<0.001
30 Months	24.75 ± 1.01	23.14 ± 1.20	20.52 ± 2.07	182.464	<0.001
F-value (Time)	137.964	37.564	1.417	/	/
P-value (Time)	<0.001	<0.001	0.227	/	/

3.2. Comparison of Pulmonary Function Indicators Among the Three Groups

After 3 months, 6 months, 12 months, and 30 months of treatment, the FEV1 and FEV1/FVC values of Groups A and B were higher than those before treatment ($P < 0.05$), while Group C showed no significant change ($P > 0.05$). In inter-group comparisons, the FEV1/FVC values of Groups A and B were higher than those of Group C at 3 months, 6 months, 12 months, and 30 months of treatment ($P < 0.05$). Additionally, at 6 months, 12 months, and 30 months, Group A had significantly higher values than Group B ($P < 0.05$). See **Table 3**.

Table 3. Comparison of Pulmonary Function Indicators Before and After Intervention Among the Three Groups (Mean±SD)

Indicator	Time Point	Group A	Group B	Group C	F-value	P-value
	Before Treatment	1.64 ± 0.23	1.59 ± 0.35	1.62 ± 0.33	0.602	0.549
	3 Months	1.92 ± 0.42	1.86 ± 0.51	1.60 ± 0.21	16.250	<0.001
FEV_1 (L)	6 Months	2.21 ± 0.54	2.04 ± 0.41	1.63 ± 0.32	42.702	<0.001
	12 Months	2.82 ± 0.42	2.56 ± 0.33	1.63 ± 0.30	219.568	<0.001
	30 Months	2.94 ± 0.23	2.66 ± 0.47	1.62 ± 0.24	344.575	<0.001
F-value (Time)	/	190.137	107.129	0.167	/	/
P-value (Time)	/	<0.001	<0.001	0.955	/	/

Table 3 (Continued)

Indicator	Time Point	Group A	Group B	Group C	F-value	P-value
	Before Treatment	66.25 ± 4.23	65.98 ± 4.46	65.53 ± 4.51	0.614	0.542
	3 Months	72.85 ± 5.61	71.82 ± 4.91	65.94 ± 4.02	45.529	<0.001
FEV_1/FVC (%)	6 Months	78.55 ± 4.67	76.15 ± 5.99	65.79 ± 5.06	149.063	<0.001
	12 Months	83.52 ± 8.31	82.61 ± 6.57	64.89 ± 3.97	232.733	<0.001
	30 Months	84.50 ± 6.51	78.14 ± 7.30	64.12 ± 5.25	238.216	<0.001
F-value (Time)	/	144.072	105.940	2.403	/	/
P-value (Time)	/	<0.001	<0.001	0.050	/	/

3.3. Safety Analysis Adverse Reactions in Groups A and B

There was no significant difference in the incidence of adverse reactions between the two groups during treatment ($P > 0.05$). See **Table 4**.

Table 4. Incidence of Adverse Reactions in Groups A and B (n,%)

Adverse Reaction	Group A	Group B	χ^2 Value	P-value
Throat Discomfort (n)	2	1	/	/
Gastrointestinal Reaction (n)	1	2	/	/
Headache (n)	1	2	/	/
Allergic Reaction (n)	0	0	/	/
Palpitations (n)	0	0	/	/
Total Incidence	4 (4.44%)	5 (5.56%)	0.117	0.732

Complications in Group C: During the follow-up period, Group C had a total of 15 cases of complications due to acute asthma exacerbation, including 14 cases of pulmonary infection and 1 case of respiratory failure. All patients improved after symptomatic treatment, and no patients died from complications.

4. Discussion

Seasonal asthma is a type of asthma associated with allergens, which can lead to asthma symptoms and respiratory inflammation. It is a common clinical asthma phenotype, and its long-term management requires a balance between "inflammation control" and "exacerbation prevention." This means alleviating bronchial spasms in patients by suppressing airway hyperresponsiveness and reducing the release of inflammatory factors, thereby controlling the progression of the disease [7-8]. Currently, ICS, LABA, and LTRA are commonly used in clinical treatment [9-11]. Therefore, this study compared the efficacy and safety of budesonide-formoterol and montelukast sodium through a 30-month follow-up.

The ACT score is an effective tool for monitoring and evaluating asthma conditions during treatment, and its changes directly reflect the effectiveness of the treatment plan. Before treatment in this study, there were no significant differences in ACT scores among the three groups ($P>0.05$). However, after prophylactic treatment in Groups A and B, the corresponding scores increased significantly, and continued to rise with the extension of follow-up time ($P<0.05$). This indicates that both budesonide-formoterol and montelukast sodium can effectively control disease symptoms in patients

with seasonal asthma, while relying solely on salbutamol treatment cannot achieve long-term disease control. Further inter-group comparisons showed that the scores in Group A were significantly higher than those in Group B at 6, 12, and 30 months of treatment ($P<0.05$). The reason is that budesonide-formoterol, as a combination preparation of ICS and LABA, can rapidly dilate the bronchi while suppressing airway inflammation, providing a dual therapeutic effect. Montelukast sodium, on the other hand, is an LTRA that can only treat the disease by antagonizing the inflammatory pathway mediated by leukotrienes, and its effect in long-term asthma management is relatively limited [12-13].

Improvements in asthma control levels are often accompanied by improvements in patients' lung function. FEV1 and FEV1/FVC are commonly used indicators for lung function assessment, which can evaluate the patient's patency and degree of airflow limitation. Three months after treatment, the FEV1 and FEV1/FVC in Groups A and B began to be significantly higher than before treatment ($P<0.05$), and the scores in Group A were significantly higher than those in Group B at 6, 12, and 30 months of treatment ($P<0.05$), while Group C remained at a consistently low level. Both types of drugs can alleviate inflammatory responses and spasms, thereby protecting lung function. However, the synergistic effect of budesonide-formoterol not only relieves immediate airflow limitation but also achieves long-term improvement by delaying airway remodeling. In contrast, montelukast sodium has a weaker intervention effect on remodeling [14-15], which is a significant reason why its long-term improvement in lung function is inferior to that of the former.

In terms of safety, the results showed that the incidence of adverse reactions was low in both Group A and Group B, with mild symptoms such as throat discomfort and gastrointestinal reactions being predominant. No inflammatory adverse reactions were observed, indicating that both drugs have favorable therapeutic effects in seasonal asthma. In Group C, 15 cases of complications were reported, including 14 cases of pulmonary infection and 1 case of respiratory failure. This further demonstrates that relying solely on symptomatic treatment without using control medications increases the risk of complications during acute asthma exacerbations, highlighting the necessity of standardized preventive treatment.

In summary, preventive treatment is crucial for patients with seasonal asthma. Both budesonide-formoterol and montelukast can effectively improve patient symptoms, with comparable safety profiles. However, budesonide-formoterol demonstrates superior performance in long-term symptom control and lung function improvement. Clinical decision-making should consider the patient's specific condition and treatment response to develop an appropriate individualized treatment plan. Nevertheless, this study has certain limitations, such as a relatively small sample size, which may affect a comprehensive assessment of the long-term safety of the drugs. Additionally, although the use of symptomatic treatment during acute exacerbations in the blank control group meets ethical requirements, it may have a certain impact on the evaluation of therapeutic efficacy. Subsequent studies will further optimize the research protocol to provide more meaningful preventive treatment strategies for asthma.

Funding

Project Title: Research on Medication for Seasonal Asthma Attacks in the Karamay Region (Project No.: 2022D01F31).

Disclosure statement

The author declares no conflict of interest.

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