



MAIN PROBLEMS AND MISTAKES IN THE TREATMENT OF ALLERGIC RHINITIS.

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ABSTRACT

Allergic rhinitis (AR) is a chronic pathological process, the main pathogenetic mechanism of which is inflammation caused by immunoglobulin E (IgE)—an indirect hypersensitivity reaction that develops as a result of allergens entering the nasal mucosa and manifesting sneezing, nasal congestion, itching and nasal discharge of various nature. Of the extranasal symptoms, complaints of poor sleep, lacrimation, redness of the eyes, stuffiness in the ears or hearing loss as a result of dysfunction of the auditory tubes, emotional instability are more often noted [1]. It is characterized by itching in the nose, difficulty breathing, sneezing and runny nose. Most often, the painful condition is associated with seasonal allergies.

The relevance of the problem

The occurrence of pathology is associated with hyperactivity of the immune system, which overreacts to the usual substances present in the surrounding air. The immune response to an irritant provokes a reaction from the nasal mucosa that is typical for cases of an attack by viruses and bacteria: itching, sneezing, exudate separation. Seizures are stopped with antihistamines. In the case of severe allergic rhinitis, a radical change of lifestyle or place of residence may be required. Due to the high prevalence in the world, the problem of allergic pathology in general and AR in particular does not lose relevance. AR is registered in 20-40% of cases, especially in developed and developing countries. In the USA alone, according to 2012 data, 19.1 million cases of AR were recorded in people over 18 years of age and 6.1 million in people under the age of 18 [2]. The costs of paying for days of disability, doctor visits, laboratory tests, treatment of AR itself and concomitant pathology, in particular bronchial asthma (BA), conjunctivitis, exacerbation of chronic rhinosinusitis, place a heavy economic burden on society [3]. We should not forget that the quality of life of allergic patients is significantly reduced. Patients with AR suffer from allergic symptoms on average 52.5 days a year [4]. The most painful symptom is nasal congestion. Violation of nasal breathing leads to the development of the main extranasal symptoms. About 48% of patients with seasonal AR and 68% with year-round AR experience problems falling asleep. The quality of sleep decreases. This is due to the fact that at night, due to the dominance of the

influence of the recurrent nerve, swelling of the nasal mucosa worsens [5]. There are often periodic awakenings during sleep, snoring with the possible development of obstructive apnea syndrome [6]. As a result, irritability, fatigue, decreased concentration and labor productivity against the background of slowing down psychomotor and mental processes [7].

Phases of allergic reaction and clinical manifestations

Aeroallergens are among the most relevant factors in the development of AR. Being in the form of a suspension in the inhaled air, they fall on the nasal mucosa and cause the development of an independent inflammatory process. The highest pollen content in the air is observed from mid-spring to early summer, when the majority (75%) of plants bloom. At the same time, the volume of sales of medicines for the treatment of allergic pathology increases sharply [10]. Due to the development of cross-reactivity between allergens in a number of patients in the summer months, symptoms of AR persist. An increase in the duration of the presence of pollen allergens in the air and the formation of pollen by plants against the background of global climate warming also negatively affects the condition of patients with AR [11]. After contact with the nasal mucosa, the causally significant allergen is processed in antigen-presenting cells, which subsequently present its individual peptides through a type II histocompatibility complex (MHC II) to naive T-lymphocytes. The latter differentiate into type 2 T-helpers (Th), which play a key role in the development of the IgE response. At the same time, other immune cells are recruited in the focus of inflammation, including eosinophils, basophils, mast cells secreting interleukins (IL) 4, 5, 6, 10 and 13. As a result, isotopic switching of B-lymphocytes into producing immunoglobulins, mainly class E, plasma cells is induced. Subsequently, IgE molecules bind to high affinity Fc receptors of mast cells and basophils. In addition, IdE is a CD23-receptor ligand on mature B-lymphocytes activated by x crofa ha x, eosinophils, follicular dendritic cells and platelets, upon binding to which IgE is transported [12]. Symptoms of AR develop with repeated exposure to a sensitizing allergen after its cross-binding with IgE, coupled with Fc receptors. This leads to the degranulation of mast cells and basophils, the release of histamine, tryptase, kininogenase, prostaglandins, leukotrienes and other active mediators of the inflammatory response. The late phase of the allergic response is characterized by eosinophilic chemotaxis. Degranulation increases the amount of biologically active substances in the mucous membrane of the nasal cavity, which contributes to increased vascular permeability, mucus secretion, irritation of nerve endings. Sensory nerve fibers are excited by non-specific stimuli, transmitting a signal to both afferent and efferent nerves (retrograde axon reflex). As a consequence, the secretion of neuropeptides (substance P, neurokinin A, etc.), reduction of smooth muscles, hypersecretion of mucus by goblet cells and an even greater increase in the permeability of small vessels [13]. Clinically, this is manifested by the main nasal symptoms of AR (sneezing, nasal congestion, itching and nasal discharge). Against the background of prolonged exposure to the allergen, the formation of cytokines increases, to which pro-inflammatory IL-1-beta, IL-6 and tumor necrosis factor alpha (TNF-alpha) are added. The inflammatory process is aggravated. As a result of neurogenic inflammation, the nasal mucosa acquires the property of hyperreactivity when exposed to non-specific stimuli unrelated to a significant allergen (cold or dry air, pungent odor, tobacco) AR symptoms occur. In the pathogenesis of AR, both Th1- and Th2-cytokines are released. Some of them, for example IL-6 and TNF-alpha, penetrating through the blood-brain barrier, are involved in cognitive disorders in AR, which is manifested by depression, anxiety or suicidal behavior [8].

Issues to be resolved

There are several problems associated with the diagnosis and treatment of AR. Firstly, patients with permanent symptoms of AR often do not seek medical help. For example, in the UK, only 18% of patients with chronic rhinitis, which bothered them during the previous two years, turned to a general practitioner, in France, 19% of 230 patients with typical symptoms of AR never sought medical help. Large-scale European studies have shown that 45-46% of

patients with the main clinical manifestations of AR have never undergone a comprehensive diagnosis for this disease [14]. This is due to the fact that patients do not realize the severity of an allergic disease and do not consider it possible to waste time on a visit to a doctor. They do not see a connection between nasal and extranasal manifestations of AR, they independently try to pick up symptomatic therapy drugs at the pharmacy. According to available data, in 2018 the majority of patients with AR (69.5%) purchased drugs based on their own preferences, without asking the opinion of a pharmacist. Only 14.9% of them were able to optimally choose medicines. 86.7% of patients explained their preferences for a certain medication during self-treatment with their own positive experience, 4.2% with recommendations from friends or family members, 3.5% with the provisions of the instructions for drugs, 3.5% with the cost of different groups of medicines. 2.8% of patients selected treatment by trial and error [15]. It should not be forgotten that patients with AR have a high risk of developing AD. The lack of drug control of AR, underestimation by patients of the severity of the condition can subsequently lead to the development of poorly controlled AD [16]. With self-treatment, only 6.3% of patients with AR and BA were able to make an adequate choice of drug therapy [15]. Secondly, the standard of diagnostic measures for the detection of allergic pathology, fixed in clinical recommendations, is not observed. As the analysis of the outpatient service of several polyclinics in Moscow showed, despite the presence of many detailed guidelines for the diagnosis and treatment of AR, in 2017, a comprehensive examination of patients with suspected AR was carried out only in 6.5% of cases. In 52.7%, the diagnosis was made empirically – based on complaints and anamnesis of the disease, skin tests were prescribed to 31.3% of patients, rhinocytogram – 10.2%. The indicators of total and specific IgE in blood serum were determined at 7.9% [17]. As a consequence, underdiagnosis of AR, an increase in the risk of disease progression, the possibility of AD joining. Thirdly, the treatment regimens of patients are violated. In accordance with ARIA recommendations, therapy of patients with AR and BA should be stepwise. According to data for 2017, antihistamines (AGP) were prescribed only in 27.3% of cases, and in 14% in the form of monotherapy, allergen-specific immunotherapy (ASIT) was carried out extremely rarely (1.9%). Leukotriene receptor antagonists were received by 9.7% of patients (together with either AGP or intranasal glucocorticosteroids (GCS)). Irrigation therapy was recommended in 35.6% of cases. There were no other barrier methods in the appointments. The leading positions were occupied by topical GCS – 77.8% of cases, and in 64% – in the form of monotherapy [18]. Finally, another problem is related to compliance with medical recommendations. Even with an adequate diagnosis to identify a significant allergen and well-chosen complex therapy, it is important that the patient takes the necessary medications daily in the indicated doses throughout the entire treatment period. In Germany, a study was conducted on the level of compliance with the intake of second-generation AGP (Erius 5 mg once a day) by adult patients with AR. It was found that with a duration of treatment of 41.6 days, 98.1% of patients followed the doctor's instructions. The combination of AR with BA had a negative effect on adherence to therapy, most likely due to the large number of medications taken. A low level of compliance was almost twice as common in patients with concomitant AD (3.1 vs. 1.8%). Sex and age characteristics, duration of the disease, severity of nasal symptoms and the level of quality of life at the beginning of therapy did not affect compliance with the treatment regimen. With high compliance, a good therapeutic effect of AGP was observed. The researchers also analyzed compliance with sublingual immunotherapy (SLIT, sublingual immunotherapy) with an average duration of 23.36 weeks. A high level of compliance was observed in 79.6% of cases, and in contrast to the treatment of AGP, gender (female), the severity of nasal symptoms and concomitant asthma positively influenced compliance with the treatment regimen. During the first year of SLIT therapy, 71% of patients registered high adherence, which decreased in subsequent years, which is typical for the treatment of many chronic diseases [19]. It follows from the above that

it is difficult to count on achieving the best result without close interaction between the doctor and the patient. The allergist must follow the algorithm of diagnostic measures, work in a team with an otorhinolaryngologist, if necessary with specialists of another profile - a pulmonologist, ophthalmologist, neurologist. When prescribing therapy, it is necessary to be guided by the latest consent documents, more often combine basic therapy with ASIT, which today is considered the only method capable of influencing all pathogenetic links in the development of the disease and forming immune tolerance to allergens (immunity to them is manifested in the absence of clinical symptoms of AR). The pharmaceutical industry, specializing in the production of drugs for ASIT, actively uses the latest achievements in the field of immunology and bioengineering. New routes of drug administration, new hypoallergenic recombinant allergen derivatives and immunogenic peptides, their combinations with monoclonal antibodies, etc. are proposed [20]. In addition, it is necessary to take into account the psychology of patients. Many of them believe that it is not necessary to treat AR, it is enough to periodically use decongestants to eliminate nasal congestion and travel outside the region of permanent residence during the flowering period of plants. To convince patients of the need for treatment, as well as to reduce the risk of complications, multiple reminders of possible negative prospects for the development of the allergic process, persistent recommendations to follow the prescribed treatment regimen and constant dynamic monitoring can help.

Treatment

For allergic rhinitis, step-by-step therapy is used, based on the severity of clinical symptoms. Upon reaching the control of symptoms, the volume of prescribed drugs and their dose decrease, in the absence of control, they increase. Antihistamines of the second generation belong to the first-line medicines, are prescribed at the first manifestations of the disease and are used as monotherapy or in combination with other medications, such as leukotriene receptor blockers, topical GCS. Ebastin (Espa-Bastin, Germany) is a second-generation AGP, available in tablet form of 10 and 20 mg. The effect of the drug begins 1-3 hours after administration. In numerous studies, the drug has demonstrated a favorable safety profile, high bioavailability. The rate of onset of the clinical effect does not depend on food intake. The drug is compatible with alcohol, does not affect the ability to drive a vehicle. Against the background of the use of the drug, there is a regression of all nasal manifestations with seasonal and year-round AR. In addition to selective binding to H1 -histamine receptors, ebastin reduces the release of pro-inflammatory cytokines, such as TNF-alpha, granulocyte-macrophage colony stimulating factor, IL-8, which additionally provides an anti-inflammatory effect and a decrease in the chemotaxis of granulocytes, including eosinophils, into the nasal mucosa. This double action of modern second-generation AGPS more effectively contributes to the regression of exacerbation of the chronic inflammatory process in AR, and consequently, the prevention of complications and the addition of other comorbid conditions.

Conclusion

The administration of patients with AR is considerably a ball-bust task. It is all-important to appropriate into explanation the characteristic characteristics of patients, supervise their deed of examination recommendations, remuneration consideration to extranasal manifestations of the affliction and contemplate each situations of characteristic and therapeutical magnitudes

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