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REVIEW PAPER

ARTYKUŁ PRZEGLĄDOWY

ALLERGIC RHINITIS TREATMENT: OVERVIEW OF THE LATEST GUIDELINES

LECZENIE ALERGICZNEGO NIEŻYTU NOSA: PRZEGLĄD NAJNOWSZYCH WYTYCZNYCH

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Summary

Allergic rhinitis (AR) is a prevalent atopic disease in Poland, affecting approximately 25% of the adult population. It is characterized by chronic inflammation induced by IgE-dependent reactions to environmental allergens, leading to symptoms such as nasal congestion, sneezing, itching, and ocular manifestations. AR can be categorized as intermittent or persistent based on symptom duration and frequency. Common allergens include dust mites, pollen, animal secretions, and occupational agents. AR often coexists with asthma, necessitating accurate diagnosis and treatment to prevent bronchial complications. Diagnosis of AR relies on clinical symptoms and diagnostic tests such as skin prick testing and immunological assays. Skin prick testing is particularly useful in identifying IgE-mediated processes and guiding allergen avoidance and treatment decisions. Pharmacotherapy options include oral antihistamines and intranasal corticosteroids, with combination therapies showing promising results. Immunotherapy, in the form of subcutaneous or sublingual administration, aims to induce immunological tolerance and alleviate symptoms. In conclusion, effective management of AR involves a multifaceted approach, including allergen avoidance, pharmacotherapy, and immunotherapy. Early intervention and personalized treatment strategies are crucial for improving patient outcomes and quality of life.

Keywords: intranasal H1-antihistamine, intranasal corticosteroids, oral antihistamines, specific immunotherapy, allergic rhinitis

Streszczenie

Alergiczny nieżyt nosa (ANN) jest powszechną chorobą atopową w Polsce, dotyczy około 25% populacji dorosłych. Charakteryzuje się przewlekłym stanem zapalnym wywołanym reakcjami IgE-zależnymi na alergeny środowiskowe, co prowadzi do objawów takich jak blokada nosa, kichanie, świąd nosa, jak również objawy oczne. ANN może być sklasyfikowany jako

okresowy lub przewlekły w zależności od częstości występowania i czasu trwania objawów. Do najczęstszych alergenów należą roztocza kurzu, pyłki, wydzieliny zwierząt oraz czynniki zawodowe. ANN często współistnieje z astmą, co sprawia, że dokładna diagnoza i leczenie są niezbędne, aby zapobiec powikłaniom oskrzelowym. Rozpoznanie ANN opiera się na ocenie objawów klinicznych oraz badaniach diagnostycznych, takich jak punktowe testy skórne (prick test) i testy immunologiczne. Testy skórne są szczególnie użyteczne do identyfikacji procesów IgE-zależnych, co pomaga w podejmowaniu decyzji dotyczących unikania alergenów i leczenia. Opcje leczenia farmakologicznego obejmują doustne leki przeciwhistaminowe i donosowe glikokortykosteroidy, przy czym terapie łączone dają obiecujące rezultaty. Immunoterapia, podawana podskórnie lub podjęzykowo, ma na celu wywołanie tolerancji immunologicznej i złagodzenie objawów. Efektywne leczenie ANN wymaga kompleksowego podejścia, które obejmuje unikanie alergenów, farmakoterapię oraz immunoterapię. Wczesne podjęcie działań oraz indywidualnie dostosowane strategie terapeutyczne są niezbędne do poprawy wyników leczenia i jakości życia pacjentów.

Słowa kluczowe: donosowe leki przeciwhistaminowe H1, donosowe glikokortykosteroidy, doustne leki przeciwhistaminowe, swoista immunoterapia, alergiczny nieżyt nosa

Introduction

Allergic rhinitis (AR) is a prevalent atopic disease in Poland, affecting approximately 25% of the adult population [1]. It is characterized by chronic inflammation induced by IgE-dependent reactions to environmental allergens [2,3], leading to symptoms such as nasal congestion, sneezing, itching, and ocular manifestations. AR can be categorized as intermittent or persistent based on symptom duration and frequency [4]. Common allergens include dust

mites, pollen, animal secretions, and occupational agents. AR often coexists with asthma, necessitating accurate diagnosis and treatment to prevent bronchial complications [5].

Aim of the work

Fundamental aim of this study was to present symptoms and diagnostic methods in AR and discuss treatment approaches.

Methods

This article is a literature review based on the ARIA-GRADE 2022 guidelines and International consensus statement on allergy and rhinology: Allergic rhinitis – 2023. The basis for the current ARIA-GRADE recommendations are ARIA 2016 and American clinical guidelines from 2017. These recommendations take into account not only randomized clinical trials but also data from real-world evidence (RWE) and chamber studies. ICAR-2023 employs the evidence-based review with recommendations (EBRR) methodology. It is also based on publications on PubMed using keywords: allergic rhinitis, oral antihistamines, intranasal corticosteroids, intranasal drugs, specific immunotherapy, intranasal H1-antihistamine, ARIA, mometasone furoate, olopatadine.

Literature review results

AR is the most commonly diagnosed allergic disease in Poland, affecting approximately 25% of the adult population [1]. It is an atopic disease, associated with a chronic inflammatory process, in approximately 90% IgE-dependent induced by the action of environmental allergens

involving many inflammatory cells accumulating in the nasal mucosa and submucosal layer [2,3]. Exposure to allergens leads to mast cell degranulation and the release of allergic reaction mediators such as histamine, tryptase, leukotrienes, prostaglandins, bradykinin, and platelet-activating factor (PAF). This process consists of two phases: an early phase characterized by immediate symptoms, and a late phase, primarily marked by nasal congestion and impaired nasal patency. Two forms of AR are distinguished: intermittent, when symptoms occur less than 4 days a week for less than 4 weeks, and persistent, when symptoms last longer than 4 days a week for more than 4 weeks [4]. Symptoms of AR primarily include watery nasal discharge, sneezing, nasal itching, nasal congestion, mucosal redness, and ocular symptoms such as tearing, burning, or eye redness. Other accompanying symptoms often include palate itching and coughing [5].

The most common allergens that can trigger AR include dust mites (the main cause of perennial AR), pollen (mainly responsible for seasonal AR), animal secretions and excretions (from cats, dogs, horses, mice), fungi, as well as allergens related to occupational exposure, e.g., flour, latex, wood dust. Additionally, environmental factors such as smoke, cold air or irritant substances such as formaldehyde or ammonia can make allergic reactions worse [5].

Plenty of research indicates that diseases involving inflammation of the respiratory mucosa, such as AR and asthma often occur together [5]. The ECAP study in Poland confirmed that AR significantly increases the risk of developing hypersensitivity in the lower respiratory tract [1]. Consequently, the accurate diagnosis and efficacious treatment of AR exert a profound influence preventing bronchial asthma.

AR negatively affects the quality of life of individuals suffering from this condition. Beyond the overt symptoms, it induces sleep disturbances, fatigue, cognitive dysfunction and irritability, as well as work-related effectiveness [6].

Diagnosis

Diagnosis of AR is based on the analysis of clinical symptoms and diagnostic test results. A significant role is played by the medical history, in which the patient describes their symptoms, the time of their occurrence and duration, the frequency and intensity with which they occur, triggering factors, and alleviating factors. Diagnostic tests used in the diagnosis of AR include skin prick testing, immunological assays (e.g., measurement of specific IgE antibody concentration in blood serum) and allergen provocation tests. In some cases other nonspecific tests such as basophil activation test, nasal endoscopy and imaging studies such as computed tomography of the nose and paranasal sinuses may also be recommended [7,8].

A valuable test that in combination with patient history, can easily differentiate AR from other types of rhinitis is skin prick testing (SPT). Identifying an IgE-mediated process can help determine what allergens to avoid and direct appropriate medications. SPT is not suitable for everyone. Reasons to avoid SPT are abnormal skin changes such as dermatographia and atopic skin, because dermatitis make SPT less reliable due to the risk of false positives [9]. A good alternative is measuring the specific IgE antibody concentration in blood serum [10].

The nasal allergen challenge (NAC) is an advanced diagnostic tool indicated to investigate seasonal and perennial allergic rhinitis, local allergic rhinitis, and occupational rhinitis and assess reactivity to specific allergens. It involves administering an allergen into the patient's nasal cavity and observing the reaction, such as sneezing, nasal itching, or a runny nose. This test is particularly useful when other diagnostic methods are inconclusive, though it requires specialized supervision and is not widely used in routine practice. NAC can provide valuable information in more challenging cases of allergy. NAC is useful in diagnosis of local allergic rhinitis (LAR). LAR is characterized by the presence of a localized inflammatory response mediated by Th2 lymphocytes, the production of allergen-specific IgE in the mucous

membrane, and the absence of allergen-specific IgE (asIgE) both on mast cells in the skin and in the serum. In patients with LAR, a beneficial effect of orally administered antihistamines (OAH), and intranasal corticosteroids (INCS), as well as the combination of INCS with intranasal antihistamines is observed – similar to the treatment in AR [11].

Treatment

When managing allergic rhinitis, the main aim is to effectively control the disease. It's important to choose treatment options that are effective, safe, and readily available, and to take into account patient preferences and the costs associated with the recommended treatment.

Therapeutic options for patients with allergic rhinitis:

1. reducing exposure to environmental allergens,
2. pharmacotherapy,
3. specific immunotherapy.

Reducing exposure to environmental allergens

Patients who have allergies to pollen are strongly advised to avoid exposure to these allergens [12]. Educating these patients is crucial, as avoiding allergens requires behavioral adjustments, especially during periods of allergen exposure. Since pollen seasons vary for different plants in different regions, it's advisable to utilize information from the Internet where pollen calendars for plants in Poland are regularly updated, for example, on the website of the Polish Society of Allergology [13]. The recommendations involve keeping windows in homes and cars closed during pollen season, changing clothes and showering after outdoor activities, minimizing outdoor exposure during periods of high pollen count [14]. For those allergic to

house dust mites, attempts are made to decrease dust mite levels indoors by eliminating plush carpets and toys, implementing regular cleaning with efficient vacuum cleaners equipped with filters and utilizing products that effectively eliminate dust mites and can be applied to different surfaces [15,16].

If efforts to reduce exposure are insufficient, pharmacological treatment becomes necessary.

According to the ARIA-GRADE recommendations the therapeutic approach is suggested to follow the MASK algorithm, which relies on the visual analogue scale (VAS). This algorithm employs a strategy of escalating treatment and reducing treatment based on the severity of symptoms [3].

Pharmacotherapy

The primary medications according to ARIA-GRADE 2022 guidelines and ICAR-2023 are: OAH of newer generations), INCS, intranasal antihistamine preparations (INAH), combination preparations. Antileukotriene receptor antagonists (LTRA) and chromones have received lower recommendation levels and are suggested as second-line treatments [3,10].

OAH remain the first-line treatment for AR [17]. These medications work by blocking histamine receptors, causing dilation of blood vessels, constriction of smooth muscle in the airways, increased endothelial permeability and stimulation of sensory nerves, leading to the characteristic symptoms of AR [18]. It is advisable to avoid using first-generation antihistamines due to their sedative effects, resulting from crossing the blood-brain barrier [19]. Second-generation antihistamines block H1 receptors peripherally, without crossing the blood-brain barrier, making them safer and less prone to causing significant side effects. The proposed dosing is presented in the table below (Table 1).

Table 1. The proposed dosing of chosen OAH, along with the onset and duration of action [8]

Medication	The beginning of action	Onset of action	Dosage – adults	Dosage – children
Bilastine	2 h	24 h	20 mg 1 x d	6-11 y 10 mg 1 x d
Deslorotadine	2-2.6 h	>24 h	5 mg 1 x d	2-5 y 1.25 mg 1 x d 6-11 y 2.5 1 x d
Fexofenadine	1-3 h	>24 h	60 mg 2 x d or 180 mg 1 x d	2-11 y 30 mg 2 x d
Loratadine	2 h	>24 h	10 mg 1 x d or 5 mg 2 x d	2-5 y 5 mg 1 x d ≥6 y 10 mg 1 x d

INCS are one of the most effective group of medications used in the treatment of AR. They exert their effects by targeting both the early and late-phase manifestations of AR such as including nasal itching, sneezing, congestion, and swelling.

By reducing inflammation in the nasal passages, they alleviate symptoms and prevent complications in the sinuses and ears. An improvement in quality of life [20] and alleviation of sleep disturbances [21] were observed in clinical studies across all age groups. Despite their delayed onset of action, due to their effectiveness, affordability, and minimal side effects, they are strongly recommended by International Consensus Statement on Allergy and Rhinology: Rhinosinusitis (ICAR) [10,22]. Individuals with seasonal AR should begin preventive treatment with INCS several days prior to the onset of the pollen season. A few weeks after starting the treatment, they should have their response assessed, including a nasal examination to check for any signs of local irritation or mechanical injury [10]. The proposed dosing is presented in the table below (Table 2).

INAH sprays are considered in the first-line treatment because of their rapid onset of action, even as early as about 15 minutes after application [23], and their reduction of nasal mucosal congestion, which is more effective than OAH [24]. They are highly effective in treating ocular symptoms, sneezing, and nasal itching. The benefits of using these drugs include

a low incidence of adverse effects and a high level of safety in their use. The proposed dosing is presented in the table below (Table 3).

Table 2. The proposed dosing of chosen INCS [8]

Medication	Dosage – adults	Dosage – children
Budesonide (32 μg per spray)	2 sprays per nostril twice a day or 4 sprays per nostril in the morning	≥ 6 y: 2 sprays per nostril twice a day or 4 sprays per nostril in the morning
Fluticasone propionate (50 μg per spray)	2 sprays per nostril every day	≥ 4 y: 1 spray per nostril every day
Mometasone furoate (50 μg per spray)	2 sprays per nostril every day or 2 sprays per nostril twice a day with polyps: 2 sprays per nostril twice a day	2-11 y: 1 spray per nostril every day ≥ 12 y: 2 sprays per nostril every day

INAH can effectively enhance the effects of INCS. The combination of these two treatments is strongly advised for treating allergic rhinitis, supported by several randomized studies [25]. In a prospective real-life study it was observed that the combination of azelastine with intranasal corticosteroid (MP-AzeFlu) provided relief in symptoms and improved the quality of life of patients. Comparative studies of the effectiveness of MP-AzeFlu with fluticasone propionate or azelastine used as monotherapy showed significant clinical efficacy, faster action, and comprehensiveness of the combined preparation compared to drugs used in monotherapy and placebo [26,27]. Currently there are products on the market that combine azelastine with fluticasone, as well as olopatadine with mometasone. The proposed dosing is presented in the table below (Table 3).

When comparing the effectiveness of azelastine + fluticasone and olopatadine + mometasone combinations, similar reductions in symptoms and clinical improvements were observed in both scenarios [28]. In summary, combination preparations exhibit a faster onset of action and are more effective in reducing symptoms compared to use of INAH or INCS in monotherapy.

Table 3. The proposed dosing of chosen nasal antihistamine sprays and the combination of INAH and INCS [8]

Medication	Dosage – adults	Dosage – children
Azelastine (INAH) (137 µg per spray)	1 spray per nostril twice a day	≥ 6 y: 1 spray per nostril twice a day
Azelastine plus fluticasone (137 µg of azelastine, 50 µg of fluticasone per spray)	1 spray per nostril twice a day	≥ 12 y: 1 spray per nostril twice a day
Mometasone furoate plus olopatadine (25 µg of mometasone furoate, 600 µg of olopatadine per spray)	2 sprays per nostril twice a day	≥ 12 y: 2 sprays per nostril twice a day

Leukotriene receptor antagonists (LTRA) are a group of medications used in the treatment of bronchial asthma, whose mechanism of action is based on blocking potent inflammatory substances – leukotrienes – released from mast cells during their degranulation. LTRA should only be used as adjunctive therapy and are not recommended as monotherapy in the treatment of allergic rhinitis. Their benefits are mainly seen in patients with asthma [25]. They are considered safe in the usual dosage.

Cromones act by stabilizing mast cells, inhibiting the release of inflammatory mediators, and preventing the development of IgE-mediated reactions [29]. Despite their side effects such as throat irritation, sneezing, runny nose and headache, due to their safety profile they are suggested as a second-line intranasal treatment if INCS therapy is ineffective [30]. They can be considered safe in particular when used at the standard dosage for use in young children (2 years and older) and pregnant women [10,31]. Disodium cromoglycate is also effective for short-term preventive use in adult patients who are at known risk of exposure [10].

Physiological saline (NaCl) solutions are commonly used to alleviate symptoms of allergic rhinitis. These preparations are available in various forms such as irrigation, spray, and

drops. The dosage depends on the type of product. Physiological saline therapy is very safe, making it suitable for pregnant women [32] and children [7].

Immunotherapy

Allergen immunotherapy (AIT) aims to modify the course of the disease by inducing immunological tolerance [33]. It is commonly used for pollen allergens. AIT is available in two forms: subcutaneous (SCIT) and sublingual (SLIT). The process of immunotherapy involves gradually introducing the allergen into the body through subcutaneous or sublingual administration. Dosage starts with very small amounts, gradually increasing to a maintenance dose. The prescribed maintenance dose is consistently given over a span of 3-5 years. Clinical symptoms improve and allergy symptoms decrease shortly after reaching this maintenance dose. The effectiveness of AIT in treating AR is demonstrated by alleviation of symptoms and reduction in the need for antiallergic medications [34]. Both forms of immunotherapy induce similar changes in the immune system, reducing the frequency of mast cell degranulation and gradually inhibiting the humoral response [35]. The most serious potential adverse effect during allergen immunotherapy is anaphylactic shock.

Conclusions

AR is a prevalent allergic condition affecting approximately 25% of adults in Poland. It is characterized by chronic inflammation, primarily IgE-dependent, triggered by environmental allergens, leading to mast cell degranulation and release of inflammatory mediators. AR presents in two forms: intermittent and persistent, with symptoms including nasal discharge, sneezing, itching, congestion, and ocular symptoms. Environmental allergens such as dust

mites, pollen, animal secretions, and occupational exposures exacerbate AR, often co-occurring with asthma. Diagnosis involves analyzing clinical symptoms and conducting tests such as skin prick testing and IgE antibody measurement. Treatment options aim to control symptoms effectively and safely, including reducing allergen exposure, pharmacotherapy, and allergen immunotherapy. Pharmacotherapy includes OAH, INCS, and combination preparations, while immunotherapy induces immunological tolerance through subcutaneous or sublingual administration of allergens. Management strategies vary based on symptom severity and patient preferences. Proper diagnosis and management of AR are crucial for improving quality of life and preventing complications such as asthma.

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