

A to Z in treatment for allergic rhinitis

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Introduction

Allergic rhinitis (AR) is defined as chronic inflammatory reactions to common allergens in the nasal mucosa with at least two AR symptoms including rhinorrhea, nasal congestion, sneezing, nasal/ocular pruritus, and postnasal drainage. AR is a common health problem, and it affects around 10-25% of general population. Its prevalence is increasing according to the environmental changes [1,2]. To date, numerous evidences indicate that allergic rhinitis may represent a component of systemic airway disease involving the entire respiratory tract. There are a number of physiological, functional and immunological relationships between the upper (nose, nasal cavity, paranasal sinuses, pharynx and larynx) and lower (trachea, bronchial tubes, bronchioles and lungs) airways. Therefore, AR and asthma frequently could coexist in the same patient and we should consider it and check for asthma to diagnose AR. [1,3]. This manuscript provides an overview of the pathophysiology, diagnosis, and appropriate management of allergic rhinitis.

Pathophysiology

Numerous inflammatory cells, including mast cells, eosinophil, macrophage, T cells, and B cells could infiltrate the allergic nasal mucosa. Generally, the infiltrating T cell are predominantly T helper 2 (Th2) cells and these cells release Th2 cytokines (e.g., IL-4, IL-5, and IL-13) that promote immunoglobulin E (IgE) production by plasma cells. Thereafter, the increased IgE triggers the release of mediators, such as histamine and leukotrienes, that induces arteriolar dilation, increased vascular permeability, mucous secretion, and smooth muscle contraction [1,2]. In addition, AR may be characterized by early-phase and late-phase responses. Each type of response is characterized by sneezing, congestion, and rhinorrhea, but congestion predominates in the late phase

Classification

Traditionally, AR is classified into seasonal (occurs during a specific season) or perennial (occurs throughout the year) types. However, not all patients fit into this classification scheme. For example, some allergic triggers, such as pollen, may be seasonal in cooler climates, but perennial in warmer climates, and patients with multiple “seasonal” allergies may have symptoms throughout most of the year. To date, AR is classified according to symptom duration (intermittent or persistent) and severity (mild, moderate or severe) [1,4]. Rhinitis symptom is considered as intermittent when the total duration of episode is less than 6 weeks, and persistent when symptoms continue throughout the year. Symptoms are classified as mild when patients are generally able to sleep normally and perform normal activities (including work or school); mild symptoms are usually intermittent. Symptoms are categorized as moderate/severe if they significantly affect sleep and activities of daily living and/or if they are considered bothersome. It is important to classify the severity and duration of symptoms as this will guide the management approach for individual patients [4].

Diagnosis

1. History

Classic symptoms of AR are followed as; nasal congestion, nasal itch, rhinorrhea and sneezing. Allergic conjunctivitis is also frequently associated with AR and its symptoms generally include redness, tearing and itching of the eyes.

Physical examination

During the nasal cavity examination, physicians could observe swollen and pale nasal mucosa combined with watery thin secretions. An internal endoscopic examination of the nose should also be considered to assess for structural abnormalities and nasal polyps.

Diagnostic tests

Although a thorough history and physical examination are required to establish the clinical diagnosis of rhinitis, further diagnostic testing is usually necessary to confirm that underlying allergies cause the rhinitis. Skin-prick testing is considered the primary method for identifying specific allergic triggers of rhinitis. Skin prick testing involves placing a drop of a commercial extract of a specific allergen on the skin of the forearms or back, then pricking the skin through the drop to introduce the extract into the epidermis. Within 15-20 minutes, a wheal-and-flare response (an irregular blanched wheal surrounded by an area of redness) will occur

if the test is positive. A reasonable alternative to skin prick testing is the use of allergen-specific IgE tests that provide an in vitro measure of a patient's specific IgE levels against particular allergens. However, skin prick tests are generally considered to be more sensitive and cost effective than allergen-specific IgE tests, and have the further advantage of providing physicians and patients with immediate results [1,4].

Treatment

1. Allergen avoidance

The avoidance of relevant allergens (e.g., house dust mites, moulds, pets, pollens) and irritants (e.g., tobacco smoke) is the first-line treatment in AR [4]. Patients allergic to house dust mites should be instructed to use allergen-impermeable covers for bedding and to keep the relative humidity in the home below 50% (to inhibit mite growth). Pollen exposure can be reduced by keeping windows closed, using an air conditioner, and limiting the amount of time spent outdoors during peak pollen seasons. For patients allergic to animal dander, removal of the animal from the home is recommended and usually results in a significant reduction in symptoms within 4-6 months.

2. Antihistamines

The first-generation antihistamines include brompheniramine, chlorpheniramine, clemastine, and diphenhydramine. These drugs may cause substantial adverse effects, including sedation, fatigue, and impaired mental status [5]. Compared with first-generation antihistamines, second-generation antihistamines have a better adverse-effect profile and cause less sedation. The second-generation oral antihistamines include desloratadine (Clarinet), levocetirizine (Xyzal), fexofenadine (Allegra), and loratadine. Second-generation antihistamines have more complex chemical structures that decrease their movement across the blood-brain barrier, reducing central nervous system adverse effects such as sedation. In general, first- and second-generation antihistamines have been shown to be effective at relieving the histamine-mediated symptoms associated with allergic rhinitis (e.g., sneezing, pruritus, rhinorrhea, ocular symptoms), but are less effective than intranasal corticosteroids at treating nasal congestion [5].

3. Intranasal corticosteroids

Intranasal corticosteroids are the mainstay of treatment of AR [6,7]. They act by decreasing the influx of inflammatory cells and inhibiting the release of cytokines, thereby reducing inflammation of the nasal mucosa. Their onset of action is 30 minutes, although peak effect may take several hours to days, with maximum effectiveness usually noted after two to four weeks of use. Intranasal corticosteroids are first-line therapeutic options for patients with mild persistent or moderate/severe symptoms and they can be used alone or in combination with oral antihistamines. The adverse effects most commonly experienced with the use of intranasal

corticosteroids are headache, throat irritation, epistaxis, stinging, burning, and nasal dryness. Although the use of intranasal corticosteroids has raised concern for potential systemic adverse effects, including the suppression of the hypothalamic-pituitary axis, the products currently available have not been shown to have such effects

4. Intranasal antihistamine

Compared with oral antihistamines, intranasal antihistamines offer the advantage of delivering a higher concentration of medication to a specific targeted area, resulting in fewer adverse effects [8]. Currently, azelastine (Astelin; approved for ages five years and older) and olopatadine (Patanase; approved for ages six years and older) are the two FDA-approved intranasal antihistamine preparations for AR treatment. Adverse effects include a bitter aftertaste, headache, nasal irritation, epistaxis, and sedation

5. Leukotriene receptor antagonists

The leukotriene receptor antagonists (LTRAs) montelukast and zafirlukast are also effective in the treatment of allergic rhinitis; however, they do not appear to be as effective as intranasal corticosteroids [9].

6. Allergen immunotherapy

Allergen immunotherapy involves the subcutaneous administration of gradually increasing quantities of the patient's relevant allergens until a dose is reached that is effective in inducing immunologic tolerance to the allergen [10]. This form of therapy has been shown to be effective for the treatment of allergic rhinitis caused by pollens and dust mites, but has limited usefulness in treating mould and animal dander allergies. Allergen immunotherapy should be reserved for patients in whom optimal avoidance measures and pharmacotherapy are insufficient to control symptoms or are not well tolerated. Since this form of therapy carries the risk of anaphylactic reactions, it should only be prescribed by physicians who are adequately trained in the treatment of allergy and who are equipped to manage possible life-threatening anaphylaxis. To date, the usefulness of sublingual immunotherapy in adults with allergic rhinitis has been supported by several large trials, but studies in children have shown with mixed results [11]. FDA has yet to approve a commercial product for sublingual immunotherapy.

7. Surgical treatment

Sometimes, we experienced allergic symptoms refractory to medical therapy, especially nasal obstruction. In this condition, inferior turbinate hypertrophy has been suggested as a major cause of nasal obstruction. In addition, nasal septal deviation and chronic rhinosinusitis are possible causes. Various procedures exist for surgical reduction of inferior turbinate volume, including lateral out fracture, partial turbinectomy, submucosal resection, laser-assisted turbinoplasty, radiofrequency-assisted turbinoplasty, and microdebrider-assisted turbinoplasty [12].

Conclusions

AR is a common disorder that can significantly impact patient quality of life. The diagnosis is made through a comprehensive history and physical examination. Further diagnostic testing using skin-prick tests or allergen-specific IgE tests is usually required to confirm that underlying allergies cause the rhinitis. The therapeutic options available for the treatment of allergic rhinitis are effective in managing symptoms and are generally safe and well-tolerated. Second-generation oral antihistamines and intranasal corticosteroids are the mainstay of treatment for the disorder. Allergen immunotherapy as well as other medications such as decongestants and oral corticosteroids may be useful in select cases.

References

1. Small P, Frenkiel S, Becker A, Boisvert P, Bouchard J MD, Carr S, et al. The Canadian Rhinitis Working Group: Rhinitis: A practical and comprehensive approach to assessment and therapy. *J Otolaryngol* 2007;36(Suppl 1):S5-S27.
2. Dykewicz MS, Hamilos DL: Rhinitis and sinusitis. *J Allergy Clin Immunol* 2010;125:S103-115.
3. Bourdin A, Gras D, Vachier I, Chanez P: Upper airway 1: Allergic rhinitis and asthma: united disease through epithelial cells. *Thorax* 2009;64:999-1004.
4. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. World Health Organization GA(2)LEN AllerGen: Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008;63(Suppl 86):8-160.
5. Bender BG, Berning S, Dudden R, Milgrom H, Tran ZV. Sedation and performance impairment of diphenhydramine and second-generation antihistamines: a meta-analysis. *J Allergy Clin Immunol*. 2003;111(4):770-776.
6. Price D, Bond C, Bouchard J, et al. International Primary Care Respiratory Group (IPCRG) Guidelines: management of allergic rhinitis. *Prim Care Respir J*. 2006;15(1):58-70.
7. Scadding GK, Durham SR, Mirakian R, Jones NS, Leech SC, Farooque S, et al. British Society for Allergy and Clinical Immunology. BSACI guidelines for the management of allergic and non-allergic rhinitis. *Clin Exp Allergy*. 2008;38(1):19-42.
8. Bousquet J, Van Cauwenberge P, Khaltaev N; ARIA Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol*. 2001;108(5 suppl):S147-S334.
9. Wilson AM, O'Byrne PM, Parameswaran K. Leukotriene receptor antagonists for allergic rhinitis: a systematic review and meta-analysis. *Am J Med*. 2004;116(5):338-344.
10. Bousquet J, Khaltaev N. Global Surveillance, Prevention and Control of Chronic Respiratory Diseases: A Comprehensive Approach. Geneva: World Health Organization; 2007.
11. Durham SR, Yang WH, Pedersen MR, Johansen N, Rak S. Sublingual immunotherapy with once-daily grass allergen tablets: a randomized controlled trial in seasonal allergic rhinoconjunctivitis. *J Allergy Clin Immunol*. 2006;117(4):802-809.
12. Seidman MD, Gurgel RK, Lin SY, Schwartz SR, Baroody FM, Bonner JR, et al. Clinical practice guideline: Allergic rhinitis. *Otolaryngol Head Neck Surg*. 2015 Feb;152(1 Suppl):S1-43.