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Rhinitis in children

Nieżyt nosa u dzieci

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ABSTRACT: Rhinitis (RN) is inflammation of the nasal mucous membrane, manifested by impaired patency, pruritus, sneezing and the presence of secretions. Depending on the mechanism of creation of an inflammatory reaction, RN is divided into: (1) allergic rhinitis (AR) and (2) nonallergic rhinitis (NAR), and in case of their overlap, it is said to be (3) mixed (MR). The basis for the diagnosis of NN are: physical examination and interview (including ENT) and properly selected auxiliary research. The fundamental approach in RN in children is: education of patients and their parents, avoiding exposure to irritants (including allergens), nasal irrigation, air humidification and proper hydration of the child, and pharmacotherapy, and in selected cases of ARN, also allergen specific immunotherapy. The basis of pharmacotherapy in RN are intranasal glucocorticoids (dnGKS) and second-generation antihistamines, although their efficacy in NAR is lower than in AR. Due to the high incidence and adverse consequences, such as: decreased quality of life, sleep and mood disorders, deterioration in school education and relationship with other diseases, including: asthma, adenoid hypertrophy, conjunctivitis, chronic inflammation of paranasal sinuses and otitis media, RN is an important clinical problem. It is necessary to further investigate the issue to better understand this problem and to avoid its negative consequences, especially in the paediatric population.

KEYWORDS: allergic rhinitis, classification, diagnosis, nonallergic rhinitis, rhinitis, treatment

STRESZCZENIE: Nieżyt nosa (NN) to stan zapalny błony śluzowej nosa, objawiający się upośledzeniem jego drożności, świądem, kichaniem i obecnością w nim wydzieliny. W zależności od mechanizmu powstawania reakcji zapalnej NN dzieli się na: (1) alergiczny nieżyt nosa (ANN) i (2) niealergiczny nieżyt nosa (NANN), a w przypadku ich nakładania się mówi się o (3) NN mieszanym. Podstawą rozpoznania NN są: badanie podmiotowe i fizykalne (w tym laryngologiczne) oraz właściwie dobrane badania pomocnicze. Zasadniczym postępowaniem w NN u dzieci jest: edukacja chorych i ich rodziców, unikanie ekspozycji na czynniki drażniące (w tym alergeny), płukanie jam nosa, nawilżanie powietrza i właściwe pojenie dziecka oraz farmakoterapia, a w wybranych przypadkach ANN, również swoista immunoterapia alergenowa. Podstawą farmakoterapii w NN są glikokortykosteroidy donosowe (dnGKS) i leki antyhistaminowe drugiej generacji, choć ich skuteczność w NANN jest mniejsza niż w ANN. Z uwagi na dużą częstość występowania oraz niekorzystne następstwa, takie jak: obniżenie jakości życia, zaburzenia snu i nastroju, pogorszenie wyników w nauce i związek z innymi chorobami, w tym: astmą, przerostem migdałka gardłowego, zapaleniem spojówek, przewlekłym zapaleniem zatok przynosowych i zapaleniem ucha środkowego, NN stanowi istotny problem kliniczny. Konieczne jest prowadzenie dalszych badań, celem większego zrozumienia tego problemu oraz uniknięcia wystąpienia jego negatywnych następstw, zwłaszcza w populacji dziecięcej.

SŁOWA KLUCZOWE: alergiczny nieżyt nosa, diagnostyka, klasyfikacja, leczenie, niealergiczny nieżyt nosa, nieżyt nosa

LIST OF ABBREVIATIONS USED IN THE PAPER

AR – allergic rhinitis
ARIA – Allergic Rhinitis and its Impact on Asthma
cIgE – total serum immunoglobulin
E (IgE) concentrations INS – intranasal corticosteroids
NPT – nasal provocation testing
EPOS – European Position Paper on Rhinosinusitis and Nasal Polyps
LAR – local allergic rhinitis
NAR – non-allergic rhinitis
NARES – non-allergic rhinitis with eosinophilia syndrome
ARS – acute rhinosinusitis
AOM – acute otitis media
PSTR – Polish standards for the treatment of rhinitis
SPT – skin prick tests
CRS – chronic rhinosinusitis
SCIT – subcutaneous immunotherapy
SLIT – sublingual immunotherapy
sIgE – specific class E immunoglobulins concentration
AIT – allergen-specific immunotherapy
OM – otitis media
RS – rhinosinusitis

DEFINITION OF RN

Rhinitis (RN) is defined as inflammation of the nasal mucosa, manifested as impaired patency, itching, sneezing and nasal discharge (anterior or posterior nasal drip), whereby these symp-

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toms should occur for more than an hour a day for at least two consecutive days [1].

CLASSIFICATION OF RHINITIS – ETIOPATHOGENESIS AND SYMPTOMS

The occurrence of rhinitis is a sum of many mechanisms which is reflected in the ARIA classification of rhinitis (Allergic Rhinitis and its Impact on Asthma), shown in Tab. I. [1, 2]. The main classification in this division is: (1) allergic rhinitis (AR) and (2) non-allergic rhinitis (NAR). In the paediatric population, AR coexisting with NAR, called (3) mixed RN, is frequently found in more than half of children with AR [2, 3].

Allergic rhinitis (AR)

AR is an IgE-mediated rhinitis caused by allergen exposure. In addition to sneezing, nasal itching, nasal discharge and nasal obstruction, in AR there are frequent ocular symptoms such as ocular pruritus, dacryorrhea, conjunctivitis [2, 3]. In children up to 3 years of age, the progress of AR is often oligosymptomatic and the symptoms – if they occur – are less specific than in older children and adults. In this youngest age group, the only symptom may be nasal discharge or obstruction, which is often confused with the symptoms of infectious RN. However, it should be noted that nasal congestion as a single symptom is rarely associated with allergies and therefore requires accurate differential diagnosis [2]. If symptoms persist for more than 2 weeks, a cause other than infection should be considered. [1, 2].

Depending on the time of incidence of symptoms, AR can be divided into: (1) periodic AR (periodic, intermittent), with symptoms occurring for less than 4 days a week or less than 4 weeks, and (2) chronic AR (permanent, continuous, persistent), with symptoms occurring for more than 4 days a week and for more than 4 weeks [4, 2]. According to the Polish Standards for Treatment of Rhinitis (PoSLeNN) from 2013, this classification is more adequate than the existing division of AR into seasonal and perennial, depending on the time of allergen exposure. [2].

However, the recalled classification was restored in the revision of the 2016 ARIA recommendations in view of the fact that most scientific studies still used it [5]. In periodic AR, the most common symptoms are sneezing, nasal itching and runny nose, with a less intense sensation of obstruction, while chronic AR is more commonly characterised by nasal congestion, coughing, and general symptoms (fatigue, weakness, sleep disorder). The factors causing periodic AR are often mould antigens and pollen antigens, while chronic AR is usually caused by allergens that occur in the patient's daily life (e.g. mites, house moulds, animal allergens) [2].

Furthermore, AR can be divided into: (1) mild AR, in which the condition does not have an adverse impact on the quality of life, performance of daily activities, leisure and/or sports activities, and does not cause sleep disorder or deterioration of academic performance (or at work), and (2) moderate/severe AR, in which the symptoms carry at least one of the above-mentioned implications [1].

Nonallergic rhinitis (NAR)

NAR is a group of rhinitis whose common feature is the absence of atopy (negative results of skin prick tests, measurements of specific IgE concentration and nasal allergen challenge) and the occurrence of IgE-independent and Th2 lymphocyte-dependent reactions. PoSLeNN divides NAR in children into 7 types: infectious (more common in children), occupational, hormonal, drug-induced, gustatory (associated with nutrients), NAR with eosinophilia syndrome (NARES) and vasomotor RN [2].

Infectious RN

Due to the anatomical continuity of the nasal mucosa and paranasal sinuses, the coexistence of inflammation is usually observed within their borders, hence currently, tend to speak of rhinosinusitis [1, 2, 4].

In children, rhinosinusitis is defined as the incidence of at least two of the following four symptoms: (1) impaired nasal patency, (2) nasal discharge (anterior or posterior nasal drip), (3) facial pain or pressure and (4) cough; whereby at least one of the first two symptoms must be present (nasal congestion and/or anterior/posterior nasal drip) [4].

In terms of duration, RS can be divided into: (1) acute (ARS), lasting less than 12 weeks, with symptom-free periods in case of relapse, and (2) chronic (CRS), with or without polyps, lasting at least 12 weeks, with partial relief of symptoms. In addition, the course of CRS may include exacerbations [4]. Medical history should include questions about allergy symptoms (i.e. sneezing, runny nose, itchy nose, itchy and watery eyes) [4].

ARS includes viral ARS (common cold) and post-viral ARS, while a small percentage of patients with post-viral ARS will develop bacterial ARS.

85–98% of acute rhinitis in children are viral infections, usually in the course of upper respiratory tract infection [2].

Viral ARS persists up to 10 days, while acute post-viral ARS is defined as the exacerbation of symptoms after 5 days or the persistence of symptoms for more than 10 days but less than 12 weeks [4].

Bacterial ARS should be suspected when at least 3 of the following symptoms occur: (1) discoloured secretion (with a predominance of one side of the nose) and purulent nasal discharge, (2) acute localized pain (with a predominance of one side), (3) fever (> 38°C), (4) increased OB/CRP, (5) so-called 'double-sickening' (i.e. repeated deterioration after initial improvement) [4].

According to PoSLeNN, 10% of children with viral rhinitis will progress to bacterial infection. Children particularly at risk of developing secondary bacterial rhinitis include patients with atopy, anatomical abnormalities of the upper respiratory tract (e.g. cleft palate), patients with cystic fibrosis and immunodeficiency. In these children, the main pathogens causing rhinitis are Staphylococcus aureus and Pseudomonas aeruginosa. In the case of infection with streptococci from the PBHA group, there may develop primary bacterial rhinitis. It should be noted that unilateral purulent nasal

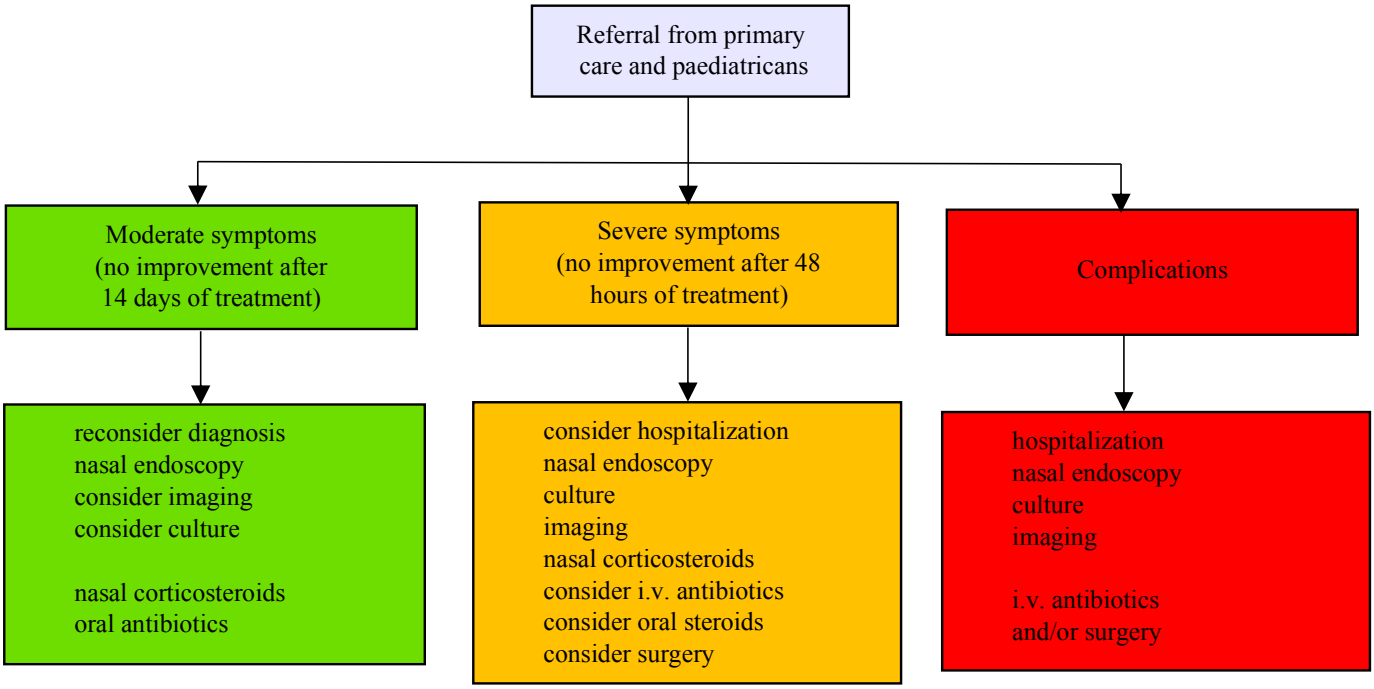

Fig. 1. Treatment regime for children with ARS in basic health care conditions according to EPOS, modified [4, cf.: 63].

discharge in a child should always raise a suspicion of the presence of a foreign body in the nose [2].

Non-infectious NAR

There are several etiopathologically different types in this group. Non-allergic rhinitis with eosinophilia syndrome (NARES) is defined as a set of chronic nasal symptoms (sneezing, nasal discharge, itching, and sometimes also loss of smell), with the presence of eosinophilia in nasal secretion, and in the absence of confirmation of allergy [1, 2]. According to the ARIA paper from 2008, NARES does not constitute a separate disease entity, but rather a subtype of idiopathic rhinitis, distinguished by a good response to intranasal glucocorticoids (INS) [1, 2]. It is rare in children, accounting for about 5% of rhinitis [2].

Drug-induced rhinitis can be caused by many substances, including acetylsalicylic acid and other nonsteroidal anti-inflammatory drugs, reserpine, guanethidine, phentolamine, methyldopa, angiotensin-converting enzyme (ACE) inhibitors, α-adrenergic antagonists, chlorpromazine, oral contraceptives and β-blockers used for conjunctival sac, whereby most of these drugs are rarely used in children [1, 2]. However, rhinitis has been also diagnosed in infants whose mothers have taken antihypertensive, antidepressant or narcotic drugs during pregnancy [2]. In the paediatric population, the so-called rhinitis medicamentosa is of importance. It is a rhinitis caused by the abuse of nasal decongestants [1, 2]. Occupational RN in children is rare, usually as a result of exposure to irritants during apprenticeships [2]. Hormonal rhinitis may occur in children during puberty [2]. Gustatory rhinitis usually occurs after eating hot or spicy foods containing capsaicin [1, 2].

In the 2008 ARIA classification [1], the term 'vasomotor rhinitis' was abandoned, since 'vasomotor' symptoms may occur in both AR and NAR. The term 'vasomotor rhinitis' is often equated with idiopathic RN, which – according to the ARIA classification of 2008 – is defined as a state of hyperresponsiveness of the upper respiratory tract in response to nonspecific environmental triggers, such as changes in ambient temperature and humidity, or exposure to tobacco smoke and strong odors [1]. PoSLeNN also identifies both of the above terms (vasomotor and idiopathic RN) with the term non-allergic rhinopathy, defined as the occurrence of chronic symptoms of rhinitis in the absence of nasal eosinophilia as well as confirmed immunological and infectious an etiology [2].

EPIDEMIOLOGY

The incidence of rhinitis in children below 6 years of age varies significantly between studies, from 2.8% to even 42.7%, depending on the definition and the assessed age groups. A similar incidence of RN is reported in school children [3]. According to PoSLeNN, children aged 1–6 may experience even 3–8 episodes of rhinitis per year, and the frequency of rhinitis symptoms is estimated at 22–46% in the 6- and 7-year-olds group and at 22–45% in the 13- and 14-year-olds [2]. In the ECAP questionnaire survey, the frequency of rhinitis in children aged 6 –7 was estimated at 37.8%, and in children aged 13 –14 it was estimated at 34.5%. [6]. The incidence and severity of AR depend on age, with the highest incidence among school-aged children. The average age at which the onset of symptoms is noted is 10 years, and the peak incidence is observed in the age group of 13. –19 [7].

The incidence of rhinitis is comparable for both sexes. A significantly higher incidence of rhinitis is observed in urban agglome-

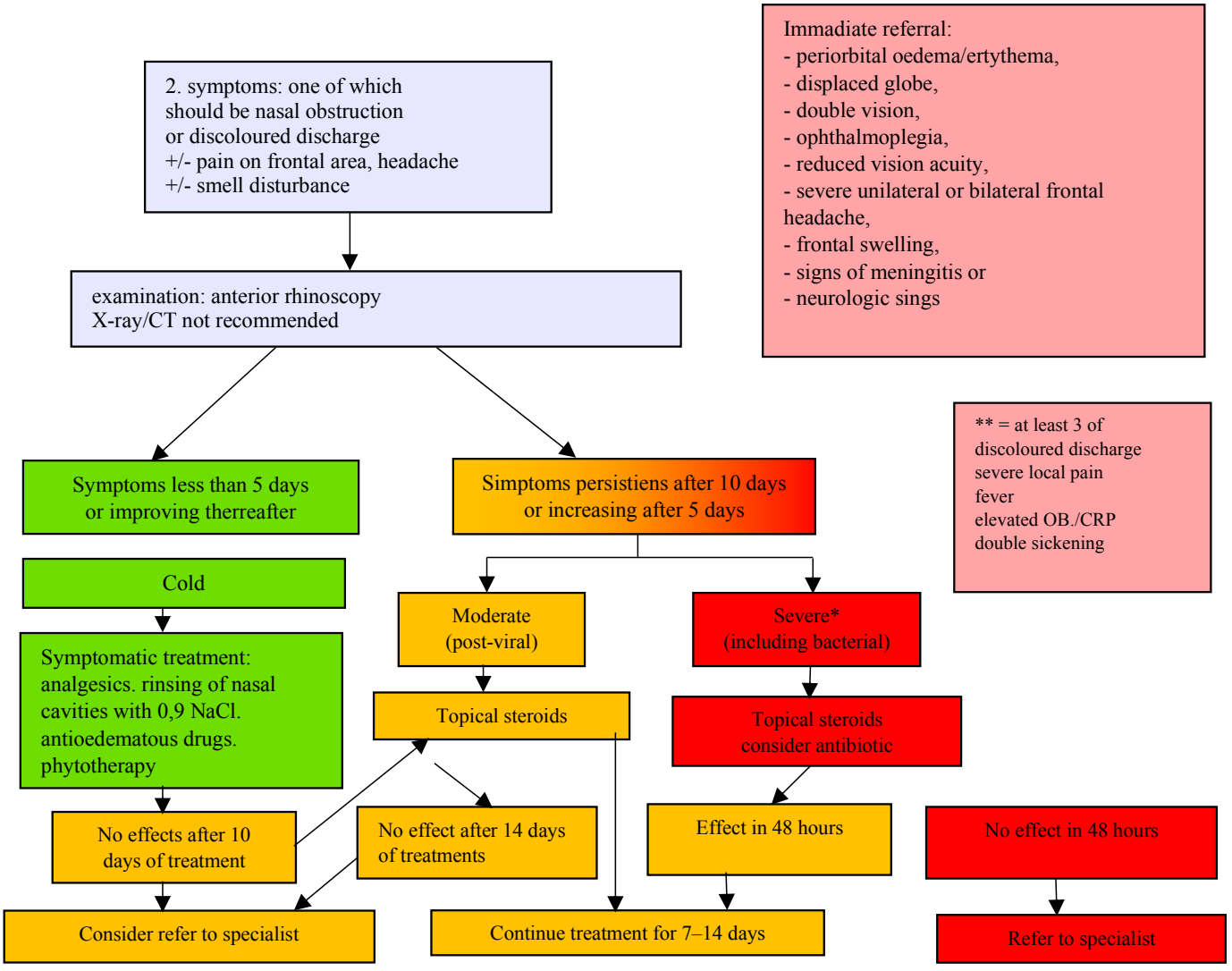

Fig. 2. Treatment regime for children with ARS for otolaryngology specialists according to EPOS [4, 63].

rations compared to people from rural areas [6]. In Poland, AR is diagnosed in 14–37% of younger children and 18–42% of older children, with an increasing incidence [2]. The ECAP study revealed that the incidence of AR symptoms was 23.6% in the group of children aged 6 –7 and 24.6% in children aged 13 –14 [6].

RISK FACTORS

Rhinitis pathogenesis is multifactorial, involving genetic and environmental factors [1, 2]. The main risk factors for AR in children are: positive family history of atopy, male sex, low birth weight, delivery in spring or autumn, caesarean delivery, maintenance of elevated serum IgE, positive result of allergy skin tests, early feeding with cow's milk, early exposure to solid foods, exposure to some aeroallergens, early infection with certain viruses, exposure to tobacco smoke and air pollution [2, 3, 8, 9]. In children under 2 years of age, the initial cause of AR is allergy to house (mites, animal dander) and food allergens, although food allergens are thought to rarely cause AR. Pollen allergy usually occurs after the second pollen season in a child' life [2]. Many factors can contribute to the pathogenesis of NAR, and some of them, such as dietary factors, exposure to air pollution and tobacco smoke are found both in AR and NAR. Establishing the risk factors characteristic of NAR is difficult due to the frequent overlap of AR and NAR in the paediatric population (so-called mixed rhinitis) and heterogeneity of the NAR group [10]. According to Deliu et al., maternal smoking and lack of breastfeeding are a stronger risk factor for NAR than for AR [11].

DIAGNOSTICS

The basis for diagnosing rhinitis are medical history (also family history), physical examination and properly selected diagnostic tests [2].

Clinical history

Clinical history should particularly involve the most common symptoms of RN, i.e. nasal discharge, obstruction, sneezing and itching of the nose, as well as other symptoms such as epistaxis, loss of

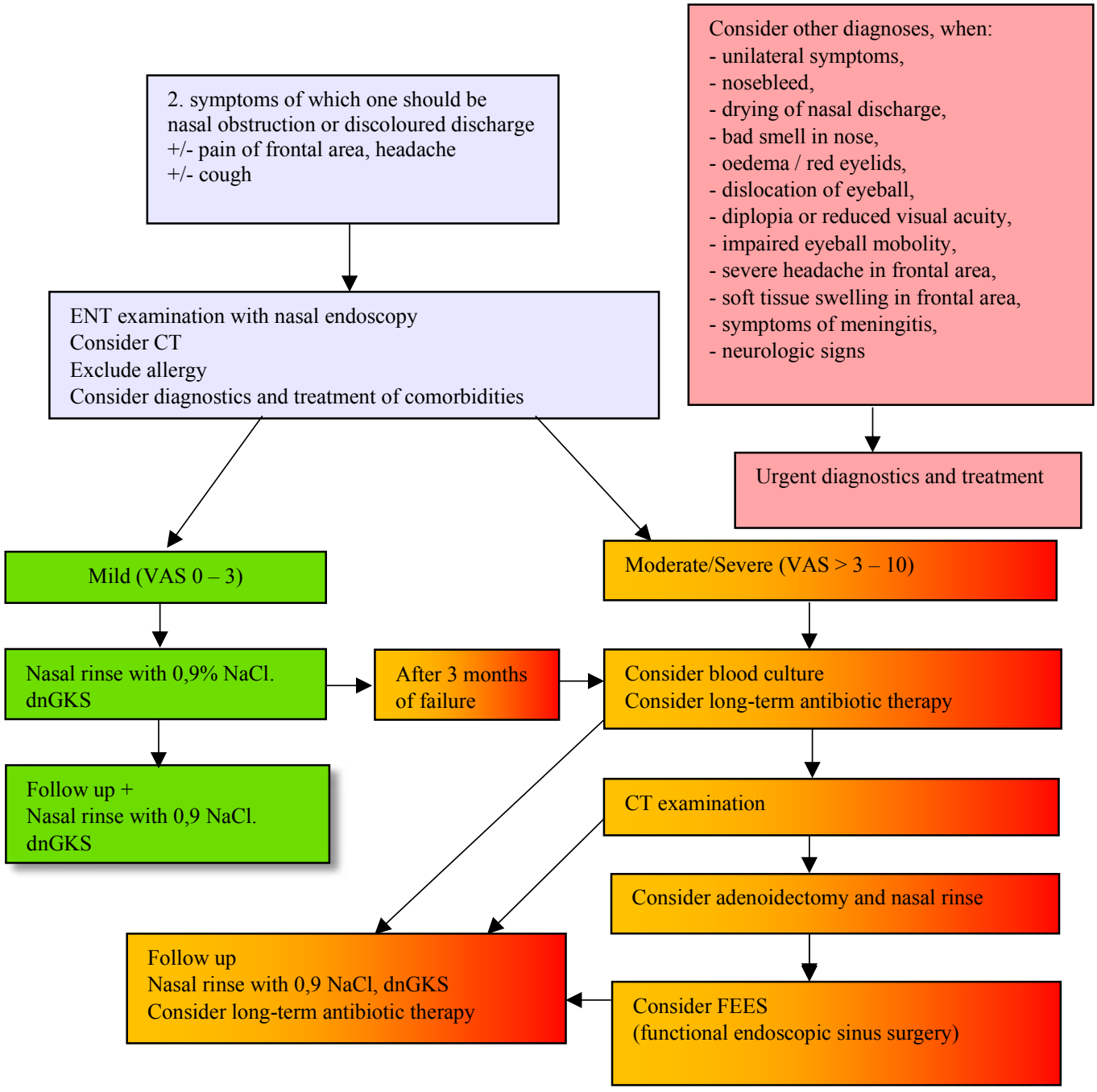

Fig. 3. Approach to CRS in young children for otolaryngology specialists according to EPOS, modified [4, 63].

smell and/or taste, headache, cough and eye symptoms (conjunctivitis, ocular pruritus) [1, 2]. Nonspecific symptoms of rhinitis include: dark circles around the eyes, probably resulting from venous circulation disorders caused by oedema of the nasal mucosa, allergic salute – i.e. rubbing the tip of the nose in an upwards manner to increase nasal patency and reduce nasal itching, allergic crease, i.e. a transverse line between the bridge and the tip of the nose resulting from an allergic salute, as well as breathing through the mouth and resulting malocclusion. The following should be established: duration of symptoms, seasonality, causative agents, factors that intensify and alleviate symptoms, past treatment and its effectiveness. In physical examination concomitant chronic diseases and medications used, as well as previous illnesses, should also be considered. Particularly important are the symptoms of comorbidities associated with AR, such as asthma and atopic dermatitis, and the possibly resulting diseases such as otitis media, rhinosinusitis, chronic cough and sleep apnoea. Family and community interview are also very important, with consideration of the occurrence of atopy in the family, lifestyle and eating habits [1, 2]. The severity of symptoms and their impact on the patient's quality of life should also be assessed, e.g. with the VAS scale [2].

Clinical history should include differential diagnosis of RN. It should be noted that the younger the child, the less likely the allergic

background of RN, so in these cases, particularly broad differential diagnosis is indicated [2].

ENT EXAMINATION

In anterior rhinoscopy, the anatomical structures of the nose (and their possible abnormalities, e.g. deviated nasal septum, and presence of abnormal structures, such as polyps or tumours, should be assessed), condition of the mucosa (including colour, humidity, swelling, atrophy), presence and type of nasal discharge and possible features of the presence of a foreign body in the nose. Endoscopic examination of the nasal cavities and nasopharynx should also be considered, including assessment of the pharyngeal ostium of the auditory tube and the adenoid [2].

ENT examination should also include otoscopy with an assessment of possible features of the auditory tube dysfunction or middle ear effusion.

DIAGNOSTIC TESTS

The basis of allergological diagnostics are skin prick tests (SPT) [1, 2]. They are characterised by low cost, promptness and availability. In the diagnosis of rhinitis, they allow the confirmation or exclusion of allergic grounds, as well as the identification of allergen causing the symptoms. Diagnosis of AR should be confirmed by a positive SPT result [2].

In case of doubt in the interpretation of the SPT result, multidirectional diagnostics can be performed, including serum IgE concentration testing or challenge tests.

Serum specific IgE (sIgE, i.e. IgE directed against specific allergens) is a useful tool in diagnosing AR, especially in cases of discrepancy between the history and SPT results. In turn, total serum IgE (tIgE) may be elevated in many non-allergic diseases, and its low value does not exclude allergies and therefore should not be used in the diagnosis of AR [1, 2]. In a nasal challenge test (NCT), allergens or irritants are administered topically to the nasal mucosa. Challenge attempts are of importance in occupational rhinitis and in local allergic rhinitis (LAR), i.e. in patients with a history typical of AR, but without systemic features of atopy, with a negative SPT result and sIgE concentration testing [1, 2].

According to PoSLeNN, cytology of the nasal mucosa (microscopic examination of the mucosa exfoliated from the inferior turbinate) was considered to be useful in the diagnosis of rhinitis, although, according to ARIA 2008, it is used rather in clinical studies [1, 2].

Various tests may be used in the differential diagnosis of rhinitis, such as bacteriological tests, rhinomanometry (assessing nasal flow and resistance), smell tests, ciliary function assessment, nasal NO concentration measurement and imaging tests.

According to the ARIA 2008 guidelines, routine nasal swabs are not beneficial in diagnosing AR [1]. Also, in infectious rhinitis, microbiological diagnostics are usually not necessary, because in most cases empirical treatment proves to be effective. Bacteriological examination should be considered in the event of failure of empirical treatment, in people with immunodeficiency, suspected of ozaena, rhinoscleroma and in some cases in chronic rhinosinusitis [2].

A swab taken under endoscopic control from the middle nasal meatus may have a greater diagnostic value than that taken in anterior rhinoscopy [1].

Imaging is not necessary for the diagnosis of AR, although may be applicable in differential diagnosis. It should be emphasised that plain sinus x-ray has limited sensitivity and should not be used in the diagnosis of ARS [4]. Computed tomography is the imaging test of choice in rhinological practice [2]. According to ARIA, computed tomography can be considered in the following cases: to exclude other abnormalities (including chronic sinusitis) and rhinitis complications, in the event of treatment failure and in patients with unilateral symptoms [4]. Magnetic resonance imaging has very limited significance, although it may be indicated in selected cases (including in the diagnosis of tumours or meningoencephalocele) [1, 2].

In children, important elements of differential diagnosis are Politzer manouver and Eustachian tube catheterisation, allowing the diagnosis of the mechanical cause of nasal obstruction, including tumours and congenital defects [2].

Furthermore, spirometry is recommended for patients with moderate or severe AR, for the diagnosis of bronchial asthma [2].

DIFFERENTIAL DIAGNOSIS

In children, the differential diagnosis of rhinitis should include, among others

- adenoid hypertrophy,
- presence of foreign body,
- anatomical abnormalities (especially in younger children; e.g. choanal atresia, arhinia, hiporhinia, cleft lip and palate),
- deviated nasal septum,
- consequences of traumas (including nasal septum hematoma, nasal bone fracture, nasal adhesions),
- tumours of the nasal cavity (including dermoid cysts, meningoencephalocele, haemangiomas, choanal polyp, glioma and other nasal neoplasms),
- nasopharyngeal tumours (including juvenile nasopharyngeal angiofibromas, rhabdomyosarcoma, lymphomas),
- cystic fibrosis,
- ciliary dyskinesia,
- chronic rhinosinusitis, including allergic fungal sinusitis,
- granulomatous vasculitis,
- cerebrospinal fluid leak [1, 2].

Nasal polyps in children are rare, and their presence should prompt diagnostics for cystic fibrosis [1, 2].

CONSEQUENCES OF RHINITIS AND RHINITIS COMORBIDITIES

Currently, the importance of rhinitis in children is increasingly emphasised due to their negative impact on the quality of life and the associated high costs incurred by healthcare systems [2].

Amongst diseases that may coexist with or be exacerbated by rhinitis, beside rhinosinusitis, asthma, conjunctivitis, eustachian tube dysfunction and associated otitis media – acute (often recurrent) and exudative (which may cause hearing loss and related speech development disorders), adenoid hypertrophy, palatine tonsillar hypertrophy and sleep apnoea can also be mentioned [3, 12, 1].

Asthma

There is a proven association of both asthma and rhinitis with allergies, which can also be caused by environmental factors. The age of the incidence of atopy may be an important factor in the development of asthma and rhinitis. In infants and young children, lower respiratory tract symptoms may precede nasal symptoms. One study found that early occurrence of atopy (under 6 years of age) is an important predictor of asthma later in childhood, while atopy acquired later is strongly associated with seasonal AR [1].

The vast majority of asthma patients have rhinitis. A higher incidence of asthma has also been reported in patients with rhinitis (10–40% compared to less than 2% in the general population), with asthma being more common in people with moderate/severe and chronic AR than in mild and periodic AR. Both AR and NAR are considered risk factors for asthma. The Children's Respiratory Study found that diagnosing AR in infancy was related with a twice as large probability of developing asthma up to the age of 11. It remains unclear whether AR is an earlier clinical manifestation of allergic disease in patients who will subsequently develop asthma, or whether AR is the causative agent of asthma. Studies have shown that in patients with asthma, eosinophilic infiltrates are found both in the bronchial mucosa and in the nasal mucosa. Furthermore, rhinitis, especially untreated, is associated with significant deterioration in asthma control, a higher incidence of asthma attacks, urgent medical consultations, and hospitalisation for asthma. Moreover, most asthma exacerbations are associated with viral infection of the nasal mucosa [1, 2].

Allergic conjunctivitis

Ocular symptoms are very common in patients with AR. Allergic conjunctivitis is an acute hypersensitivity reaction with conjunctival hyperaemia, intense lacrimation, itching and burning eyes as a result of contact with the allergen. According to some studies, in patients with pollen allergy, allergic conjunctivitis occurs in up to 75% of patients with rhinitis Other forms of conjunctivitis are not associated with an IgE-dependent allergic reaction [1].

Chronic rhinosinusitis

The role of allergies in diseases of the paranasal sinuses is unclear. In studies in patients with AR, a similar inflammatory response is observed in the nasal mucosa and in the paranasal sinus mucosa.

Tab. I. Classification of rhinitis according to ARIA [2].

CLASSIFICATION OF RHINITIS ACCORDING TO ARIA.
INFECTIOUS:
viral
bacterial
caused by other infectious agents
ALLERGIC:
periodic
chronic
OCCUPATIONAL (ALLERGIC AND NON-ALLERGIC):
periodic
chronic
INDUCED BY DRUGS:
acetylsalicylic acid (ASA)
other drugs
HORMONAL:
CAUSED BY OTHER REASONS:
Nonallergic rhinitis with eosinophilia (NARES)
irritants o food ingredients
??????????????????????
??????????????????????
emotional factors o atrophic rhinitis
gastroesophageal reflux disease*
IDIOPATHIC:

*included in PoSLeNN 2013 classification, not included in ARIA 2008 classification

There was a correlation between total serum IgE concentration and thickness of the paranasal sinus mucosa observed in computed tomography images. Several epidemiological studies have found a high incidence of hypersensitivity to inhaled allergens in both acute and chronic rhinitis and rhinosinusitis patients. Among people undergoing reoperation of the paranasal sinuses, the frequency of hypersensitivity to inhaled allergens is estimated to be as high as 84% (compared to 6% in the general population) [1]. In the study of Sadeghat et al. it was found that AR is the most common disease comorbid with RS in children. Nevertheless, the relationship between AR and RS has still not been clearly proven. The relationship between allergies and nasal polyps remains even more unclear. Despite numerous similarities in the inflammatory reaction observed in AR and RS with nasal polyps, there is still no clear confirmation of the relationship between these disease entities in epidemiological studies [1].

Adenoid hypertrophy

Many factors may be involved in the etiopathogenesis of adenoid hypertrophy, such as mould and irritants (tobacco smoke). Symptoms of adenoid hypertrophy include nasal congestion, open-mouth breathing, or snoring, and therefore rhinitis-like symptoms. For this reason, adenoid hypertrophy in children should always be included in the differential diagnosis of rhinitis. A relationship between AR and adenoid hypertrophy is also suspected. The effects of hypersensitivity to inhaled allergens on adenoid immune

changes, including increased numbers of Langerhans CD1a+ cells, eosinophils, as well as IgE, IL-4 and IL-5 producing cells have been reported. However, no correlation was observed between the severity of the allergy and the degree of adenoid hypertrophy. However, it seems advisable to carry out allergological diagnostics in all children with adenoid hypertrophy [1].

Eustachian tube dysfunction and otitis media with effusion.

According to the concept of 'global allergy' in the respiratory tracts, the eustachian tube, lined with respiratory epithelium, may participate in the inflammatory response after contact with the allergen. Inflammatory infiltration typical of an allergic reaction was found in patients with AR at the pharyngeal ostium of the auditory tube. Mucosal oedema in patients with rhinitis may cause tube dysfunction. This facilitates the penetration of microorganisms from the nasopharynx to the middle ear, as well as the accumulation of fluid in the tympanic cavity, which can lead to the development of acute otitis media (AOM) or otitis media with effusion (OME) [1, 14]. In middle ear effusion, a greater number of eosinophils and cells producing interleukins IL-4 and IL-5 were found in patients with OME. Furthermore, IgE-dependent hypersensitivity and respiratory symptoms of the allergy have been shown to be independent risk factors for the development of EOM [1]. A study of Fasunla et al. [15] found a higher incidence of type B and C tympanograms and OME in children with AR compared to the control group. For these reasons, it is recommended to perform allergological diagnostics in children with OME [1].

Chronic cough

Post-nasal drip in rhinitis is one of the most common causes of chronic cough. Children with coughing attacks during exercise, laughter, play or at night, are recommended to undergo asthma diagnostics [1].

Impact of rhinitis on sleep, academic performance and quality of life

Insufficient control of AR symptoms can lead to insomnia or sleep disorders. The relationship between rhinitis and sleep apnoea has also been described, although it remains unclear. Difficulty in learning may be a direct result of rhinitis, due to the deterioration of cognitive functions, and may also result from more frequent absences from school, as well as from fatigue and increased daytime sleepiness, caused by sleep disorder. Conductive hearing loss in the course of otitis media with effusion can also have an adverse effect on academic performance. In addition, deterioration in academic performance can be further exacerbated using antihistamines, especially older generations. Rhinitis can cause mood changes ('irritable child syndrome'), depression and anxiety. Deterioration of the quality of life is often observed in patients with RN [2, 1, 16].

TREATMENT

Basics of RN treatment and nonpharmacological methods.

The fundamental approach in rhinitis is education of patients and their parents, avoiding exposure to irritants (especially tobacco smoke), and in AR also to allergens, pharmacotherapy and – in selected cases of AR – allergen-specific immunotherapy (SIT) [2, 1]. Humidification of air and proper hydration of the child, as well as nasal irrigation with isotonic and hypertonic NaCl/sea water solutions (in the form of aerosols or irrigation), allowing mechanical removal of secretions, allergens, irritants and inflammatory mediators, and improving mucociliary clearance, are also important in the treatment of rhinitis [2, 10, 17]. Nasal irrigation is safe and is very rarely associated with side effects [18, 19]. Studies have found its beneficial effect in reducing the severity of rhinitis symptoms [18, 19], however, it is less effective than the use of intranasal glucocorticoids. For this reason, it should rather be used as an adjuvant rather than pharmacological treatment [20]. In the study of Li et al. hypertonic solutions were found to be more effective than isotonic in reducing rhinitis symptoms, although, according to the authors of this paper, in another study no differences were found [19]. Furthermore, the literature indicates a beneficial effect of the use of moisturising nasal ointments in relieving symptoms of rhinitis [21, 22].

Tab. II. Antihistamines - H1-receptor antagonists, used in children [65, modified in accordance with current Summary of Product Characteristics: 36, 37, 38, 39, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56].

DRUG	INDICATIONS AND AGE OF REGISTRATION	RECOMMENDED DOSE
Cetirizine	Chronic and seasonal AR > 2 years of age	2–6 years of age: 2x2.5 mg 6-12 years of age: 2x5 mg >12 years of age: 2x10 mg
Levocetirizine	Chronic and seasonal AR > 2 years of age	2–6 years of age: 2x1.25 mg > 6 years of age: 1x5 mg
Fexofenadine	Seasonal AR > 12 years of age	1x120 mg
Loratadine	Chronic and seasonal AR > 2 years of age	2–12 years of age: < 30 kg b.w. 1x5mg; > 30 kg b.w. 1x10 mg > 12 years of age: 1x10 mg
Desloratadine	Seasonal AR >1 years of age	1-5 years of age: 1x1.25 mg 6-11 years of age: 1x2.5 mg ≥ 12 years of age: 1x5 mg
Rupaditine	Chronic and seasonal AR > 2 years of age	2-11 years of age: 10–25 kg b.w. 1x2.5 mg; ≥ 25 kg b.w. 1x5 mg ≥ 12 years of age: 1x10 mg
Bilastine	Chronic and seasonal AR > 6 years of age	6–11 years of age (b.w. > 20 kg): 1x10 mg ≥ 12 years of age: 1x20 mg

Pharmacotherapy

AR treatment should be individualised. It should take into account: the severity and duration of the disease, patient preferences, as well as the effectiveness, availability and cost of therapy [1]. The basis of pharmacotherapy in AR are intranasal glucocorticosteroids (INCS) and second-generation antihistamines [2]. The use of INCS and antihistamines can also be considered in NAR, although their effectiveness is lower than in AR [2, 10]. Some studies indicate that topical administration of azelastine may be beneficial in NAR, especially in combination with INCS [10]. Drugs used in AR do not give a long-term effect after discontinuing use, hence they are used chronically. However, not all patients with moderate/severe AR manage disease control

Tab. III. Guidelines for the treatment of ARS in children as recommended in the non-hospital of community-acquired respiratory infections, National Program for the Protection of Antibiotics, 2016 [17].

	ANTIBIOTIC	DOSAGE IN CHILDREN WITH B.W. > 40 KG	DOSAGE IN CHILDREN WITH B.W. < 40 KG
Treatment of first choice	amoxicillin	1500–2000 mg every 12 hours	75–90 mg/kg/day in 2 divided doses
Corrected treatment	amoxicillin with clavulanate	such that the dose of amoxicillin is 1500–2000 mg every 12 hours for 10 days	such that the dose of amoxicillin is 70–90 mg/kg/day in 2 divided doses for 10 days
in a reaction of immediate hypersensitivity to penicillins	cefuroxime axetil	2 x 500 mg/day	30 mg/kg/day in 2 partial doses for 10 days not exceeding in a single dose of 500 mg
in the reaction of immediate hypersensitivity to β-lactam antibiotics	clarithromycin	250-500 mg every 12 hours	15 mg/kg/day in 2 partial doses

despite optimal treatment. Minimimising the amount of taken medications is also important [1].

In AR, drugs are usually applied orally or intranasally. The advantages of intranasal administration include: the possibility of local administration of a higher dose of the drug while reducing the risk of systemic side effects, and a faster onset of action. However, in some patients, nasal administration of drugs may cause epistaxis and retention of mucous discharge. Furthermore, in some patients the coexistence of other atopy-related diseases if found, such as asthma and allergic conjunctivitis, which requires systemic drugs (although, according to literature, INCS are effective in the treatment of allergic conjunctivitis) [1].

Intranasal glucocorticoids (INCS)

INCS are significantly more effective at treating AR than oral and topical antihistamines, particularly in improving nasal patency. They are also the most effective drugs in the treatment of NAR. In the case of nasal obstruction or frequent recurrence of symptoms, INCS should be the first-line treatment. Onset of action is seen after 7-8 hours, but the maximum effectiveness is only achieved after two weeks, although newer studies show that in some patients the first effects of INCS are observed after two hours. Fluticasone propionate has been shown to reduce nasal symptoms of AR when used on an ad hoc basis [1].

New INCS formulations are safe and free from most systemic side effects seen with oral corticosteroids. Previous generation of INCS with high bioavailability, such as betamethasone and beclomethasone, should not be used. Although there was a slight decrease in growth rate for long-term (over a year) intake of beclomethasone, this effect was not seen in children treated with fluticasone propionate or mometasone furoate. New INCS preparations also do not have a significant effect on the hypothalamus – pituitary – adrenal axis, which was confirmed in a study with fluticasone propionate, used simultaneously in intranasal and inhalation forms [1]. The main side effects of INCS include dryness and irritation of the nasal mucosa and epistaxis. To prevent them, it is recommended to use moisturising preparations, such as natural oils (e.g. olive oil) [1, 23, 24].

In Poland, among INCS, mometasone furoate is approved for use in children over 3 years of age (3-11 years: 1x1 dose, > 12 years 1x2 dose) [25, 26, 27, 28, 29, 30, 31], fluticasone propionate in children over 4 years of age (4–11 years: 1x1 dose, > 12 years 1–2x2 dose) [32, 33], and fluticasone furoate in children over 6 years of age (6–11 years: 1x1 dose, > 12 years 1x2 dose) [34].

Due to their side effects, the use of intramuscular corticosteroids and long-term therapy with oral corticosteroids is not recommended [1].

Oral antihistamines

Antihistamines are histamine H1 receptor antagonists. They are effective in the treatment of symptoms associated with histamine-dependent reactions, such as nasal discharge, sneezing, nasal itching and ocular symptoms, but show less effectiveness in the treatment of nasal obstruction, hence their effectiveness in the treatment of persistent AR is low [1]. Oral antihistamines improve the patients' quality of life. Their special significance in the paediatric population is due to the fact that it is often easier for younger children to be given an oral medicine due to their lack of cooperation when administering intranasal preparations [1]. First-generation antihistamines have significant side effects due to their sedative and anticholinergic effects, as well as paradoxical effects, sometimes causing hyperactivity and irritability, and therefore should not be currently used, especially in children. Newer preparations do not cause sedation or cause it to a small extent and do not show or show little anticholinergic effect. On the contrary, due to the reduction of AR symptoms, such as fatigue, new generation antihistamines may improve academic performance. It has been shown that the use of newer-generation antihistamines in children is effective and safe. They are also approved for use in young children. It was found that taking cetirizine delayed the development of asthma (and in some cases even prevented asthma) in infants with atopic dermatitis and allergy to grass pollen (and to a lesser extent in children with allergy to house dust mites) [1].

In the NAR group, antihistamines are used in the treatment of NARES [2]. Their role in the other types of NAR remains unclear [35]. Dosage of the most commonly used second-generation antihistamines in children is presented in Tab. II. [2, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56]. The choice of preparation should include authorisation for use depending on the child's age, effectiveness and safety profile.

In the meta-analysis of Mösges et al., which compared four antihistamines (desloratadine, ebastine, fexofenadine and levocetirizine), it was found that levocetirizine was more effective in relieving the symptoms of AR compared to the other studied agents [57].

In turn, in the paper by Kawauchi et al. [58] attention was drawn to the potential differences in the safety of individual second-generation antihistamines in children, especially in the context of their sedative and depressive effects on the central nervous sys-

tem (associated with binding to the brain H1 receptor). Bilastine and fexofenadine preparations were found to be the safest in this respect, as drugs not penetrating into the central nervous system. In addition, loratadine and desloratadine have the potential to have anticholinergic effects, whereas bilastine, fexofenadine, cetirizine and levocetirizine have high specificity for the H1 receptor and do not display such activity [58]. This work also quoted the results of studies comparing various antihistamines, which include lower tendency to cause drowsiness and deterioration of psychomotor functions by fexofenadine and bilastine compared to cetirizine and similar efficacy in the relief of symptoms of seasonal AR for bilastine, cetirizine and desloratadine (although less for fexofenadine) [58]. At present, there are no studies indicating unequivocally the advantage of any of the second-generation antihistamines.

Topical antihistamines

Intranasal antihistamines are effective in reducing nasal itching, sneezing, nasal discharge and nasal congestion. Administered into the conjunctival sac, they are effective in relieving eye symptoms. Onset of action is observed after 20 minutes. Topical antihistamines should be administered twice a day. Intranasal antihistamines do not affect ocular symptoms [1]. The 2016 ARIA revision found greater efficacy of INCS monotherapy compared to monotherapy with nasal antihistamines in AR [5]. However, no significant differences were observed between the use of oral and nasal antihistamines in AR [5]. In Poland, intranasal azelastine is approved for use in the treatment of AR in children over 6 years of age. The drug is administered 2 times a day, 1 dose in each nasal cavity. In children, therapy should not last longer than 6 months [59, 60].

Anti-leukotriene drugs

Study results indicate that montelukast is more effective than placebo, similar to antihistamines and lower than INCS in the treatment of AR. It can be used to treat seasonal AR in patients over 6 years of age [1]. In the 2016 revision of the ARIA guidelines, compared to the effectiveness of anti-leukotriene drugs and oral antihistamines in the treatment of seasonal AR, the advantage of one of the methods was not clear. On the one hand, antihistamines in many cases remain more cost-effective, on the other, in patients with concomitant asthma, especially exercise and aspirin-dependent asthma, montelukast treatment can yield better effects [5]. In the treatment of perennial AR, antihistamines are superior to anti-leukotriene drugs, although montelukast may be more effective in selected cases (as above) [5].

Drug combinations

According to the revision of the ARIA recommendations of 2016, INCS as monotherapy or in combination with an oral antihistamine is recommended for patients with seasonal AR. The inclusion of antihistamine treatment is especially recommended in situations where INCS does not provide full control of symptoms, with severe ocular symptoms, and when the rapid effect of treatment is important. In patients with perennial AR, INCS was recommended as monotherapy rather than in combination with an oral antihistamine [5]. The use of INCS alone or in combination with intranasal antihistamines is equivalent in both seasonal and perennial AR, with the combination being particularly preferred in the first two weeks of treatment to achieve a faster therapy effect [5]. In Poland, a complex intranasal preparation containing fluticasone propionate and azelastine is approved for use in the treatment of AR in children over 12 years of age. The drug is administered 2 times a day, 1 dose in each nasal cavity [61]. At the same time, in patients with seasonal AR, greater efficacy of the combination of INCS and nasal antihistamines has been reported compared to nasal antihistamines alone [5]. The combination of antihistamines and montelukast is not more effective than either of these drugs alone and is less effective than INCS alone.

Other drugs used to treat rhinitis

Topical cromones are recommended for the treatment of AR and allergic conjunctivitis, but their efficacy is low. Intranasal administration of ipratropium preparations may be effective in treating watery nasal discharge. Intranasal decongestants may be taken for a short time in patients with severe nasal congestion, but the possibility of rhinitis medicamentosa with their long-term use should be noted. Oral decongestants (and their combinations with oral antihistamines) may be used to treat AR in adults, but side effects such as insomnia and hyperactivity are often observed, especially in children. Other drugs used to treat NAR in children include mucolytics, anti-reflux drugs, and NSAIDs.

Specific immunotherapy

Specific immunotherapy (SIT) is based on administering an allergen-containing solution, usually at gradually increased levels, to reduce the symptoms associated with repeated allergen exposure. An accurate diagnosis of IgE-dependent allergy is necessary to start SIT. Traditionally, SIT has been associated with subcutaneous immunotherapy, or SCIT, although nasal and sublingual preparations are currently available (sublingual immunotherapy, or SLIT), some of which do not require an increase in allergen concentration. The ARIA 2010 revision recommend the use of SCIT in children with AR regardless of the co-existence of asthma. Intranasal SIT and SLIT are recommended in AR only for patients allergic to pollen, but not for those allergic to house dust mites. SCIT is not usually recommended for children under 5 years of age due to both safety and difficulty in repeated injections over months or years. Research is currently undertaken on the effectiveness of SLIT in younger children. The results achieved to date indicate their safety in children, as well as the possibility of preventing the development of asthma in children with AR, however, further research is needed to confirm their effectiveness [1, 62].

Treatment of rhinosinusitis

Treatment of ARS

ARS usually tends to subside spontaneously, hence in most cases, treatment reducing the inflammatory response, especially INCS0, is sufficient. Flushing the nose with isotonic NaCl solutions (e.g. sea water) may also be beneficial. Nasal decongestants may be used as auxiliary treatment; however, it should be emphasised that

these preparations should not be taken for more than 5-7 days. Analgesic, antipyretic and anti-inflammatory drugs are also used, whereby ibuprofen is the drug of choice. The role of antihistamines, mucolytics and phytotherapy (herbal preparations) is unclear. According to European guidelines from 2012 (European position paper on rhinosinusitis and nasal polyps, EPOS 2012), there are no indications for the use of antihistamines, unless concomitant AR is suspected, and Polish recommendations allow the use of antihistamines in combination with pseudoephedrine [4, 17]. The antibiotic should only be used in acute bacterial ARS in combination with INCS. Amoxicillin is the antibiotic of choice. Amoxicillin with clavulanate should be adminstered for corrected treatment of ARS (especially if previous treatment with amoxicillin has been ineffective), cefuroxime axetil - for immediate hypersensitivity reactions to penicillin, and clarithromycin - for immediate hypersensitivity to beta-lactam antibiotics (Tab. III.) [17]. The treatment regimen for children with ARS in primary health care according to EPOS is presented in Fig. 1., while the diagrams for otolaryngology specialists are presented in Fig. 2.

Septic complications of ARS are rare but severe and all basic health care physicians should be aware of 'red flags' in the course of this disease, that require urgent specialist consultation, such as periorbital oedema, displacement of the eyeball, blurred vision, severe headache, swelling in the frontal area, or neurological symptoms In these cases, the imaging test of choice is computed tomography. In addition to the above-mentioned treatment, blood culture, hospitalisation, intravenous antibiotic therapy, oral glucocorticosteroids and surgery should also be considered [4].

Treatment of CRS

The treatment of CRS mainly involves nasal rinse with an isotonic solution of NaCl and INCS. Long-term targeted antibiotic therapy and surgical treatment can also be considered (firsr adenoidectomy, and, if necessary, endoscopic sinus surgery) [4]. The approach to CS in young children for otolaryngology specialists is presented in Fig. 3.

CONCLUSION

Due to the wide variety of causes and course of rhinitis described above, and their important impact on the development of other conditions, they constitute a significant diagnostic and therapeutic problem. It is necessary to further investigate in order to better understand this problem and to avoid its negative consequences, especially in the paediatric population [2, 3].

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