

Recent Trends in Management of Allergic Rhinitis

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ABSTRACT

Allergic rhinitis is an inflammatory, immunoglobulin E (IgE)-mediated disease, characterized by nasal congestion, rhinorrhea, and sneezing with or without nasal itching. It can significantly interfere with patient's quality of life. The goals of treatment are to provide the patient with symptomatic relief and improve the quality of life with minimal adverse effects. Prevention has been a large focus in the treatment of allergic rhinitis, but few interventions have proven effective. Although dust mite allergies are more common.

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INTRODUCTION

Allergic rhinitis (AR) is recognized as a global health care problem affecting 10 to 30% of adults and up to 40% of children. However, prevalence may be significantly underestimated due to misdiagnosis, underdiagnosis, and failure of the patient to seek medical attention.¹ Allergic rhinitis is an inflammatory, immunoglobulin E (IgE)-mediated disease, characterized by nasal congestion, rhinorrhea, and sneezing with or without nasal itching.² About 500 million people worldwide are affected by AR, while in India it is about 100 million, and the prevalence differs from one region to another.³ Symptoms that may develop later include⁴

- Stuffy nose (nasal congestion)
- Running nose
- Coughing
- Clogged ears and decreased sense of smell
- Sore throat
- Dark circles under the eyes
- Puffiness under the eyes

- Fatigue and irritability
 - Headache
- It may be classified by²
- Temporal pattern of exposure to a triggering allergen, such as seasonal-like pollen, perennial-like dust mite, or episodic as visiting a home with pets
 - Frequency of symptoms
 - Severity of symptoms, such as a classification to assist in choosing the appropriate treatment strategy
- Independent risk factors associated with AR in India⁵:
- Overcrowding
 - Absence of cross ventilation
 - Occupational exposure to dust or smoke
 - Tobacco smoking
 - Family history of allergic diseases and clinical allergy
 - Sedentary lifestyle.

If a patient has more than one symptom, such as nasal congestion; sneezing; rhinorrhea; itching of nose, eyes, palate; postnasal drip; frequent throat clearing; and cough with positive allergic history, then the clinician should make a diagnosis of AR. Clinicians should initiate empirical therapy including environmental controls, avoidance of allergen, or medical. The management of AR consists of three major categories of treatment: (1) Environmental control measures and allergen avoidance, (2) pharmacological management, and (3) immunotherapy.²

Management for AR is mostly without confirmation of IgE allergy. However, in certain cases, there is need to perform IgE allergy test, such as²

- When patients do not respond to empiric treatment
- When diagnosis of AR is not clear
- When diagnosis of the specific allergen could affect therapy decisions
- When immunotherapy is required, the recommended tests being skin prick, intradermal tests, and blood tests.

The allergic reaction is characterized by activation of two types of inflammatory cells called mast cells and basophils. These cells produce inflammatory substances, such as histamine, which cause congestion (fluid builds up in the nasal tissues), itching, sneezing, and runny nose. Over several hours, these substances activate other inflammatory cells that can cause persistent symptoms.⁶

Seasonal *vs* perennial AR can be seasonal (occurring during specific seasons) or perennial (occurring year-

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round). The allergens that most commonly cause seasonal AR include pollens from trees, grasses, and weeds, as well as spores from fungi and molds.^{2,6}

The allergens that most commonly cause perennial AR are dust mites, cockroaches, animal dander, and fungi or molds. Perennial AR tends to be more difficult to treat.^{2,6}

Optimal treatment includes allergen avoidance, targeted symptom control, immunotherapy, and asthma evaluation, when appropriate.⁷ In 2001, AR and its impact on asthma guidelines were published in cooperation with the World Health Organization, suggesting that the treatment of AR makes use of a combination of patient education, allergen avoidance, pharmacotherapy, and immunotherapy.⁷ In contrast with previous guidelines, these recommendations are based on symptom severity and age, rather than the type or frequency of seasonal, perennial, or occupational exposure.⁸ Allergic rhinitis treatment based on symptoms is summarized in Table 1.

PHARMACOTHERAPY

Pharmacologic options for the treatment of AR include intranasal corticosteroids, oral and topical antihistamines, decongestants, intranasal cromolyn, intranasal anticholinergics, and leukotriene receptor antagonists.^{9,10} The International Primary Care Respiratory Group, British Society for Allergy and Clinical Immunology, and American Academy of Allergy Asthma and Immunology recommend initiating therapy with an intranasal corticosteroid alone for mild to moderate disease and using second-line therapies for moderate to severe disease.⁹⁻¹² Table 2 gives a summary of pharmacologic treatments for AR.⁸

INTRANASAL CORTICOSTEROIDS

Intranasal corticosteroids are the mainstay of treatment of AR. They act by decreasing the influx of inflammatory cells and inhibiting the release of cytokines, thereby reducing inflammation of the nasal mucosa.¹³ Their onset of action is 30 minutes, although peak effect may take several hours to days, with maximum effectiveness usually noted after 2 to 4 weeks of use.¹⁴ Use of these

agents in seasonal disease leads to reduction in inflammatory cells and cytokines within the nasal mucosa and secretions of patients with AR. It also reduces the antigen-induced hyperresponsiveness of nasal mucosa to subsequent challenge by antigen and histamine release. Continuous use is recommended and more efficacious than intermittent use. Along with diminished nasal symptoms, intranasal steroids have beneficial effects on allergic eye symptoms including itching, tearing, redness, and puffiness.²

Many studies have demonstrated that nasal corticosteroids are more effective than oral and intranasal antihistamines in the treatment of AR.^{15,16} One randomized controlled trial (RCT) looking at quality-of-life measures compared the antihistamine loratadine with the nasal corticosteroid fluticasone in 88 adults over a 4-week period.¹⁷ The study's results showed that symptom scores were comparable, but quality-of-life scores were superior in the nasal corticosteroid group.¹⁷ The adverse effects most commonly experienced with the use of intranasal corticosteroids are headache, throat irritation, epistaxis, stinging, burning, and nasal dryness.^{8,9}

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.^{8,18} There are few studies that looked specifically at the effects of intranasal corticosteroids on skeletal growth and adrenal activity. A well-designed prospective study did not show any difference in growth in children using nasal corticosteroids for at least 3 years.¹⁹ Although nasal fluticasone has been shown to reduce endogenous cortisol excretion in one study,²⁰ its impact on growth is unknown.¹⁸ Despite the data, all intranasal corticosteroids carry a warning that long-term use may restrict growth in children.⁸ Fluticasone propionate nasal spray improved nasal symptoms, quality of life, and verbal memory in children with seasonal AR.²¹ One of the benefits of intranasal application is targeted delivery and increased dosage to nasal tissues while limiting systemic side effects.

Table 1: Allergic rhinitis treatment based on symptoms

Treatment type	Ocular symptoms	Nasopharyngeal itching	Sneezing	Rhinorrhea
Intranasal corticosteroids	✓	✓	✓	✓
Oral antihistamines	✓	✓	✓	✓
Intranasal antihistamines	—	✓	✓	✓
Decongestants	✓	—	—	✓
Intranasal cromolyn	—	✓	✓	✓
Intranasal anticholinergics	—	—	—	✓
Leukotriene receptor antagonists	✓	—	—	✓
Nasal saline irrigation	—	—	—	✓
Immunotherapy	✓	—	✓	✓

Table 2: Summary of pharmacologic treatments for allergic rhinitis

<i>Treatment</i>	<i>Minimum age</i>	<i>Mode and onset of action</i>	<i>Adverse effects</i>
<i>Intranasal corticosteroids</i>			
Beclomethasone	6 years	Inhibits the influx of inflammatory cells; onset of action is less than 30 minutes	Bitter aftertaste, burning, epistaxis, headache, nasal dryness, potential risk of systemic absorption, rhinitis medicamentosa, stinging, throat irritation
Budesonide	6 years		
Ciclesonide	6 years		
Flunisolide	6 years		
Fluticasone furoate	2 years		
Fluticasone propionate	12 years		
Mometasone	2 years		
Triamcinolone	12 years		
<i>Oral antihistamines</i>			
Cetirizine	6 months	Blocks H1 receptors; Cetirizine : 1 to 2 hours	Dry mouth, sedation at higher than recommended doses
Desloratadine	6 months	Fexofenadine: 30 to 60 minutes	
Fexofenadine	6 months		
Levocetirizine	12 years		
Loratadine	2 years	1 hour 42 minutes	
<i>Intranasal antihistamines</i>			
Azelastine	5 years	Blocks H1 receptors; onset of action is 15 minutes	Bitter aftertaste, epistaxis, headache, nasal irritation, sedation
Olopatadine	6 years		
<i>Oral decongestants</i>			
Pseudoephedrine	12 years	Vasoconstriction; onset of action is 15 to 30 minutes	Arrhythmias, dizziness, headache, hypertension, insomnia, nervousness, tremor, urinary retention
<i>Intranasal cromolyn</i>			
Cromolyn	2 years	Inhibits histamine release; results typically noted in 1 week, but may take 2 to 4 weeks for full effect	Epistaxis, nasal irritation, sneezing
<i>Intranasal anticholinergics</i>			
Ipratropium	6 years	Blocks acetylcholine receptors; onset of action is 15 minutes	Epistaxis, headache, nasal dryness
<i>Leukotriene receptor antagonists</i>			
Montelukast	6 months	Blocks leukotriene receptors; onset of action is 2 hours	Elevated levels of alanine transaminase, aspartate transaminase, and bilirubin

Note: Listed in order of treatment preference

ORAL ANTIHISTAMINES

Histamine is the most studied mediator in early allergic response. It causes smooth muscle constriction, mucus secretion, vascular permeability, and sensory nerve stimulation, resulting in the symptoms of AR.²² The first-generation antihistamines include brompheniramine, chlorpheniramine, clemastine, and diphenhydramine.²³ They may cause substantial adverse effects, including sedation, fatigue, and impaired mental status. These adverse effects occur because the older antihistamines are more lipid soluble and more readily cross the blood-brain barrier than second-generation antihistamines. The use of first-generation antihistamines has been associated with poor school performance, impaired driving, and an increase in automobile collisions and work injuries.^{21,22,24,25}

Compared with first-generation antihistamines, second-generation antihistamines have a better adverse

effect profile and cause less sedation, with the exception of cetirizine.^{21,22} The second-generation oral antihistamines include desloratadine, levocetirizine, fexofenadine, 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. Although cetirizine is a second-generation antihistamine and a more potent histamine antagonist, it does not have the benefit of decreased sedation. As a group, the second-generation oral antihistamines are thought to stabilize and control some of the nasal and ocular symptoms, but have little effect on nasal congestion.²²

In general, first- and second-generation antihistamines have been shown to be effective at relieving the histamine-mediated symptoms associated with AR (e.g., sneezing, pruritus, rhinorrhea, ocular symptoms), but are less effective than intranasal corticosteroids at treating

nasal congestion. Because their onset of action is typically within 15 to 30 minutes and they are considered safe for children older than 6 months, antihistamines are useful for many patients with mild symptoms requiring "as needed" treatment.²⁶

INTRANASAL ANTIHISTAMINES

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.¹³ Currently, azelastine (approved for ages 5 years and older) and olopatadine (approved for ages 6 years and older) are the two Food and Drug Administration (FDA)-approved intranasal antihistamine preparations for the treatment of AR. As a class, their onset of action occurs within 15 minutes and lasts up to 4 hours. Adverse effects include a bitter after-taste, headache, nasal irritation, epistaxis, and sedation. Although intranasal antihistamines are an option in patients whose symptoms did not improve with second-generation oral antihistamines, their use as first- or second-line therapy is limited by their adverse effects and cost compared with second-generation oral antihistamines, and by their decreased effectiveness compared with intranasal corticosteroids.^{27,28}

ROLE OF MONTELUKAST

Investigations studied that a combination of antileukotrienes and fexofenadine abolished early- and late-phase reactions. It seems histamine and cysteinyl leukotriene together are the greatest mediators of early and late reactions. Furthermore, antileukotriene therapy reduces nasal congestion and improves sense of smell.²⁹ While few studies demonstrate clinical responses to the new antileukotriene oral medication in AR, Kaliner³⁰ noted 30 to 50% clinical improvement in patients with rhinosinusitis.

DECONGESTANTS

Oral and topical decongestants improve the nasal congestion associated with AR by acting on adrenergic receptors, which causes vasoconstriction in the nasal mucosa, resulting in decreased inflammation.^{7,9,13} Although the most commonly available decongestants are phenylephrine, oxymetazoline, and pseudoephedrine, the abuse potential for pseudoephedrine should be weighed against its benefits.

Common adverse effects that occur with the use of intranasal decongestants are sneezing and nasal dryness. Duration of use for more than 3 to 5 days is usually not recommended, because patients may develop rhinitis medicamentosa or have rebound or recurring congestion.¹³

However, a study of 35 patients found no rebound when oxymetazoline was used for 10 days.³¹

Because oral decongestants may cause headache, elevated blood pressure, tremor, urinary retention, dizziness, tachycardia, and insomnia, patients with underlying cardiovascular conditions, glaucoma, or hyperthyroidism should only use these medications with close monitoring.^{7,9,13}

COMBINATION THERAPY

Although many studies have looked at the combination of an intranasal corticosteroid with an antihistamine or leukotriene receptor antagonist, most have concluded that combination therapy is no more effective than monotherapy with intranasal corticosteroids.^{17,32-34} Therefore, although patients should not have therapy initiated with more than one agent, combination therapy is an option for patients with severe or persistent symptoms. Since antileukotrienes display synergism with antihistamines, they are often used for combination treatment of AR and asthma. Antihistamine-antileukotriene combination exerts additional anti-inflammatory activity as evidenced by reduction of inflammatory infiltrate and cytokine levels in patients with seasonal AR and mild intermittent asthma, and is therefore thought to be as effective as corticosteroids.^{35,36}

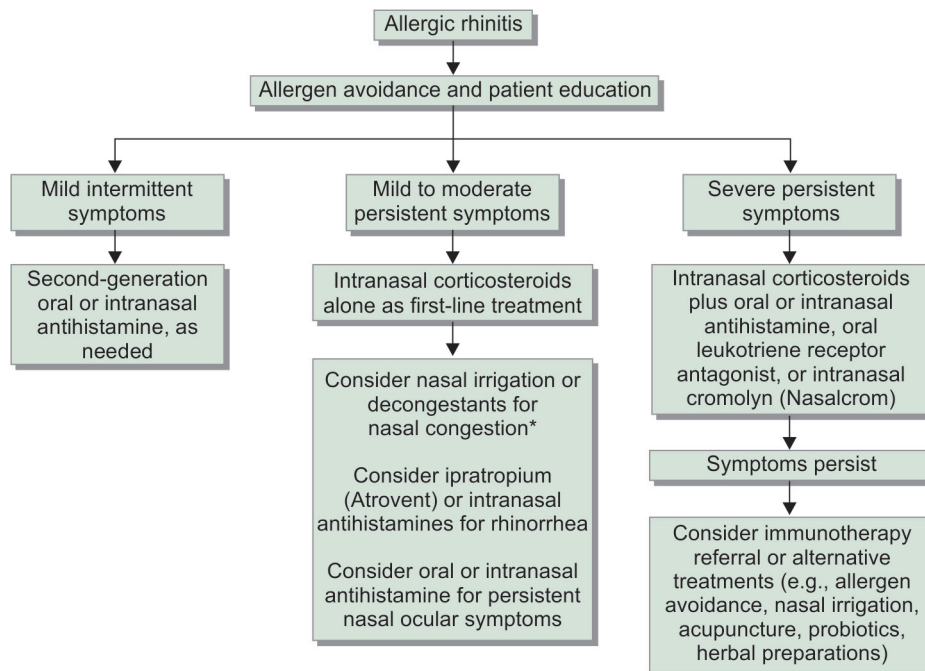
Several drugs of antihistamine and antileukotriene classes have been employed in patients with AR-asthma comorbidity. However, optimal choice of therapy is fundamental to maximize clinical effectiveness and attain desirable outcomes. Montelukast, a cysteinyl leukotriene antagonist, and fexofenadine, a second-generation antihistamine, have evolved to become the preferred drugs for managing these patients.^{37,38}

Immunotherapy

Immunotherapy should be considered for patients with moderate or severe persistent AR, i.e., not responsive to usual treatments. Targeted immunotherapy is the only treatment that changes the natural course of AR, preventing exacerbation.² It consists of a small amount of allergen extract given sublingually or subcutaneously over the course of a few years, with maintenance periods typically lasting between 3 and 5 years. The greatest risk associated with immunotherapy is anaphylaxis.² Although the usefulness of sublingual immunotherapy in adults with AR has been supported by several large trials, studies in children have met with mixed results, and the FDA has yet to approve a commercial product for sublingual use.⁸

Recombinant deoxyribonucleic acid technology has also played a role in immunotherapy, allowing for the development of allergen-specific vaccines. In a multi-

Flow Chart 1: Treatment of allergic rhinitis



center RCT involving 134 adults receiving a recombinant birch pollen vaccine for 12 consecutive weeks followed by monthly injections for 15 months, patients noted statistically significant improvements in rhinosinusitis symptoms, medication use, and skin sensitivities when compared with placebo.³⁹

Omalizumab (Xolair), an anti-IgE antibody, has been shown to be effective in reducing nasal symptoms and improving quality-of-life scores in patients with AR.⁸ The main limitations of its current use are its high cost (average wholesale price is \$679 to \$3,395 per month) and lack of FDA approval for home use.⁸

OTHER

Patients with AR should avoid exposure to cigarette smoke, pets, and allergens to which they have a known sensitivity. Nasal irrigation is beneficial in the treatment of chronic rhinorrhea and may be used alone or as adjuvant therapy. Irrigation using a Neti pot is superior to saline sprays; it may also be done with a low-pressure squeeze bottle.⁸

Prevention has been a large focus in the study of AR, but few interventions have proven effective. Although dust mite allergies are common, studies have not found any benefit to using mite-proof impermeable mattress and pillow covers. Other examples of proposed interventions without documented effectiveness include breastfeeding, delayed exposure to solid foods in infancy, and use of air filtration systems. Flow Chart 1 provides an algorithm for the treatment of AR with pharmacologic and nonpharmacologic therapies.⁸

CONCLUSION

Individuals with AR suffer from impaired cognitive function and reduced work productivity and performance. It can affect children's learning ability and performance at school and cause somnolence and inability to concentrate. Adolescents with AR have difficulty getting a good night's sleep and experience problems doing school work, and children with rhinitis and snoring have poorer school performance.

Allergic rhinitis is a common disorder that can significantly interfere with patient's quality of life. The goals of treatment are to provide the patient with symptomatic relief and improve the quality of life with minimal adverse effects.

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