Management of Allergic Rhinitis: A Review for the Community Pharmacist



J. Russell May, PharmD¹; and William K. Dolen, MD²

¹University of Georgia College of Pharmacy, Augusta, Georgia; and ²Augusta University, Augusta, Georgia

ABSTRACT

Purpose: Allergic rhinitis is a highly prevalent disease affecting the quality of life of millions of North Americans. The management of allergic rhinitis includes allergen avoidance, pharmacotherapy, and immunotherapy. Current pharmacologic options include oral and intranasal antihistamines, intranasal corticosteroids, oral and intranasal decongestants, oral and intranasal anticholinergics, and leukotriene receptor antagonists. Second-generation oral antihistamines and intranasal corticosteroids are the mainstays of treatment, with practice guidelines recommending intranasal corticosteroids as first-line treatment for moderate to severe allergic rhinitis.

Methods: Clinical trials studying a widely used intranasal corticosteroid, fluticasone propionate, in comparison with second-generation oral antihistamines, cetirizine, loratadine, or montelukast, were selected to support the comparative review of the efficacy and tolerability of these 2 classes of medications. Studies evaluating the combination of fluticasone propionate with an oral antihistamine were also included to review the efficacy and tolerability of combination therapy to treat allergic rhinitis.

Findings: Studies comparing fluticasone propionate with cetirizine had mixed findings; fluticasone propionate was found to have equal or greater efficacy in reducing nasal symptom scores. Combination therapy of fluticasone propionate and the oral antihistamine, loratadine, was found to have efficacy comparable with that of intranasal corticosteroid alone.

Implications: Many of these medications are available over the counter in the pharmacy, and the community pharmacist plays an important role as part of the patient's health care team in managing this disease. Pharmacotherapy is patient-specific, based on type, duration, and severity of symptoms, comorbidities, prior treatment, and patient preference. This article aims to provide an overview of the pathophysiology, available treatment options, guideline recommendations, and role

of the pharmacist for this disease. (*Clin Ther.* 2017;39:2410–2419) © 2017 The Authors. Published by Elsevier HS Journals, Inc.

Key words: allergic rhinitis, antihistamines, community pharmacy, corticosteroids, pharmacists.

INTRODUCTION

Allergic rhinitis (AR) is a chronic inflammatory disease that affects 10% to 30% of Americans¹ and 20% to 25% of Canadians.² Prevalence of AR is increasing worldwide, affecting up to 40% of the global population.³ AR is part of a systemic inflammatory process and is associated with other inflammatory disorders, including asthma, rhinosinusitis, and allergic conjunctivitis.⁴ AR reduces quality of life by affecting sleep, school, work productivity, and social life.⁴ Due to its high prevalence and impact on quality of life, AR has been classified as a major chronic respiratory disease.³ The financial burden is also significant, with direct medical costs in the United States increasing from \$6.1 billion in 2000 to \$11.2 billion in 2005, greater than for diabetes, coronary heart disease, and asthma.⁵

Practice guidelines and parameters have been developed to classify and manage treatment of AR. Many patients who have AR do not seek care from a primary care physician or specialist and instead choose to self-treat their symptoms or even ignore them. Therefore, the community pharmacist can be a valuable resource in recognizing and assessing the symptoms of AR. Whether or not a patient has been

http://dx.doi.org/10.1016/j.clinthera.2017.10.006 0149-2918/\$ - see front matter

Disclaimer: The views expressed in this article are those of the authors and do not necessarily represent the views of their respective institutions. *Accepted for publication October 5*, 2017.

^{© 2017} The Authors. Published by Elsevier HS Journals, Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

diagnosed previously with AR, the pharmacist should be aware of common symptoms and understand when to refer the patient to a primary care physician. The knowledge and skills of the pharmacist allow optimization of therapy and appropriate treatment selection based on symptom presentation, duration, severity, and minimizing adverse events.

Definition

AR is an immunoglobulin E-mediated inflammatory reaction in the nasal mucosa caused by inhaled allergens, such as pollen, mold, or animal dander.¹ The allergic response occurs in 2 phases-early and late. Allergen exposure leads to the allergens crosslinking with immunoglobulin E antibodies bound to mucosal mast cells and subsequent release of inflammatory mediators, such as histamine, prostaglandins, and leukotrienes.^{6,7} These mediators initiate the early (or acute) phase of an allergic reaction, which develops within minutes of exposure and causes AR symptoms.⁷ Symptoms include sneezing, nasal pruritus (itching), upper airway obstruction (congestion or blockage), rhinorrhea (clear nasal discharge), and itchy or watery eyes.¹ The inflammatory mediators attract, recruit, and activate additional inflammatory cells-eosinophils, neutrophils, and T lymphocytes-into the nasal mucosa. These cells release more inflammatory mediators, initiating the late-phase response, which occurs several hours after initial allergen exposure.^{1,8} This late response is associated with chronic inflammation and includes the same symptoms seen in the early-phase response, with nasal congestion becoming the primary symptom due to mucosal edema.^{1,8} These symptoms begin 6 to 12 hours after allergen exposure, peaking at 12 to 24 hours.⁷ Priming is a clinical feature of AR and is thought to be related to the latephase allergic response. Although the initial influx of inflammatory cells does not induce allergy symptoms, repeated or later exposure of a smaller amount of the same allergen will induce a symptomatic response because of increased mucosal sensitivity.⁸ Due to this sensitivity, which can persist for a few days, symptoms can be provoked by other allergens and are not limited to the priming allergen.⁸

There are 2 symptom patterns of AR, seasonal (also known as hay fever, or intermittent) and perennial (or persistent). Seasonal allergic rhinitis (SAR) symptoms are usually easily identifiable and directly associated with seasonal allergen exposure, such as tree, grass, and weed pollens, or fungi.¹ The length of the "season" can vary based on location and climate conditions,¹ as well as the range of allergens to which the patient is sensitized. Intermittent symptoms are present <4 days per week or for <4 weeks.⁴ Perennial allergic rhinitis (PAR) symptoms occur for up to 75% of the year, are present for >4 days per week and for >4 weeks, and are less easy to identify because they overlap with symptoms seen in sinusitis, respiratory infections, and other types of rhinitis.^{4,9} Symptoms are often caused by nonseasonal allergens, such as dust mites, animal dander, or mold.¹

Treatment Options

There are many options for the treatment of AR, both nonpharmacologic and pharmacologic. A number of medications are also available over the counter (OTC) without a prescription, and product selection should be based on patient factors, including their symptoms and medical history. The goal of treatment is to reduce or eliminate current symptoms while preventing future attacks and long-term complications. Appropriate treatment selection should allow for minimal adverse effects and enable the patient to maintain a normal lifestyle.

Three approaches of AR management include allergen avoidance, pharmacotherapy, and immunotherapy. Nonpharmacologic interventions, such as allergen avoidance, can reduce or eliminate AR symptoms and the amount of pharmacotherapy needed for symptom control. Allergen avoidance is a practical option when allergens have been identified, either by the patient or by allergy testing. Patients can take steps to reduce exposure to triggers based on the specific allergen, whether it is pollen, mold, or animal dander. Allergen avoidance should be part of an overall treatment strategy that includes pharmacotherapy.

Selection of pharmacotherapy (OTC and prescription) should take into account efficacy, tolerability, patient preference, and cost. Treatment options for AR are generally administered orally or intranasally. Pharmacologic treatment of AR proposed by the guidelines is a stepwise approach based on classification of symptoms in terms of course and severity.^{1,10}

Available treatment classes include antihistamines, corticosteroids, decongestants, leukotriene receptor antagonists (LTRAs), and anticholinergics. Immunotherapy is also an option for patients who are refractory to pharmacotherapy.¹⁰ The most common pharmacologic treatment options include intranasal corticosteroids, H_1 receptor inverse agonists (antihistamines), and LTRAs. These medications have proven to be efficacious in treating SAR, and a few trials have supported their use in PAR as well.^{11–13}

Intranasal corticosteroids (INCS) are first-line therapy for moderate to severe AR and are the most effective medication for controlling AR symptoms.^{1,10} INCS have also demonstrated efficacy in certain types of nonallergic rhinitis as well. INCS exhibit potent antiinflammatory action due to effects on several cell types, including topically on nasal mucosa.¹⁴ They decrease release of inflammatory mediators and cytokines, thereby reducing nasal mucosal inflammation. They provide symptomatic and effective relief when used continuously or as needed. However, they are most effective when used regularly, as onset of action is 7 to 12 hours, reaching maximum benefit within 2 weeks.¹⁵ Local adverse effects include epistaxis, nasal drying, and septal perforation (although rare), and are most likely due to incorrect administration technique.¹⁶ Intranasal corticosteroids are less likely to display the systemic effects of oral steroids-adrenal suppression, bone fractures (especially in the elderly), growth suppression, and ocular effects-that are normally a concern for some prescribers and patients, due to reduced exposure. Studies have found that, due to the lower dose and lower bioavailability of the intranasal formulations compared with inhaled steroids, there is less risk of adverse events associated with systemic absorption.¹⁴ Although the available intranasal corticosteroids vary in terms of solubility, binding affinity, and topical potency, overall clinical response does not significantly vary when comparing within the class.¹ All of the available intranasal corticosteroids are efficacious in controlling AR symptoms.¹ Thus, product differentiation involves factors such as cost, ease of dosing, and sensory issues, such as aroma and taste, which can affect patient preference.¹⁷

 H_1 -receptor inverse agonists were previously thought to block histamine at the H_1 receptor and were termed, erroneously, as *receptor antagonists*. However, research on the mechanism of action found that H_1 -receptor inverse agonists downregulate receptor activity, and some can additionally stabilize mast cells.^{18,19} These agents are most effective against symptoms primarily mediated by histamine, that is, sneezing, pruritus, and ocular symptoms.¹⁶ Rhinorrhea can be multifactorial, and individual patients differ in clinical an antihistamine. their response to Antihistamines are less effective for nasal congestion and may need to be given in combination with a decongestant or intranasal corticosteroid.¹⁹ Older, firstgeneration, oral antihistamines nonselectively interact with other receptors and are therefore associated with sedation and mental impairment, as well as potential anticholinergic side effects, such as dry mouth, dry eves, urinary retention, and constipation.¹⁹ Newer, second-generation oral H1 antihistamines are more selective and are recommended, as they are equally effective with less sedation and anticholinergic side effects.¹ Second-generation antihistamines can also be dosed once daily as opposed to the multiple doses required for first-generation antihistamines, with a rapid onset of action between 1 and 2 hours. Antihistamines are also available for intranasal administration and their efficacy is similar to that for oral formulations. They work rapidly, effectively reducing nasal symptoms in <30 minutes.¹

Oral and intranasal decongestants produce vasoconstriction, which decreases inflammation and nasal congestion.¹ Intranasal formulations are more effective in reducing obstruction than oral decongestants.⁴ Oral decongestant use is limited by adverse effects, including insomnia, loss of appetite, elevated blood pressure, and tachycardia.²⁰ Due to the adverse effects and tolerability concerns of oral decongestants, they should be used for a short duration, with caution in certain patient populations, such as the elderly and patients with hypertension, hyperthyroidism, urinary retention, or closed-angle glaucoma.²⁰ Some adverse effects of intranasal decongestants include nasal burning, stinging, or dryness.²⁰ Consecutive use of intranasal decongestants should be limited to no more than 3 days in a row, as overuse can lead to dependence, and patients can experience rebound nasal congestion due to a-receptor downregulation, or rhinitis medicamentosa.^{3,20} It is a condition of nasal hyper-reactivity, swelling, and tolerance induced or aggravated by overuse of topical decongestant.¹ This condition can be reversed using a topical intranasal corticosteroid to allow the rebound congestion to resolve, although underlying anatomic abnormalities can make this a difficult process requiring consultation with upper airway specialists.²¹

Decongestants are effective in providing short-term relief of nasal congestion, but have no effect on other AR symptoms, such as itching, sneezing, or rhinorrhea.

Leukotrienes cause bronchial smooth muscle constriction, which leads to airway inflammation. LTRAs block the inflammatory effects of leukotrienes at the Cys-LT4 receptor, relieving nasal congestion.³ They can be used alone or in combination with antihistamines or INCS and may be beneficial in patients who have comorbid asthma.¹

Anticholinergics can reduce watery rhinorrhea, but have no effect on other nasal symptoms.¹ They can be used in combination with an antihistamine or intranasal corticosteroid in patients whose primary symptom is rhinorrhea or is refractory to other treatments.⁴ They are commonly given as an intranasal spray with minimal absorption, thus with minimal systemic anticholinergic effects.¹

While pharmacotherapy works to suppress AR, allergen-specific immunotherapy can be used to cure AR.²² It results in relief of symptoms for the patient with long-lasting preventative effects.³ Subcutaneous immunotherapy is effective in reducing symptoms and medication requirements in the long term. It is reserved for patients with severe AR whose symptoms are not sufficiently managed by pharmacotherapy.²² It involves repeated subcutaneous injections containing allergens, and patients are at small risk of having a systemic allergic reaction.³ The treatment must be supervised by physician specialists, and patients should be observed for 30 to 60 minutes after injection.³ Sublingual immunotherapy is also available for some allergens. The first dose must be given in a physician's office, and the patient should be monitored for 30 to 60 minutes for signs of an allergic reaction.³ Patients should also be prescribed autoinjectable epinephrine. If the patient tolerates the first dose, subsequent doses of sublingual immunotherapy can be given at home, repeated from 3 days per week to daily. Sublingual administration is thought to be better tolerated than subcutaneous, and most side effects are limited to the respiratory and gastrointestinal tracts. However, the allergens covered are currently limited to a few grass and tree pollens.

Guideline Recommendations

Within North America, there are many practice guidelines, protocols, and recommendations for the management of AR. In the United States, an updated practice parameter established by the American Academy of Allergy, Asthma & Immunology and the American College of Allergy, Asthma and Immunology, guides the management and treatment decisions for AR.¹ In Canada, the rhinitis guidelines present a practical and comprehensive approach to assessment and therapy, providing a consensus on the etiology and treatment of rhinitis for Canadian health care providers.¹⁰ A global guidance was also developed in collaboration with the World Health Organization, that is, the Allergic Rhinitis and its Impact on Asthma guidelines. The most recent revision of this guidance provides clinicians with recommendations, strong or conditional based on quality of evidence, to guide treatment decisions in management of their patients with AR.²³

Across all guidelines, one of the first steps in managing patients with AR is to classify their disease. Classification and treatment are based on symptom duration and severity.²³ Symptoms are classified as intermittent or persistent and mild or moderate to severe (Figure).²³

The US guidelines recommend second-generation antihistamines over first-generation due to adverse effects, such as sedation, mental impairment, and anticholinergic effects.¹ Intranasal antihistamines may be considered for first-line use and are equally efficacious or superior to oral antihistamines.¹ INCS are considered the most effective medication for controlling symptoms of AR, and most studies have found they are more effective than the combined use of an antihistamine and LTRA in the setting of SAR.¹

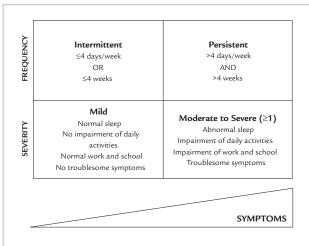


Figure 1. Relationship Between Range of Symptoms and Frequency/Severity.

Class	Classification	Treatment Recommendation
l	Mild, intermittent	Allergen avoidance
		Oral H1 antihistamines
		Intranasal corticosteroids
II	Moderate, intermittent	Allergen avoidance
	Moderate to severe, intermittent	Oral H1 antihistamines
	Severe, intermittent	Intranasal corticosteroids
	Mild, persistent	Leukotriene receptor antagonists
		Immunotherapy
111	Moderate, persistent	Allergen avoidance
		Oral H ₁ antihistamines
		Intranasal corticosteroids
		Immunotherapy
		Surgery
IV	Moderate to severe, persistent	Allergen avoidance
	Severe, persistent	Oral H ₁ antihistamines
		Intranasal corticosteroids
		Oral steroids [†]
		Immunotherapy
		Surgery

Table. Canadian guideline treatment recommendations based on allergic rhinitis class	ification. ¹⁰
--	--------------------------

The guidelines do suggest that topical decongestants or oral corticosteroids can be used for short-term management, but due to adverse effects, prolonged use is not recommended.¹

The Canadian guidelines recommend nonsedating oral antihistamines for the relief of sneezing, pruritus, and rhinorrhea in patients who present with milder symptoms.¹⁰ The Canadian guideline for rhinitis treatment recommendations based on classification is summarized in the Table. Intranasal corticosteroids should be used to treat moderate to severe intermittent symptoms or mild persistent rhinitis alone or in combination with an antihistamine.¹⁰ This recommendation is analogous to asthma guidelines that recommend an inhaled steroid as "controller therapy" and a β -2 adrenergic receptor agonist as "reliever therapy."²⁴ INCS are highly effective in reducing nasal obstruction and congestion. LTRAs have also been found to be useful in reducing nasal congestion alone or in combination with antihistamines.¹⁰ Surgery to reduce the size of, or remove, inferior turbinates may be an option in

managing AR in patients who have chronic sinus disease that is refractory to pharmacotherapy.¹⁰

The Allergic Rhinitis and its Impact on Asthma guidelines²³ strongly recommend INCS for the treatment of AR in adults and suggest INCS in children with AR. INCS are suggested over oral antihistamines in adults for both seasonal and persistent AR due to higher efficacy. Secondgeneration oral H1 antihistamines are recommended over the older generation, placing value on reduction of adverse effects and low value on comparative efficacy. Oral formulations for antihistamines are recommended over intranasal in adults with SAR or PAR. If used, intranasal H₁ antihistamines are only recommended in patients with SAR, not PAR, due to lack of evidence and uncertain efficacy. Oral LTRAs are also only recommended in patients with SAR due to limited efficacy and high cost. Oral decongestants should not be used regularly. An anticholinergic, such as ipratropium, can be used for rhinorrhea or a short course of oral or nasal decongestant (< 5 days) can be used for nasal obstruction. If treatment fails, health care providers should consider compliance issues, and be sure that patients have been correctly instructed on how to use and take their medication, especially intranasal sprays.

ORAL ANTIHISTAMINES VERSUS INTRANASAL CORTICOSTEROIDS

Intranasal corticosteroids are recommended as firstline therapy for patients with mild to persistent and any moderate to severe presentation of AR symptoms. As established by the guidelines, oral antihistamines can be used for any symptom classification of AR. Some patients report satisfactory relief of symptoms with antihistamine monotherapy. These 2 classes of medications are used most commonly by patients and are readily available without a prescription. Many studies have evaluated and compared the tolerability and efficacy of both treatment classes in reducing AR symptoms. Clinical trials evaluating the widely used intranasal corticosteroid, fluticasone propionate (FP) in comparison with second-generation oral antihistamines, cetirizine, loratadine, or montelukast, were selected. Additional studies evaluating use of this intranasal corticosteroid as monotherapy and in combination with an antihistamine are also important to review, as these treatment regimens are commonly utilized in practice.

Efficacy

One study²⁵ enrolled 237 patients with SAR and studied intranasal FP (200 µg daily) versus cetirizine (10 mg daily). Intranasal FP was significantly more effective than cetirizine for reducing nasal symptom scores and had comparable tolerability. A more recent study²⁶ also evaluated intranasal FP with cetirizine and enrolled 682 patients with SAR. In the 2-week study, investigators found FP and cetirizine were equally effective in treating fall SAR, with significant reductions in nasal symptom scores in patients receiving the active treatments versus patients receiving placebo. Another study²⁷ aimed to evaluate the potential efficacy of combination therapy. Six hundred patients with SAR were enrolled and received intranasal FP or loratadine, alone or in combination. FP plus loratadine and FP monotherapy were comparable in efficacy in almost all evaluations; for some patient-rated symptoms, the

combination was found to be superior. A similar study²⁸ (n = 100) compared intranasal fluticasone monotherapy versus FP plus cetirizine versus FP plus montelukast versus cetirizine plus montelukast, and found FP to be highly effective, with efficacy exceeding that of cetirizine plus montelukast in combined therapy. In addition, the combined therapy of FP plus cetirizine or plus montelukast did not show a significant advantage when compared with FP alone.

With many intranasal corticosteroids available with similar proven efficacy as monotherapy, a study²⁹ was conducted to determine the efficacy of combination intranasal FP and azelastine (AZ), an antihistamine, versus FP monotherapy versus AZ monotherapy versus placebo. The study enrolled 779 patients with SAR and found the combination therapy significantly improved total ocular symptom scores when compared with placebo, providing a clinically important improvement in the overall Rhinoconjunctivitis Quality of Life Questionnaire score, and was well tolerated. In this study, the combination of FP and AZ provided more symptom relief than 2 commonly used first-line AR treatments and it was well tolerated.

A systematic review¹⁵ of the efficacy of INCS versus oral antihistamines, a meta-analysis of 16 trials, confirmed intranasal corticosteroids were significantly more effective at relieving nasal congestion, discharge, pruritus, and postnasal drip than oral antihistamines. INCS were more effective at relieving sneezing and reducing total nasal symptoms than antihistamines. Only 1 of 13 studies showed oral antihistamines produced greater relief of sneezing than INCS. None of the 9 studies found antihistamines to have significantly improved total nasal symptom scores. Pooled data on ocular symptoms found there was no difference in treatment effectiveness between groups. One explanation for this observation is the difference in onset of action between drug classes. Histamine suppression by antihistamines is initially rapid, with clinical onset in a matter of hours.³⁰ INCS effects can take 3 to 10 days before a benefit is observed, although studies have reported significant relief of nasal symptoms within 12 to 24 hours.^{31,32}

Safety

INCS are considered well tolerated, while mild local side effects, such as mucosal irritation or epistaxis, may be commonly seen. Some health care providers are concerned that INCS produce adverse effects similar to those reported for systemic steroids. In 7 randomized, controlled trials in both adults and children, no significant effects were found on the hypothalamic-pituitary-adrenal axis in patients receiving FP nasal spray at varying doses.³³ Multiple studies of FP nasal spray in children with AR found no significant growth changes or cortisol concentrations.^{34,35} A recent study evaluated the effect of the newer fluticasone furoate nasal spray (FFNS) on growth in young children.³⁶ Due to the large sample size and narrow age range of the patients studied, investigators were able to determine a small, but statistically significant reduction in growth velocity after 52 weeks of treatment with FFNS once daily compared with placebo.³⁶ No clinically significant adverse events were observed on any other safety profile end points. Additional studies will need to be done to determine potential long-term effects. Clinicians should discuss the potential risks of longterm steroid treatment with their patients or caregivers and use the lowest effective dose to manage symptoms to prevent such side effects.

First-generation oral antihistamines are generally well tolerated but do have sedative, cognitive, and anticholinergic effects that can present challenges for some patients. Second-generation oral antihistamines generally do not have these sedating effects and are well tolerated. Fexofenadine, loratadine, and desloratadine do not cause sedation at recommended doses. Cetirizine and intranasal AZ can case sedation at recommended doses.¹

Summary

INCS are the most effective treatment for nasal symptoms of AR.¹⁵ They are the first-line option for treating moderate to severe SAR or PAR and are more effective than a combination of oral antihistamines and LTRAs, and are at least as effective as or more effective than intranasal antihistamines. INCS are preferred over all other agents for mild persistent or moderate to severe symptoms. Compared with antihistamines and LTRAs, INCSs are superior in reducing nasal symptom scores and nasal congestion. Oral antihistamines are considered first-line treatment of patients with mild to moderate intermittent AR symptoms.^{1,4}

ROLE OF THE PHARMACIST

Management of AR begins in the pharmacy aisles, as pharmacists are trusted health care professionals

expected to provide guidance and education for patients. A pharmacist should be able to recognize AR symptoms, assess the quality of a patient's symptoms, and determine whether the patient should be referred to a primary care physician. If OTC management is appropriate, the pharmacist should be able to select optimal treatment in accordance with the patient's symptom and medication profile. Patients might have been diagnosed previously by a physician, self-diagnosed, misdiagnosed, or not diagnosed at all. The symptoms of AR are often confused with those of an infection or cold.³ Normal symptoms associated with AR are watery anterior rhinorrhea, sneezing (especially sudden or recurrent), nasal obstruction or congestion, and nasal pruritus, with or without conjunctivitis.¹ Patients presenting with unilateral symptoms, congestion without other symptoms, purulent rhinorrhea with thick mucus, posterior rhinorrhea (postnasal drip), pain, recurrent epistaxis, or loss of smell should be referred to a physician and should not be treated OTC for AR.³ Patients should also be referred to a physician if the patient is pregnant, has asthma, shows signs of dyspnea, is on any medication that may be causing symptoms, or fails to respond to OTC therapy.³ Medications that can cause such symptoms include aspirin, nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, α blockers, and β blockers. As with any new prescription medication, a patient should be counseled on any product they select OTC and be educated on the importance of compliance. A patient should be educated on when to expect relief of symptoms and, in the case of intranasal steroids, informed that the full benefit may not be evident for 2 weeks. Patients should be encouraged to continue using their medication as directed to achieve maximum symptom relief. Patients should also be counseled on appropriate administration technique for intranasal formulations, especially in avoiding the nasal septum, which could lead to unnecessary harm. Improper administration, such as failing to prime the device correctly, can also lead to decreased effectiveness due to the patient not receiving the full recommended dose. In the case of medications that contain pseudoephedrine, many of which are now kept behind the counter (BTC) in the United States, it is imperative that the pharmacist emphasize that such medication should only be used in the short term for congestion relief. It is important that patients be aware of the common side effects that they can expect and the serious adverse events that should be reported to their physician. Patients should also be educated on reading product labels and being aware of active ingredients. Many OTC or BTC medications are combination products, and caution should be taken when using multiple products, including nonallergy medications. Proper patient education and counseling can make the difference in optimizing patient outcomes by improving a patient's health literacy and compliance. The community pharmacist plays an impactful role in the identification of undiagnosed or untreated disease, increasing collaboration among all health care providers to provide optimal health care and treatment for the patient, improving patient quality of life, and reducing the burden of AR and associated comorbidities.

PATIENT CASES

To illustrate how the community pharmacist can play a significant role in the successful management of patients with AR, the following 2 case examples are presented.

CASE 1

An 18-year-old male comes to the pharmacy looking for relief for his "allergies." He says it is really bad when he plays football, and that 2 different OTC antihistamines have not helped. In consultation with a pharmacist, he reports that symptoms are so bad that he cannot breathe through his nose when wearing a mouth guard. He snores but does not believe that his breathing is interrupted. He initially notes some clear rhinorrhea and that he does have some nasal and ocular itching and sneezing when not taking an antihistamine. He denies having nosebleeds. He reports no other medical or surgical problems and is taking no medications.

You advise him to start fluticasone nasal spray in accordance with the prescribing information and demonstrate appropriate technique. You ask him to come back in 2 weeks to let you know how it is working. He returns a month later, looking for an alternative. He reports that the nasal spray has helped his congestion a little, but that he still has trouble breathing during football practice. He states that he used the nasal spray as directed for 3 weeks but has since stopped using it.

Due to his failure to respond sufficiently to therapy, you advise him to consult with his doctor.

Six weeks later, he returns to report that allergy testing was positive to trees, grasses, weeds, and dust mites. Because of a prominent nasal blockage, the allergist sent him to see an otolaryngologist who diagnosed adenoidal hyperplasia with sleep disturbance and performed an adenoidectomy. His breathing and snoring issues have resolved, but he still reports some nasal and ocular pruritus, sneezing, and rhinorrhea, and he states that both his allergist and otolaryngologist have advised him to try the intranasal corticosteroid again.

This patient has AR, with the symptom of nasal blockage predominating. This suggests an anatomic problem in the upper airway, such as nasal septal deviation or upper airway pathology. In his age group, adenoidal hyperplasia, nasal polyposis, and angiofibroma of the nasopharynx warrant consideration. Nasal examination is necessary to identify the source of blockage. However, a short trial of an intranasal corticosteroid is worthwhile. After adenoidectomy, an intranasal steroid is the agent of choice for controlling his rhinitis symptoms, with the addition of an antihistamine if needed and with immunotherapy being an additional option.

CASE 2

A 65-year-old male comes to the pharmacy for advice on the recent onset of the following symptoms: waking up several times during the night to urinate, difficulty with urination, daytime drowsiness, and fatigue. These symptoms started at the beginning of the spring allergy season when he started taking an antihistamine to prevent the symptoms he experienced last spring when he moved into the area. His medical history includes hypertension and diabetes, both controlled on current medications. His current medications include lisinopril 20 mg once daily, metformin 500 mg twice daily, ibuprofen 400 mg twice daily as needed for knee pain, and diphenhydramine 25 mg twice daily.

The patient is experiencing anticholinergic side effects from the diphenhydramine. This side effect can be particularly troublesome in older males who are at risk for an enlarged prostate. The pharmacist should advise the patient to stop the diphenhydramine and start an intranasal steroid, such as fluticasone nasal spray, once daily. A decongestant would not be used first line in this patient due to his history of hypertension. The patient should be properly instructed on how to use his intranasal spray, when to start therapy, and how to administer the product. The patient should return for a follow-up after 2 weeks to re-evaluate symptoms and medication. This patient returned 2 weeks later with improved symptoms, no daytime drowsiness, and improved urination.

CONCLUSIONS

Many classes of medications available to treat AR are effective and well tolerated. Evidence supports the use of intranasal steroids or second-generation oral antihistamines. INCS have been proven to be superior to other drug classes, with a significant reduction in AR symptoms and a favorable safety profile. Antihistamines can be recommended for patients who experience mild, intermittent AR for symptom relief. Both classes of drugs are available without a prescription and enable the community pharmacist to play a major role in treating this disease by helping select a product based on symptoms, educating the patient on the appropriate use of the product, and referring the patient to a physician when necessary.

ACKNOWLEDGMENTS

This article was supported by GlaxoSmithKline Consumer Healthcare, Canada.

Both authors contributed equally to all phases of manuscript development. Rachel Reji, PharmD (Precept Medical Communications) provided medical writing assistance (editing of the manuscript, preparation of figures and tables) that was funded by GlaxoSmithKline Consumer Healthcare, Canada.

CONFLICTS OF INTEREST

The authors have indicated that they have no conflicts of interest regarding the content of this article.

REFERENCES

- Wallace DV, Dykewicz MS, Bernstein DI, et al. The diagnosis and management of rhinitis: an updated practice parameter. *J Allergy Clin Immunol.* 2008;122(Suppl): S1–S84.
- 2. Keith PK, Desrosiers M, Laister T, et al. The burden of allergic rhinitis (AR) in Canada: perspectives of physicians and patients. *Allergy Asthma Clin Immunol.* 2012;8:1-11.
- 3. Bousquet J, Van Cauwenberge P, Khaltaev N. ARIA in the pharmacy: management of allergic rhinitis symptoms in

the pharmacy. Allergic rhinitis and its impact on asthma. *Allergy*. 2004;59:373-387.

- Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol. 2001;108(Suppl):S147-S334.
- Hay JW, Kaliner MA. Costs of second-generation antihistamines in the treatment of allergic rhinitis: US perspective. *Curr Med Res Opin*. 2009;25:1421–1431.
- 6. Barnes PJ. Pathophysiology of allergic inflammation. *Immunol Rev.* 2011;242:31-50.
- Derendorf H, Meltzer EO. Molecular and clinical pharmacology of intranasal corticosteroids: clinical and therapeutic implications. *Allergy*. 2008;63:1292–1300.
- 8. Dykewicz MS, Hamilos DL. Rhinitis and sinusitis. J Allergy Clin Immunol. 2010;125(Suppl):S103–S115.
- 9. Skoner DP. Allergic rhinitis: definition, epidemiology, pathophysiology, detection, and diagnosis. J Allergy Clin Immunol. 2001;108(Suppl):S2–S8.
- Small P, Frenkiel S, Becker A. Rhinitis: A practical and comprehensive approach to assessment and therapy. *J Otolaryngol.* 2007;36(Suppl):S5–S27.
- 11. Bruttmann G, Charpin D, Germouty J, et al. Evaluation of the efficacy and safety of loratadine in perennial allergic rhinitis. *J Allergy Clin Immunol*. 1989;83:411–416.
- Philip G, Williams-Herman D, Patel P, et al. Efficacy of montelukast for treating perennial allergic rhinitis. *Allergy Asthma Proc.* 2007;28:296–304.
- 13. Banov CH, Woehler TR, LaForce CF, et al. Once daily intranasal fluticasone propionate is effective for perennial allergic rhinitis. *Ann Allergy*. 1994;73:240–246.
- Benninger MS, Ahmad N, Marple BF. The safety of intranasal steroids. *Otolaryngol Head Neck Surg.* 2003;129: 739-750.
- Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ*. 1998;317:1624–1629.
- **16.** Scadding GK, Durham SR, Mirakian R, et al. BSACI guidelines for the management of allergic and non-allergic rhinitis. *Clin Exp Allergy*. 2008;38:19–42.
- 17. Meltzer EO. Intranasal steroids: managing allergic rhinitis and tailoring treatment to patient preference. *Allergy Asthma Proc.* 2005;26:445-451.
- Leurs R, Church MK, Taglialatela M. H1-antihistamines: inverse agonism, anti-inflammatory actions and cardiac effects. *Clin Exp Allergy*. 2002;32:489–498.
- Bousquet J, Khaltaev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008. *Allergy*. 2008;63 (Suppl 86):8–160.
- 20. Platt M. Pharmacotherapy for allergic rhinitis. *Int Forum Allergy Rhinol.* 2014;4(Suppl 2):S35–S40.
- 21. Vaidyanathan S, Williamson P, Clearie K, et al. Fluticasone reverses oxymetazoline-induced tachyphylaxis of

response and rebound congestion. *Am J Respir Crit Care Med.* 2010;182: 19–24.

- 22. Greiner AN, Hellings PW, Rotiroti G, Scadding GK. Allergic rhinitis. *Lancet*. 2011;378:2112–2122.
- 23. Brozek JL, Bousquet J, Baena-Cagnani CE, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 revision. J Allergy Clin Immunol. 2010;126:466–476.
- 24. Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Summary Report 2007. J Allergy Clin Immunol. 2007;120(Suppl):S94–S138.
- 25. Vervloet D, Charpin D, Desfougeres JL. Intranasal Fluticasone Once Daily Compared with Once-Daily Cetirizine in the Treatment of Seasonal Allergic Rhinitis: Results of a Multicentre, Double-Blind Study. *Clin Drug Investig.* 1997;13: 291–298.
- 26. Ford LB, Matz J, Hankinson T, et al. A comparison of fluticasone propionate nasal spray and cetirizine in ragweed fall seasonal allergic rhinitis. *Allergy Asthma Proc.* 2015;36:313–319.
- 27. Ratner PH, van Bavel JH, Martin BG, et al. A comparison of the efficacy of fluticasone propionate aqueous nasal spray and loratadine, alone and in combination, for the treatment of seasonal allergic rhinitis. *J Fam Pract.* 1998;47:118-125.
- 28. Di LG, Pacor ML, Pellitteri ME, et al. Randomized placebo-controlled trial comparing fluticasone aqueous nasal spray in mono-therapy, fluticasone plus cetirizine, fluticasone plus montelukast and cetirizine plus montelukast for seasonal allergic rhinitis. *Clin Exp Allergy*. 2004;34:259–267.
- 29. Meltzer EO, LaForce C, Ratner P, et al. MP29-02 (a novel intranasal formulation of azelastine hydrochloride and fluticasone propionate) in the treatment of seasonal allergic rhinitis: a randomized, doubleblind, placebo-controlled trial of efficacy and safety. *Allergy Asthma Proc.* 2012;33:324–332.

- **30.** Meltzer EO, Weiler JM, Widlitz MD. Comparative outdoor study of the efficacy, onset and duration of action, and safety of cetirizine, loratadine, and placebo for seasonal allergic rhinitis. *J Allergy Clin Immunol*. 1996;97:617-626.
- Selner JC, Weber RW, Richmond GW, et al. Onset of action of aqueous beclomethasone dipropionate nasal spray in seasonal allergic rhinitis. *Clin Ther.* 1995;17:1099– 1109.
- 32. Munk ZM, LaForce C, Furst JA, et al. Efficacy and safety of triamcinolone acetonide aqueous nasal spray in patients with seasonal allergic rhinitis. *Ann Allergy Asthma Immunol.* 1996;77: 277–281.
- **33.** Sastre J, Mosges R. Local and systemic safety of intranasal corticosteroids.

J Investig Allergol Clin Immunol. 2012; 22:1–12.

- **34.** Allen DB, Meltzer EO, Lemanske RF Jr., et al. No growth suppression in children treated with the maximum recommended dose of fluticasone propionate aqueous nasal spray for one year. *Allergy Asthma Proc.* 2002;23: 407–413.
- **35.** Fluticasone Propionate Collaborative Pediatric Working Group. Treatment of seasonal allergic rhinitis with once-daily intranasal fluticasone propionate therapy in children. *J Pediatr.* 1994;125:628-634.
- 36. Lee LA, Sterling R, Maspero J, et al. Growth velocity reduced with oncedaily fluticasone furoate nasal spray in prepubescent children with perennial allergic rhinitis. J Allergy Clin Immunol Pract. 2014;2:421–427.

Address correspondence to: J. Russell May, PharmD, University of Georgia College of Pharmacy, HM 124, AU Campus, 1120 15th Street, Augusta, GA 30912. E-mail: jmay@augusta.edu