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Local Therapy for Allergic Rhinitis In Children

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The article describes the current view of the topical treatment of allergic rhinitis (AR). Today in the world there is an increase in the incidence of AR, its prevalence in different countries of the world ranges from 4% to 32% of the population, in Uzbekistan – 10-24%. Most often, the disease debuts in the first half of life. AR is often associated with bronchial asthma, which is detected in 15-38% of patients with AR. Recently, the attention of researchers has been focused on local AR, which is diagnosed in patients with negative skin and serum tests, when AR is confirmed by provocative tests with significant allergens for the patient with the detection specific IgE in the nasal cavity. When conducting local therapy, nasal sprays are used to eliminate allergens and restore the protective role of epithelial barriers, decongestants are prescribed in a short course, and topical antihistamines are used to relieve allergic inflammation. The main drugs for the treatment of moderate to severe AR are topical glucocorticosteroids: mometasone furoate, azelastine, f luticasone furoate, f luticasone propionate, beclomethasone dipropionate and budesonide. A good effect in the treatment of infectious-allergic rhinitis was obtained with saline solutions.

Allergic rhinitis (AR) is a disease characterized by IgE-mediated inflammation of the nasal mucosa (which develops under the influence of allergens) and the presence of at least two of the following symptoms daily for an hour or more: nasal congestion (obstruction), nasal discharge (rhinorrhea), sneezing, itching in the nasal cavity. AR is often combined with other allergic diseases such as allergic conjunctivitis, atopic dermatitis, and bronchial asthma [1-8]. The prevalence of AR in different countries of the world is 4-32%, in Russia – 10-24% [7, 9]. Attention is drawn to the low incidence of AR patients in the early stages of the disease and late diagnosis. Most often, the disease debuts in the first half of life. AR is often associated with asthma, which is detected in 15-38% of AR patients [9]. At the same time, 55-85% of patients with ASTHMA have AR symptoms [10, 11]. AR is a widespread disease [6]. The average prevalence of AR symptoms is 8.5% (1.8- 20.4%) in 6-7-year-olds and 14.6% (1.4-33.3%) in 13-14-year-olds (International Study of Asthma and Allergy in Childhood– ISAAC). According to the results of a study conducted according to the GALEN protocol (Global Allergy and Asthma European Network – Global Network on Allergy and Asthma in Europe) in 2022-2024, the prevalence of AR symptoms in adolescents aged 15-18 years was 34.2%, with an in-depth examination in 10.4% of cases, the diagnosis of AR was confirmed, which largely prevails working on official statistics [5-7]. Since similar studies have been conducted, there has been an increase in the observed prevalence of AR worldwide [5]. The leading step in the treatment of AR is to determine the phenotypes and endotypes of rhinitis [7, 12]. The phenotype is determined by the leading clinical picture, while the endotype is determined by the underlying pathophysiological mechanisms [7, 12]. AR usually differs from non-allergic rhinitis by the presence of positive skin screening tests with high levels of serum-specific IgE [7]. Recently, there has been a growing interest in local art. Local AR is diagnosed in patients with negative skin and serum tests. The medical history of these patients is similar to the medical history of children with AR, with this variant of the course of AR, patients show a positive response to local provocation by allergens and/or specific IgE in the nasal cavity to various allergens [11]. Non-allergic rhinitis also has a number of phenotypes and endotypes, including infectious, medicinal, hormone-induced, and idiopathic rhinitis [7, 12]. AR–like symptoms can occur as a result of structural or mechanical problems such as choan atresia, adenoid hypertrophy, septal curvature, as a result of systemic diseases such as cystic fibrosis, primary ciliary dyskinesia, eosinophilic granulomatosis, and other diseases. Often, patients may suffer from AR with a mixed phenotype and endotype [7]. In 2015, the PRACTALL report "Rhinitis Phenotypes and Endotypes: Diagnosis and Treatment" was published, the result of a consensus reached by experts from the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma and Immunology [6]. The PRACTALL report describes the phenotypes and endotypes of rhinitis, presents approaches to its

diagnosis and treatment based on the phenotype/endotype [6, 7, 9]. The treatment concept is based on the control of the clinical picture and covers all variants of rhinitis. The proposed classification based on phenotype/endotype promotes the transition to stratified and personalized medicine in the field of rhinitis [9]. The document is intended for practicing physicians. Let's consider the main positions outlined in it. Rhinitis is traditionally divided into three main clinical phenotypes: allergic, infectious, and non-allergic/non-infectious. A number of patients may have a combined (mixed) course. Phenotypes/endotypes do not have clear boundaries, are dynamic, and are able to move from one to another, which makes it difficult to clearly systematize [6]. It is possible that classification based on endotypes will to some extent explain the variability of both clinical manifestations and response to treatment. But until we learn how to identify all the endotypes that lead to the development of a particular phenotype, this problem cannot be solved [6].

Classifying rhinitis based on phenotypes, various clinical criteria can be used, in particular, age at the time of onset of the disease, its severity, external manifestations and provoking factors. Cluster approaches are also being developed. However, unlike the concept of AD phenotyping, the concept of rhinitis is subject to refinement [8]. The need to perform and optimize cluster analysis is due to the increasing variety of symptoms of rhinitis. In addition, each group of patients probably reacts differently to the proposed treatment options. In this sense, promising therapies will not be an exception [7]. Phenotypes are taken into account: • severity of the disease – mild, moderate/severe, severe combined upper airway disease (SCUAD); • duration of the course (acute or chronic, intermittent or persistent); • Time pattern (seasonal or year-round); • the predominant symptom (rhinorrhea or nasal congestion); • ability to control the disease (amenable/uncontrollable); • trigger factor, if known (allergen, infectious agent, drug, etc.); • response to specific treatment (intranasal glucocorticosteroids [7]. Comorbid pathology (respiratory allergy, rhinoconjunctivitis) is additionally taken into account or a combination of AR and asthma in the same patient. Phenotypes can be combined with some endotypes. Their definition is based on pathomorphological (non-allergic rhinitis with eosinophilia syndrome) or pathophysiological (AR) symptoms. It is also possible to identify relevant biomarkers. Phenotypes are quite clearly defined, as well as their combination with various endotypes [7]. AR diagnosis It is necessary to carefully collect allergy history data. The clinical manifestations of the disease are being evaluated. Laboratory diagnostics includes: clinical blood analysis, in vivo allergodiagnostics (setting up scarification skin tests, conducting a prik test with various types of allergens: house dust mites (Dermatophagoides pteronyssinus and Dermatophagoides farinae species), pollen, epidermal, mold spores, food). In vitro allergodiagnostics (determination of specific class E immunoglobulins). To date, the most accurate definitions of immunoglobulin E are the ImmunoCAP method and the Fouquet method. Instrumental examination methods are performed: rhinoscopic, otoscopic examination, pharyngoscopy, endoscopic examination of ENT organs, cytology of nasal secretions (sometimes it can be very informative, although it is not included in the main laboratory examination), examination of the microflora of the nasal cavity, nasal provocative tests (rarely performed in children), rhinomanometry, computed tomography of the paranasal sinuses - according to indications, an ophthalmological examination is performed according to indications (if the eyes are involved in allergic inflammation) [7, 9, 13, 14]. In the 1990s, instead of allergen extracts, it was proposed to use separate highly purified allergenic molecules (allergen components). Individual allergenic proteins were called allergocomponents. An allergenic molecule (component, allergen; protein or glycoprotein) is a molecule derived from the allergen source, which is determined by SiGe antibodies. Allergocomponents can be obtained from natural sources (natural highly purified allergens) or using molecular biological methods (recombinant allergens) [7, 12, 15]. Allergocomponents are divided into "major" – the main allergens and "minor" – secondary, depending on the frequency of occurrence in the population responding to this source. "Major" – allergenic molecules, antibodies to which are found in more than 50% of patients in the population with allergies to the same source, "minor" – in less than 10% of patients. "Major" allergenic components are resistant to heat and more immunogenic. They are large in size and are contained in this allergen in larger quantities. "Minor" allergenic molecules are smaller in size and less immunogenic, which are usually contained in smaller quantities in the allergen, but are present in many allergens, sometimes not closely related, providing cross–allergy [7, 15, 16]. Molecular diagnostics makes it possible to increase the accuracy of the diagnosis and prognosis of allergic diseases, more accurately determine the indications for allergen-specific immunotherapy and the prognosis of its effectiveness, and individualize the appointment of elimination measures and diets [12, 15].

Differential diagnosis of AR To exclude asthma, it is necessary to determine the parameters of the function of external respiration and a test with a bronchodilator for the reversibility of bronchial obstruction. In doubtful cases,

a physical activity test is performed. If obstructive sleep apnea is suspected, a polysomnography is performed. Anterior rhinoscopy and otoscopy are necessary for symptoms of hearing loss. Additional studies are performed under the supervision of an ENT doctor: tympanometry, acoustic impedance measurement, and, if necessary– consultation with a sign language specialist [7]. Differential diagnosis is performed with diseases such as infectious rhinitis, rhinosinusitis, choan atresia or stenosis, immunodeficiency, encephalocele, adenoid vegetation, foreign body, cystic fibrosis, primary ciliary dyskinesia, coagulopathy, systemic autoimmune diseases (Wegener's granulomatosis) [7]. Clinical manifestations of AR in children: mucous discharge from the nasal passages, sneezing, itchy nose (the so-called "allergic salute"), sometimes itchy palate and pharynx, itchy ears, nasal obstruction, mouth breathing, changes and nasal nasal tones, sniffling, snoring, apnea. Wet cough, mainly in the morning (more typical for younger children), "allergic circles" under the eyes, decreased sense of smell, ear pain, chronic exudate in the middle ear and eustachian tube dysfunction, prolonged and frequent respiratory tract infections [7, 9]. All these clinical manifestations of AR greatly reduce the quality of life of patients: patients experience increased fatigue, weakness, headache, irritability, sleep disorders, impaired concentration, decreased academic performance at school, limited physical activity, lack of sense of smell, the need for frequent use of a handkerchief, maceration of the skin under the nose, physical suffering – excruciating desire scratching the nose, painful appearance, emotional suffering [6, 7, 9]. Additional symptoms of AR develop due to excessive nasal secretions, impaired drainage of the paranasal sinuses and patency of the auditory (Eustachian) tubes. Manifestations may include coughing, decreased and lack of sense of smell; irritation, swelling, hyperemia of the skin above the upper lip and at the wings of the nose; nosebleeds due to forced expectoration; sore throat, coughing (manifestations of concomitant allergic pharyngitis, laryngitis); pain and cracking in the ears, especially when swallowing; hearing impairment (manifestations of allergic tubositis). Among the common nonspecific symptoms observed in AR are weakness, malaise, irritability; headache, fatigue, impaired concentration; sleep disorders, depressed mood; rarely fever [7, 9]. The AP classification is presented in Table No. 1. Local AR therapy in children First of all, they consider moisturizing agents and barrier drugs that help eliminate the allergen from the nasal mucosa and restore the protective function of the epithelial barrier. Moisturizers help to moisturize and cleanse the nasal mucosa and have proven effectiveness. Rinsing the nasal cavity with saline solution or sterile seawater solution is an inexpensive method of treating rhinitis with low but proven effectiveness [7]. Currently, Nasaval and Aqua Maris Ectoin nasal spray are considered among the drugs used to eliminate allergens. They create a natural barrier between the nasal mucosa and various aero-allergens and pollutants. There is also a mechanical means of protecting the nasal mucosa – an invisible respirator. It contains a filter material, a cellulose micro-sponge. An invisible respirator is inserted into the anterior nasal passages and prevents the penetration of allergens to the nasal mucosa: nasal filter "Nose Mask Kit" and nasal filter "Hit Stopper". Topical antihistamines are widely used for the treatment of arthritis today – Allergodil (azelastine) (nasal spray for children from 6 years old) for 1 instillation 2 times a day, from 12 years old – 2 instillations 2 times a day, Tizine Alert (levocabastine) (nasal spray from 6 years old) for 2 instillations 2 times (up to 4 times) per day. Topical antihistamines have a number of advantages and positive properties: the absence of side effects that may occur with their systemic use, the easy achievement of high local concentrations of the drug on the mucosa, the rapid onset of therapeutic action (10-15 minutes), significantly lower single doses than when using similar systemic drugs. In the treatment of AR in children with a short course, it is possible to use decongestants – naphazoline (Naphthyzine, Sanorin), oxymetazoline (Nazivine, Nazol, Afrin), xylometazoline (Xymelin, Otrivine, Foranos, Xylometazoline, Xylene, Tizine Xylo), tuaminoheptan (as part of Rhinofluimucil), phenylephrine hydrochloride (Nazolkids), irifrin (as part of Polydexes). Decongestants are used for up to 5 days in severe and moderate cases of the disease to improve the quality of life of patients and for the best effect from the use of topical glucocorticosteroids [2, 3]. It is convenient to use a combined topical preparation containing an antihistamine and a decongestant – vibrocil (dimethinden maleate and phenylephrine), nasal spray – for children from 6 years old, with a course of no more than 2 weeks. Nasal drops for children from 1 year old – 1 drop 2 times a day, gel for children from 1 year old 2 times a day. For children under 1 year of age, nasal drops are prescribed 1 drop once a day. The main drugs used to treat moderate and severe AR are topical glucocorticosteroids: mometasone furoate (Nasonex, Momat Reno, Nosephrine), Momat Reno Advance– a combined drug of mometasone furoate with azelastine from the age of 2, fluticasone furoate (Avamis) from the age of 2, fluticasone propionate (Nazarelle, Flixonase) from 4 years old, beclomethasone dipropionate (Nasobek) from the age of 6, budesonide (Tafennazal) from the age of 6 [10]. The mechanisms of action of topical glucocorticosteroids are widely known: they simultaneously inhibit the early and

late phases of allergic inflammation and inhibit all symptoms of AR: sneezing, itching, mucus secretion from the nasal passages, nasal obstruction [1]. It is necessary to remember about the side effects that can occur from prolonged or uncontrolled use of topical nasal corticosteroids: symptoms of irritation of the nasal mucosa (burning, sneezing), nosebleeds, atrophic processes in the nasal mucosa, its dryness, nasocandiasis of the pharynx and esophagus, hoarseness and cough [1]. AR is often accompanied by infectious complications. For infectious complications of AR, Polydex with phenylephrine (decongestane) has been used since the age of 2.5 years. It consists of: dexamethasone sodium metasulfobenzoate, neomycin sulfate, polymyxin B sulfate, phenylephrine. Sialor (a silver-based drug) is also used from 1 month of life and framecitin sulfate (Isofra, Tramicent) from 1 year [6]. A very good effect for the treatment of infectious allergic rhinitis is provided by Rhinorin (evidence level 1++A) [8]. The preparation contains isotonic saline solution and benzalkonium chloride (antiseptic). Isotonic saline solution eliminates viruses, bacteria, and allergens from the nasal mucosa and helps to normalize its function and the rheological properties of mucus. Benzalkonium chloride has an antiseptic effect. The mechanism of action of benzalkonium chloride is to disrupt the integrity of the cell membranes of microorganisms. It has a wide range of antimicrobial and antifungal activity, is non-addictive, non-toxic, and has no systemic effect. Rhinorin reduces the manifestations of the local inflammatory process in the nasopharynx [8]. Rhinorin is used in children for 1-3 instillations 1-3 times a day. The drug is approved for use by pregnant and lactating women. Rhinorin can also be used to eliminate nasal congestion before using topical glucocorticosteroids. There is a rating scheme for assessing the level of evidence. Evidence levels: Description 1++ – high-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs) or RCTs with a very low risk of systematic errors. 1+ – well-conducted meta-analyses, systematic or RCTs with a low risk of systematic errors. 1 – Systematic meta-analyses or RCTs with a high risk of systematic errors. 2++ – High-quality systematic reviews of case-control or cohort studies. High-quality reviews of case-control studies or cohort studies with a very low risk of confounding effects or systematic errors and an average probability of causation. 2+ – well-conducted case-control studies or cohort studies with an average risk of confounding effects or systematic errors and an average probability of causation. 2- Case–control studies or cohort studies with a high risk of confounding effects or systematic errors and an average probability of causation. 3 – non-analytical studies (for example, case descriptions, case series). 4 – expert opinion [4, 7].

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