Khalmatova B.T

Doctor of Medical Sciences, Professor, Head of the Department of Children's Diseases No. 1 of the Tashkent Medical Academy, Republic of Uzbekistan

Tashmatova G.A.

PhD, Senior Lecturer of the Department of Children's Diseases No. 1 of the Tashkent Medical Academy, Republic of Uzbekistan

ESTIMATION OF THE EFFICIENCY OF THE DOMESTIC PREPARATION MONTELUKAST IN THE COMPLEX THERAPY OF BRONCHIAL ASTHMA IN CHILDREN

Abstract. *This article is devoted to the study of the efficacy and tolerability of the domestic drug montelukast in comparison with a foreign analogue in the treatment of children diagnosed with bronchial asthma. The data obtained showed that the use of the domestic drug montelukast improves clinical and laboratory parameters in children with bronchial asthma.*

Keywords. *Bronchial asthma, children, montelukast.*

Relevance. Bronchial asthma (BA) remains one of the most common chronic diseases, especially among children and adolescents, due to its early onset [5]. Prevalence of asthma in children in the world: on average, 4.3% of the respondents registered asthma diagnosed by a doctor, 4.5% had clinical manifestations with the appointment of therapy for asthma, 14.4% of the study participants noted the presence of asthma symptoms [2]. Depending on the participating country, these figures fluctuated significantly, reaching a difference of 21 times. This study shows that bronchial asthma is placing a heavy burden on health care worldwide. As you know, bronchial asthma is based on allergic inflammation, which involves numerous cells and mediators, including cysteinyl leukotrienes (cis-LT), which include LTC, LTD, LTE, and LTB. These lipid substances, formed from arachidonic acid under the action of 5-lipoxygenase (5-LO), are powerful pro-inflammatory mediators that cause bronchoconstriction, hypersecretion of mucus and impaired mucus clearance, stimulate the influx of eosinophils and other inflammatory cells, and increase the permeability of blood vessels 100 times more

efficiently. histamine, stimulate the proliferation and differentiation of myofibroblasts, thus promoting the development of subepithelial fibrosis [7, 8, 9, 10]. Acetylsalicylic acid (ASA) and non-steroidal anti-inflammatory drugs (NSAIDs) are inhibitors of cyclooxygenase-1 (COX-1), an enzyme that, along with 5-LO, participates in the metabolism of arachidonic acid and controls the formation of prostaglandins and thromboxanes, therefore, with aspirin BA accompanied by ASA intolerance and NSAIDs and polypous rhinosinusitis, the level of cis-LT is especially significant [1–3].

According to the latest revisions of the international recommendations GINA (2014, 2016, 2018) [5-7], antileukotriene drugs are considered as an alternative to inhaled glucocorticosteroid (ICS) therapy in the treatment of mild persistent asthma and virus-induced bronchial obstruction, in children, with intermittent asthma and as component of basic anti-inflammatory therapy (for addition to ICS) of persistent moderate asthma. The effectiveness of antileukotriene drugs has been proven in many studies. For example, the results of the PREVIA (Prevention of Viral-Induced Asthma) study showed a 39.9% reduction in the frequency of asthma exacerbations with the use of montelukast in children 2-5 years old [6]. However, the use of montelukast in adolescent and adolescent children with asthma as a single control drug is usually less effective than ICS; at the same time, it is considered an alternative to ICS when it is possible to carry out step down therapy [2].

The urgency of the problem of bronchial asthma is due to its socio-economic component, since, being a chronic disease, this disease significantly reduces the quality of life and leads to loss of working capacity. In modern conditions, the goal of treatment is to achieve control of bronchial asthma and improve the quality of life of patients.

One of the effective montelukast drugs is Neoclast® (manufactured by the pharmaceutical company "NOBEL PHARMSANOAT" (Uzbekistan). This drug is indicated as an alternative method of treatment instead of low doses of inhaled corticosteroids for patients with mild persistent asthma who have not recently had serious asthma attacks, requiring oral corticosteroids, as well as for those patients

who are found to be intolerant to inhaled GCS, according to experimental and clinical data [1] prevents bronchoconstriction caused by physical exertion, inhalation of cold air and allergens, the action of aspirin and sulfur dioxide.

Purpose of the study. Study of antiallergic efficacy and tolerability of the drug NEOCLAST 4 mg, 5 mg chewable tablets manufactured by FE LLC "NOBEL PHARMSANOAT", Uzbekistan, in comparison with the drug NOTTA (registered in Uzbekistan under the name AKRETAN SANOVEL) tab 4 mg, 5 mg chewable tablets manufactured by Sanovel Ilac Sanayi ve Ticaret AS Turkey, in patients with bronchial asthma, to identify the possibility of recommending the drug for clinical use in the Republic of Uzbekistan.

Materials and methods. Clinical trials were carried out in accordance with the Law of the Republic of Uzbekistan "On Medicines and Pharmaceutical Activities", "National Standard of Uzbekistan - GCP - Good Clinical Practice" and taking into account the rules of GCP applied in international practice, the Regulation "On the Procedure for Conducting Clinical Trials and Expertise of Materials of Clinical Trials pharmacological and medicinal products "(Appendix 1 to the Order of the Ministry of Health of the Republic of Uzbekistan No. 40 dated January 26, 2015), ethical principles of the Declaration of Helsinki. Ethical and moral and legal aspects of the clinical trial were considered and approved at a meeting of the National Ethics Committee at the Ministry of Health of the Republic of Uzbekistan. (protocol No. 20, dated 19.10.2016). A limited, comparative, open-label, controlled, randomized study with two parallel groups was conducted. The studies were carried out in patients undergoing inpatient and outpatient treatment in the departments of allergology, pulmonology and in the polyclinic. A total of 60 children were examined, aged 2 to 18 years, who are inpatient treatment in the allergy department with a diagnosis of bronchial asthma. In the group that received the study drug, as well as in the group that received the reference drug, there were 30 patients. The groups were matched by sex and age.

Results. The main group included 30 children, of which children under 3 years old - 23.3% (n = 7), children from 3-7 years old - 33.3% (n = 10), and children over

7 years old - 43.3 % (n = 13). Among the surveyed children there were 16 boys (53.3%), 14 girls (46.7%). The control group consisted of 20 children. Patients of the main group received the drug "NEOCLAST" once a day. The patients who made up the comparison group (30 people) received NOTTA, also once a day. The chewable tablet was chewed 2 hours after a meal, in the evening, before bedtime. The course of treatment was 28 days. The drug treatment regimen, depending on the patient's condition, was established by the doctor.

Adjunctive treatments: excluded other drugs with a similar effect. The basic therapy drugs necessary for the treatment of the underlying disease and other drugs compatible with the studied drugs, as well as the necessary physiotherapeutic methods of treatment, were used. The data of the studies obtained, as well as other indicators reflecting the effectiveness of the drug used are presented.

The dynamics of changes in some clinical data shows pronounced, reliable improvements in the studied parameters. Improvements in both groups proceeded almost the same (Table 1):

Table 1

Dynamics of changes in clinical indicators (M±m, n=60)

Examination terms	**NEOCLAST (Nobel)**			**NOTTA (Turkey)**		
	INDICATORS					
	Breathlessness *(score)*	**Cough** *(score)*	**Suffocation** *(score)*	**Breathlessness** *(score)*	**Cough** *(score)*	**Suffocation** *(score)*
Before treatment	1,73±0,07	2,67±0,1	0,93±0,05	1,90±0,05	2,40±0,13	0,77±0,08
After treatment	0,00±0,00	0,27±0,06	0,00±0,00	0,00±0,00	0,23±0,08	0,00±0,00
P	*<0,001*	*<0,001*	*<0,001*	*<0,001*	*<0,001*	*<0,001*

This table shows that in terms of the severity of the patients, they were more worried about coughing, then shortness of breath, and to a lesser extent attacks of suffocation.

And if, after a course of treatment in both groups, these signs of allergy, such as shortness of breath and attacks of suffocation, passed, then a mild cough remained in less than a third of patients in both groups (Table 2).

Table 2

Dynamics of distribution in groups of allergy signs (%) by severity

(in%, n = 60)

Expressiveness (score)	**NEOCLAST (Nobel)**			**NOTTA (Turkey)**		
	INDICATORS					
	Breathlessness	**Cough**	**Suffocation**	**Breathlessness**	**Cough**	**Suffocation**
Before treatment						
0	--	--	6,7%	--	--	*23,3%*
1	26,7%	3,3%	93,3%	*10%*	*13,3%*	*76,7%*
2	73,3%	26,7%	--	*90%*	*33,3%*	--
3	--	70%	--	--	*53,4%*	--
After treatment						
0	*100%*	*73,3%*	*100%*	*100%*	*76,7%*	*100%*
1	--	*26,7%*	--	--	*23,3%*	--
2	--	--	--	--	--	--
3	--	--	--	--	--	--

0 - no sign *2 - moderately expressed*

1 - mild *3 - severe*

The number of leukocytes and eosinophils in the blood, ESR in the dynamics of studies also indicated a tendency to improve the studied parameters. So, if the decrease in the number of blood leukocytes was within the limits of physiological fluctuations, then the dynamics of markers of allergic inflammation in patients under the influence of the studied drugs had a unidirectional character: in all patients there was a significant decrease in the content of eosinophils in peripheral blood at the 4th week of therapy - the level of eosinophils in blood showed a picture of its significant decrease by 47.6% (Neoclast) and 42.6% (Notta).

In the group taking Neoclast, the IgE value decreased by 53%, in the control group by 59%. At the same time, in the experimental group, the IgE index and in the control group, a decrease was observed in almost the same number of patients.

Критерии оценки переносимости изучаемого препарата. Tolerability of the drug was assessed on the basis of subjective symptoms and sensations, which the patient reported independently and taking into account the objective data obtained by the doctor. The dynamics of laboratory parameters, as well as the

frequency of occurrence and nature of adverse reactions were taken into account. The assessment of the tolerance of the study drug was carried out on the basis of the above criteria in points on a scale from 0 to 4 points:

The studies carried out have established that in the dynamics of changes in the level of the number of erythrocytes and leukocytes, ESR during the entire test period varied significantly within physiological fluctuations, with the exception of a certain increased index of eosinophils in the blood before treatment.

Other indicators of laboratory studies, such as the activity of the enzymes ALT, AST, the level of bilirubin in the blood also remained within the range of physiological fluctuations, although sometimes they were reliable in the dynamics of changes. The drugs were well tolerated; there were no subjective complaints about changes in the state of health from the patients.

CONCLUSION. The data obtained allow us to conclude that the drug NEOCLAST 4 mg, 5 mg chewable tablets produced by FE LLC "NOBEL PHARMSANOAT", Uzbekistan is an effective drug in the treatment of patients with bronchial asthma. The drug NEOCLAST 4 mg, 5 mg chewable tablets (montelukast) is comparable in clinical efficacy and tolerability to the drug NOTTA 4 mg, 5 mg chewable tablets (registered in Uzbekistan under the name AKRETAN SANOVEL) manufactured by Sanovel Ilac Sanayi ve Ticaret AS Turkey.

Our experience of using the drug NEOCLAST 4 mg, 5 mg chewable tablets shows that it has sufficient clinical activity, efficacy, good tolerance and can be recommended for registration and medical use in the Republic of Uzbekistan as an antiallergic agent.

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