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SAFETY AND CLINICAL EFFECTIVENESS OF BILASTINE IN THE TREATMENT OF ALLERGIC RHINITIS IN CHILDREN

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The purpose of the study was to evaluate the effectiveness and safety of bilastine in relieving symptoms in patients aged 6–12 years with allergic rhinitis. In this prospective, randomized study, 50 patients aged 6 to 12 years with newly diagnosed allergic rhinitis and confirmed sensitization to allergens of household or pollen group participated; 46 completed the course of treatment within 4 weeks. Patients received bilastine orally at a dose of 10 mg daily for 4 weeks. Before starting treatment, the average level of severity of eye and nasal symptoms was assessed using the total nasal symptom score questionnaire for 5 days, with further assessment in 7, 14 and 28 days after starting bilastine intake. In general, at the endpoint of monitoring after 4 weeks, the reduction in the severity of symptoms was 49.1 %. A total of 89.1 % of patients (n=41) who received bilastine at a dose of 10 mg had no adverse reactions during the study. All adverse reactions were classified as mild, with headache being the most common, reported in 2 (4.3 %) cases.

Key words: allergic rhinitis, children, symptomatic therapy, antihistamines, bilastine

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БЕЗПЕЧНІСТЬ ТА КЛІНІЧНА ЕФЕКТИВНІСТЬ БІЛАСТИНУ У ЛІКУВАННІ АЛЕРГІЧНОГО РИНІТУ У ДІТЕЙ

Метою роботи було оцінити ефективність та безпеку біластину щодо полегшення симптомів у пацієнтів віком 6–12 років з алергічним ринітом. У цьому проспективному, рандомізованому дослідженні прийняли участь 50 пацієнтів віком від 6 до 12 років з вперше встановленим діагнозом алергічного риніту та підтвердженою сенсибілізацією до алергенів побутової або пилкової групи, з них повністю завершили курс лікування протягом 4 тижнів 46 осіб. Пацієнти отримували біластин перорально у дозі 10 мг 1 раз на добу протягом 4 тижнів. До початку прийому середній рівень вираженості очних та назальних симптомів був оцінений за опитувальником Total nasal symptom score протягом 5 днів, з подальшою оцінкою через 7, 14 та 28 днів після початку прийому біластину. Загалом у кінцевій точці моніторингу через 4 тижні зменшення вираженості симптомів становило 49,1 %. У цілому 89,1 % пацієнтів (n=41), які отримували біластин у дозі 10 мг, не мали побічних реакцій під час дослідження. Усі побічні реакції були класифіковані як легкі, а найпоширенішим був головний біль, зареєстрований у 2 (4,3 %) випадках.

Ключові слова: алергічний риніт, діти, симптоматична терапія, антигістамінні препарати, біластин

The work is a fragment of the research project "Effectiveness of modern methods of combined treatment (specific immunotherapy and pharmacotherapy) of allergic respiratory diseases", state registration No. 0116U003349.

Allergic rhinitis is defined as symptoms of sneezing, nasal pruritus, airflow obstruction, and mostly clear nasal discharge caused by IgE-mediated reactions against inhaled allergens [12].

Often, allergic diseases manifest quite early, although in early childhood sometimes the characterizing of the symptoms can be a problem. The International Study of Asthma and Allergy in Childhood (ISAAC) reported an approximately 10–20 % prevalence of childhood allergic rhinoconjunctivitis in most countries [6]. The prevalence of allergic rhinoconjunctivitis varies considerably between regions and countries, but worldwide it is reported to be 8.5 and 14.6 % at 6–7 and 13–14 years, respectively [10]. In Ukraine, allergic diseases in general and allergic rhinitis, in particular, continue to remain a significant socio-economic problem due to the high incidence rate, which continues to grow, the inconsistency of official statistical data with the real picture of prevalence, as well as often untimely diagnosis of these diseases and inadequate treatment of the relevant categories of patients. Optimization of

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diagnostic algorithms [3], transition to personalized therapy of both allergic rhinitis and bronchial asthma, based on endo- and phenotyping [1], can improve the situation with these diseases.

Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines puts second-generation antihistamines at the center of treatment options for allergic rhinitis, regardless of its severity. Second-generation antihistamines are also recommended as the first-line approach for treatment of pediatric allergic rhinitis [2].

Bilastine is a representative of non-sedating H1-antihistamine drugs, which was first approved in the European Union in 2010 for the symptomatic treatment of allergic rhinoconjunctivitis (seasonal and perennial) and urticaria in patients aged 12 years and older and is now available in approximately 100 countries worldwide [11]. Several years ago, it was approved in Europe for use in children aged 6 to 12 years, and more recently, a similar approval for use was received in Ukraine.

The purpose of the study was to evaluate the effectiveness and safety of bilastine in relieving symptoms in patients aged 6–12 years with allergic rhinitis.

Materials and methods. The study was prospective, and randomized. The research group included 50 patients aged 6 to 12 years (the target group for receiving bilastine in a dosage of 10 mg) with a newly established diagnosis of allergic rhinitis and confirmed sensitization to allergens of the household or pollen group. Patients with allergic rhinitis were considered to meet the criteria for inclusion in the study during the screening visit if they met the following criteria: age 6–12 years, suspected sensitization to allergens of the pollen or household group, absence of allergen-specific therapy in the anamnesis.

The criteria for inclusion in the study were as follows: a positive result of detection of specific immunoglobulin E (IgE) to at least one pollen or household allergen, a total score of nasal symptoms (TNSS) of more than 8 points, of which the sum of the points of rhinorrhea and sneezing is at least 4 points.

Exclusion criteria from the study: active infections, ulcers or polyps of the nasal septum, or other diseases of the nose, ears, eyes that may interfere with the correct interpretation of the treatment effect, asthma, allergen-specific immunotherapy in history, underwent immunotherapy or received corticosteroid injections or treatment with anti-IgE therapy (omalizumab) previous 180 days; have taken other symptomatic drugs for the treatment of allergic rhinitis in the previous 7 days, poor compliance.

Patients received bilastine ("Nixar", manufacturer A. Menarini Manufacturing Logistics and Services S.r.L.) orally at a dose of 10 mg once a day for 4 weeks. Mean symptom severity was assessed using the TNSS questionnaire for 5 days prior to initiation, with follow-up assessments at 7, 14, and 28 days after bilastine initiation. The survey according to the TNSS point scale was carried out using a standardized questionnaire, adapted to the Ukrainian language.

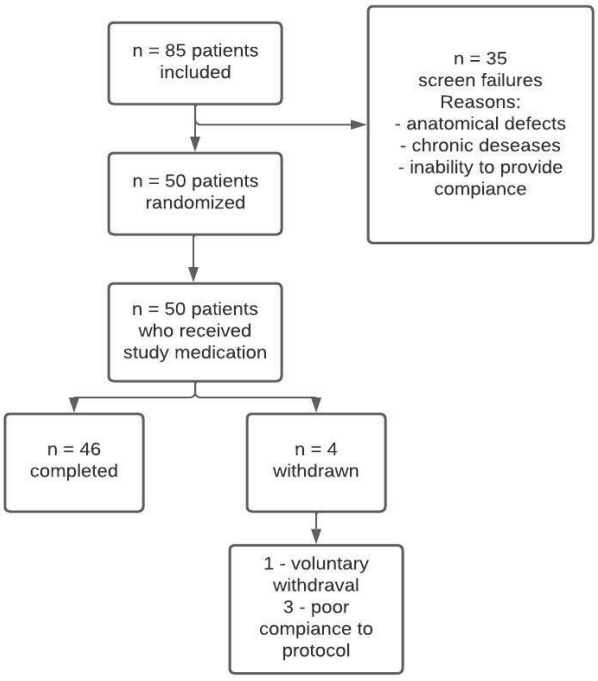

Fig. 1. Patient disposition.

Parents or persons authorized to do it by the laws of Ukraine of all patients gave informed consent to participate in the study. The safety assessment was carried out by the frequency of adverse drug reactions, changes in the results of clinical laboratory tests, electrocardiogram (ECG) and vital signs. According to the WHO, we defined an adverse drug reaction as "a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for the modification of physiologic function" and did not register all the adverse drug events.

Statistical processing of the results was performed using IBM IPSS Statistics 21.

Results of the study and their discussion. Of 85 patients screened, 50 patients were randomized to receive bilastine 10 mg, and 46 patients completed 4 weeks of treatment. Four patients in the treatment group were withdrawn before the end of the study for various reasons (fig.1).

The mean age of the patients was 10.21 years with a standard deviation (SD) of 2.06 years. In general, among them there were more female patients (n=28; 56.5 %) than male patients (n=18; 43.5 %), and the majority were patients aged 9–11 years (n=32; 69.5 %).

Most of the patients had no comorbidities (n=36; 78.2 %), other comorbidities included atopic dermatitis (n=6; 13.0 %) and adenoid vegetations (n=4; 8.6 %). Compliance among patients in the study group was 100 %.

The initial mean score for the TNSS questionnaire was 11.6 points (95 % CI: 10.3, 12.9).

The results of all planned monitoring of the TNSS score are shown in fig. 2.

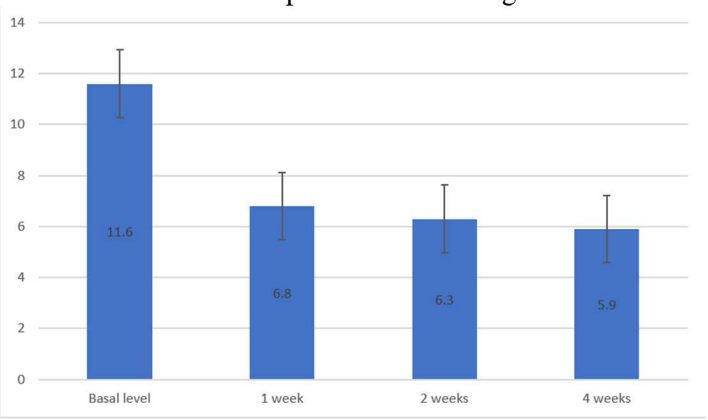

Fig. 2. Dynamics of the TNSS score in patients during 4 weeks of treatment

As can be seen from the above data, after one week of bilastine treatment (first control point), the total severity of symptoms by the TNSS scale decreased to 6.8 (95 % CI: 5.3, 8.3) points, or by 41.4 %. Subsequently, after 2 (second control point) and 4 (third control point) weeks of reception, the total severity of symptoms according to the TNSS scale was, respectively, 6.3 (95 % CI: 5.3, 7.3) and 5.9 (95 % CI: 4.8, 7.0) points. In general, at the end point of monitoring after 4 weeks, the reduction in severity of symptoms amounted to 49.1 %.

Analyzing the relief of the severity of symptoms in patients, it was determined that bilastine at a dose of 10 mg most reliably reduced the severity of sneezing (-1.5 points (95 % CI: 1.3; 1.7)), rhinorrhea (-1.2 points (95 % CI: 1.0; 1.4)), itching (-1.1 points (95 % CI: 0.9; 1.3)), to a lesser extent – eye symptoms (-0.9 points (95 % CI: 0 .8; 1.0) and nasal congestion (-0.6 points (95 % CI: 0.5; 0.7)), which is consistent with the mechanism of action of the active substance.

A total of 89.1 % of patients (n=41) treated with bilastine 10 mg were free of adverse drug reactions during the study. All adverse drug reactions were classified as mild and the most common was headache, recorded in 2 (4.3 %) cases. Other adverse drug reactions were: gastroenteritis (1 case, 2.2 %), somnolence (1 case, 2.2 %), fatigue (1 case, 2.2 %), and upper abdominal pain (1 case, 2.2 %). No moderate or severe adverse drug reactions were registered during the study.

The significance of the problem of allergic rhinitis is related not only to its growing prevalence, but also to the negative impact on the patient's quality of life and significant economic costs. Seasonal allergic rhinitis causes nasal congestion, rhinorrhea, itching, sneezing, headache, which ultimately disrupts sleep, leads to increased fatigue, reduced work capacity of adults and academic success in children. people of working age. Middle – age patients and children usually prevail among patients with seasonal allergic rhinitis, and this disease disrupts physical, psychological, and also social aspects of life. Choosing the optimal treatment method directly improves the quality of life of such patients, increases compliance and reduces the likelihood of complications.

The purpose of the study was to evaluate the effectiveness and safety of bilastine in relieving symptoms in patients aged 6-12 years with allergic rhinitis. In general, both parameters are significant for a modern antihistamine drug and determine the possibility of its wide use in the pediatric population for a long time (most allergic diseases in general and allergic rhinitis, in particular, require this) with a minimal risk of adverse events and sufficient effectiveness. This position is confirmed by the ARIA guidelines, which define the requirements for an ideal antihistamine drug, which, however, currently cannot be fully met by any of the existing active substances. Modern guidelines for the management of patients with allergic rhinitis categorically do not recommend the use of sedative antihistamines (first generation), however, the choice of a drug to prescribe among second generation drugs is not always easy.

Analyzing the results of the effectiveness of bilastine in reducing the severity of symptoms of allergic rhinitis in patients, a rapid statistically significant decrease in the TNSS symptom score at the first control point of administration (7 days) with a subsequent gradual decrease in the severity of symptoms at other control points is noticeable. Probably, the gradual decrease in the severity of symptoms in the following weeks is associated with several factors, namely: the absence of a recommendation to carry out elimination therapy (only in this way it was possible to assess the effectiveness of the pharmacological effect of the drug), which involves periodic contact with the allergen; a weaker effect of the drug on nasal congestion (this is a common problem of all oral antihistamines), which generally increased the number of points in patients with significant severity of this symptom; some percentage of patients resistant to taking oral antihistamines, requiring further treatment with intranasal corticosteroids and other drugs according to ARIA recommendations. In ARIA recommendations, effectiveness in nasal congestion and the like is one

of the requirements for effective oral antihistamines, which means they must have a concomitant anti-inflammatory effect. And in fact, H1 receptor blockers have been shown in studies to inhibit Th1, interferon, and interleukin-IL-2, increasing production of Th2, IL-4, and IL-13. However, in clinical practice, the anti-inflammatory effect is meant only empirically, therefore the choice of antihistamines should be based on effectiveness, safety, sedative effects and the possibility of increasing the dosage in case of ineffectiveness of standard doses. In general, data on the effectiveness of bilastine in reducing the severity of symptoms of allergic rhinitis in children correspond to similar data on effectiveness studies in adults [4, 6, 7].

With respect to safety, there did not appear to be any cause for concern following long-term administration of bilastine in children. The frequency of adverse events was low, expected according to the instructions of the drug and corresponding to the frequency of side effects when taking a placebo from similar data in the literature [8, 9]. In addition, absolutely all adverse events were mild and none of them led to the withdrawal of patients from the study.

Conclusions

1. After 4 weeks of management of allergic rhinitis in children aged 6–12 years by 10 mg bilastine, the reduction in severity of symptoms by TNSS scale amounted to 49.1 %.

2. Bilastine at a dose of 10 mg most reliably reduced the severity of sneezing (-1.5 points (95 % CI: 1.3; 1.7)), rhinorrhea (-1.2 points (95 % CI: 1.0; 1.4)), itching (-1.1 points (95 % CI: 0.9; 1.3)), to a lesser extent – eye symptoms (-0.9 points (95 % CI: 0 .8; 1.0) and nasal congestion (-0.6 points (95 % CI: 0.5; 0.7).

3. A total of 89.1 % of patients (n=41) treated with bilastine 10 mg were free of adverse drug reactions during the study. All adverse drug reactions were classified as mild and the most common was headache, recorded in 2 (4.3 %) cases.

4. Obtained data on the effectiveness and safety of taking bilastine in a dose of 10 mg for the treatment of allergic rhinitis in children 6–12 years old allow us to recommend this drug for long-term use.

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