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EXPERIENCE OF LONG-TERM OMALIZUMAB TREATMENT FOR PEDIATRIC ASTHMA IN ASTRAKHAN REGION

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ABSTRACT — The efficacy of the addition of the genetically engineered drug Omalizumab in complex anti-inflammatory therapy in children with moderate-to-severe uncontrolled bronchial asthma (BA) living in the Astrakhan region was evaluated. In the study, it was proved that the recombinant humanized monoclonal antibodies (IgG1) — Omalizumab (Xolair) leads to a sharp decrease in the frequency of exacerbations, reduces the dose of inhaled glucocorticosteroids (ICS), which characterizes gaining control over bronchial asthma and improving the quality of life in patients.

KEYWORDS — bronchial asthma, children, Omalizumab (Xolair).

INTRODUCTION

Today, the high growth rate of the urbanization of the population, the deep introduction of biologically unsafe products into the diet, massive air pollution trigger an increase allergic diseases in childhood, including bronchial asthma. According to the Guideline (GINA 2019), in order to achieve control in patients with moderate to severe form of BA, if the use of medium or high doses ICS plus long-acting β2-agonists (LABA) and/or leukotriene modifiers (LM) is not effective, it is suggested to add a genetically engineered drug anti-IgE therapy of Omalizumab (Xolair). Based on the central role of immunoglobulins E in the genesis of inflammation of bronchial asthma in children, it can be regarded as the most successful target for pathogenetic therapy [1, 2].

OBJECTIVE

This study evaluates the efficacy of Omalizumab in baseline treatment of children with moderate-to-severe bronchial asthma in Astrakhan.

MATERIALS AND METHODS

The study enrolled 14 patients age 6 to 17 years (mean age 10.8 + 2.1 years) with bronchial asthma in baseline treatment with Omalizumab.

According to modern international consensus documents (GINA, 2019), the diagnosis of Bronchial Asthma was verified based on the bronchodilator reversibility test or airway hyperresponsiveness in combination with a characteristic clinical performance, laboratory findings and the presence of atopy. The research was carried out on the basis of the analysis of medical documentation, a survey of patients, as well as their parents according to the developed questionnaire. The questionnaire consisted of three blocks of questions. The first block contained the patient's passport data and clinical and anamnestic features of the disease (degree of severity and duration of BA, the presence of comorbid allergic pathology, the frequency and intensity of symptoms, the level of treatment to relieve exacerbations, the degree of tolerance of physical and emotional stress, lung function measures and Asthma Control Test results) before Xolair therapy. The second block was aimed at identifying the side-effects of the drug, with the refinement of local and general adverse reactions. The third section of the questionnaire included questions characterizing the course of the disease and the degree of control in patients receiving the genetically engineered drug Omalizumab, specifying the dosage and duration of administration.

All patients were reviewed once a month and received the prescribed dose of the drug in the Pulmonology Department of the State Budgetary Institution of Health Care of Astrakhan Region Regional Children's Clinical Hospital named after N.N. Silischeva in Astrakhan. Monthly, it was monitored patients' general clinical indicators of blood and urine, the level of total immunoglobulin E, carried out functional breathing test and filled in tests–questionnaires to objectify the patient's subjective attitude to his/her disease (ACT test: scores of 20 or more were classified as well-controlled asthma, less than 19 points as not-well controlled).

RESULTS AND DISCUSSION

The examined cohort was consisted of 7 boys and 7 girls. The age of patients is presented as follows: 6–10 years — 6 children, 11–14 years — 5 children, 15 and more years — 3 children. The duration of treatment of bronchial asthma before addition of Xolair in baseline anti-inflammatory therapy was up to 8 years in 8 children; from 8 to 10 years — in 3 patients; more than 10

years — in 3 patients. Taking into account the combination of clinical features and functional indicators 12 children form 14 patients were diagnosed with severe bronchial asthma, 2 patients — moderate asthma. As a baseline therapy, 12 patients received a fixed high-dose ICS plus LABA (1000 mcg of fluticasone propionate or budesonide 720 mcg) and plus leukotriene modifiers or long-acting M-anticholinergics. Two patients with a moderate disease, anti-inflammatory therapy was represented by a combination of ICS/LABA (in moderate therapeutic doses of ICS) plus AM.

The frequency of daily and nocturnal symptoms before omelizumab add-on ranged from 2 times a week to daily. At the same time, exacerbations requiring medical assistance, including in-hospital, were observed in 8 patients once in a month and in 6 patients more than 2 times a month. 78.5% from 100% of responders were required a short-term course of treatment with systemic corticosteroids 3 or more times a year to relief attacks. Exercise intolerance and sharp limitation of emotional stress were common in all patients. When assessing the level of control according to the Asthma Control Test, asthma was interpreted as uncontrolled in all children (the total number of points varied from 8 to 16). It should be noted the high compliance to therapy in families of patients (strict adherence to hypoallergenic life and the recommendations of the attending physician) and the correct technique for applying an individual inhaler by the patient. The following co-existing allergic diseases were identified: atopic dermatitis in 5 patients, year-round allergic rhinitis in 11 patients, drug allergy in 5 children, food allergy in 11 children.

Given the lack of control over the disease during the baseline anti-inflammatory therapy of 4 and 5 steps, as well as the high adherence to therapy of patients' families according to federal clinical guidelines for the treatment of bronchial asthma in children, the genetically engineered drug Omalizumab (Xolair) was added to the therapy. Dosing was determined for each individual patient according to the dosing table based on the initial level of immunoglobulins E and the patient's body weight. 7 patients were receiving 150 mcg of Omalizumab; 1 patient — 225 mcg; 6 children — 300 mcg. The drug was administered subcutaneously 1 time in 4 weeks. Following administration of the drug, the following local and general adverse reactions were noted. In 4 children, mild headache and dizziness were noted, in 4 children, slight hyperemia and edema were observed at the injection site. According to the manufacture's recommendations, these side-effects of the drug are not a contraindication for further therapy. Therefore, Xolair administration was continued. One child had an anaphylactic reaction in the form of acute urticaria following the first administration of Omalizumab, so the drug was canceled and the patient was excluded from further observation.

At the time of the study, Xolair was used from 6 months to 4 years. For 6 months, Xolair was a component of baseline anti-inflammatory therapy in 1 patient, from 6 to 18 months — in 7 patients, 2 children received Omalizumab for 2 years and 3 children for more than 3 years. The results of the study indicate that 69.2% (n = 9) of patients achieved stable control of the disease: relief of both nocturne and daily attacks (within a few months to a year), satisfactory exercise tolerance and low interest in short-acting β2 agonists. 4 (30.8%) patients had partial control of the disease: daily and nocturne symptoms of a mild degree 1–2 times per month. 2 out of 3 patients had a restriction of physical activity, which was more associated with parental hyper-care than with persistent bronchial hyperresponsiveness associated with physical activity. Asthma Control Test results show the disease control, which are ranged from 18 to 25 points in all patients.

With regular Omalizumab treatment, the basline anti-inflammatory therapy in 11 patients (84.6%) was stepped down by reducing ICS dose due to long-lasting drug remission and a high level of disease control. Thus, if before Xolair therapy 12 children had been receiving high-dose ICS therapy, 2 children — medium dose ICS, then, with genetically engineered drug add-on 10 children reduced ICS to medium dose, 2 children — to low dose ICS. One patient continued to receive high dose of inhaled hormones to achieve disease control. When analyzing the lung function measures all patients had a significant increase in the level of FEV1.

CONCLUSION

The study results indicate that the recombinant humanized monoclonal antibodies (IgG1) — Omalizumab (Xolair) in complex of baseline anti-inflammatory therapy in children with moderate-to-severe bronchial asthma leads to a sharp decrease in the frequency of exacerbations and emergence department visits, reduces the dose of inhaled (ICS), increase lung function which characterizes gaining control over bronchial asthma and improving the quality of life in patients.

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