

Management of Seasonal Allergies in Adults

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Abstract

Introduction: Seasonal allergies are a group of conditions that are related to atopy. Atopy is an immunological response to normally harmless ubiquitous allergens in a form of abnormal production of specific Immunoglobulin E. Allergic rhinitis is the most encountered type of rhinitis. Although the condition is usually seasonal, some individuals with allergic rhinitis may have persistent inflammation.

The Aim of Work: In this review, we will spotlight the latest available data regarding the management of chronic allergic rhinitis in adult patients.

Methodology: A thorough search of MEDLINE database between 1966 and 2020 was conducted using Medical Subject Heading (MeSH) on PubMed. All relevant full article were reviewed and included.

Conclusion: Allergic rhinitis is usually diagnosed clinically upon the presence of characteristic symptoms, suggestive clinical history, and supportive findings on physical examination. Mild intermittent symptoms related to predictable allergen exposures can be managed with as needed second-generation oral antihistamine. For patient with persistent pattern, moderate to severe symptoms, Glucocorticoid nasal sprays are the most effective pharmacologic therapy.

Keywords: Seasonal Allergies; Allergic Rhinitis; Allergic Rhinosinusitis; Acute Attack Control; And Chronic Management

Introduction

Seasonal allergies are a group of conditions that are related to atopy. Atopy is an immunological response to normally harmless ubiquitous allergens in a form of abnormal production of specific Immunoglobulin E (IgE) [1]. Atopic diseases include seasonal allergy as allergic

rhinitis (AR), rhinosinusitis, conjunctivitis, and seasonal asthma, in addition to atopic dermatitis and food allergies. The nose and sinuses are usually affected simultaneously, hence some experts prefer the term rhinosinusitis instead of the separate terms rhinitis and sinusitis. As the management may differ, we choose to distinguish between these terms. Rhinitis can be simply defined as an inflammation of nasal membrane and mucosa [2]. Allergic rhinitis is the most encountered type of rhinitis [3]. Although the condition is usually seasonal, some individuals with allergic rhinitis may have persistent inflammation. Seasonal allergies greatly impact social life, school adherence and performance, and work productivity, especially with severe symptoms and inadequate management [4,5].

According to one estimate, seasonal allergies are responsible for at least 2.5 percent of clinical visits, two million of missing school days, and six million of missing work days [4]. The prevalence ranges between 10 and 30 percent in the developed countries [6]. Many reports indicate similarly high prevalence on developing countries.

In this review, we will spotlight the latest available data regarding the management of chronic allergic rhinitis in adult patients. Although the management of allergic conjunctivitis might be very similar, it will not be the focus of this review.

Methods

A thorough search of MEDLINE database between 1966 and 2020 was conducted using Medical Subject Heading (MeSH) on PubMed. The result were screened and all full article relevant to seasonal allergies were reviewed and included. The terms used in the search process include seasonal allergies, allergic rhinitis, allergic rhinosinusitis, acute attack control, and chronic management.

Risk factors and clinical presentation

Many factors were suggested or confirmed to play a role in developing atopy and allergic diseases [7]. Genetic plays important role, many chromosomal loci have been linked with the risk of atopy [1]. Seasonal allergies are more prevalent in young male than female. Male sex is considered to have a positive likelihood ratio for the diagnosis of allergic rhinitis [8]. Birth during pollen season and firstborn carry a higher risk of developing seasonal allergy.

Patient with seasonal allergic rhinitis typically present with paroxysms of sneezing, rhinorrhea, nasal obstruction, and nasal itching. Other common symptoms include postnasal drip, cough, irritability, and fatigue [9]. Patients who have allergic conjunctivitis may experience bilateral itching, tearing, and/or burning of the eyes. Allergic conjunctivitis is seen in about 60 percent of patient with allergic rhinitis. In addition, about 50 percent of patients with asthma have allergic rhinitis.

The symptoms could be classified according to their pattern and/or severity [10]. Pattern include intermittent or persistent symptoms while by severity the symptoms are either mild or moderate to severe. Intermittent symptoms persist less than 4 days per week or less than four weeks. Symptoms are classified as persistent, however, when present for more than that. The symptoms are considered moderate to severe if there is sleep disturbance, impairment of school or work performance, Impairment of daily activities, leisure, and/or sport activities, or troublesome symptoms. Otherwise, the symptoms are classified as mild. Patients with episodic symptoms are often more conscious of the disability caused by allergic rhinitis, whereas patients with persistent symptoms often adapt over time and do not seek medical help until symptoms become severe [11]. Persistent/perennial symptoms are more common than purely intermittent or seasonal symptoms, although many patients have perennial symptoms with seasonal exacerbations [9]. Seasonal allergy rhinitis is usually triggered by pollen from trees and grasses. Pollination time varies by geographic area and it is, usually, well known for certain types of plants. Hence, colloquial names usually used to indicate the triggering pollen. Examples include cedar fever, rose fever, or hay fever. Symptoms of seasonal allergic rhinitis are predictable and reproducible from year to year.

Clinician should be aware that it is possibly difficult to distinguish symptoms of allergic rhinitis from the nonallergic forms of rhinitis, since not all seasonal symptoms are unique to allergy [9]. As an example, chronic nonallergic rhinitis can be triggered by changes in

weather and temperature and may appear to have a seasonal pattern in some patients. Thus, for an accurate diagnosis of allergic rhinitis, diagnostic testing may be required. Continuous exposure to an allergen leads to persistent nasal mucosal inflammation. This leads to over sensitivity in these patient that is believed to result from lowering of the threshold for a clinical response. Clinically, this manifests as more severe symptoms of rhinitis on exposure to lower doses of allergen (priming) and to nonspecific irritants (hyper-reactivity).

Clinical inspection of patient with suspected allergic rhinitis can yield many physical findings [12]. Allergic shiners is used to refer for infraorbital edema and darkening due to subcutaneous venodilation. Patient may show accentuated lines or folds below the lower lids that called Dennie-Morgan lines; the presence of these line suggests concomitant allergic conjunctivitis. In addition, careful inspection may detect a transverse nasal crease caused by repeated rubbing and pushing the tip of the nose up with the hand. Physical findings that appear on examining the internal structures of the nose, oropharynx, and ears may include pale bluish hue or pallor along with turbinate edema in the nasal mucosa of patients with active allergic rhinitis. Clear rhinorrhea may be clearly visible in the anterior part of the nose, or when the nasal passages are obstructed; rhinorrhea may also be visible as posterior dripping down the pharynx. Physician can also see hyperplastic lymphoid tissue resembling the cobblestones lining the posterior pharynx. Ear examination may demonstrate retracted tympanic membranes or accumulated serous fluid behind tympanic membranes in patients with significant nasal mucosal swelling and eustachian tube dysfunction.

Routine laboratories usually show no abnormality in patient with allergic rhinitis. Peripheral blood eosinophil counts is not sensitive to aid the diagnosis. Total serum immunoglobulin E (IgE) level is seen elevated in less than half of the patient and hence it has no adequate sensitivity to be relied upon.

Diagnosis

Allergic rhinitis is usually diagnosed clinically upon the presence of characteristic symptoms, suggestive clinical history, and supportive findings on physical examination. Skin testing for allergy confirms the presence of sensitivity to aeroallergens. However, it is not necessary for the initial diagnosis. Further evaluation may be needed in case of robust symptoms against management or the trigger is not obvious. The aim of further evaluation is to demonstrate that the patient is sensitized to aeroallergens. Sensitization can be demonstrated with either allergy skin testing or in vitro tests for allergen-specific immunoglobulin E (IgE).

Typically, there is no need for imaging studies in patient with presentation suggestive of allergic rhinitis. An exception is when concomitant condition as chronic rhinosinusitis (CRS) is suspected or there is a history of facial trauma or features to suggest anatomic abnormalities. Diagnosis based on clinical response to therapeutic trial of either topical nasal glucocorticoids or topical antihistamines is not does not conclusive. This is due to the fact that these therapies are also effective in the treatment of nonallergic rhinitis [9].

Although the use of diagnostic testing to identify culprit allergens has been associated with improved patient outcomes, routine practice does not involve testing for allergen-specific IgE. Primary care clinicians treat the majority of patients with allergic rhinitis and often initiate therapy empirically, identifying possible triggers only through the clinical history. This approach is reliable and sufficient for most patients. For selective cases, test for patient's sensitized allergen is beneficial. Types of patient that benefit the most include patient with an unclear diagnosis based upon the history and physical examination, patients with poorly controlled symptoms, such as persistent nasal symptoms and/or an inadequate clinical response to nasal glucocorticoids, patient with coexisting persistent asthma and/or recurrent sinusitis/otitis, and patient who prefers to try to avoid the allergen rather than take medications to control symptoms. One method is immediate hypersensitivity skin testing; a quick and cost-effective to identify the allergen-specific IgE [13]. Although these tests are generally safe, they should be performed under supervision of allergy specialist, for the fear of rare systemic allergic reactions. Positive results in sensitive patients appear as a wheal-and-flare reaction within 20 minutes. The skin testing should be avoided in a very symptomatic pollen-allergic patient during peak pollen season due to the fear of further aggravating symptoms. In addition, the test in these circumstances may be associated with higher rates of systemic reactions during testing. Hence, the optimal approach is empiric treatment of patient's symptoms, the testing should be deferred until the patient is less symptomatic after the season.

Serum test by IgE immunoassays provide similar diagnostic information to allergen skin tests. However, these tests are more expensive and less sensitive for the diagnosis of allergy to inhalant allergens compared with skin tests. Generally, they can be useful in some situations as skin testing is not available or cannot be performed because patients have extensive skin disease, cannot discontinue antihistamines or other interfering medications, dermatographic patient, or have other issues that complicate skin testing [14].

Management: the aim

Traditionally, all management efforts aimed toward improving the symptoms of allergic rhinitis rather than the interest in patients' quality of life. Nowadays, it is become clearer that the burden of allergic rhinitis extends beyond the discomfort caused by symptoms as it could affect healthy life in many ways [15]. For examples, in addition to missing school and work days, the disturbed adherence to social events could result in emotional disturbances that manifest as anger, sadness, frustration, and withdrawal [16]. School performance is worsen by allergic rhinitis according to one report about children aged 15 - 16 years in the UK, this is particularly evident in case of using antihistamines that have high sedation as an adverse effect [17]. Severe chronic upper-airway disease has been proposed to arise when rhinitis is not controlled by adequate pharmacotherapy.

Management: general approach

The management of allergic rhinitis involves 3 main component: allergen avoidance, pharmacotherapy, and allergen immunotherapy.

Allergen avoidance is a helpful measure to overcome symptoms of allergic rhinitis. However, complete avoidance is difficult to achieve especially for pollen which is wildly present in the outdoor air [18]. Attempts to minimize outdoor exposure during the season in which the incriminated pollen is thought to be circulating can be beneficial. For indoor allergens, patient can apply some environmental control measures. For example, covering the mattress and pillows with impermeable covers help reduce exposure to dust mites, washing bed linens every 2 weeks in hot water (>130°F) to kill any mites present. Some allergic source is easier to be avoided as animal allergy, hence, complete avoidance is the best option.

The general approach to manage patients with mild or episodic symptoms that are related to predictable allergen exposures can include regular or as needed administration of a second-generation oral antihistamine. As needed method is ideally achieved by using the drug 2 - 5 hours before the expected exposure. Other possible option is antihistamine nasal spray. Example of this group include azelastine, which could be used safely for adult and children older than 5 years. Glucocorticoid nasal spray is more effective than antihistamines. It can be used regularly or as needed. However, a relatively long period (2 days) before predictable exposures is needed to achieve optimal result, and for 2 days after the end of exposure [19]. Examples of this group include mometasone furoate, fluticasone fu roate, and triamcinolone acetoneide.

For patient with persistent pattern, moderate to severe symptoms, Glucocorticoid nasal sprays are the most effective pharmacologic therapy. Guidelines consider glucocorticoid sprays as the best single therapy for these type of patients [20]. If the initial management with glucocorticoid basal sprays was not sufficient to adequate control of symptoms, a second agent can be added. Options include an antihistamine nasal spray, oral antihistamines, and antihistamine/decongestant combination products. There are few clinical trials directly comparing different combinations of these therapies, and the choice of additional agents should be based upon the patient's residual symptoms, preferences, and coexistent conditions.

Some glucocorticoid nasal sprays carry additional benefits in relieving eye symptoms associated with allergic conjunctivitis. However, additional agent is required in many patient to achieve adequate relief. Patients with concomitant allergic conjunctivitis benefit from a combination of a glucocorticoid nasal spray and ophthalmic antihistamine drops much more. Epinastine and azelastine are common examples of these drops. This method is preferred over the combination of glucocorticoid spray and oral antihistamine.

Management: pharmacotherapy

Most patients with allergic rhinitis respond to pharmacotherapy. Options include glucocorticoid nasal spray, systemic glucocorticoid, oral and nasal antihistamines, mast cell stabilizers (cromolyn), leukotriene modifiers, and ipratropium. Some of these drugs may be sufficient to manage mild intermittent cases, while other is usually reserved for more severe illness. A combination between some types is also practical. This section include a rapid review of pharmacological agents used in the setting of AR.

Nasal irrigation with saline is simple method to manage mild symptoms. Additional use is before other topical medications so that the mucosa is freshly cleansed when the medications are applied. Nasal irrigation is safe, has a minimal risk of side effect, and could be used in all age groups.

Glucocorticoid nasal sprays are considered the most effective drug in the line of managing allergic rhinitis. It is able to control most, if not all, nasal symptoms as nasal blockage, nasal discharge, nasal itch, sneezing, and postnasal drip [21]. Data have shown that studies nasal steroids are more effective than monotherapy with nasal cromolyn or antihistamines [22]. They have a rapid onset of action during few hours. However, the maximal effect may take several days to weeks to appear, especially in patients with longstanding untreated symptoms. With adherence to prescribed dose, glucocorticoid nasal sprays are not commonly associated with substantial systemic side effects and have minor local side effects. Nasal inflammation and bleeding may occur. Oral glucocorticoids are typically indicated in patients with serious allergic rhinitis causing symptoms that interfere with the everyday work of patients. Some studies have shown that oral glucocorticoids effectively eliminate symptoms of allergic rhinitis [23]. This approach was more commonly used until nasal glucocorticoids and non-sedating antihistamines were widespread. However, systemic glucocorticoids should not be used repeatedly or over prolonged periods of time [24].

Oral antihistamines effectively reduce itching, sneezing, and rhinorrhea. However, the less impact on nasal congestion compared with intranasal glucocorticoids. Antihistamines are divided into first- and second-generation group. The metabolites of second generation (as desloratadine, the metabolite of loratadine) are sometimes called the third-generation. Second and third generation antihistamines are preferred over the first-generation because they have similar efficacy and fewer side effect on the central nervous system (CNS). Prominent examples of second-generation antihistamines include loratadine and cetirizine. Second- and third-generation antihistamine are lipophobic, hence they lack the anticholinergic and central nervous system side effects in contrast to the lipophilic first-generation antihistamines agent drugs [25]. They demonstrate a rapid onset of action within one hour for most agents, peak serum level within 2 - 3 hours, long duration of action so they are used once or twice daily, and anti-inflammatory properties as decreased mast cell mediator release. Second-generation antihistamines are equally or more efficacious than cromolyn in relieving symptoms [26]. Intranasal antihistamines have significant clinical effect on nasal congestion with faster duration of action than that of glucocorticoid nasal sprays. The estimated time for onset of action is less than 15 minutes. Therefore, antihistamine nasal spray could be used as "on demand." [27] In spite of these advantages, glucocorticoids nasal sprays are better than antihistamine sprays as shown by many reports [23].

Nasal decongestant sprays such as Phenylephrine and oxymetazoline are potent vasoconstrictive agents with very rapid onset of action in about 10 minute [18]. However, these drugs are not recommended as monotherapy in the chronic treatment of allergic rhinitis due to downregulation of the alpha-adrenergic receptor that develops after three to seven days. Downregulation causes rebound nasal congestion. Nasal decongestants are helpful option before air travel in patients who have difficulties with middle ear and/or sinus equilibration with flying or in patients who have problems with altitude changes. Some studies have indicated that non-sedating antihistamines paired with decongestant pseudoephedrine offer greater symptom relief than antihistamines alone [28]. However, decongestants have a number of adverse effects, including hypertension, insomnia, irritability, and headache.

Cromolyn sodium acts as mast cell stabilizer that inhibits the release of histamine and other inflammatory mediators from mast cells. The mechanism is believed to be through inhibiting the intermediate conductance chloride channel pathways of mast cells, eosinophils,

epithelial and endothelial cells, fibroblasts, and sensory neurons. Although some studies suggest that cromolyn sodium is more effective than placebo in the treatment of seasonal allergic rhinitis with no serious side effects, most data conclude that it is less effective than glucocorticoid nasal sprays and second-generation antihistamines [29].

Less commonly used pharmacological agent include montelukast and ipratropium bromide. Montelukast is a leukotriene receptor antagonist. It is usually prescribed for patient who refuse the use of nasal spray. A systematic review has confirmed that montelukast provides relief of symptoms similar to loratadine. However, montelukast is less effective than glucocorticoid nasal sprays for controlling the symptoms of allergic rhinitis [30]. It usually used for patients refuse nasal sprays or cannot tolerate them. It could be prescribed alone or combined with antihistamine.

Ipratropium bromide is not recommended as a first-line drug in allergic rhinitis. It shows beneficial effect in controlling rhinorrhea, yet less effective than glucocorticoid nasal sprays for sneezing, pruritus, or nasal obstruction [31]. It can be used in children or adults with profuse rhinorrhea not otherwise controlled with topical nasal corticosteroids.

Allergen immunotherapy

Immunotherapy is a method that aim to change the immune system. Subcutaneous immunotherapy has demonstrated success in patients with allergic rhinitis with long-lasting reduction of symptoms and medication specifications. These are typically used in people with severe agonizing allergic rhinitis whose symptoms are not managed by pharmacotherapy or who have side effects from medications. Sublingual immunotherapy in another way of administering immunotherapy. Studies have shown that this route may have prolonged benefit that continue after 3 years. The result are comparable to subcutaneous immunotherapy.

Conclusion

Allergic rhinitis is the most encountered type of rhinitis. Although the condition is usually seasonal, some individuals with allergic rhinitis may have persistent inflammation. Patient with seasonal allergic rhinitis typically present with paroxysms of sneezing, rhinorrhea, nasal obstruction, and nasal itching. Allergic rhinitis is usually diagnosed clinically upon the presence of characteristic symptoms, suggestive clinical history, and supportive findings on physical examination. Skin testing for allergy confirms the presence of sensitivity to aeroallergens. However, it is not necessary for the initial diagnosis. Clinician should be aware that it is possibly difficult to distinguish symptoms of allergic rhinitis from the nonallergic forms of rhinitis. Routine laboratories usually show no abnormality in patient with allergic rhinitis. The management of allergic rhinitis involves 3 main component: allergen avoidance, pharmacotherapy, and allergen immunotherapy. Mild intermittent symptoms related to predictable allergen exposures can be managed with as needed second-generation oral antihistamine. For patient with persistent pattern, moderate to severe symptoms, Glucocorticoid nasal sprays are the most effective pharmacologic therapy.

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