Allergic Rhinitis: Update on Your Therapeutic Choices

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Many pharmacological options exist for allergic rhinitis. Intranasal corticosteroids are the most effective medication class for patients with moderate to severe symptoms; those with milder intermittent symptoms can be treated with a second-generation oral or intranasal antihistamine.

ABSTRACT: Many pharmacological options exist for allergic rhinitis. Intranasal corticosteroids are the most effective medication class for patients with moderate to severe symptoms; those with milder intermittent symptoms can be treated with a second-generation oral or intranasal antihistamine. Allergen avoidance measures may also be helpful. In patients whose symptoms are refractory to standard pharmacological therapy, allergen immunotherapy can be effective. A 3- to 5-year treatment course of subcutaneous injection immunotherapy can produce lasting benefit years after completion of therapy. In the future, sublingual immunotherapy may emerge as an alternative approach in the United States as it has in Europe in recent years.

Key words: allergic rhinitis, nonallergic rhinitis, primary care

Allergic rhinitis is a common disorder that dramatically affects patients' quality of life and consumes billions of dollars each year in health care costs and lost productivity. Rhinitis may be allergic (IgE-mediated) or nonallergic. Pure allergic rhinitis is about 3 times more prevalent than pure nonallergic rhinitis; however, many patients have both types.

In this article, we review pharmacological treatments for the different types of rhinitis; we focus on their relative efficacy and the symptoms for which each is best employed (Table). We also discuss immunotherapy options for the treatment of allergic rhinitis. In a previous article ("Allergic Rhinitis: Update on Diagnosis"), we addressed issues related to the diagnosis of allergic rhinitis.

INTRANASAL CORTICOSTEROIDS

Intranasal corticosteroids are the most effective class of medication for allergic rhinitis, and they are effective for all of its symptoms. While a patient may prefer and/or respond better to a given agent, none of the currently available intranasal corticosteroids has known superior efficacy over another. Intranasal corticosteroids are also effective in nonallergic rhinitis, including vasomotor rhinitis and rhinitis medicamentosa. Even though symptoms may initially abate within approximately 12 hours, maximum efficacy requires several weeks of daily use.

In our experience, most patients who report that allergic rhinitis symptoms have not responded to an intranasal corticosteroid are not using the medication regularly. Advise patients to give the medication at least a 1-month trial. In addition, teach them to direct the spray laterally within the nasal vestibule; this technique minimizes the nasal irritation and bleeding that can be associated with intranasal corticosteroids. These strategies should improve adherence and consequently efficacy. Intranasal corticosteroids are generally free from significant systemic side effects, including growth suppression in children.

<table>
<thead>
<tr>
<th>Class</th>
<th>Agent</th>
<th>Trade name</th>
<th>Mechanism</th>
<th>Symptom(s) treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Second-generation oral antihistamine</td>
<td>Cetirizine, Fexofenadine, Levocetirizine, Loratadine, Desloratadine</td>
<td>Zyrtec, Allegra, Xyzal, Claritin, Clarinex</td>
<td>Stabilizes H&lt;sub&gt;1&lt;/sub&gt; receptor in inactive conformation&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Itching, sneezing, rhinorrhea; not as effective for nasal congestion</td>
</tr>
</tbody>
</table>
Intranasal antihistamine

- **Azelastine**, Olopatadine
- **Astepro**, **Patanase**

**Stabilizes H$_1$ receptor in inactive conformation**

- **Itching, sneezing, rhinorrhea and nasal congestion**

Leukotriene receptor antagonist

- **Montelukast**, **Singulair**

- **Leukotriene receptor antagonist**

- **Itching, sneezing, rhinorrhea; not as effective for congestion**

Anticholinergic agent

- **Ipratropium nasal spray**, **Atrovent nasal spray**

**Anticholinergic**

- **Rhinorrhea (only)**

Intranasal corticosteroid

- **Fluticasone propionate**, Fluticasone furoate, Mometasone, Budesonide, Triamcinolone, Flunisolide, Ciclesonide

- **Flonase**, **Veramyst**, **Nasonex**, **Rhinocort Aqua**, **Nasacort AQ**, **Nasarel**, **Omnaris**

**Multiple anti-inflammatory effects (corticosteroid)**

- **Itching, sneezing, rhinorrhea and nasal congestion; the most effective class of agents**

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**ANTIHISTAMINES**

Second-generation oral antihistamines (loratadine, desloratadine, fexofenadine, cetirizine, levocetirizine) are effective for pruritus and rhinorrhea in allergic rhinitis, although they are less effective for nasal congestion and are of no proven use in nonallergic rhinitis. They can be used as needed for rhinitis symptoms, but they generally are more effective with continuous use. As a group, the second-generation agents have fewer side effects than first-generation agents (diphenhydramine, chlorpheniramine, hydroxyzine, and others), which can cause sedation and anticholinergic side effects.

In a double-blind study, the performance in a driving simulator of participants who took 50 mg of diphenhydramine was similar to or worse than that of persons with a blood alcohol concentration of 0.1%, whereas the performance of participants who took 60 mg of fexofenadine was not significantly different from that of those who received placebo. First-generation antihistamines have also been associated with impaired learning and school performance in children.

Among the second-generation oral agents, loratadine and desloratadine generally have somewhat less efficacy and slower onset of action than other agents. The intranasal antihistamines (azelastine, olopatadine) have rapid onset of action and may be more effective than oral antihistamines, but combining agents from the 2 classes may not be better than using the intranasal antihistamine by itself. Unlike oral antihistamines, intranasal antihistamines have proven utility for vasomotor rhinitis. The principal adverse effects of intranasal antihistamines include bad taste and somnolence.

**DECONGESTANTS**

Intranasal decongestants, such as oxymetazoline, cause vasoconstriction and decrease nasal congestion, although they do not substantially affect itching, sneezing, and rhinorrhea. They can be useful in the short term in severely congested patients to allow other agents (eg, nasal corticosteroids or nasal antihistamines) to reach their site of action. While there is some evidence that intranasal decongestants can be safely tolerated for weeks, rebound congestion (rhinitis medicamentosa) may begin to develop within 3 days. Generally speaking, intranasal decongestants should not be recommended for longer than 3 days of continuous use.

Oral decongestants, such as pseudoephedrine and phenylephrine, are α-agonists and work similarly...
to topical agents. They alleviate congestion caused by both allergic and nonallergic rhinitis. Although they do not cause rhinitis medicamentosa, they have the potential for systemic adverse effects, including palpitations, irritability, and elevated blood pressure. However, the effect on blood pressure is probably overestimated: in a well-done meta-analysis, pseudoephedrine raised systolic blood pressure by an average of 1 mm Hg, increased pulse by 3 beats per minute, and did not affect diastolic blood pressure. Because of significant individual patient variability in these parameters, close monitoring remains important.

**OTHER AGENTS**

An intranasal preparation of the anticholinergic drug ipratropium is useful for the treatment of rhinorrhea in both allergic and nonallergic rhinitis as well as in rhinitis caused by the common cold.

The efficacy of the leukotriene receptor antagonist montelukast in the treatment of allergic rhinitis is similar to that of oral antihistamines, and select studies suggest an additive benefit in combination with oral antihistamines. However, this combination is less effective than singleagent use of an intranasal corticosteroid for most patients. Montelukast is also useful in the treatment of asthma. Cromolyn, a mast cell stabilizer available as a nasal spray or eyedrops, is effective in preventing allergic rhinitis symptoms before allergen exposure. However, given a 4 times daily dosing regimen and limited efficacy following symptom onset, topical cromolyn preparations are of modest practical value for most patients.

**INITIAL CHOICE OF AGENT**

The selection of initial therapy involves several factors. In general, patients with moderate to severe allergic rhinitis symptoms should start with an intranasal corticosteroid, whereas those with milder intermittent symptoms can be treated with a second-generation oral or intranasal antihistamine. In patients with nonallergic rhinitis, either an intranasal corticosteroid or an intranasal antihistamine is appropriate; however, an oral antihistamine is not likely to be effective. Patients with prominent nasal congestion can be treated with an intranasal corticosteroid or perhaps an intranasal antihistamine. Patients whose most prominent symptom is clear anterior rhinorrhea, such as those with gustatory rhinitis, benefit most from intranasal ipratropium.

**COMBINATION THERAPY**

Frequently, a single agent does not sufficiently relieve the symptoms of allergic rhinitis. Because oral antihistamines treat all allergic rhinitis symptoms effectively except congestion, and oral decongestants treat only congestion, the combination makes pharmacological sense. Indeed, the evidence shows that this combination is superior to either agent alone for symptoms of allergic rhinitis. However, the adverse effects of oral decongestants make this combination untenable for sustained use in many patients.

An oral antihistamine plus montelukast may be superior to either agent alone for allergic rhinitis, but this combination is inferior to an intranasal corticosteroid by itself. Nevertheless, select patients may demonstrate marked clinical improvement, even the minority in whom intranasal corticosteroids have failed. For rhinorrhea, intranasal ipratropium and an intranasal corticosteroid are more effective than either agent alone.

Other frequently used combinations, such as an oral antihistamine plus an intranasal corticosteroid and an oral antihistamine plus an intranasal antihistamine, are not supported by clearly convincing data that indicate additive benefit. However, from a practical standpoint, the combination of an intranasal corticosteroid used daily and an oral second-generation antihistamine used as needed is often quite effective. In patients who do not respond to this regimen, an intranasal antihistamine and an intranasal corticosteroid may be the most potent 2-agent combination.

**CLINICAL HIGHLIGHTS**

- Intranasal corticosteroids are the most effective medications for allergic rhinitis; they treat all of its...
symptoms. These agents are also effective in nonallergic rhinitis, including vasomotor rhinitis and rhinitis medicamentosa. Most patients who report that allergic rhinitis symptoms have not responded to an intranasal corticosteroid are not using the medication regularly. Advise patients to give the medication at least a 1-month trial. In addition, teach them to direct the spray laterally within the nasal vestibule; this technique minimizes the nasal irritation and bleeding that can be associated with intranasal corticosteroids.

Second-generation oral antihistamines are effective for pruritus and rhinorrhea in allergic rhinitis, although they are less effective for nasal congestion and are of no proven use in nonallergic rhinitis.

To prevent the development of rebound congestion (rhinitis medicamentosa), advise patients not to use intranasal decongestants for more than 3 days.

In general, patients with moderate to severe allergic rhinitis symptoms should start with an intranasal corticosteroid, whereas those with milder intermittent symptoms can be treated with a second-generation oral or intranasal antihistamine.

Consider referral to an allergist for patients whose rhinitis remains symptomatic or whose quality of life remains impaired despite treatment.

Subcutaneous injection allergen immunotherapy has been shown to be effective in numerous randomized, controlled trials in children and adults. Immunotherapy also appears to prevent sensitization to new allergens and may reduce the risk of asthma in patients with allergic rhinitis.

ALLERGEN AVOIDANCE

For persons with allergic rhinitis, a number of allergen avoidance recommendations are advocated in practice parameters and reviews. For those with pollen allergy, these measures include wearing dust masks (although supporting data are limited, and even high-efficiency respirators, such as N95 respirators, do not perform well if not fitted properly) and limiting time outdoors. For persons with mold allergy, avoidance measures include limiting soil-disturbing activity or wearing masks while doing so, and for indoor mold, eliminating moisture sources, removing moisture-damaged materials, and cleaning nonporous surfaces with bleach.

To control dust mite antigen, reducing indoor humidity, using dust mite sheet covers, washing bedding in hot water, replacing carpeting with hard flooring, using acaricides, and using high-efficiency particulate air (HEPA) filters in vacuums and in heating/air conditioning units have all been advocated. However, the effectiveness of some of these measures is controversial.

Roach antigen control focuses on extermination and good sanitation to prevent reinfection. Pet allergen is most effectively avoided by removing the pet, after which time it can take months for allergen to disappear from the home.

INDICATIONS FOR SPECIALTY REFERRAL

Consider referral to an allergist for patients whose rhinitis remains symptomatic or whose quality of life remains impaired despite treatment. Allergy skin testing may confirm suspected triggers or lead
to the diagnosis of nonallergic rhinitis. Frequently, the combination of allergen avoidance and ongoing pharmacological therapy controls symptoms. For those patients with positive skin test results consistent with their symptoms (eg, peak symptoms in the fall in a patient with ragweed allergy) who remain uncontrolled with pharmacotherapy or who wish to limit the need for medication, consider allergen immunotherapy.

**IMMUNOTHERAPY FOR ALLERGIC RHINITIS**

Allergen immunotherapy involves exposing patients to initially escalating and then maintenance amounts of the allergens that cause the majority of their symptoms. Subcutaneous injection immunotherapy has been shown to be effective in numerous randomized, controlled trials in children and adults. Allergen immunotherapy also appears to prevent sensitization to new allergens and may reduce the risk of asthma in patients with allergic rhinitis. Further, allergen immunotherapy is the only treatment known to alter the natural history of allergic rhinitis, and the clinical benefits are usually sustained for years following a successful 3- to 5-year treatment period.

In the United States, immunotherapy is usually administered by subcutaneous injection, although sublingual immunotherapy may prove to be an effective alternative. While substantial positive data about European sublingual extracts have accumulated over the past several years, data about sublingual extracts in the United States are limited and results have been mixed. It is important to note that allergen extract potency is not uniformly standardized; different standardization methods are used in Europe. Thus, data from European sublingual immunotherapy trials (even with similar allergens) cannot be extrapolated directly for use with extracts manufactured in the United States. Currently, no form of sublingual immunotherapy is approved by the FDA.

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**Therapeutic Agents in This Article**

Azelastine (Astelin, Astepro)
Budesonide (Rhinocort Aqua)
Cetirizine (Zyrtec)
Chlorpheniramine (Chlor-Trimeton)
Ciclesonide (Omnaris)
Cromolyn (Nasalcrom)
Desloratadine (Clarinex)
Diphenhydramine (Benadryl)
Fexofenadine (Allegra)
Flunisolide (Nasarel)
Fluticasone furoate (Veramyst)
Fluticasone propionate (Flonase)
Hydroxyzine (Atarax)
Ipratropium (Atrovent)
Loratadine (Claritin)
Levocetirizine (Xyzal)
Mometasone (Nasonex)
Montelukast (Singulair)
Olopatadine (Patanase)
Oxymetazoline (Afrin, Dristan)
Phenylephrine (Neo-Synephrine)
Pseudoephedrine (Sudafed)
Triamcinolone (Nasacort AQ)

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