# The effect of budesonide on the quality of life in patients with bronchial asthma

Shukhrat Ziyadullaev, Samarkand State Medical Institute. Samarkand, Uzbekistan Jasur Rizaev Alimdjanovich, Rector of the Samarkand State Medical Institute. Uzbekistan Irina Agababyan Rubenovna, Samarkand State Medical Institute. Uzbekistan Jamshid Ismailov Abduraimovich, Samarkand State Medical Institute. Uzbekistan Soatboy Yuldashev Jiyanboyevich, Samarkand State Medical Institute. Samarkand, Uzbekistan. jamshidismailov@mail.ru

Abstract: In recent years, serious and numerous advances have been made in the treatment of bronchial asthma. These results are associated with the significant efficacy of inhaled corticosteroids in topical diagnosis and pathogenetic treatment of bronchial asthma. However, despite the results achieved, the fight against this disease is not satisfactory. In patients with severe bronchial asthma, inhaled corticosteroids are more effective when used in combination with  $\beta$ 2-agonists. Almost every second asthma patient is concerned about nighttime attacks. More than half of the patients had limited physical activity, and one in three lost the ability to work. Most patients are forced to see a doctor because of the exacerbation and progression of the disease.

Keywords: bronchial asthma, budesonide, prednisolone, nebulizer

**Introduction:** Corticosteroid drugs are one of the most effective drugs in the treatment of bronchial asthma and in reducing the number of attacks [2,15]. Inhaled corticosteroid drugs bind to specific receptors in the cytoplasm, activate them, forming a complex, which then penetrates the cell nucleus, binds to DNA and interacts with key enzymes, receptors, and transcription mechanisms of other complex proteins. This leads to pharmacological and therapeutic effects.

The disadvantages of systemic inhaled corticosteroids in the treatment of bronchial asthma attacks are their late exposure and the risk of developing other side effects. The effectiveness of treatment with systemic corticosteroids begins in 5-10 hours, therefore, their early prescription for patients with bronchial asthma is recommended [1,4,].

Inhaled glucocorticosteroids (IGS) reduce the synthesis of prostaglandins, including pro-inflammatory cytokines and leukotrienes; reduce capillary permeability (stabilize biological membranes, leading to the development of an antiexudative effect). Inhaled glucocorticosteroids stabilize lysosomal membranes, reduce the release of proteolytic enzymes from lysosomes and prevent the development of destructive processes in tissues. Inhaled glucocorticosteroids increase the synthesis of anti-inflammatory proteins (lipocortin-1), increase apoptosis, and decrease the number of eosinophils by inhibiting interleukin-5. Inhaled corticosteroids increase the stability of cell membranes, reduce vascular permeability, improve the activity of b-receptors, synthesize new ones and increase their sensitivity, and stimulate epithelial cells [3,8,9].

Nebulizer therapy with corticosteroids for hormone-dependent bronchial asthma has been well studied in several studies to reduce the dose of systemic corticosteroids and significantly reduce side effects [6,7]. The role of IGS in the exacerbation of bronchial asthma is currently the subject of numerous disputes and controversies. Although the anti-inflammatory effect of inhaled corticosteroids also manifests itself after the activation of systemic corticosteroid receptors and a prolonged cascade of subsequent biochemical reactions, IGS, as a consequence of a direct effect on the bronchial mucosa, have a faster

clinical effect [10, 14]. The combination of inhaled corticosteroids with  $\beta$ 2-agonists has a more bronchodilator effect than monotherapy with  $\beta$ 2-agonists. During an exacerbation of bronchial asthma, the effect of inhaled corticosteroids is observed after 1.5-2 hours [12]. However, the properties of budesonide (good solubility in the water period) have a positive effect on the functional parameters of respiration after 1 hour and on the symptoms of inflammation after 3-4 hours [11].

Currently, few studies have been conducted to study the effects of nebulizer therapy with corticosteroids in exacerbation of bronchial asthma [13]. Some studies show that nebulizer therapy with budesonide is no less effective than oral corticosteroids in treating exacerbations of bronchial asthma.

The aim of the study was to study the effectiveness of the use of corticosteroids (through a nebulizer using budesonide) in the treatment of bronchial asthma.

Materials and methods

Over the past 2 years, observation was observed in 105 patients admitted to the pulmonary department in connection with acute attacks of bronchial asthma. Patients were diagnosed based on clinical criteria such as the presence of aggressive cough and shortness of breath, the presence of distant wheezing, a history of allergies and genetic predisposition. The diagnosis was confirmed by general clinical studies, determination of the total level of IgE in the blood and the results of spirographic examination. In 93% of patients (98 patients) the diagnosis of bronchial asthma was made earlier, and in 7% (8 patients) the diagnosis of bronchial asthma was made for the first time.

# Distribution of patients admitted with an acute attack of bronchial asthma by age and sex

Table 1.

Gender	20-24 ages	25-29 ages	30-34 ages	35-39 ages	40-45 ages
Men	7 (6,5%)	8 (7,6%)	10 (9,5%)	15 (14,3)	18 (17%)
Women	4 (3,8%)	7 (6,5%)	12 (11,4%)	10 (9,5%)	14 (13,3%)

According to the severity of an attack of bronchial asthma, patients are as follows: intermittent 12 (11.4%), mild persistent 38 (36.2%), moderately persistent 42 (40%), severe persistent 13 (12.4).

The severity of the attack was assessed in accordance with the recommendations for the treatment of bronchial asthma, taking into account such clinical parameters as respiratory rate, heart rate, emotional state of the patient, physical activity, involvement of accessory muscles in breathing, auscultatory changes, blood oxygen saturation.

Patients were taken to the hospital by ambulance 85 (81%), the rest - 20 (19%) - asked for help on their own. The distribution of bronchial asthma by severity is as follows: mild - 15 (14.3%), medium - 62 (59%), severe - 28 (26.7%).

The exacerbation of asthma, accompanied by an attack, in 35 (33.3%) patients was caused by bacterial and viral infections. In these patients, leukocytosis is detected in a general blood test in case of intoxication syndrome simultaneously with attacks of bronchial asthma. In 45 (43%) patients, discontinuation of inhalation medications without the doctor's permission led to an increase in bronchial asthma attacks. In 25 (23.7%) patients, the duration and number of attacks increased as a result of exposure to allergens.

Patients with a severe attack of bronchial asthma did not receive adequate primary anti-inflammatory therapy and cannot be included in the group of patients with "controlled asthma". In 8 (7.6%) patients with moderate to severe bronchial asthma, cromones were used in primary therapy, while 18 (17%) patients received uncontrolled inhaled corticosteroids. In 23 (21.9%) patients, the causative agent was an exacerbation of bronchial obstruction against the background of viral infections of the upper respiratory tract, especially in the elderly.

We followed the algorithm shown in Figure 1 to stop an asthma attack.

## A therapy algorithm used to relieve an acute attack of bronchial asthma Table 2.

Rapid nebulization of the bronchodilator (berodual solution)									
Positive answer	The answer is not enough								
Inhalation bronchodilator every 1-3	continue inhalation of a								
hours, continued inhalation in high	bronchodilator every 20 minutes for								
doses (metered dose inhaler)	one hour								
Positive answer	The answer is not enough								
Inhalation bronchodilator every 1-3	oral prednisolone or budesonide								
hours, continued inhalation in high	tablet via a nebulizer, repeated								
doses (metered dose inhaler)	inhalation of a bronchodilator								
Positive answer	The answer is not enough								
We continue to inhale bronchodilators	intravenous prednisone infusion,								
every 1-3 hours, and continue to	oxygen therapy, bronchodilator								
inhale high doses of corticosteroids	nebulization repeated every 30								
	minutes aminophylline infusion								
Positive answer	The answer is not enough								
oral prednisolone or budesonide tablet using a nebulizer, bronchodilator nebulization every 1-4 hours, oxygen therapy	transfer to intensive care								
Positive answer									
decreased breathing rate with									
bronchodilators									

A compressor nebulizer was used for inhalation. Berodual is prescribed in 20-25 drops. To prevent exacerbation of bronchial obstruction, it is important to dissolve the drug (up to 2 ml) with water, and not with isotonic sodium chloride solution [15]. Duration of inhalation is 8-10 minutes.

Subsequently, these patients were assigned to a bronchodilator in the form of a metered-dose inhaler, measured through a spacer, if necessary for primary therapy.

These patients were divided into 2 groups. Twenty-eight patients of the first group additionally received oral prednisolone at a dose of 0.5 to 1 mg/kg per day for 3 days.

Thirty-two patients in the second group received budesonide at a dose of 2 mg twice daily via a nebulizer.

The first group included patients with a high risk of adverse outcomes: patients with hormone-dependent bronchial asthma, patients with a history of asthma, hyperexcitatory patients with fear of death. Also included are patients who sought help when the duration of an emergency attack exceeded 48 hours.

## Research results

The condition of the patients of both groups stabilized after 14 hours, and after 24 hours it improved significantly. After 72 hours, only a few patients developed dry rales against the background of a slight lengthening of the breathing time.

Table 3.

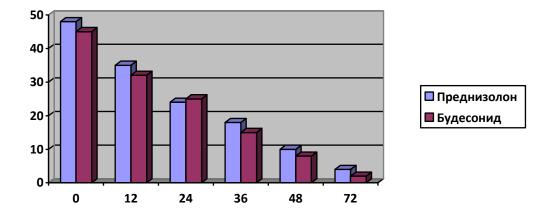
DynamIGS of high expiratory flow rate in patients of the first and second groups (% of the corresponding value)										
Time periods										
Originally	42,9±4,0	45,2±3,8	1,895	>0,05						
After 24 h.	56,4±3,1	60,2±4,4	1,948	>0,05						
After 48 h.	68,1±2,5	72,6±3,25	3,275	<0,05						

Table4.

Clinical ef	fectiv	eness	of tre		nt in t		st and	second	group	of pat	ients	
Clinical manifestations	Clinical manifestations Group 1 prednisolone n = 26					Group 1 - budesonide n = 28						
	Before treatment	12	24	36	48	72	Before treatment	12	24	36	48	72
Dyspnea	24	23	9	2	1	0	20	19	11	8	2	1
Tachycardia	24	24	10	4	2	1	20	18	10	4	2	1
Weakness	24	17	7	1	0	0	20	14	6	4	3	1
Excitement	20	4	0	0	0	0	15	2	0	0	0	0
Limitations of speech	24	2	0	0	0	0	17	2	1	0	0	0
Involvement of accessory muscles in breathing	24	20	8	1	1	0	20	9	3	1	0	0
Distension of the chest	24	22	12	3	3	1	20	16	9	2	0	0
Weakening	24	22	7	3	2	0	20	20	6	6	4	0

breathing												
Extended exhalation	24	24	18	15	8	1	20	14	8	6	2	0

Figure. 1.



DynamIGS (by hour) of the severity of clinical symptoms (by mean values of points) in the observed patients with bronchial asthma of the first (prednisone, blue bars) of the second (budesonide, bard bars) groups during treatment.

During treatment with corticosteroids, the severity of clinical symptoms was taken into account in points every 12 hours. Measurements of peak blood flow have been studied and evaluated separately only in middle-aged patients (Table 3). The dynamIGS of clinical symptoms is presented in Table 4 and Figure 1.

The dynamIGS of clinical parameters and high expiratory flow rate indicate the effectiveness of both regimens of corticosteroid therapy. Comparing the dynamIGS of clinical symptoms in the two groups, it should be noted an improvement in the group of patients receiving budesonide suspension in the first 12 hours, and the maximum expiratory flow rate after 48 hours was also significantly higher in the group receiving budesonide. Given the particular subjectivity of the assessment of clinical symptoms, it can be noted that the effectiveness of prednisolone (in tablets) and budesonide (in a nebulizer solution) can be compared. The median duration of treatment with systemic corticosteroids was 3.8 days. Side effects of systemic action and nebulizer-stabilization of the state, patients were switched to inhaled corticosteroids (fluticasone, budesonide) in two doses.

### **Conclusions**

- 1. Inhalation of budesonide in combination with  $\beta$ 2-agonists through a nebulizer is effective for the treatment of patients with moderate to severe attacks of bronchial asthma.
- 2. It was found that budesonide has a higher clinical efficacy compared to systemic corticosteroids.
- 3. Early administration of systemic corticosteroids is indicated in patients with severe asthma and risk of death.
- 4. With the combined use of inhaled corticosteroids and  $\beta$ 2-agonists, the duration of bronchial asthma attacks is reduced and the quality of life of patients is significantly improved.

### **References:**

- [1] S. B. de Nijs, E. J. M. Krop, L. Portengen, L. H. Rijssenbeek-Nouwens, J. W. J. Lammers Effectiveness of pulmonary rehabilitation at high-altitude compared to sealevel in adults with severe efractory asthma// Respiratory Medicine September 2020 Volume 171 Article 106123
- [2] J.Mark FitzGerald, Sofie Arnetorp, Caitlin Smare, Danny Gibson, Karen Coulton, Kirsty Hounsell, Sarowar Golam, Mohsen Sadatsafavi The cost-effectiveness of as-needed budesonide/formoterol versus low-dose inhaled corticosteroid maintenance therapy in patients with mild asthma in the UK. Respiratory Medicine September 2020 Volume 171Article 106079
- [3] Guy Brusselle A new once-daily long-acting β2-adrenoceptor agonist—inhaled corticosteroid combination therapy for asthma The Lancet Respiratory MedicineIn press, corrected proofAvailable online 9 July 2020
- [4] M Sean, R Marybeth, M.D Jones, Nicolas Goldstein, Kristin Riekert, Maria Fagnano, S.Jill Knowledge of Inhaled Therapy and Responsibility for Asthma Management Among Young Teens With Uncontrolled Persistent Asthma Academic PediatrIGSApril 2018Volume 18, Issue 3Pages 317-323
- [5] Akramovich, B.T., Askarovna, S.O., Hamidovna, M.D., Samiyevich, B.S. Features of sexual development, state of the pituary-gonad system and measures of secondary prevention in sick children with chronic bronchitis. International Journal of Pharmaceutical Research 2020 12(1), c. 384-388
- [6] Anna Pomés, Jill Glesner, Agustin Calatroni, Cindy M Visness, Robert A Wood, George T O'Connor, Meyer Kattan, Leonard B Bacharier, Lisa M Wheatley, James E Gern, William W Busse Cockroach allergen component analysis of children with or without asthma and rhinitis in an inner-city birth cohort Journal of Allergy and Clinical ImmunologyOctober 2019Volume 144, Issue 4Pages 935-944
- [7] Ishbel Henderson, Elisabetta Caiazzo, Charles McSharry, Tomasz J. Guzik, Pasquale Maffia Why do some asthma patients respond poorly to glucocorticoid therapy? Pharmacological ResearchOctober 2020Volume 160Article 105189
- [8] L.P. Tavares, H.Y. Peh, W.S.D. Tan, H. Pahima, P. Maffia, E. Tiligada, F. LeviSchaffer, Granulocyte-targeted therapies for airway diseases, Pharmacol. Res. 157 (2020), 104881.
- [9] C. van der Heijden, J. Deinum, L.A.B. Joosten, M.G. Netea, N.P. Riksen, The mineralocorticoid receptor as a modulator of innate immunity and atherosclerosis, Cardiovasc. Res. 114 (7) (2018) 944–953.
- [10] M.C. Peters, S. Kerr, E.M. Dunican, P.G. Woodruff, M.L. Fajt, B.D. Levy, E. Israel, B.R. Phillips, D.T. Mauger, S.A. Comhair, S.C. Erzurum, M.W. Johansson, N. N. Jarjour, A.M. Coverstone, M. Castro, A.T. Hastie, E.R. Bleecker, S.E. Wenzel, J. V. Fahy, Refractory airway type 2 inflammation in a large subgroup of asthmatic patients treated with inhaled corticosteroids, J. Allergy Clin. Immunol. 143 (1) (2019), 104-113.e14.
- [11] S.D. Harding, E. Faccenda, C. Southan, A.J. Pawson, P. Maffia, S.P.H. Alexander, A.P. Davenport, D. Fabbro, F. Levi-Schaffer, M. Spedding, J.A. Davies, The IUPHAR

- Guide to immunopharmacology: connecting immunology and pharmacology, Immunology 160 (1) (2020) 10–23.
- [12] Eyal Oren Fernando D. Martinez Stress and asthma: Physiological manifestations and clinical implications Annals of Allergy, Asthma & ImmunologyIn press, corrected proofAvailable online 24 July 2020
- [13] Tzu-Jung Tseng, RN PhD, Assistant Professor, Chiung-Jung (Jo). Wu, RN DrHlthSc FACN, Associate Professor, Honorary Research Fellow, Anne M. Chang, RN PhD FRCNA, Adjunct Professor Theoretical asthma self-management program for Taiwanese adolescents with self-efficacy, outcome-expectancy, health behaviour, and asthma symptoms: A randomized controlled trial Contemporary Clinical Trials Communications September 2020Volume 19Article 100624
- [14] FitzGerald JM, Bleecker ER, Menzies-Gow A, Zangrilli JG, Hirsch I, Metcalfe P, et al. Predictors of enhanced response with benralizumab for patients with severe asthma: pooled analysis of the SIROCCO and CALIMA studies. Lancet Respir Med 2018; 6:51-64.
- [15] Nair P, Bardin P, Humbert M, Murphy KR, Hickey L, Garin M, et al. Efficacy of Intravenous Reslizumab in Oral Corticosteroid-Dependent Asthma. J Allergy Clin Immunol Pract 2020; 8:555-64.